Ansgar M. Brambrink
Jeffrey R. Kirsch
Editors

Essentials of Neurosurgical Anesthesia & Critical Care

Strategies for Prevention, Early Detection, and Successful Management of Perioperative Complications

Second Edition

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To our life mentors:

Dr. Nelly Tsouyopoulos, Dr. Donna Stark, Dr. Jeffrey R. Kirsch, and Dr. John W. Olney. Above all else, to my wife, Petra Brambrink, who has supported and challenged me since we first met (AMB)

Dr. Louis G. D'Alecy, Dr. Richard J. Traystman, and my loving and tolerant wife, Robin (JRK)

– Thank you

Foreword

The great success of the first edition of this book, *Essentials of Neurosurgical Anesthesia & Critical Care*, encouraged the editors, the authors, and the publisher to publish this second edition. It appeals to a wide variety of readers, including anesthesiologists, intensivists, neurosurgeons, neurologists, physician assistants, perioperative/advanced practice nurses, trainees, or even colleagues, interested in the "neuro" field. The essentials of neuroanesthesia and critical care are presented in a concise manner, guiding the reader from anatomical/pathophysiological backgrounds to scientific-based anesthetic treatment. It considers many special aspects of individual care, covering a wide variety of problems which may occur in patients with or without comorbidities over the whole perioperative period.

To my knowledge, there no other book on the market which in 100 chapters covers almost all aspects pertinent to modern neuroanesthesia and neuro-critical care. The editors are to be commended on gathering worldwide renowned experts as authors to present the state of the art for understanding neurosurgical/neurological diseases and their respective anesthetic/intensive care treatments of standard "and complex" neuro patients. For this second edition, each chapter has been rigorously updated with nine more chapters added. In addition, the problem-oriented approach helps the daily practitioner to understand not only the development of a patient's condition during the course of treatment, but also the acutely changing situation of the patients, which may need a precise intervention, to ensure optimized treatment and recovery. All of this can be achieved only by a multidisciplinary approach which is reflected by the authors from different disciplines.

The new edition of *Essentials of Neurosurgical Anesthesia and Critical Care* closes the gap between classical textbooks and other available sources on neuroanesthesia/neuro-critical care and the need for a scientific-based reference guide with a focus on a day-to-day clinical practice.

Munich, Germany — Eberhard Kochs

Preface

Today, treatment decisions are expected to be evidence-based, and the pursuit of excellence in clinical practice is an essential element for achieving success in the current healthcare environment.

Perioperative care of patients with central nervous system diseases is evolving rapidly as increasing numbers of operative interventional techniques and strategies are developed. Physicians, nurses, nurse practitioners, and physician assistants treat patients throughout the immediate perioperative period, including during diagnostic procedures and interventional radiology procedures, and frequently participate in critical care treatment for this patient population.

We believe that the broad spectrum of neuroanesthesiology and neurocritical care providers should have a clear understanding of (1) the disease process including pathophysiology, specific diagnostics, and treatment options, (2) the concepts and relevant details of the available neurosurgical interventions and techniques, and (3) the means necessary to provide safe and comfortable anesthesia and perioperative care for these patients.

This book, *Essentials of Neurosurgical Anesthesia & Critical Care*, is intended to serve as a quick reference guide for those involved in the perioperative care of neurosurgical patients. It is not meant to substitute for a full-length textbook in this field.

As a guide, this book focuses on day-to-day clinical practice and supports the first-line healthcare provider by anticipating problems and complications in neurosurgical anesthesia and critical care, and by suggesting solutions and appropriate management. All chapters are dedicated to a single area of concern and are designed to walk the reader from the problem to the solution, using a structured, algorithmic approach. In addition, each chapter summarizes key knowledge for the practitioner in the field as necessary, and tables and illustrations are included for quick and easy reference. At the end of each chapter, the most important elements are highlighted, and references for further reading are provided.

Our book is conceived and edited out of the strong belief that perioperative medicine is a true multi-specialty discipline and that patient care is best delivered with a genuine collaborative approach. Therefore, we hope that it will be useful for all healthcare providers involved in the perioperative treatment of neurosurgical patients, including trainees in anesthesiology and neurosurgical critical care as well as faculty members in both fields, physician assistants, nurse practitioners, nurse anesthetists, and perioperative nurses.

We believe the reference guide format is best because it allows the clinician to have immediate access to solutions to problems in the operating room, post-anesthesia care unit, intensive care unit, or wherever they may occur. Even if the practitioner has the best text on the office shelf, it is not helpful when acute problems occur at the bedside. This book, however, will be portable to every place of practice and will make it easy for the practitioner to identify or quickly review several good solutions for a given problem at any time.

We have been fortunate that so many international leaders in the field agreed to contribute to our project, and we are convinced that clinicians in both private practice and academic medicine will benefit from the concise information provided by authorities from multiple institutions worldwide.

We hope that this book may help to improve further the safety and comfort of our patients who must undergo risky procedures to receive relief from diseases affecting the central nervous system.

New York, NY, USA — Ansgar M. Brambrink
Portland, OR, USA — Jeffrey R. Kirsch

Acknowledgments

The editors wish to express their great respect and gratitude for the contribution of W. “Scott” Jellish, MD, PhD to the field of anesthesiology and perioperative medicine in general, and to this book in particular. Scott was a gifted physician who served in multiple leadership positions at the Loyola University Medical Center/Stritch School of Medicine. He retired from Loyola as one of the longest serving Chairs in Anesthesiology in the United States. With his direction, anesthesia services across the disciplines flourished at Loyola. Scott was a highly regarded neuro-anesthesiologist, and a national leader with numerous prominent roles including President of the Illinois Society of Anesthesiologists and Full Examiner for board certification with the American Board of Anesthesiology. He also was an innovative researcher, a warm and generous educator, a talented editor, and a prolific writer. Above all, as a clinician, Scott had remarkable expertise in intraoperative management and critical care, and he supported patients with the most complex conditions through surgical procedures with grace and kindness.

The editors are tremendously grateful to Jennifer Young for her amazing dedication in developing and finalizing the second edition of this book. Her commitment to keeping us on track, tirelessly communicating between authors, editors, and the publisher, and skillfully managing the complex process of revising existing chapters and supporting new authors were of paramount importance in making this new publication possible.

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Part I

Basics of Neuroanesthesia Care

The Adult Central Nervous System: Anatomy and Physiology

1

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Overview

The human brain consists of three basic subdivisions – the cerebral hemispheres, the brain stem, and the cerebellum. Speech is represented by two main areas – Broca's area in the inferior frontal lobe (expressive speech) and the Wernicke's area in the temporoparietal cortex (interpretation of language) (Fig. 1.1). Language localization is found in 96% of population in the left. The basal ganglia are a collection of nuclei deep in the white matter of cerebral cortex and contain the substantia nigra. A decrease in function of the dopaminergic neurons located in the substantia nigra causes Parkinson's disease. The cerebral hemispheres are connected together medially by the corpus callosum. The limbic areas of the brain include the hypothalamus, amygdala, hippocampus, and limbic cortex. Optic nerve (second) leaves the retina of the eye and travels to the optic chiasm, located just below and in front of the pituitary gland. In the optic chiasm, the optic nerve fibers arising from the nasal half of each retina cross over to the other side; but the nerve fibers originating in the temporal retina do not cross over. The nerve fibers become the optic tract and the optic radiation and reach the visual cortex in the occipital lobe of the cerebrum.

The brain stem is located at the juncture of the cerebrum and the spinal column. It consists of the midbrain, pons, and medulla oblongata. Two cranial nerves are associated with the midbrain, the oculomotor (third) which emerges from the interpeduncular fossa and the trochlear (fourth) cranial nerves which emerge from the dorsal surface of the brain stem. The cranial nerves associated with the pons are the trigeminal (fifth), abducens (sixth), facial (seventh), and the two components of the auditory (eighth). The fifth cranial nerve passes through the rostral part of the middle cerebellar peduncle. The sixth lies on the floor of the fourth ventricle, is partially encircled by the seventh cranial nerve, and emerges from the ventral surface of the brain stem at the junction between the pons and medulla. The seventh and eighth cranial nerves emerge from the lateral surface of the pons at the cerebellopontine angle. The red nucleus is a structure in the rostral midbrain involved in motor coordination. It is less important in its motor functions for humans than in many other mammals because, in humans, the corticospinal tract is dominant. The reticular formation is composed of a number of diffuse nuclei in the medulla, pons, and midbrain. The ascending reticular formation is also called the reticular activating system (RAS) and is responsible for the sleep–wake cycle. The descending reticular formation is involved in posture, equilibrium, and motor movement. It is also responsible for autonomic nervous system activity (vasomotor center), and stimulation of different portions of this center causes either a rise in blood pressure and tachycardia (pressor area) or a fall in blood pressure and bradycardia (depressor area). Medulla is the most caudal part of the brain stem. The cranial nerves associated with the medulla are the glossopharyngeal (9th), vagus (10th), accessory (11th), and hypoglossal (12th) (Fig. 1.2).

The cerebellum is a trilobed structure, lying posterior to the pons and medulla oblongata and inferior to the occipital lobes of the cerebral hemispheres, that is responsible for the regulation and coordination of complex voluntary muscular movement as well as the maintenance of posture and balance. In contrast to the neocortex, cerebellar lesions produce ipsilateral disturbances.

The skull consists of the anterior, middle, and posterior cranial fossa. Anterior cranial fossa accommodates the anterior lobe of the brain. Middle cranial fossa contains the two temporal lobes, the parietal and part of the occipital lobe of the brain. The posterior cranial fossa is part of the intracranial cavity located between the foramen magnum and tentorium cerebelli. It contains part of the occipital lobe, brain stem, and cerebellum. The brain is covered by the dural membranes which enclose the venous sinuses.

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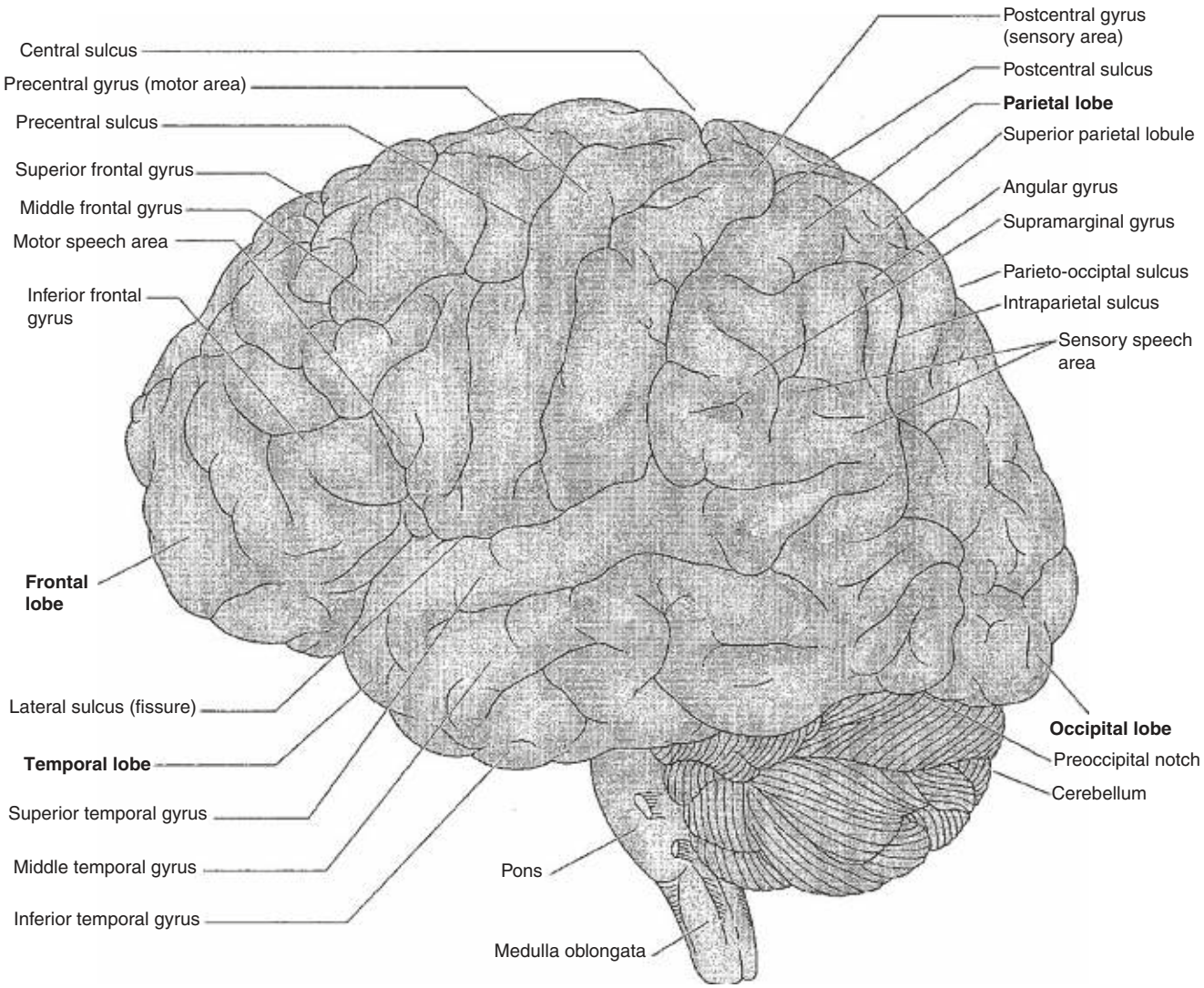

Fig. 1.1 Lateral surface of the brain

The cavernous sinuses are paired, venous structures located on either side of the sella turcica (Fig. 1.3). They contain the carotid artery, its sympathetic plexus, and the third, fourth, and sixth cranial nerves. In addition, the ophthalmic branch and occasionally the maxillary branch of the fifth nerve traverse the cavernous sinus. The nerves pass through the wall of the sinus, while the carotid artery passes through the sinus itself. The pituitary gland is located inside the sella turcica, a round bony cavity that is separated from the sphenoid sinuses by a thin bone, the floor of the sella, which forms part of the roof of the sphenoid sinuses.

The circle of Willis provides the blood supply to the cerebrum. It is formed by the two internal carotid arteries, which are responsible for 80% blood supply to the brain, and the vertebral artery, which is responsible for about 20% blood supply to the brain. The internal carotids and vertebral arteries anastomose together at the base of the brain. The circle of Willis is associated with frequent anatomical variations, and a complete circle of Willis is found only in 50% of the population. The anterior and middle cerebral arteries, which originate from the circle of Willis, form the anterior circulation and supply the forebrain. Each gives rise to branches that supply the cortex and branches that penetrate the basal surface of the brain, supplying deep structures such as the basal ganglia, thalamus, and internal capsule. The lenticulostriate arteries arise from the middle cerebral artery and supply the basal ganglia and thalamus. The posterior circulation of the brain supplies the posterior cortex, the midbrain, and the brainstem and comprises arterial branches arising from the posterior cerebral, basilar, and vertebral arteries. Midline arteries supply medial structures; lateral arteries supply the lateral brainstem; and dorsal–lateral arteries supply dorsal–lateral brainstem structures and the cerebellum (Fig. 1.4).

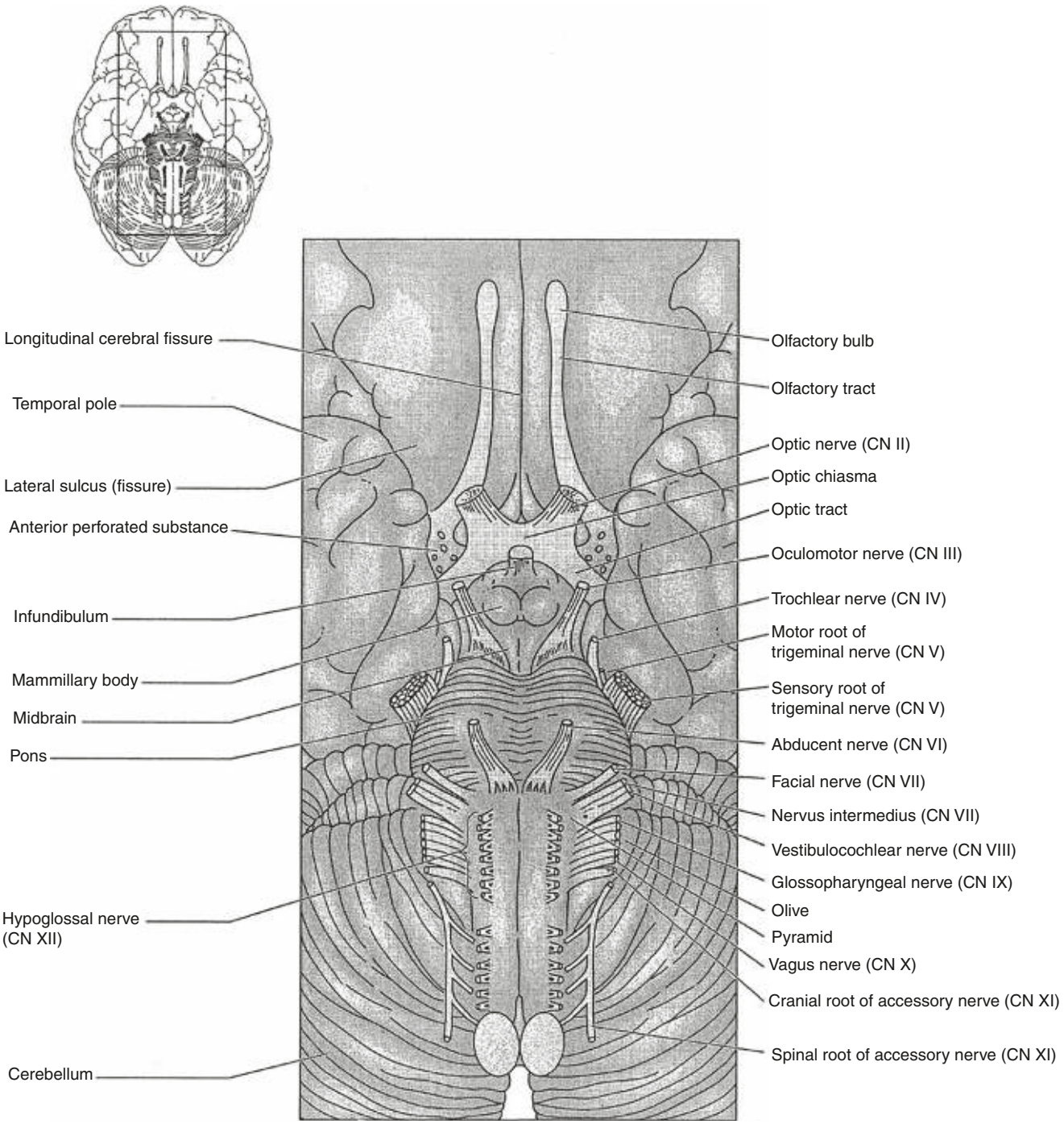

Fig. 1.2 Cranial nerves at the base of brain

Most of the blood in the brain can be found in its venous system. Blood is drained into superficial and deep cerebral veins and veins of the posterior fossa. The superficial veins drain the surface of the brain cortex and lie within the cortical sulci. The deep cerebral veins drain the white matter, basal ganglia, diencephalon, cerebellum, and brain stem. The deep veins join to form the great cerebral vein. The veins of posterior fossa drain blood from the cerebellar tonsils and the posteroinferior cerebellar hemispheres. In addition, the diploic veins drain the blood between layers of the bone in the skull. Emissary veins connect the veins near the surface of the skull to the diploic veins and venous sinuses. All the blood is drained into the meningeal sinuses, which mainly drain into the internal jugular vein. Usually, the right jugular vein is the dominant one, receiving most of the blood from the brain. The veins and sinuses of the brain lack valves.

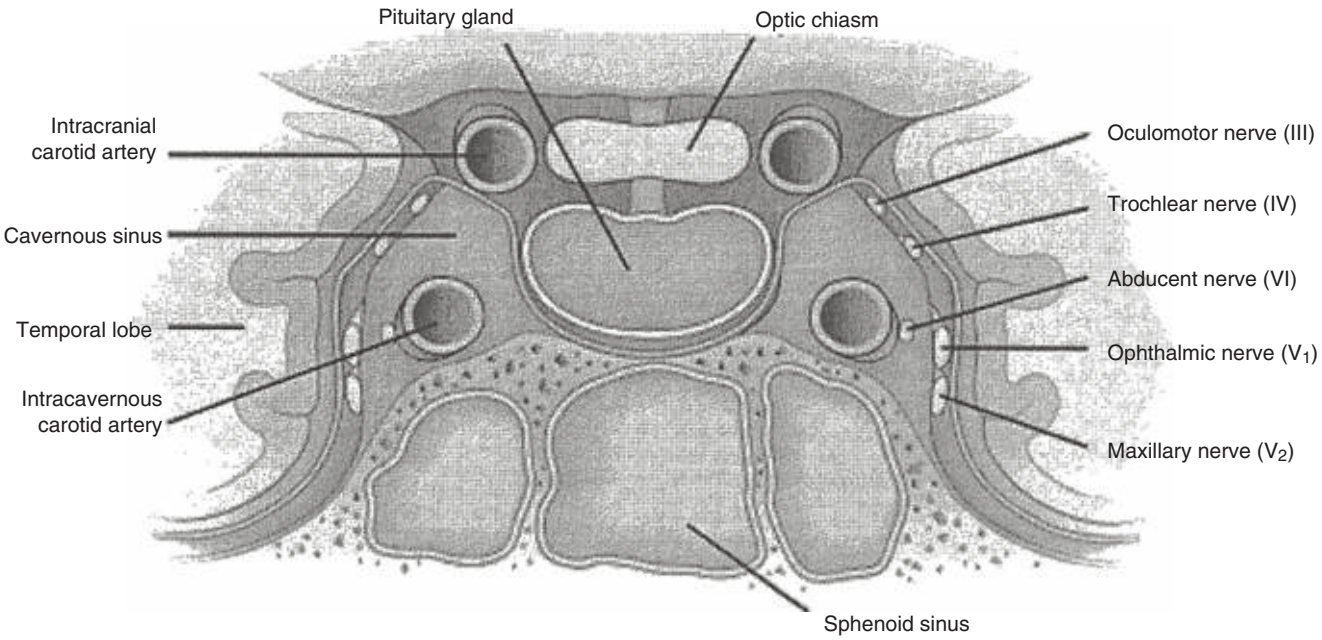

Fig. 1.3 Anatomical structure of cavernous sinus

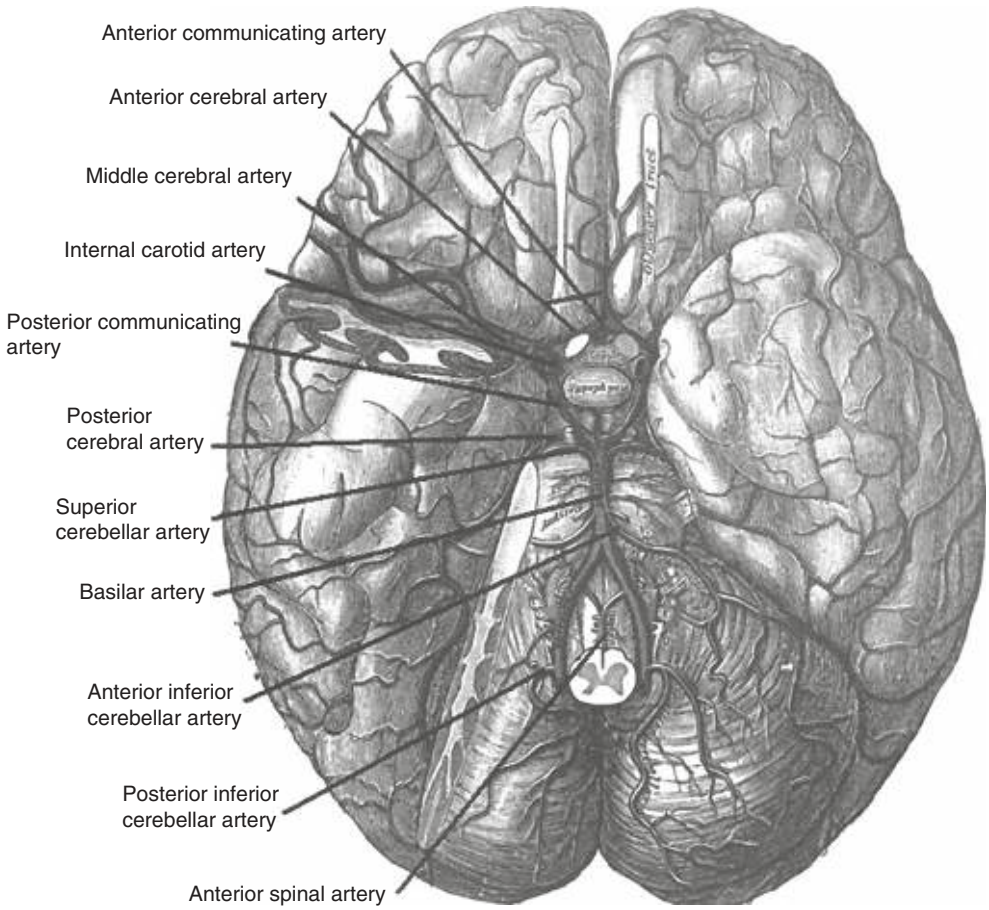

Fig. 1.4 Arterial supply of the brain

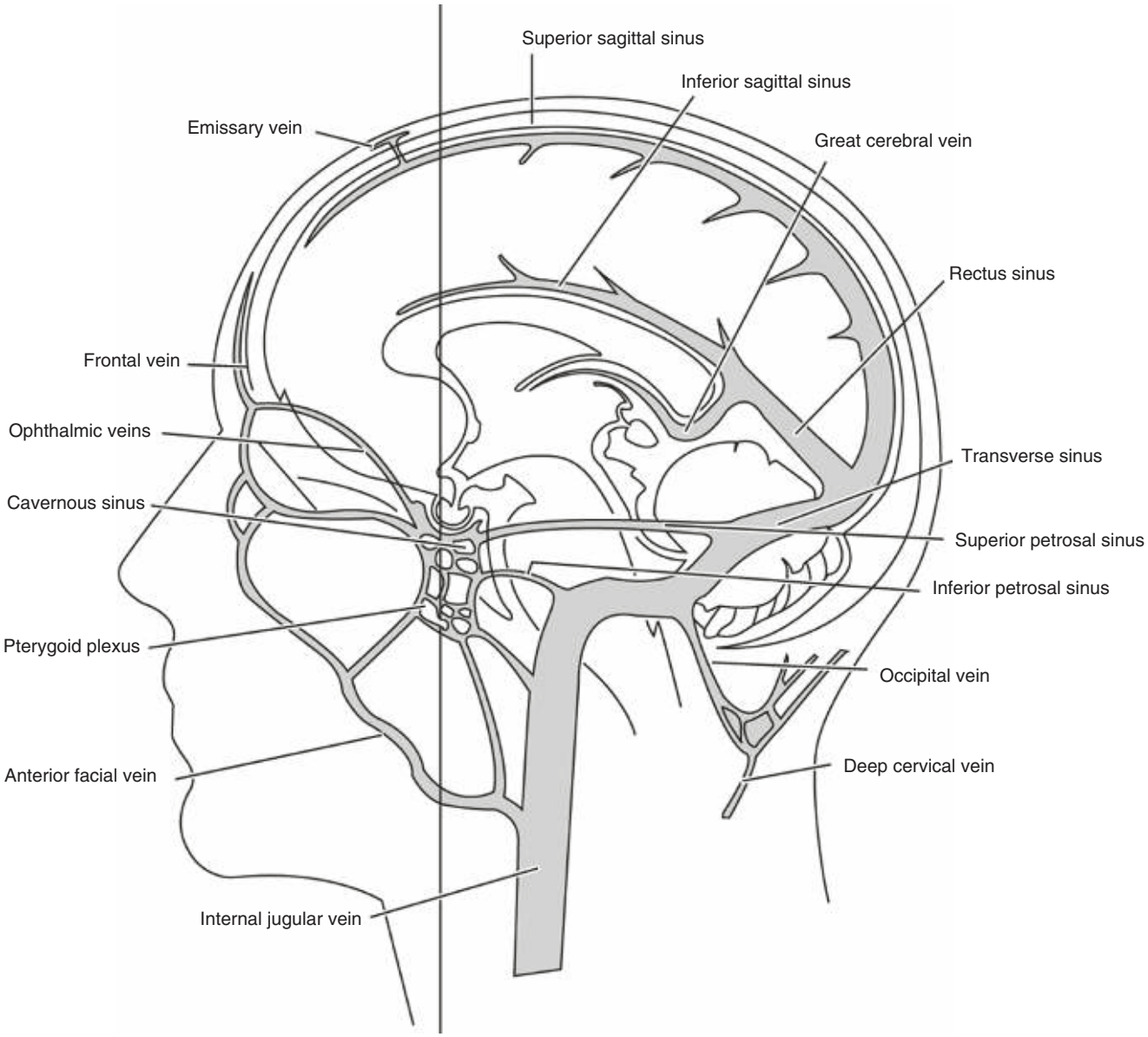

Fig. 1.5 Venous drainage of the brain

Pressure of drainage vessels in the neck is directly transmitted to intracranial venous structures (Fig. 1.5).

The vertebral column is composed of 33 vertebrae. Each vertebra is composed of a vertebral body, neural arch, pedicle, and lamina (Fig. 1.6). The two laminae join together posteriorly to form the spinous process. The ligaments stabilizing the vertebral column from exterior to interior are the supraspinous, interspinous, ligamentum flavum, posterior longitudinal, and anterior longitudinal ligaments (Fig. 1.7). The ligaments provide flexibility without allowing excessive movement which could damage the cord. The human spine is also affected by aging. The intervertebral disks become drier, more fibrous, and less resilient.

The spinal cord is a long cylindrical structure covered by membranes which lies in the vertebral canal. The spinal cord is the continuation of the medulla. It extends from the foramen magnum to the lower border of first lumbar vertebral. It has two enlargements, cervical and lumbosacral, corresponding to the innervation of the upper and lower extremities. It ends in the conus medullaris. The anterior portion of the spinal cord contains the motor tracts, while the posterior cord contains the sensory tracts. The mean spinal cord blood flow in the cervical and lumbar segments is 40% higher than the thoracic segment. The watershed area of the spinal cord blood flow is the mid-thoracic region. The spinal cord receives its blood supply principally from three longitudinal vessels. The

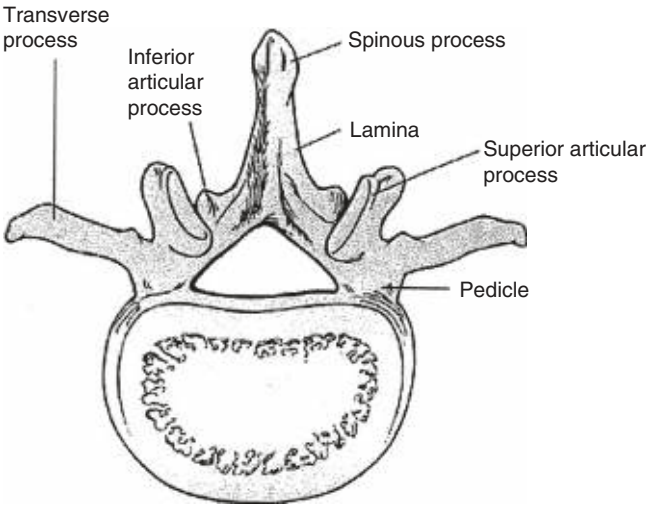

Fig. 1.6 Lumbar vertebra

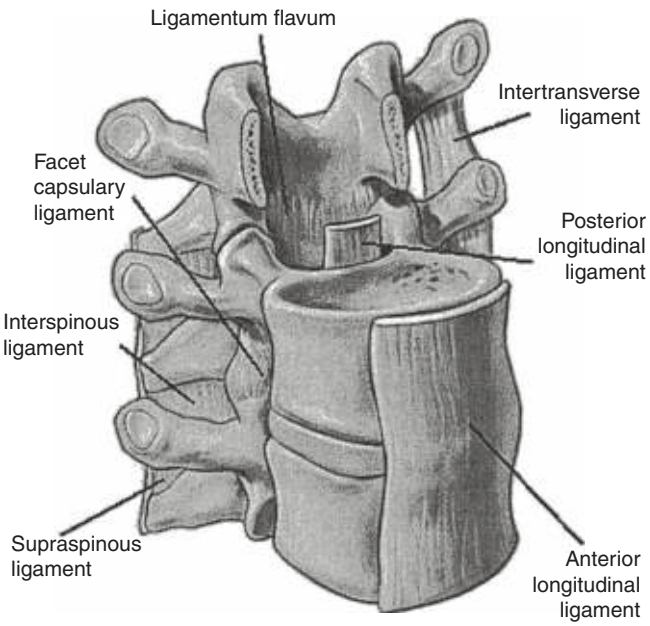

Fig. 1.7 Ligaments supporting the vertebrae

single anterior spinal artery is formed by the two vertebral arteries which supply the anterior 75% of the cord and the two posterior spinal arteries formed by the posterior inferior cerebellar artery and supply the posterior 25% of the cord (Fig. 1.8). The anterior and posterior arteries alone can only supply enough blood to maintain the upper cervical segments of the spinal cord. The blood supply to the lower levels of the spinal cord is provided by the radicular arteries which anastomose with the anterior and posterior spinal arteries. The artery of Adamkiewicz, a major radicular artery located in lower thoracic or upper lumbar region, provides most of the blood supply to the lower cords. Autoregulation maintains spinal cord blood flow by altering vascular resistance in response to changes in the mean arterial blood pressure (MAP).

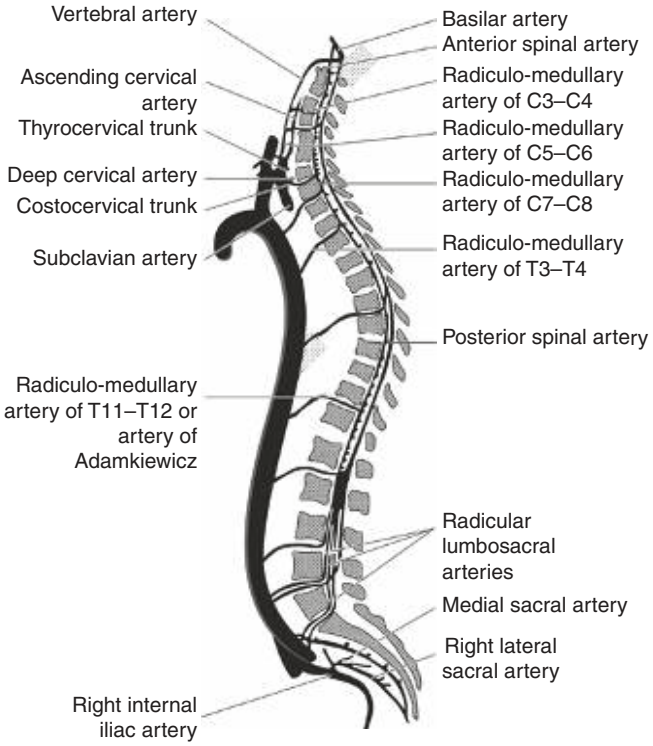

Fig. 1.8 Blood supply of the spinal cord

The ascending spinal tracts are contained in the posterior column of the spinal cord and terminate in the medulla. They are sensory in nature. After decussation in the medulla, the second-order neurons form an ascending bundle and terminate in the thalamus from where they reach the postcentral gyrus via third-order neurons (Fig. 1.9). The descending tract, called the corticospinal tract, is motor in nature. Corticospinal tract fibers originate in the cerebral cortex in the precentral gyrus, and 90% decussate at the level of the medulla. Lesions above the medullary decussation cause contralateral paralysis, and those below medullary decussation cause ipsilateral paralysis (Fig. 1.10).

The ventricular system of the brain is composed of two lateral ventricles and two midline ventricles called the third and fourth ventricles which contain the cerebrospinal fluid (CSF). The chambers are connected to allow the flow of CSF between two lateral ventricles to the third ventricles through the foramen of Monro. This then communicates through the aqueduct of Sylvius (mesencephalic aqueduct) to the fourth ventricle (Fig. 1.11). The CSF flows out into the subarachnoid spaces of the brain and the spinal cord through the medial foramen of Magendie and lateral foramen of Luschka. The chambers of the ventricular system are lined with ependymal cells and are continuous with the central canal enclosed within the spinal cord. CSF is a dynamic medium, which is produced and absorbed constantly, and functions as the brain's drainage system. Under normal circumstances, a human being produces

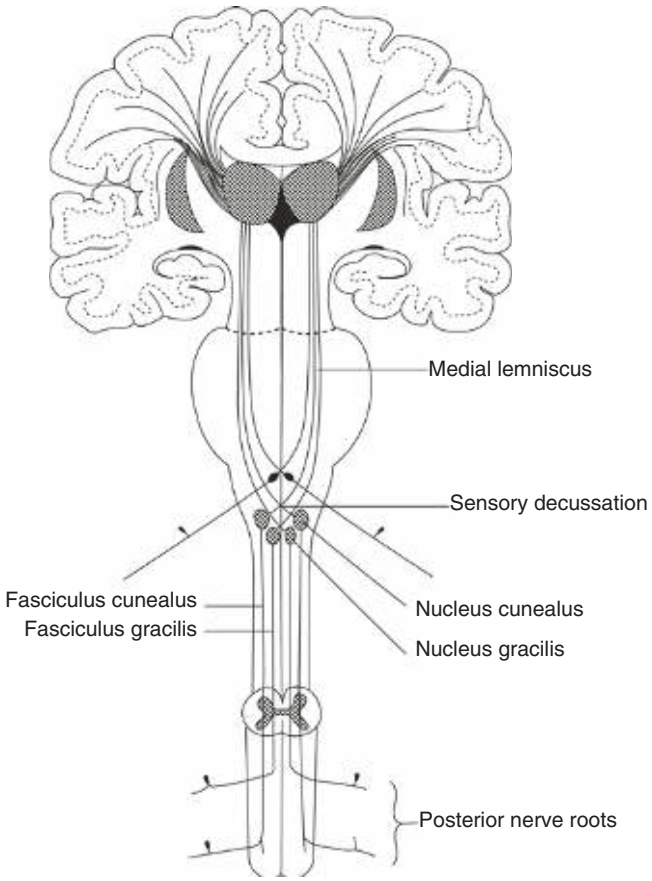

Fig. 1.9 Sensory pathway

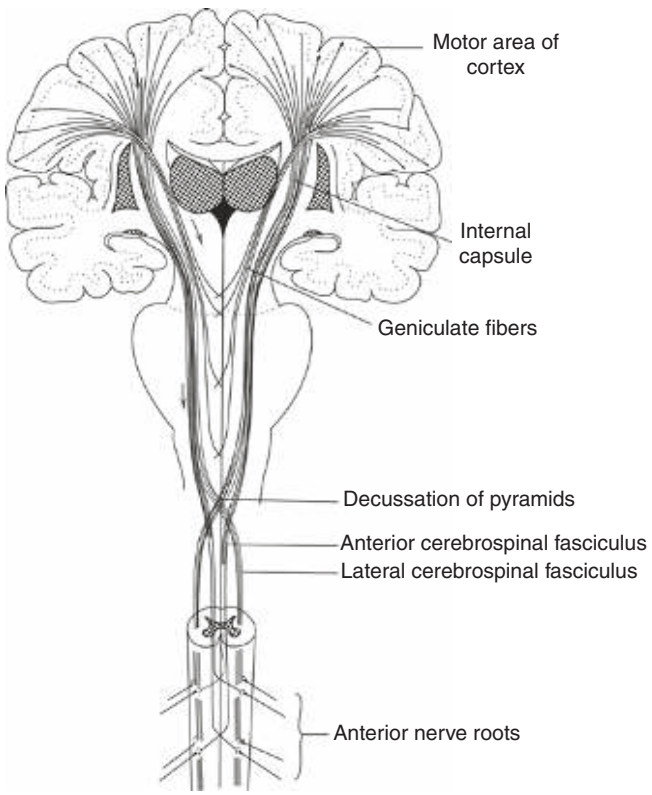

Fig. 1.10 Motor pathway (corticospinal tract)

approximately 0.35 ml/min (500 ml/day) of CSF. The total volume of CSF at a given time is 150 ml, which means that the CSF is replaced approximately four times a day. The majority of CSF is formed in the choroid plexus of the lateral ventricles by filtration of plasma through fenestrated capillaries and also by the active transport of water and dissolved substances through the epithelial cells of the blood–CSF barrier. CSF may also be formed by the lymph-like drainage of the brain's extracellular fluid. Reabsorption of CSF takes place mostly in the arachnoid villi and granulations into the circulation. The mechanism behind the CSF reabsorption is the difference between the CSF pressure and venous pressure. CSF formation is reduced by decreased blood flow through the choroid, hypothermia, increased serum osmolarity, and increased ICP. The main compensatory mechanism for an increase in CSF volume includes displacement of CSF from cranial to spinal compartment, increase in CSF absorption, decrease in CSF production, and a decrease in cerebral blood volume (mainly venous).

The blood–brain barrier (BBB) isolates the brain from the plasma and is formed by the interaction of capillary endothelial cells with astrocytes in the brain. Water, gases, glucose, and lipophilic substances are freely permeable through the BBB. Proteins and polar substances are poorly permeable through the BBB. The brain is protected from the circulating toxins by the BBB.

The brain tissue has a high energy requirement and is responsible for about 20% of total body oxygen consumption. The cerebral metabolic rate, expressed as oxygen consumption ($CMRO_2$), averages 3.5 ml/100 g/min in adults. $CMRO_2$ is greatest in the gray matter of the cerebral cortex. Brain oxygen consumption supports two major functions – basic cellular maintenance (45%) and nerve impulse generation and transmission (55%). Glucose is the main substrate for energy production in the brain.

Normal cerebral blood flow (CBF) varies with the metabolic activity. Blood flow in gray matter is about 80 ml/100 g/min and in white matter is 20 ml/100 g/min. The average CBF is about 50 ml/100 g/min. There is coupling between the CBF and $CMRO_2$. The precise mechanism responsible for this coupling has not been identified, but it has been suggested that local by-products of metabolism (K+, H+, lactate, adenosine) are responsible for this coupling. Nitric oxide, a potent vasodilator, has also been suggested to play a role. Glial processes may serve as a conduit for the coupling.

Cerebral autoregulation maintains CBF relatively constant between cerebral perfusion pressures of 50 and 150 mmHg (Fig. 1.12). The mechanism of autoregulation is not understood but is probably due to myogenic and metabolic factors. Cerebral perfusion pressure (CPP) is calculated by subtraction of intracranial pressure (ICP) from mean arterial pressure, CPP = MAP − ICP.

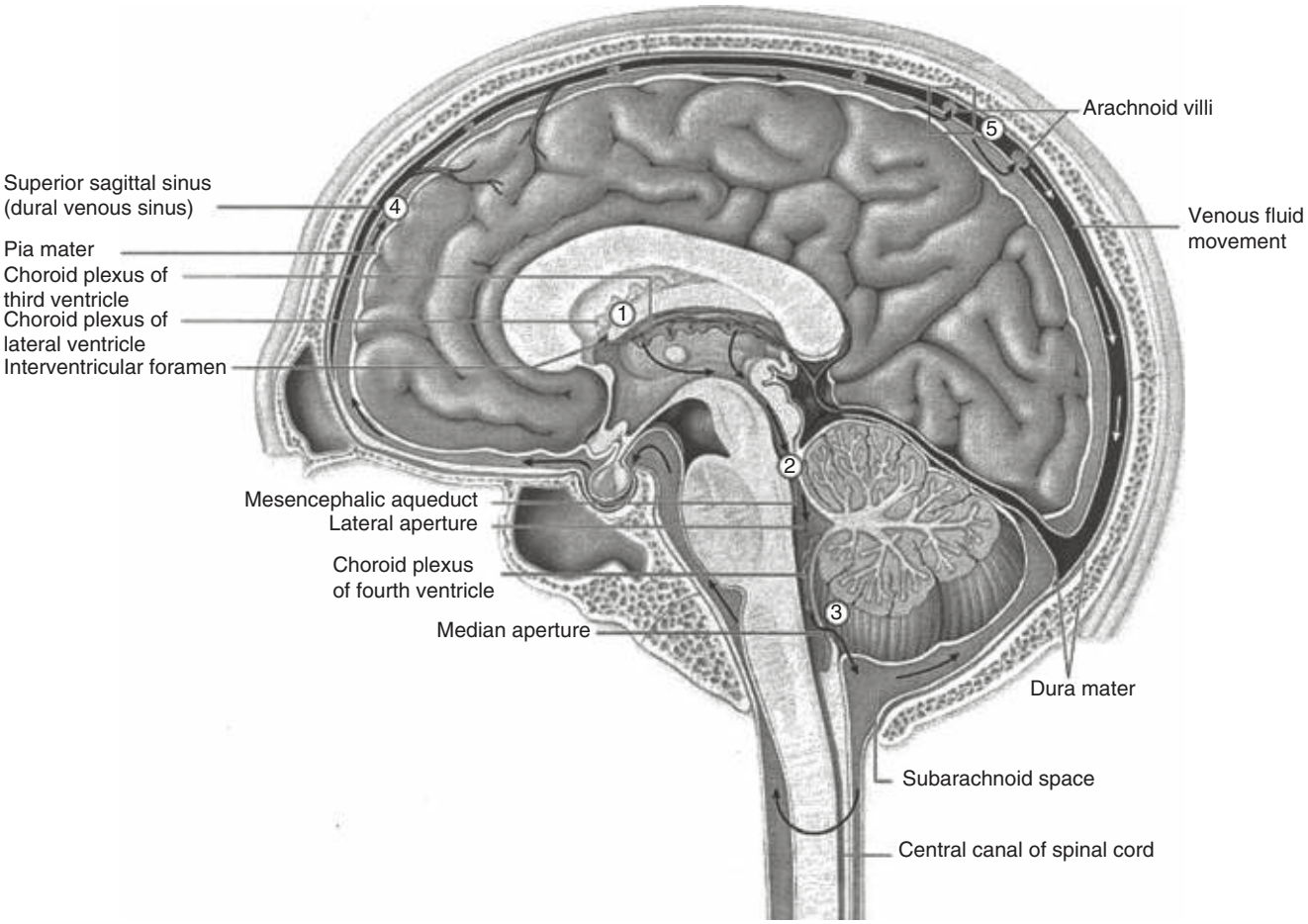

Fig. 1.11 Circulation of cerebrospinal fluid. (1) CSF formation, (2) circulation of CSF in the ventricle, (3) CSF flow into subarachnoid space, (4) CSF circulation around the brain, and (5) absorption into circulation

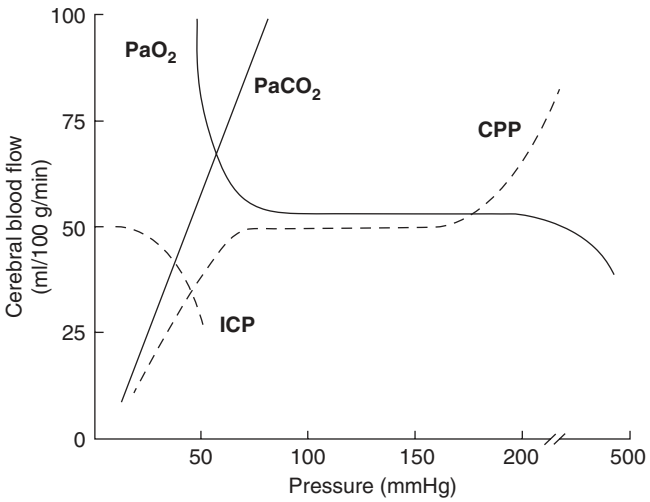

Fig. 1.12 Autoregulation of cerebral blood flow (CPP curve). Perfusion is increased in the setting of hypoxia or hypercarbia

The cranial vault is a rigid structure with fixed total volume, consisting of brain (80%), blood (12%), and CSF (8%). An increase in one component must be offset by an equivalent decrease in another to prevent a rise in the ICP. Intracranial compliance is measured by change in ICP in response to a change in intracranial volume ($\Delta V/\Delta P$). Intracranial elastance ($\Delta P/\Delta V$) is high because a small change in intracranial volume, ΔV, can cause a large change in ICP, ΔP. The pressure–volume relationship between ICP, volume of CSF, blood, and brain tissue and CPP is known as the Monro–Kellie hypothesis (Fig. 1.13).

Anatomical changes that occur in the brain during normal aging are reduction in brain weight and volume with ventriculomegaly and sulcal expansion. The white matter volume of the cerebrum, cerebellum, corpus callosum, and pons remains fairly intact across all ages. Global CBF decreases about 10–20% because there is less brain mass to perfuse as we age.

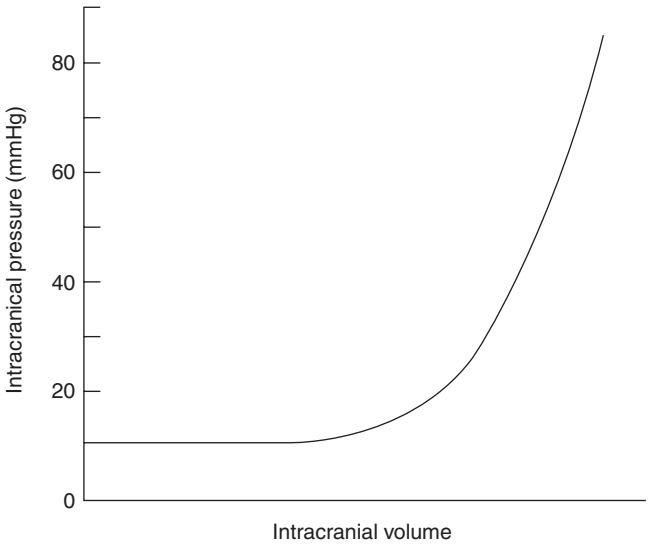

Fig. 1.13 Intracranial compliance curve – initial change in volume causes a slight rise in ICP; further increase causes a marked rise in ICP

Implications for the Neurosurgical Patient

Brain anatomy is important in identifying the different non-silent areas of the brain with respect to the surgical procedure being performed and helps to prevent devastating deficits. For instance, awake craniotomy or cortical mapping may be performed when tumors or epileptic foci are close to cortical areas for speech or motor function or temporal structures critical to short-term memory. The Wada test determines the dominant lobe for suitability of temporal lobectomy. Deep brain stimulation of the globus pallidus interna or subthalamic nucleus improves many features of advanced Parkinson's disease. In addition, surgical approach and intraoperative events have anatomical implications. A frontotemporal craniotomy is used to approach anterior circulation aneurysms. Aneurysms originating from the posterior circulation require a subtemporal exposure, suboccipital exposure, or a combined subtemporal and suboccipital exposure. Brain stem stimulation can cause ventricular and supraventricular arrhythmias. Profound arterial hypertension can result from stimulation of the fifth cranial nerve. Significant bradycardia and escape rhythms can be caused from the stimulation of vagus nerve. Arterial hypotension can result from pontine or medullary compression. Brain stem lesions may result in abnormal breathing patterns.

Cranial nerve injury is a significant risk in surgery of the cerebellopontine angle and brain stem; therefore, intraoperative stimulation, monitoring, and recording of electromyographic potential of the cranial nerve with motor component are utilized to preserve the integrity of these nerves. Direct injury to portions of the RAS located within the pons, midbrain, or diencephalon (hypothalamus and thalamus) produces unconsciousness. Locked-in syndrome occurs with focal injury to the ventral pons and is often associated with basilar artery stroke. It results in patients who are quadriplegic, nonverbal, but awake and alert as the RAS is spared and volitional eye blinking is preserved.

The signs of corticospinal pathway dysfunction include initial weakness, followed by flaccid paralysis and then decorticate rigidity. Extensor (Babinski) toe response indicates acute or chronic injury of the corticospinal tracts in the brain and spinal cord. A Hoffman's response, which is the upper extremity equivalent of a Babinski response, can also provide additive lateralizing information. When damage involves subcortical structures (basal ganglia), decerebrate rigidity occurs. Basal ganglia damage may also lead to athetoid or choreiform movements. The absence of vestibuloocular and oculocephalic reflex suggests brain stem damage in the pons between the vestibular nuclei (CN VIII) and oculomotor (CN III) and abducens (CN VI) nuclei, which control lateral eye movements. Flexor posturing (decorticate) indicates brain dysfunction above the level of the red nucleus in the midbrain (the area which mediates flexor response). Extensor posturing (decerebrate) indicates brain stem dysfunction below the level of the red nucleus. A hemispheric injury presents with contralateral hyporeflexia. Patients with acute spinal cord shock are hyporeflexive below the level of involvement (Table 1.1).

During spinal surgery, evoked potential monitoring may be used to evaluate spinal cord integrity. Sensory evoked potentials (SEP) evaluate the functional integrity of the ascending sensory pathways, mostly ending in the somatosensory cortex. Motor evoked potentials (MEP) test the functional integrity of the corticospinal tracts, which mainly originate in the motor cortex. The wake-up test is also utilized to document the anterior motor component of the spinal cord (anterior column).

CBF is linearly related to $PaCO_2$ from 20 to 70 mmHg, when the autoregulation is intact. Hypocapnia causes cerebral vasoconstriction. Hypercapnea causes vasodilatation and increases the CBF. This change is mainly dependent on the pH alteration in the extracellular fluid of the brain. Change in PaO_2 from 60 to over 300 mmHg has little influence on CBF (Fig. 1.12). Hematocrit alters blood viscosity and affects blood flow; a low hematocrit increases blood flow by decreasing viscosity. Hypothermia decreases neuronal metabolism and reduces CBF, whereas hyperthermia has the opposite effect. $CMRO_2$ decreases by 6–7% for each reduction in 1 °C.

Increased ICP may occur through one of several mechanisms: increase in CSF volume (due to blockage in CSF circulation or absorption), increase in brain tissue volume (tumor or edema), or increase in cerebral blood volume (intracranial bleed or vasodilatation). Communicating hydrocephalus occurs when the obstruction is at the point of CSF absorption (arachnoid granulation) and herniation

Table 1.1 Diagnosis of cranial nerve damage in ICU

Cranial nerve	Test cranial nerve	Cerebral lobe affected	Presentation
Cranial nerve 1 (olfactory nerve)	Not practical in ICU	Frontal lobe, pituitary tumor, anterior cranial fossa fracture	Loss of sense of smell (anosmia)
Cranial nerve 2 (optic nerve)	Limited in unconscious patient	Distal to optic chiasm Lesion pressing on optic chiasm Lesion proximal to chiasm	Monocular blindness Bitemporal hemianopia Homonymous hemianopia
Cranial nerve 3 (oculomotor nerve)	Pupillary exam	Uncal and temporal lobe herniation	Ptosis, divergent squint, pupillary dilatation, loss of accommodation, and light reflexes
Cranial nerve 4, 5, 6 (trochlear, trigeminal, abducent)	Lightly poking the patient's cheeks with a sharp object or stimulating the nasal cavity with a cotton swab (CN V)	Cavernous sinus lesion, injury to the base of skull	Loss of corneal reflex 5 (corneal damage), convergent squint 6
Cranial nerve 7 (facial)	Facial movement	Large cerebellopontine tumors	Muscles of face, anterior two-thirds of tongue
Cranial nerve 8 (auditory)		Cerebellopontine tumors, acoustic neuromas	Unilateral deafness
Cranial nerve 9, 10 (glossopharyngeal, vagus)	Gag reflex by tongue blade or suction catheter	Posterior third of tongue and pharynx	Absence of gag reflex (increased risk of aspiration), nasal speech, vocal cord paralysis 10
Cranial nerve 11 (accessory)	Limited	Central branch arising from the medullary nuclei and spinal accessory branch arising in the first five to six cervical spinal segments from the lateral portion of the ventral horn	Central branch supplies the larynx and spinal accessory to trapezius and sternocleidomastoid – inability to shrug
Cranial nerve 12 (hypoglossal)	Limited in unconscious patient	Muscle of tongue, damaged during carotid surgery	Aspiration

is less likely to occur. In noncommunicating hydrocephalus, obstruction occurs within the ventricular system, and herniation syndrome may be seen. Once there is a critical increase in ICP, brain herniation may occur. Ventriculostomy may be performed to decrease ICP in such cases. If drainage of CSF is performed via lumbar puncture in the presence of increased ICP, there is a risk of brain stem herniation through the foramen magnum. Aging increases intracranial CSF volume due to cerebral atrophy and creates nonpathological low-pressure hydrocephalus.

Concerns and Risks

Spinal cord lesions above C 3 lead to diaphragmatic paralysis, and the patient is totally ventilator dependent. This is because the phrenic nerve, which is the principal nerve supply of the diaphragm, is formed by C 3, 4, and 5 nerve roots. Acute spinal cord injury at the level of C 6 presents as spinal shock from a total loss of impulses from the higher centers. Epidural hematoma (EDH) is a traumatic accumulation of blood between the inner table of the skull and the stripped-off dural membrane. EDHs are usually arterial in origin with 70–80% located in the temporoparietal region where skull fractures cross the path of the middle meningeal artery or its dural branches. Expanding high-volume EDHs can produce a midline shift and subfalcine herniation of the brain resulting in compression of cerebral tissue and impingement on the third cranial nerve. This results in ipsilateral pupillary dilation and contralateral hemiparesis or extensor motor response. On the other hand, subdural hematomas are generally the result of venous bleeding of bridging veins (between the cortex and venous sinuses).

The brain is vulnerable to ischemic injury because of its high oxygen consumption and near-total dependence on aerobic glucose metabolism. Prolonged reduction of CBF below 20–25 ml/100 g/min is associated with cerebral impairment (slowing of EEG) and between 15 and 20 ml/100 g/min produces a flat EEG, while values below 10 ml/100 g/min are associated with irreversible structural brain damage. Autoregulation is impaired by hypoxia, ischemia, hypercapnia, trauma, and certain anesthetic agents. A rightward shift in the autoregulatory curve occurs with chronic hypertension and sympathetic activation (shock or stress). A leftward shift occurs in hypoxia, hypercarbia, and vasodilators. When CPP exceeds the upper limit of autoregulation, the BBB may be disrupted, leading to cerebral edema.

Any increase in ICP is initially well compensated; however, once the compliance is exhausted, a small increase in volume causes an exponential rise in ICP leading to herniation (see Fig. 1.14). Herniation syndromes (Table 1.2) can be reversible if treated immediately and effectively and are encountered when the pressure in one compartment of the brain results in extrusion of the contents into an adjacent compartment with accompanying mechanical damage. Depressed level of consciousness with dilated pupils is the first clinical sign of a herniation syndrome and is usually accompanied by a Cushing response (elevation in the systolic blood pressure with accompanying bradycardia).

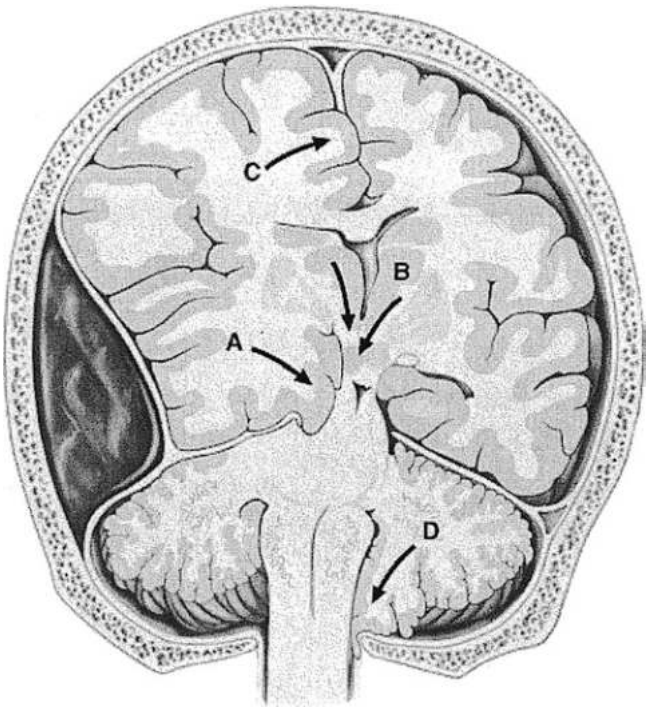

Fig. 1.14 Potential sites of brain herniation (A) uncal, (B) central, (C) subfalcine, (D) tonsillar. Transcalvarial is not shown in this figure

Table 1.2 Herniation syndromes and their clinical manifestations

Herniation of uncus of temporal lobe	Supratentorial	Pressure on ipsilateral oculomotor nerve, posterior cerebral arteries and cerebral peduncle–pupillary abnormalities, contralateral hemiplegia, possible ipsilateral medial occipital lobe infarction
Central herniation (midline structure)	Supratentorial	Downward movement of diencephalon through tentorial notch against immobile basilar artery may cause brain stem hemorrhage
Subfalcine (when the brain is pushed into the opposite half of the cranium under the falx cerebri)	Supratentorial	Cingulate gyrus injury, ischemia in anterior cerebral artery distribution
Tonsillar herniation	Supra- or infratentorial	A rapid and fatal event unless it is recognized immediately and treated; the cerebral tonsil descends through the foramen magnum leading to the compression of brain stem and respiratory arrest; rarely posterior fossa mass pushing the posterior fossa contents through the tentorium cerebelli into the supratentorial compartment
Transcalvarial herniation	Supra- or infratentorial	Any area beneath a defect in the skull

Key Points

- In the corticospinal tract, lesions above the medullary decussation cause contralateral paralysis, and those below medullary decussation cause ipsilateral paralysis.
- Brain anatomy is important in identifying the different non-silent areas of the brain with respect to the surgical procedure being performed and helps to prevent devastating deficits.
- Cranial nerve injury is a significant risk in surgery of the cerebellopontine angle and brain stem.
- Lumbar puncture for drainage of CSF is performed below the L1 vertebra to prevent damage to the spinal cord. Most spinal cord injuries occur at the mid-cervical or thoracolumbar region. The watershed area of the spinal cord blood flow is the mid-thoracic region.
- CBF is linearly related to $PaCO_2$ from 20 to 70 mmHg when the autoregulation is intact. Hypocapnia causes cerebral vasoconstriction and can lead to brain ischemia. Hypercapnea causes vasodilatation and increases the CBF.
- Increased ICP may occur through one of several mechanisms: increase in CSF volume (due to blockage in CSF circulation or absorption), increase in brain tissue volume (tumor or edema), or increase in cerebral blood volume (intracranial bleed or vasodilatation).
- The brain is vulnerable to ischemic injury because of its high oxygen consumption and near-total dependence on aerobic glucose metabolism.
- Any increase in ICP is initially well compensated; however, once the compliance is exhausted, a small increase in volume causes an exponential rise in ICP leading to herniation.

Suggested Reading

Bendo AA, Kass IS, Hartung J, Cottrell JE. Anesthesia for neurosurgery. In: Barash PG, Cullen BF, Stoelting RK, editors. Clinical anesthesia. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 746–89.

Cottrell JE, Smith DS. Anesthesia and neurosurgery. 4th ed. St Louis: Mosby; 2001.

Drummond JC, Patel PM. Neurosurgical anesthesia. In: Miller's anesthesia. 6th ed. Philadelphia: Elsevier, Churchill Livingstone; 2005. p. 2127–73.

Newfield P, Cottrell JE, editors. Handbook of neuroanesthesia. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

Patel PM, Drummond JC. Cerebral physiology and effects of anesthetics and techniques. In: Miller's anesthesia. 6th ed. Philadelphia: Elsevier, Churchill Livingstone; 2005. p. 813–57.

Neuroendocrine Physiology: Fundamentals and Common Syndromes

2

Jason D. Walls, Mitchell L. Weinstein, and Joshua H. Atkins

Introduction

By supporting the control of volume status, blood pressure, cellular metabolism, and intracellular signaling, hormonal signaling systems are critical to basic homeostatic functions. The hypothalamic–pituitary–adrenal (HPA) axis, in particular, contains systems that regulate sodium and water balance, steroid hormone production, glucose metabolism, and thyroid function. Each hormonal system is controlled via negative and positive feedback loops with the goal of maintaining homeostasis. However, these feedback mechanisms often cloud accurate hormonal measurement and diagnosis in the critically ill patient. Any intracranial pathology including traumatic brain injury (TBI), stroke, or cerebral hemorrhage disrupts the HPA axis resulting in deleterious clinical sequelae. In addition, endocrine disorders unrelated to neuropathology have significant impact on neurophysiology. Dysfunction of the HPA axis and other endocrine systems must be recognized and carefully managed during the perioperative period.

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Overview

Sodium and Water Balance

The extracellular fluid volume reflects total body sodium. Under healthy physiologic conditions, the plasma sodium concentration reflects total body water. Plasma osmolality is sensed by the hypothalamus and tightly regulated. Abnormalities of serum sodium are common in neurocritical care patients. Hypo- or hypernatremia may be acute or chronic and have many etiologies including trauma, surgery, perioperative volume resuscitation, medications, and pre-existing medical conditions. Dysfunctions of the hypothalamus, pituitary, or adrenal glands are common secondary causes of sodium and water imbalance.

Antidiuretic Hormone (Arginine, Vasopressin, Desmopressin [Synthetic])

Antidiuretic hormone (ADH) is produced by the hypothalamus but is stored and secreted by the posterior pituitary in response to (1) increased plasma osmolality detected by the hypothalamus; (2) decreased plasma volume detected by peripheral and central baroreceptors; (3) general stress, pain, or increased intracranial pressure (ICP); and (4) decreased plasma angiotensin.

Circulating ADH promotes free water absorption in the renal collecting ducts (receptor, V2 G protein-coupled receptor [GPCR]), stimulates the release of corticotropin-releasing hormone (CRH)/adrenocorticotropic hormone (ACTH) (receptor, V1b GPCR in hypothalamus), increases blood pressure (receptor, V1a), and causes the release of atrial natriuretic peptide (ANP).

Natriuretic Peptides

Natriuretic peptides (e.g., ANP, brain natriuretic peptide [BNP], C-type natriuretic peptide [CNP]) are released by the cardiac atria and the hypothalamus in response to increased

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intravascular volume as detected by changes in atrial wall tension and increases in ICP. Natriuretic peptides increase renal sodium excretion and vascular permeability. They also antagonize ADH and angiotensin II. Natriuretic peptides, produced in the brain, modulate the systemic effects of circulating ANP (does not cross the blood–brain barrier) via receptors in the hypothalamus (decreasing water and salt appetite) and decrease sympathetic tone via actions on the brain stem. ANP that is produced in the brain can affect localized increases in cerebral blood flow, decrease cerebral spinal fluid (CSF) production, and is actively transported out of the brain across the blood–brain barrier. Plasma BNP levels may increase as a result of cerebral ischemia from multiple etiologies including vasospasm after subarachnoid hemorrhage (SAH). Increased plasma BNP can potentiate hypovolemia and signal an associated cardiac dysfunction. Little is known about the role and clinical significance of CNP.

Implications for the Neurosurgical Patient

Sodium and Water Balance

Derangements of sodium and water in the neurosurgical patient, especially acute changes, can have serious and sometimes fatal consequences. These include cerebral edema, altered mental status, seizure, coma, increased ICP, cerebral hypoperfusion, cerebral vasospasm, and rupture of bridging veins with associated subdural hemorrhage. Frequently, the astute clinician is alerted to underlying sodium and water derangements by changes in urinary output or by an abnormal serum sodium concentration. A thorough investigation of these changes must take into consideration the wide differential diagnoses of the causes of an altered serum sodium concentration.

Hyponatremia (<135 mEq/L)

A lower than normal serum sodium concentration reflects an excess of free water (e.g., fluid overload) or improper sodium loss. Clinical symptoms usually manifest with an acute decrease in the serum sodium concentration to lower than 125 mEq/L. Symptoms include muscle weakness, cerebral edema, lethargy, confusion, seizures, and coma. Hyponatremia that develops over many days and continues chronically can be tolerated for quite some time without major signs or symptoms. However, chronic hyponatremia still increases overall mortality.

ADH and ANP are the main hormonal mediators of hyponatremia. The differential diagnosis of hyponatremia includes the syndrome of inappropriate ADH secretion (SIADH), cerebral salt wasting syndrome (CSW), and dilutional states (e.g., volume overload, hyperproteinemia). Hyponatremia is also found in Addison's disease due to a reduced production of aldosterone and an inability to increase reabsorption of sodium in the renal tubules. A careful assessment of the fluid/volume status should guide diagnosis and management. The total sodium deficit may be estimated via the following formula: 0.5–0.6 × (weight in kg) × (goal Na^+-measured Na^+).

Syndrome of Inappropriate ADH Secretion

SIADH is an umbrella classification for the clinical presentation of hyponatremia with euvolemia or mild hypervolemia (Table 2.1). SIADH is a common diagnosis after TBI, brain surgery, and in association with intrinsic neuropathology and many other confounding etiologies. The hallmark laboratory finding of SIADH is a continued secretion of ADH despite decreased plasma osmolality. However, elevated serum ADH concentration is not specific to SIADH. Elevated ADH levels have been reported in the context of opioid treatment, general anesthesia, the perioperative stress response, brain tumors, and CSW. ADH levels are also increased in the treatment phase of diabetes insipidus (DI).

Treatment of hyponatremia must be accomplished gradually (Table 2.2), as too rapid correction may result in osmotic demyelination (e.g., central pontine myelinolysis). In addition, hyperchloremic metabolic acidosis is a common finding when the primary treatment for hyponatremia involves administration of large volumes of normal saline. To avoid this concern, many clinicians administer sodium as a mixture of chloride and acetate salts.

Table 2.1 Diagnostic criteria for SIADH

Volume status: euvolemia or mild hypervolemia; cannot be hypovolemia
Urine output: low urine output (as low as 500 mL/day)
Urine osmolality: concentrated urine (>800 mOsm/L)
Plasma osmolality: ↓plasma osmolality (us. <280 mOsm/L)
Consider or exclude CSW (see below and Table 2.3)

Table 2.2 Treatment of SIADH

Correct Na^+ levels gradually
Normal saline with free water restriction usually adequate
Loop diuretics (cause net free water loss)
Correct deficit gradually
10 mEq/L over 24 h; or 1–2 mEq/L in first hour in symptomatic patients
3% hypertonic saline to correct severe Na^+ deficit
Tolvaptan (Samsca) – renal ADH receptor antagonist (15–60 mg PO daily)
Demeclocycline (1–2 mg PO/d) blocks renal action of ADH
Side effect profile similar to tetracyclines
May be nephrotoxic

Cerebral Salt Wasting Syndrome

CSW is a diagnosis of exclusion that presents as a hypovolemic hyponatremia (secondary to renal sodium loss) with maintained or elevated urine output. Unfortunately, there is no simple method available to accurately determine a patient's intravascular volume status. Measuring central venous pressure (CVP) may be useful to guide treatment and follow an overall trend of intravascular volume. Serial cardiac echo examinations can assess intravascular volume but require significant expertise and are beyond the scope of routine practice. Systolic pulse pressure variation as measured by the pulse oximetry plethysmograph or arterial line waveform can be helpful in assessing volume status in patients receiving positive pressure ventilation. CSW may be particularly common in subarachnoid hemorrhage. Typically, CSW develops secondary to the derangement of neurohumoral signals resulting in increased ANP and decreased renal sympathetic input (Tables 2.3 and 2.4).

Hypernatremia (>145 mEq/L)

Severe elevation of serum sodium (>160 mEq/L) is associated with increased mortality in neurocritical care patients. Symptoms include mental status changes, seizure, myoclonus/hyperreflexia, and nystagmus. Acute hypernatremia may result in permanent structural injury in the brain stem (e.g., central pontine myelinolysis). Patients may show signs of intravascular volume depletion, cerebral hypoperfusion, and/or cerebral vasospasm. Intravascular hypernatremia will cause water to move from brain cells, resulting in decreased brain volume. Decreasing the brain volume carries the risk of disrupting bridging veins and subsequent subdural hematoma.

Hypernatremia can have several etiologies including loop or osmotic diuretics, iatrogenic through aggressive administration of normal or hypertonic saline, and mineralocorticoid excess, as in Conn's or Cushing's syndrome. It may also be caused by central or nephrogenic diabetes insipidus (DI). It is important to differentiate between central and nephrogenic DI because the treatment is different. Central DI is caused by an interruption of hypothalamic signaling (e.g., anatomic, ischemic), with subsequent reduction in ADH secretion from the posterior pituitary (e.g., after TBI, tumor resection, vasospasm of the anterior circulation, pituitary surgery, brain death). Nephrogenic DI is characterized by a lack of renal response to serum ADH associated with critical illness, specific antibiotics, intravenous contrast, or renal insults.

Common symptoms for both central and nephrogenic DI are hypernatremia, hyperosmolality, and dilute polyuria. Central DI presents with severely reduced urine osmolatity: <200 mOsm/L versus 200–500 mOsm/L with nephrogenic DI. Table 2.5 lists diagnostic criteria for DI, while Table 2.6 list strategies for initial management of DI.

Table 2.3 Diagnostic criteria for CSW

Likely present if criteria for SIADH are met, *but*
1. Patient demonstrates ↓↓Na^+ with trial of fluid restriction
Fluid restriction may be deleterious in some patients (e.g., SAH)
2. Clinical indicators of hypovolemia
Decreased skin turgor, ↓ serial body weights, hypotension (esp. orthostasis), low CVP
3. Other markers (serum BUN, uric acid, ANP, ADH) are nonspecific and not clinically useful
4. Measurement of urine Na+ excretion and urine osmolality may support the diagnosis but is seldom of practical clinical utility
Complicated in the neurosurgical setting by concurrent use of diuretics, mannitol, or the stress response ↑ in ADH

Table 2.4 Treatment of CSW

1. 0.9% saline resuscitation corrects Na^+ in many cases. Consider hypertonic saline if inadequate response or need for rapid initial correction (i.e., severely symptomatic hyponatremia)
2. Consider fludrocortisone in refractory cases (0.1–0.2 mg/day PO)
Hypokalemia and hypertension are possible side effects of fludrocortisone
3. Closely monitor sodium levels and fluid balance

Table 2.5 Diagnostic criteria for DI

Classic triphasic response (confusing later interpretation of SIADH/hyponatremia) evolves over days
Commonly presents >12 h after surgery
Rarely presents intraoperatively
Intraoperative presentation (phase 1) is associated with hypovolemia
↓Plasma volume may ↑ risk of venous air embolism during surgery
Differentiate polyuria vs. diuresis associated with fluid resuscitation or osmotic/pharmacologic diuresis
Response of Na^+ and urine output to fluid restriction (unless contraindicated)
No increased UOsm (30 mOsm/L) within hours of fluid restriction → central DI
Hyperosmolar serum

Table 2.6 Initial management of DI

Fluid restriction for diagnosis
Volume/free water replacement (0.9% or 0.45% saline)
Patient should be allowed water ad lib if able to take PO
Synthetic desmopressin for central DI
5–50 mcg/day IV
Give intranasal in non-critically ill patients
Timed urine volumes, serum Na^+ and urine osmolality/specific gravity guide therapy
Correct gradually over days to avoid rebound cerebral edema

Concerns and Risks

Sodium and Water Balance

The use of diuretic and osmotic agents will invariably complicate the clinical assessment of sodium derangements. A careful assessment of the overall volume status is critical in determining the appropriate diagnosis and treatment plan. For example, treatment should consist of fluid replacement in patients with a water deficit versus fluid restriction in patients with SIADH. Fluid and sodium administration would be the best treatment for patients with CSW. In contrast, volume restriction in a patient with CSW would further worsen the volume deficit and hyponatremia. Aggressive treatment of hyponatremia can lead to overcorrection (i.e., hypernatremia) and an associated demyelination syndrome, while aggressive treatment of hypernatremia may result in cerebral edema.

Key Points: Sodium and Water Balance (Table 2.7)

- Always consider the possibility of a Na^+ abnormality in the setting of pituitary tumor, intracranial surgery, hypothalamic injury, TBI, or cerebral vasospasm/stroke or with clinical symptoms of mental status changes and seizure.
- Na^+ derangements may be related to iatrogenic fluid management (e.g., hypertonic saline, diuretics, or normal saline).
- The clinical presentation is often more helpful than formal diagnostic testing in establishing a diagnosis.
- Other endocrine diseases (e.g., adrenal, thyroid) must be considered.
- If hypernatremia, consider DI or over-resuscitation with normal saline.
- If hyponatremia, consider SIADH or CSW.
- Correct abnormalities gradually with frequent laboratory testing and monitoring.

Table 2.7 Features of common Na^+ derangements

Central DI	CSW	SIADH
Serum Na^+ >145 mEq/L	Serum Na^+ <135 mEq/L	Serum Na^+ <135 mEq/L
PE suggests hypovolemia	PE suggests hypovolemia	PE = euvolemia/ hypervolemia
	↑Na^+ with saline admin	↓Na with saline admin
1° defect in water handling	1° defect in Na^+ handling	1° defect in water handling
↑Serum osmolality	↓Serum osmolality	↓Serum osmolality
Low urine osm	High urine osm	High urine osm
IV desmopressin	↓Na with fluid restriction	↑Na with fluid restriction
	HTS if severe ↓Na^+	HTS if severe ↓Na^+
	Oral salt tablets	Oral tolvaptan

Overview

Steroid Hormone Physiology

Cortisol is the primary glucocorticoid hormone of clinical relevance regulating energy metabolism, electrolyte homeostasis, and immune function. The secretion of cortisol is tightly controlled through the HPA axis. It is secreted by the zona fasciculata of the adrenal gland in response to ACTH. In turn, ACTH is secreted by the anterior pituitary in response to CRH produced by the hypothalamus. At the cellular level, cortisol interacts with nuclear receptors found throughout the body and brain. Dysregulation at any point of the HPA axis will result in excess or deficiency of cortisol with marked clinical consequences. To replace cortisol in states of adrenal insufficiency, 10–12 mg/m^2 of hydrocortisone is required daily (conversions, prednisone = 0.25 × hydrocortisone; dexamethasone = 0.04 × hydrocortisone). Cortisol production fluctuates in a circadian fashion with the highest levels upon waking in the morning. However, a host of physiologic factors modulate cortisol production and secretion. Measurement of a random cortisol level is rarely useful in the clinical assessment of the HPA axis, although AM cortisol levels may be useful in conjunction with other tests and the clinical presentation. Overall, laboratory testing using cortisol levels or ACTH stimulation tests do not appear to be helpful in the majority of patients and does not always correlate with clinical symptoms.

During periods of physiologic stress (e.g., infection, shock, surgery), cortisol requirements may increase up to five times the basal requirements. Inadequate steroid administration during stress can result in hemodynamic instability (primarily hypotension), hypoglycemia, hyponatremia, and hyperkalemia. However, for most surgeries, "stress dosing" of steroids for patients requiring chronic steroid supplementation is no longer routine because there is no strong supporting evidence for their effectiveness. Current evidence supports maintenance dosing (i.e., the usual daily dose) on the day of surgery and additional rescue supplementation with intravenous hydrocortisone to treat unresponsive or unexplained hypotension.

Aldosterone is the primary mineralocorticoid of clinical concern. Mineralocorticoid activity is central to the maintenance of effective plasma volume via the renin–angiotensin–aldosterone axis. Aldosterone is secreted by the outermost zona glomerulosa of the adrenal cortex in response to either an increased production of ACTH, the release of adrenoglomerulotropin from the pineal gland, or many other physiologic events (e.g., hypotension, hypovolemia, acidosis). Aldosterone acts to promote sodium and water reuptake and potassium secretion from the glomerulo-filtrate in the kidney. Central nervous system aldosterone receptors also contribute to the modulation of fluid balance. Fludrocortisone is

the only available therapeutic drug that approximates natural aldosterone activity. Dexamethasone, a commonly prescribed steroid, has no mineralocorticoid activity.

Adrenal Insufficiency

Frequently, patients with adrenal insufficiency remain free of clinical signs and symptoms during normal daily activities. Those who do develop symptoms often have nonspecific complaints such as lethargy, muscle weakness, anorexia, dizziness, syncope, and abdominal pain. However, adrenal insufficiency can present as an acute crisis secondary to infection, physiologic stress (e.g., trauma), or the abrupt withdrawal of steroid supplementation. Adrenal insufficiency should always be considered in the setting of refractory hypotension/shock. If adrenal insufficiency goes undiagnosed or untreated, it can result in death.

Primary Adrenal Insufficiency (Addison's Disease)

Intrinsic failure of the adrenal glands causes primary adrenal insufficiency and is very rare (5 in 100,000 cases in the USA). The most common form of primary adrenal insufficiency is caused by an autoimmune reaction followed by tuberculous adrenalitis. Other uncommon causes include cancer metastasis (e.g., lung, stomach, breast, colon), lymphoma, bilateral adrenal hemorrhage, and surgical adrenalectomy. In children, the most common cause is congenital adrenal hyperplasia. Overall, primary insufficiency is associated with inadequate production of both glucocorticoid and mineralocorticoid hormones requiring pharmacologic replacement (e.g., hydrocortisone, fludrocortisone). The pathophysiology of primary adrenal insufficiency is described in Table 2.8.

Central Adrenal Insufficiency

If adrenal insufficiency develops in the absence of intrinsic adrenal pathology, the symptom complex is called central adrenal insufficiency and consists of secondary and tertiary forms. Secondary and tertiary adrenal insufficiency indicates a problem with the pituitary and hypothalamus, respectively.

Table 2.8 Pathophysiology of primary adrenal insufficiency

Absence of glucocorticoid and mineralocorticoid production by the adrenal gland
$\downarrow[Na^+]_p$, $\uparrow[K^+]_p$ (absent aldosterone effects)
Primary clinical issue: hypotension/hypovolemia/shock
May lead to cerebral hypoperfusion and cerebral ischemia
Hyperpigmentation 2° ↑ pituitary secretion of ACTH precursor → ↑α-MSH

Table 2.9 Causes of central adrenal insufficiency

Secondary adrenal insufficiency (low ACTH secretion)
Pituitary tumors
Pituitary surgery/irradiation
Pituitary infectious/infiltrative processes (tuberculosis, meningitis, sarcoidosis, hemochromatosis)
Sheehan's syndrome (peripartum pituitary ischemia)
Genetic disorders
Tertiary adrenal insufficiency (low CRH secretion)
Glucocorticoid therapy
Hypothalamic tumors
Hypothalamic surgery/irradiation
Infectious/infiltrative process (see above)
Trauma

Table 2.10 Diagnosis of adrenal insufficiency

Diagnostic goals include (1) confirmation of low cortisol secretion, (2) differentiation of type of adrenal insufficiency, and (3) investigation of pathophysiologic cause
Clinical suspicion based on presentation or response to empiric therapy. In many conditions (e.g., acute illness, pregnancy, cirrhosis) conventional tests lack sensitivity
↓ Random plasma cortisol levels or no ↑ levels in the presence of physiologic stress
Simultaneous cortisol and ACTH concentration
↓ Cortisol and ↑ ACTH diagnostic for primary adrenal insufficiency
ACTH stimulation test (standard dose, low-dose)
Decreased cortisol production 30/60 min after IV/IM ACTH c/w diagnosis
Prolonged ACTH stimulation test differentiates primary and central causes
CRH stimulation test
Differentiates secondary (pituitary) from tertiary (hypothalamus) disease
Insulin tolerance test
Confirmation of secondary adrenal insufficiency
Insulin (0.1–0.15 U/kg)-induced hypoglycemia
If HPA normal, accompanied by an ↑ serum cortisol
Once the diagnosis of adrenal insufficiency is confirmed, further tests can differentiate causes (e.g., autoantibodies in autoimmune disease, CT scan for tuberculous adrenalitis)

A multitude of causes can lead to central adrenal insufficiency and are summarized in Table 2.9. Diagnostic criteria and treatment options for adrenal insufficiency are described in Tables 2.10 and 2.11, respectively.

Cushing's Disease and Syndrome

Cushing's syndrome or cortisol hypersecretion results from both ACTH-dependent and ACTH-independent causes. Cushing's disease specifically refers to ACTH overproduction from the anterior pituitary (e.g., pituitary adenoma, hyperplasia) causing cortisol hypersecretion from the adrenal glands. Other less common causes of ACTH-dependent

Table 2.11 Treatment of adrenal insufficiency

Treat empirically in cases of high clinical suspicion
Chronic adrenal insufficiency
Hydrocortisone (most physiologic option) 10–12 mg/m^2 daily
During illness/surgery may need to increase dose to prevent crisis
Fludrocortisone (0.05–0.2 mg/day) provides mineralocorticoid replacement (Addison's only)
Acute adrenal crisis
Treat hypotension and reverse electrolyte abnormalities
Rapid hydration with normal saline
Hydrocortisone 100 mg IV, followed by 100–200 mg IV every 24 h by continuous infusion
No need for specific mineralocorticoid replacement (hydrocortisone 50 mg equivalent to 0.1 mg fludrocortisone)
Supplemental steroids must be tapered to avoid recrudescence

Table 2.12 Causes, diagnosis, and treatment of Cushing's syndrome/disease

Causes
Cushing's disease
Cushing's syndrome
Exogenous corticosteroids
Diagnosis
Screening tests
1. Late night salivary cortisol
2. 24 h urine free cortisol
3. Dexamethasone suppression test
Plasma ACTH level
Bilateral inferior petrosal sinus sampling (BIPSS): pituitary versus ectopic ACTH
CRH stimulation test (desmopressin test)
Pituitary imaging (MRI) and adrenal imaging (CT, MRI, PET)
Treatment
Surgery (transsphenoidal selective tumor resection, adrenalectomy), radiotherapy, and medical pharmacotherapy with dopamine agonists (bromocriptine, cabergoline), somatostatin receptor ligands (pasireotide), glucocorticoid/progesterone receptor antagonists (mifepristone), and direct cortisol synthesis inhibitors (ketoconazole, metyrapone, mitotane)

Cushing's syndrome include neuroendocrine and gastroenteropancreatic neuroendocrine tumors producing ectopic ACTH. A primary overproduction of cortisol from the adrenal glands independent of ACTH can occur secondary to adrenal adenomas/carcinoma and various forms of adrenal hyperplasia. Additionally, Cushing's syndrome can be caused by excessive exposure to exogenous glucocorticoids in the treatment of asthma, arthritis, or even during immune suppression for organ transplantation patients (Table 2.12).

Implications for the Neurosurgical Patient

Steroid Hormone Derangements

Hypercortisolism is associated with significant morbidity and mortality. Patients are likely to develop a metabolic syndrome with glucose intolerance, elevated blood pressure, central obesity, and dyslipidemia. Vascular disease is a major cause of increased mortality in this patient population. Additionally, patients are at an increased risk for thromboembolic disease, major depression, memory dysfunction, difficult airway, and opportunistic infections. These patients may also have depression, anxiety, and cognitive deficits that can confuse a perioperative neurologic examination. Remission of Cushing's syndrome after successful treatment does not guarantee the normalization of comorbidities in all patients. Therapeutic application of exogenous steroids should be guided with great caution. Some patients treated with exogenous hydrocortisone may, in fact, show an enhanced response to vasopressors/catecholamines, which can be used favorably in the context of circulatory compromise or shock. In rare instances, patients with Cushing's disease present with complications related to mass effect (e.g., visual loss, cavernous sinus compression) from an enlarging pituitary macroadenoma.

Decreased plasma cortisol levels expose the critically ill neurosurgical patient to the risk of severe complications. These include (1) systemic hypotension with decreased cerebral perfusion pressure, (2) hyponatremia with associated effects (see above), (3) decreased mental status, (4) hypoglycemia, (5) fever with increased cerebral metabolic rate, and (6) diminished response to catecholamines/vasopressors.

Concerns and Risks

Of particular concern in the neurocritical care patient population is the missed diagnosis of overt adrenal insufficiency, inadequate perioperative steroid supplementation, and uncontrolled hyperglycemia associated with increased cortisol levels. The use of etomidate for the induction of anesthesia or sedation is a risk factor for secondary adrenal insufficiency in patients with poor physiologic reserve. The increased risk of cardiovascular disease in patients with Cushing's syndrome should be assessed as a part of a comprehensive preoperative exam in an attempt to prevent serious morbidity and mortality prior to any operation.

Key Points: Steroid Physiology

- Cortisol helps regulate energy metabolism, electrolyte homeostasis, and immune function.
- Cortisol requirements significantly increase during physiologic stress.
- Accurate assessment of the HPA axis in critical illness is very challenging.
- Adrenal insufficiency should always be considered with shock in the setting of critical illness.
- Cushing's syndrome results from the hypersecretion of cortisol or from exogenous corticosteroid treatment.

- Hypercortisolism increases the risk of cardiovascular disease, thromboembolism, depression, cognitive dysfunction, difficult airway, and challenging intravenous access.

Table 2.13 Pathophysiology of hypothyroidism

Primary hypothyroidism
Decreased production of thyroid hormone by the thyroid gland
Causes: iodine deficiency, autoimmune thyroiditis, medications, congenital, surgical
Commonly subclinical
Often associated with adrenocortical insufficiency
Laboratory studies typically indicate elevated TSH and low free T4 and total T3
Laboratory values (especially TSH) may be influenced by critical illness
Secondary/tertiary hypothyroidism
Associated with neurologic processes involving the pituitary or hypothalamus
↓TSH or ↓TRH
Causes: pituitary adenoma, craniopharyngioma, traumatic brain injury, Sheehan syndrome, iron overload, sarcoidosis, syphilis, tuberculosis

Overview

Thyroid Hormone

Thyroid hormone is produced by the thyroid gland in response to thyroid-stimulating hormone (TSH) released from the anterior pituitary. Thyrotropin-releasing hormone (TRH), secreted by the hypothalamus, stimulates the anterior pituitary to release TSH. Nearly every organ system within the body relies on thyroid hormone for baseline physiologic function. Thyroid hormone is present in the serum as triiodothyronine (T3) and thyroxine (T4), which is then peripherally converted to T3, the active form of the hormone, by 5′-deiodinases. T3 and T4 are 99% protein bound to thyroid-binding globulin (TBG), transthyretin, and albumin. Free thyroid hormone levels are dependent on a variety of factors that influence protein binding including critical illness. Careful analysis of the clinical presentation with an emphasis on specific syndromes and thyroid ultrasonography are useful during the diagnostic workup of thyroid dysfunction. Alterations of thyroid hormone levels lead to either hypothyroidism or hyperthyroidism/thyrotoxicosis. Tables 2.13 and 2.14 summarize the pathophysiologic characteristics of these two states. Table 2.15 lists the therapeutic interventions in case of a hyperthyroid crisis ("thyroid storm"). Table 2.16 summarizes the clinical implications for the neurosurgical patient.

Table 2.14 Pathophysiology of hyperthyroidism

Elevated thyroid activity most commonly associated with
Graves' disease (stimulating autoantibodies against thyrotropin [i.e., TSH] receptor)
Thyroiditis/toxic multinodular goiter/toxic adenoma
Laboratory values: depressed TSH; elevated free T4 level
TSH may be elevated in pituitary adenoma
Thyrotoxicosis can transform into life-threatening thyroid storm during acute physiologic stress: infection, sepsis, surgery, trauma, exogenous iodine bolus
Thyroid storm clinical presentation
Hyperthermia (often high fever, profuse sweating)
Tachycardia
Increased carbon dioxide production/metabolic rate
Cardiac arrhythmia, especially atrial fibrillation
Gastrointestinal disturbance (nausea, vomiting, diarrhea)
Agitation/delirium/seizure/coma
Severe hypertension, increased cardiac output, and tachyarrhythmia advancing to heart failure and shock

Table 2.15 Management of thyroid storm

1. Delay non-emergent surgery
2. Acetaminophen and active cooling if indicated
3. Intravenous fluid resuscitation (possible invasive monitoring if heart failure)
4. Nonselective β-adrenergic blockade for control of tachycardia (propranolol, atenolol, metoprolol decrease the peripheral conversion of T4 to T3 at high doses)
5. Methimazole or propylthiouracil (PTU) (Inhibit new thyroid hormone synthesis. PTU also decreases peripheral conversion of T4 to T3)
6. Potassium or sodium iodide (prevents thyroid hormone synthesis and release). If patient cannot tolerate iodine (anaphylaxis), then lithium treatment will decrease T3 and T4 synthesis and release
7. Hydrocortisone IV (prevents adrenal insufficiency and decreases peripheral conversion of T4 to T3)
8. Therapeutic plasma exchange (if failed conventional therapy)

Table 2.16 Implications for the neurosurgical patient: thyroid function

Hypothyroidism (especially severe or late; rarely in subclinical)
Goiter with airway compromise (PE, symptomatology, CT)
Macroglossia can occur
Preoperative hypovolemia
Nonspecific ECG changes (especially low voltage and T-waves)
Possible prolonged Q–T interval and risk of torsades de pointes with myxedema
Decreased gastric emptying
Impaired ventilatory response to hypoxia or hypercapnea
Weakness of accessory muscles (respiratory function)
Possible coagulopathy
Decreased metabolic rate with hypothermia
Depressed myocardial contractility
Delayed emergence
Opioid sensitivity
Associated hypoglycemia, anemia, SIADH
Myxedema coma

(continued)

Table 2.16 (continued)

Decreased mental status, hypothermia, non-pitting LE edema
Very elevated TSH, extremely low T3 and T4
No effect on minimum alveolar concentration of potent agents or nitrous oxide
Hyperthyroidism
Goiter (as above)
Fever with increased cerebral metabolic rate
Hypercapnia with increased cerebral blood flow/volume
Cardiac arrhythmias – especially atrial fibrillation
Cardiomyopathy with clinical heart failure syndrome
Neurologic features: visual symptoms, muscle weakness, tremor
Change in mental status, seizures, or coma in thyroid storm
Possible hypercortisolism 2° to accelerated glucocorticoid metabolism
Hyperglycemia

Concerns and Risks

Thyroid Function

Advanced hypothyroidism can manifest in the perioperative period with neurologic symptoms, respiratory failure, or delayed emergence that may potentially confound postoperative assessment. Patients with hypothyroidism presenting for surgery should be adequately treated with thyroid hormone when possible before their operation. Similarly, hyperthyroidism must be treated preoperatively because of the risk of surgically inducing thyroid storm, increasing the risk of major cardiovascular and neurologic complications.

Key Points: Thyroid Function

- Thyroid hormone affects nearly every organ system in the body.
- Thyroid dysfunction can be difficult to assess in the setting of a physiologic stress response or critical illness.
- Clinical hyperthyroidism can advance to life-threatening thyroid storm in the perioperative setting and should be medically suppressed prior to any surgical procedure.
- Thyroid function should be normalized prior to elective surgery.

Overview

Additional Neuroendocrine Systems

Pheochromocytoma

Pheochromocytoma is a metabolically active neuroendocrine tumor of chromaffin cells commonly found in the adrenal gland but can be found in other extra-adrenal sites. Pheochromocytoma should be ruled out in neurosurgical patients with a history of neurofibromatosis type I, Von Hippel–Lindau disease, multiple endocrine neoplasia type 2A and 2B, and paraganglioma. Routine screening is recommended prior to elective surgery in these patients and should be considered for patients with severe hypertension of unknown etiology, especially in patients 30–40 years of age. Overall, pheochromocytoma represents 0.2–0.6% cases of all hypertension. Presenting symptoms often include headache, excessive truncal sweating, palpitations, or panic attacks. These tumors secrete norepinephrine and sometimes epinephrine and dopamine, resulting in hemodynamic instability, paroxysmal swings in blood pressure, and severe hypertension. The release of catecholamines is triggered by physiologic stress, physical manipulation of the lesion, or potentially certain medications (e.g., metoclopramide, corticosteroids, monoamine oxidase inhibitors, intravenous contrast agents). As many as 11% of patients with pheochromocytoma have a reversible catecholaminergic cardiomyopathy.

Standard diagnostic tests include measurement of plasma-free metanephrines and 24-h urine metanephrines. Plasma-free metanephrines have the highest sensitivity and specificity at 99% and 89%, respectively. The clonidine suppression test is sometimes employed. Physiologic tests are complemented by sensitive imaging modalities, including magnetic resonance imaging, computed tomography scans, positron emission tomography, and metaiodobenzylguanidine (MIBG) scintigraphy.

Pheochromocytoma can often go undiagnosed and then manifest as an exaggerated autonomic response during anesthesia for unrelated surgical procedures. In the untreated patient with pheochromocytoma, desensitization of beta-receptors may occur and be associated with a decreased response to exogenously administered catecholamines. Significant volume contraction occurs in the setting of elevated sympathetic tone and vasoconstriction. As a result of these derangements, cardiovascular collapse may occur during induction and maintenance of general anesthesia unless appropriate volume resuscitation is undertaken.

In patients with known pheochromocytoma, preoperative antagonism of catecholamine effects (over several weeks preceding surgery) is essential. Typically, therapy starts with a nonselective alpha-adrenergic antagonist such as phenoxybenzamine, followed by the addition of beta-antagonists. Beta-adrenergic selective antagonists should not be administered before alpha blockade, as negative inotropy in the setting of unopposed alpha-receptor-mediated vasoconstriction can result in acute ventricular dysfunction. Furthermore, beta-blockade alone is contraindicated because it does not prevent and can actually augment the effects of catecholamines at alpha-adrenoreceptors. Metyrosine, an inhibitor of tyrosine kinase that limits the formation of catecholamines, can be used in combination with alpha and beta blockade,

but severe adverse effects limit its use. Preoperative volume repletion is clearly beneficial, and patients taking alpha-antagonists are encouraged to consume liberal amounts of salt and water. Adequate preoperative preparation may be demonstrated by controlled hypertension, minimal orthostasis, and limited ectopy on heart rhythm monitoring.

Intraoperative management consists of intravenous infusions of titratable antihypertensive medications, including alpha- and beta-blockers as well as direct vasodilators. Administration of indirectly acting vasopressors, such as ephedrine, may have unpredictable effects and are best avoided. If the surgical plan includes tumor excision (or clamping of veins draining the mass), dramatic hypotension should be anticipated shortly thereafter due to the loss of catecholamines in a patient aggressively alpha-blocked. The anesthesia plan should include invasive arterial blood pressure monitoring with preparation for post-excision resuscitation, hemodynamic support, and cortisol supplementation (if adrenal).

Growth Hormone/Acromegaly

Growth hormone is secreted by the anterior pituitary gland and is a diffuse regulator of cellular metabolism. This hormone stimulates the production of insulin-like growth factor I, of which serum levels may be diagnostic for the disorder. Growth hormone excess due to a hyperactive pituitary macroadenoma is common in neurosurgical patients presenting for pituitary surgery.

Acromegaly, from excess growth hormone, is associated with an increased mortality specifically related to cardiovascular disease and respiratory complications. Additionally, acromegaly has many important anesthetic considerations. These include:

1. Potential for a difficult airway (including postoperative airway obstruction) due to diffuse soft-tissue enlargement, laryngeal calcification, and recurrent laryngeal nerve involvement
2. Increased risk of sleep apnea syndromes
3. Cardiac dysfunction including conduction abnormalities, arrhythmias, hypertrophic cardiomyopathy, valvular dysfunction (e.g., aortic and mitral regurgitation), and hypertension
4. Insulin resistance and type 2 diabetes mellitus
5. Challenging intravenous access due to diffuse skin thickening
6. Possible increased risk of positioning-related nerve injury due to pre-existing nerve compression or entrapment in fascial compartments.

The primary treatment for most patients is surgical excision of the pituitary adenoma via a transsphenoidal approach. Special attention and careful planning are necessary for airway management. Preoperatively the patient should be evaluated for signs of a potential difficult intubation or mask ventilation. Additionally, the patient should be screened for obstructive sleep apnea and possibly undergo a formal preoperative sleep study/polysomnography. In addition to specific preparations for the management of a difficult airway, the impact of anesthetic agents (e.g., benzodiazepines, opioids) on postoperative respiratory function must be considered in the setting of obstructive sleep apnea. Preoperative cardiac assessment including ECG and echocardiography should be strongly considered. Electrolytes should be checked prior to surgery and serially after resection in the intensive care unit (see diabetes insipidus above).

Pineal Gland

The pineal gland is a neuroendocrine structure situated midline in the subarachnoid space below the third ventricle with no blood–brain barrier. Its physiologic function is the secretion of melatonin, which is synthesized from serotonin. Melatonin is involved in the neurohumoral modulation of human sleep–wake cycles as well as pubescence. Currently, melatonin neurochemistry is an area of research interest. Adrenoglomerulotropin produced by the pineal gland is one of the triggers of aldosterone secretion. Tumors of the pineal gland may present for resection. Symptoms may include abnormal pubescence, gaze palsy, and increased ICP due to obstruction of CSF flow in the cerebral aqueduct by the tumor. Surgical resection of pineal tumors may require the patient to be in the sitting position.

Insulin

Insulin is a peptide hormone secreted by the β-cells of the pancreas. It modulates glucose metabolism via a variety of receptors and signaling pathways. In certain disease states (e.g., metabolic syndrome, infection, critical illness, shock), the physiologic effects of insulin are decreased. Insulin exerts anti-inflammatory properties that may improve perioperative neurologic outcome. Glucose management using insulin for neurosurgical patients remains a controversial topic of high clinical interest. Optimal target ranges for glucose in the neurosurgical patient have not been determined. There is general agreement that severe hyperglycemia is a marker of injury severity, enhances brain injury, and potentially negatively effects long-term outcomes following major neurologic injury including TBI and stroke. This is counterbalanced by the concern for hypoglycemia and subsequent neurological injury that frequently accompanies tight control regimens. Until future research delineates more precise parameters for glucose control, plasma glucose should be maintained in the range of 140–180 mg/dL. Glycemic control must be carefully planned and individualized to each patient and neurologic condition.

Key Points: Additional Neuroendocrine Systems

- Pheochromocytoma is a metabolically active neuroendocrine tumor associated with severe paroxysmal hypertension.
  - Increased prevalence in certain conditions including neurofibromatosis type I, Von Hippel–Lindau disease, and multiple endocrine neoplasia type 2A and 2B.
  - Plasma-free metanephrines have the highest diagnostic sensitivity and specificity. Optimal perioperative management requires preoperative therapy with anti-catecholaminergic agents.
- Acromegaly results from growth hormone excess.
  - Tissue changes associated with growth hormone excess predispose patients to difficult airway management, obstructive sleep apnea, and cardiomyopathy.
  - Insulin is a primary regulatory hormone of glucose metabolism.
  - Insulin action is frequently impaired during physiologic stress or injury resulting in hyperglycemia.
  - Hyperglycemia (>200 mg/dL) is deleterious to patients with neurologic injury.
  - Treatment of hyperglycemia should target a moderate glucose reduction to avoid the significant risks of plasma or cerebral hypoglycemia.

Suggested Reading

Adler S. Disorders of body water homeostasis in critical illness. Endocrinol Metab Clin N Am. 2006;35:873–94.

Atkins JH, Smith DS. A review of perioperative glucose control in the neurosurgical population. J Diabetes Sci Technol. 2009;3(6):1352–64.

Bouillon R. Acute adrenal insufficiency. Endocrinol Metab Clin N Am. 2006;35:767–75.

Burch HB, Cooper DS. Management of graves disease – a review. JAMA. 2015;314(230):2544–54.

Charmandari E, Nicolaides NC, Chrousos GP. Adrenal insufficiency. Lancet. 2014;383:2152–67.

Chiha M, Samarasinghe S, Kabaker AS. Thyroid storm: an updated review. J Intensive Care Med. 2015;30(3):131–40.

Devereaux D, Tewelde SZ. Hyperthyroidism and thyrotoxicosis. Emerg Med Clin N Am. 2014;32:277–92.

Dubbs SB, Spangler R. Hypothyroidism – causes, killers, and life-saving treatments. Emerg Med Clin N Am. 2014;32:303–17.

El Beheiry H. Protecting the brain during neurosurgical procedures: strategies that can work. Curr Opin Anesthesiol. 2012;25:548–55.

Katznelson L, Laws ER, Melmed S, Molitch ME, Murad MH, Utz A, et al. Acromegaly: an endocrine society clinical practice guideline. J Clin Endrocinrol Metabol. 2014;99(11):3933–51.

Kelly KN, Domanjnko B. Perioperative stress-dose steroids. Clin Colon Rectal Surg. 2013;26:163–7.

Koga M, Yamagami H, Okuda S, Okada Y, Kimura K, Shiokawa Y. Blood glucose during the initial 72 h and 3-month functional outcomes in acute intracerebral hemorrhage: the SAMURAI-ICH study. J Neurol Sci. 2015;350:75–8.

Lacroix A, Feelders RA, Stratakis CA, Nieman LK. Cushing's syndrome. Lancet. 2015;386:913–27.

Langouche L, Van den Berghe G. The dynamic neuroendocrine response to critical illness. Endocrinol Metab Clin N Am. 2006;35:771–91.

Loh JA, Verbalis JG. Disorders of sodium and water metabolism associated with pituitary disease. Endocrinol Metab Clin N Am. 2008;37:213–34.

Nayak B, Burman K. Thyrotoxicosis and thyroid storm. Endocrinol Metab Clin N Am. 2006;35:663–86.

Nemergut EC, Zuo Z. Airway management in patients with pituitary disease. J Neurosurg Anesthesiol. 2006;18(1):73–7.

Pappachan JM, Raskauskiene D, Sriraman R, Edavalath M, Hanna FW. Diagnosis and management of pheochromocytoma: a practical guide to clinicians. Curr Hypertens Rep. 2014;16:442.

Powlson AS, Gurnell M. Cardiovascular disease and sleep disordered breathing in acromegaly. Neuroendocrinology. 2016;103(1):75–85.

Sterns RH, Silver SM. Cerebral salt wasting syndrome versus SIADH: what difference? J Am Soc Nephrol. 2008;19:194–6.

Taub PR, Fields JD, Wu AHB, Miss JC, Lawton MT, Smith WS, et al. Elevated BNP is associated with vasospasm-independent cerebral infarction following aneurysmal subarachnoid hemorrhage. Neurocrit Care. 2011;15(1):13–8.

Wolf S. Routine management of volume status after aneurysmal subarachnoid hemorrhage. Neurocrit Care. 2011;15:275–80.

Cerebral Edema: Pathophysiology and Principles of Management

3

Ross Martini and Andrea Orfanakis

Overview

Edema is almost always of clinical significance when it occurs within the cranial vault. Brain tissue, blood, and cerebrospinal fluid (CSF) maintain a consistent presence within the cranium and spinal cord areas. When the volume of any single component increases, the other two have a limited capacity to shift into accessory spaces so as to avoid a rise in intracranial pressure. Once that capacity to buffer is reached, small increases in volume produce an exponential rise in pressure (Fig. 3.1). It is at this point that the risk of herniation and/or decreased cerebral perfusion pressure becomes a threat.

Implications for the Neurosurgical Patient

Cerebral edema is a common comorbidity in the neurosurgical patient, but the etiology and severity may vary significantly. The anesthesiologist will encounter patients ranging from those presenting to the operating room for an elective tumor resection with local edema to those with critical intracranial hypertension for urgent decompressive hemicraniectomy. Understanding the therapies available and when to employ them allows for targeted optimization of each patient in the perioperative period.

Preoperative Evaluation

A thorough neurologic exam, if permitted by the urgency of the procedure, provides important information about the degree to which a patient is at risk for secondary neurologic damage associated with cerebral edema. For example, an unconscious patient with a unilaterally dilated pupil might necessitate more aggressive and immediate interventions and monitoring than someone with complaints of a headache and nausea. Imaging studies can also be used to assess the degree of preexisting edema, compression of brain, or impending herniation. If the patient has an intracranial pressure monitor, the ICP trend should be noted preoperatively and monitored in the operating room. Pertinent labs such as starting serum sodium and plasma osmolarity may be helpful, as well as an arterial blood gas if the patient is being mechanically ventilated.

Opioids and anxiolytics in the preoperative area, or in any patient spontaneously breathing, should be used carefully.

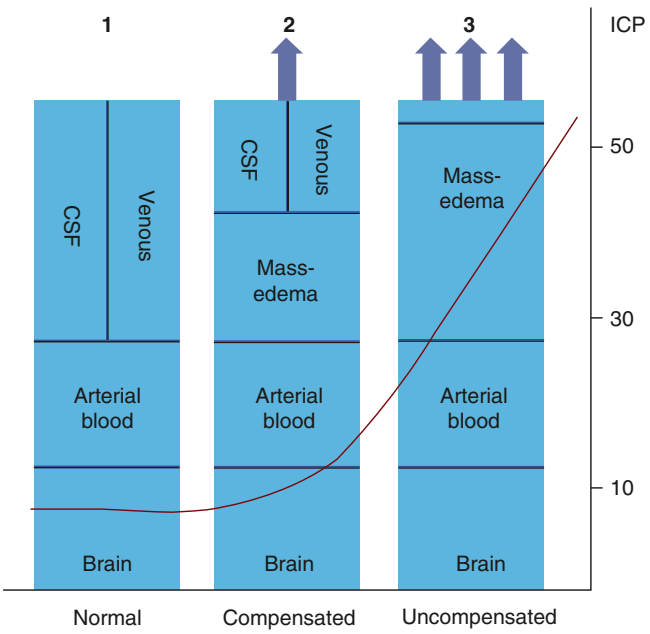

Fig. 3.1 Relationship between intracranial pressure and volume. Initially, increases in volume of one cranial component (i.e., brain edema) result in small increases in pressure (due to shifting of cerebrospinal fluid and venous blood out of the cranium). Once this compensation is exhausted, pressure increases rapidly

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Decreased minute ventilation after light sedation may increase $PaCO_2$, cerebral vasodilatation, and a consecutive rise in intracranial pressure.

Induction/Maintenance

The induction strategy for patients with cerebral edema should focus on avoiding an increase in intracranial pressure and decreases in cerebral perfusion pressure and oxygenation. Any combination of medications and airway management techniques that satisfies these criteria is appropriate. Succinylcholine will cause a transient increase in ICP and should be avoided if possible. However, it may be appropriate in select situations where airway management would otherwise be high risk.

At very high volatile anesthetic MAC (i.e., >1.5), cerebral blood flow increases, despite a decrease in cerebral metabolic rate, which can result in cerebral vasodilation and increased brain volume. At normal anesthetic concentrations, this phenomenon is not clinically significant, and intraoperative use of hyperventilation and mannitol is adequate to counteract the effect. In unique situations where high MAC is required, however, one must anticipate increased brain volume. Propofol total intravenous anesthesia (TIVA) is not associated with cerebral vasodilation and, in select cases where the brain is extremely edematous, may be a more appropriate technique. Delayed emergence and hypotension limit the usefulness. In cases where intracranial hypertension is a concern, ketamine and nitrous oxide should be avoided due to their effects on ICP and cerebral metabolic rate.

When positioning, the head and neck should ideally be midline (little to no rotation) and without towels or dressings which could compromise venous drainage of the neck. Head elevation, for instance, via reverse Trendelenburg position should be considered to further improve venous outflow.

An arterial line is often helpful when cerebral edema is a concern due to ease of estimation of CPP and frequent blood gas analysis to determine the degree of hyperventilation. If hyperosmolar therapy is employed to "relax" the brain in order to optimize surgical approach or respond to brain edema, plasma sodium and osmolarity can be checked regularly.

If rapid correction of cerebral edema is warranted, such as in acute herniation syndromes, immediate hyperventilation so as to lower $PaCO_2$ to no lower than 28 mmHg, combined with rapid administration of hyperosmolar solutions, is the most acutely responsive strategy. Hyperventilation will only demonstrate efficacy for several hours, as the brain will eventually readjust its autoregulatory thresholds. Sudden swings in the opposite (hypercapnic) direction can produce equally rapid increases in intracranial pressure and should be avoided.

Emergence

The decision to extubate the trachea must take into account the patient's ability to trigger respirations at an appropriate carbon dioxide level and to have a neurologic exam compatible with protection of the airway. Continuous $EtCO_2$ monitoring is recommended. Patients with cerebral edema may emerge from anesthesia with focal neurologic deficits. These deficits, if new, should be investigated promptly to exclude other problems such as postoperative hematoma, ischemic stroke, seizure, etc. Gr eat care should be taken to avoid coughing or vomiting as both can raise intracranial pressure.

Upon transport to the PACU or ICU, the same care that was given to maintenance of $PaCO_2$, head and neck positioning (including avoiding restrictive dressings or endotracheal tube circumferential tape), and avoidance of cough or emesis should be continued.

Pathophysiology

There are four pathophysiologic subtypes of cerebral edema: cytotoxic, vasogenic, osmotic, and interstitial. A single type rarely manifests in isolation. The division of edema types aids in the mechanistic understanding of edema formation and in the selection of effective treatments to minimize secondary injury (Table 3.1).

Table 3.1 Cerebral edema subtypes

Category	Clinical disease state
Vasogenic	Inflammatory state (e.g., meningitis) High-altitude cerebral edema Encephalopathy of HELLP Traumatic brain injury Intracranial hemorrhage Venous sinus thrombosis Hypertension Ischemia Tumor PRES
Cytotoxic	Intracerebral hemorrhage Venous sinus thrombosis Traumatic brain injury Toxin exposure Ischemia Reyes syndrome
Interstitial	Hydrocephalus Transependymal edema
Osmotic	Acute hepatic failure Diabetic ketoacidosis encephalopathy Hemodialysis encephalopathy

Cytotoxic Edema

Cytotoxic edema occurs when metabolically active cells are depleted of their energy (ATP) stores. Key cellular functions are interrupted, for example, the maintenance of cell membrane functionality and organized neurotransmitter release. The former results in rapid ion currents via respective ion channels and the latter in an excessive neurotransmitter release (e.g., glutamate) into the interstitial space. Both ion flux and transmitter release potentiate each other. Excessive ion currents, in particular sodium and calcium influx, cause water to enter the cell, resulting in rapid development of cellular edema leading to loss of cellular integrity.

If the brain areas are immediately reperfused, affected cell groups may eventually replenish energy stores and reestablish electrolyte balance. Cells in continuously underperfused areas are at risk of a subsequent insult via multiple intracellular pathways triggered by excess calcium: The active elimination of calcium to the outside of the cell results in a trade of sodium ions to the interior. This trade contributes to significant osmotic gradient, worsening cellular edema. Excess calcium causes further disruption of intracellular signaling and ultimately can lead to the activation of apoptotic pathways. Once the cellular integrity is lost, the damage is irreversible, causing "cytotoxic" brain edema (Fig. 3.2). Cytotoxic edema is commonly associated with some degree of vasogenic edema. Cell membrane leakage exposes normally intracellular contents to the extracellular environment, which results in inflammation and blood–brain barrier disruption.

Cytotoxic edema is typical after ischemic stroke or anoxia but may occur after trauma or toxin exposure. Cytotoxic edema can affect both gray and white matter. As the blood–brain barrier has been damaged, osmotic therapy has little effect to decrease volume of the damaged brain. Cerebral autoregulation is also likely to be impaired in brain regions affected by cytotoxic edema, making the response to hyperventilation and changes in blood pressure unpredictable.

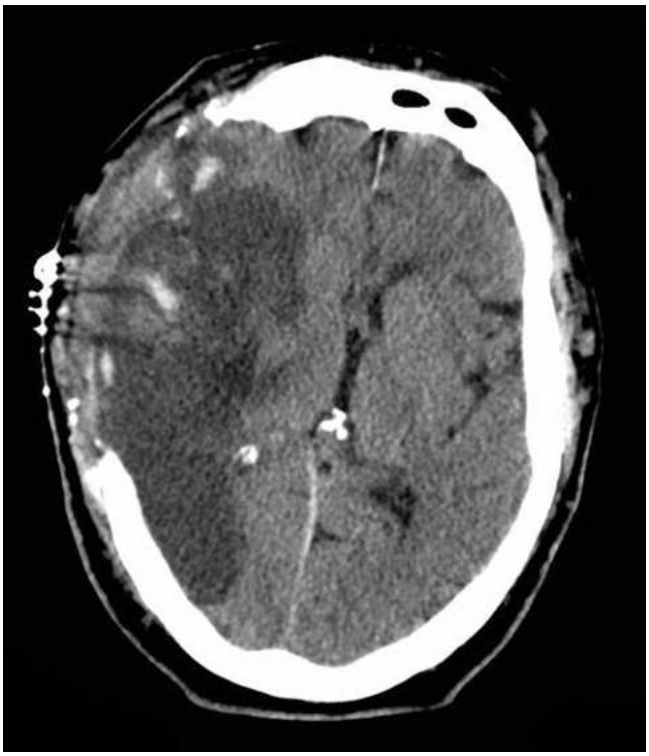

Fig. 3.2 Hemispheric cytotoxic brain edema 72 h after large middle cerebral artery ischemic stroke and decompressive hemicraniectomy. Note the loss of gray white differentiation and fungating appearance of brain tissue exiting the cranial vault

Vasogenic Edema

Damage to capillaries and a loss of tight junction integrity/basal laminar structure by proteases and free radicals result in vasogenic edema. Common etiologies include traumatic brain injury, tumor, ischemia, and inflammatory conditions such as meningitis. Hypertensive encephalopathy syndromes such as RPLS (reversible posterior leukoencephalopathy syndrome; formerly known as "PRES") and hepatic encephalopathy of HELLP (hemolysis, elevated liver enzymes, low platelets) are two other etiologies of vasogenic edema.

Increased capillary permeability as a result of inflammation and blood–brain barrier breakdown results in proteins and inflammatory mediators leaking into the brain interstitial space. Neutrophils drawn to the area further activate inflammatory cascades and may lead to permanent cellular damage. Additionally, the leak of proteins offsets the carefully controlled osmotic gradient within the brain and leads to an increase in free water movement into the interstitial spaces. Vasogenic edema typically affects white matter only (Fig. 3.3). As the cellular structure is largely maintained, vasogenic edema can be highly responsive to osmotic therapy and steroids.

Interstitial Edema

Inadequate cerebral spinal fluid absorption and resultant hydrocephalus can cause interstitial edema. Hydrostatic pressure pushes fluid into the brain interstitium. This type of edema may be more pronounced around the lateral ventricles. Medical therapy for this class of edema has questionable benefit. While diuretics such as acetazolamide and furosemide can decrease CSF production, the effect on intracranial pressure and outcomes are inconsistent. CSF diversion with an intraventricular catheter or permanent shunt is the definitive therapy.

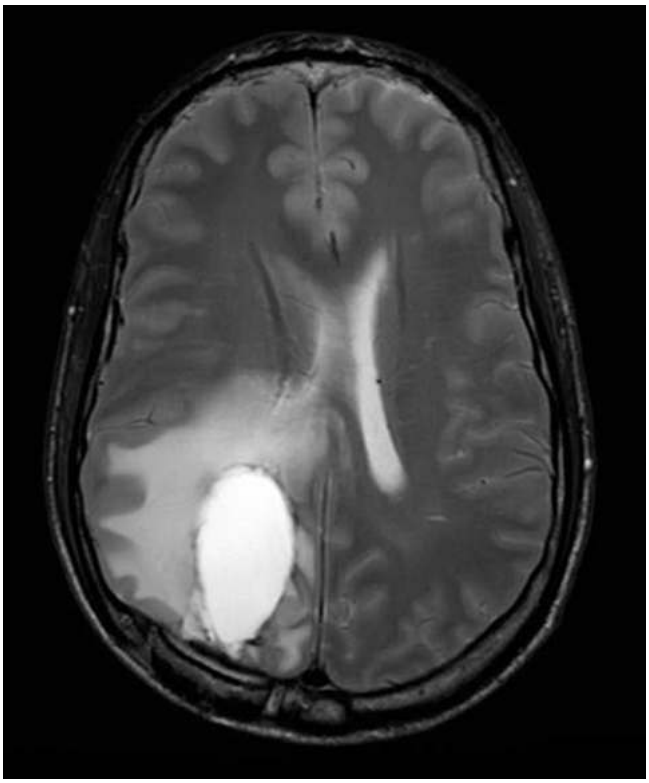

Fig. 3.3 Vasogenic edema surrounding well-demarcated brain tumor

Osmotically Driven Edema

Osmotically driven cerebral edema loosely describes a group of disorders whose pathophysiology involves acute changes in osmolarity. Acute hepatic failure can lead to extensive and difficult to treat cerebral edema. The exact mechanism of this insult is poorly understood but may be associated with ammonia accumulation and transit across the blood–brain barrier. Plasma hyperosmolar states will result in an equilibration of the brain osmolarity over time. When blood osmolarity is corrected rapidly, fluid will shift into the brain across the blood–brain barrier to reestablish equiosmolar conditions. Hemodialysis encephalopathy and diabetic ketoacidosis are two such examples. Hemodialysis encephalopathy can be seen following first-time initiation of hemodialysis and should be a concern in patients presenting with blood urea nitrogen above 50 mg/dL. Aggressive first-time dialysis is often avoided for this reason. Diabetic patients presenting in acute ketotic acidosis are similarly at risk when rapidly corrected.

Concerns and Risks

Key elements of management for patients with cerebral edema or those at risk include continuous neurologic monitoring, avoidance of both hypoosmolar and hyponatremic states, and maintenance of cerebral perfusion.

Monitoring

The cornerstone of cerebral monitoring is frequent, repeated neurologic examination. Subtle changes can be detected by an experienced examiner and may be the earliest indication of clinically significant cerebral edema. When a patient is unable to be frequently examined due to decreased alertness, sedation, or neuromuscular paralysis, serial neuroimaging may be warranted. Direct ICP monitoring can be useful in appropriate situations and is recommended in patients with traumatic brain injury and a Glasgow Coma Scale less than 8. Intraventricular catheters are most commonly used; they provide accurate and continuous pressure measurement as well as the option to drain CSF as a therapeutic means. Risks associated with intraventricular catheters include but are not limited to bleeding upon placement, infection, clotting of the catheter, and assumed risk associated with withholding prophylactic anticoagulation. Various intraparenchymal ICP monitors are a useful second option for monitoring intracranial hypertension. Certain risks are lower with this device such as injury upon placement, bleeding, and infection. The main drawback is the inability to drain CSF.

Treatment

Treatment of cerebral edema should occur in a stepwise fashion from least to most invasive interventions (Table 3.2). Non-pharmacologic options should be initiated in all patients. Raising the head of the bed at least 30° and maintaining a midline position without neck rotation help to optimize venous drainage from the brain. Obstructed venous drainage results in increased ICP and a reduced arterial perfusion.

Hyperventilation

If a definitive airway has been placed, hyperventilation is a reasonable option for treatment in the very short term. Vasoconstriction associated with decreased arterial CO_2 level is a useful rescue technique, but the effectiveness will be lost in 6–8 h as the brain resets its acid/base equilibrium. An arterial PCO_2 28–32 should be the aim; lower partial pressures can lead to excessive vasoconstriction and ischemia. Just as the vasoconstrictive effects of a low arterial PCO_2 are rapid, a sudden rise in arterial PCO_2 can produce equally rapid vasodilatation. It is therefore important to carefully follow the $PaCO_2$ in patients whose $PaCO_2$ had recently been lowered. This is of particular importance in the postoperative care unit or in any head injury patient who is spontaneously breathing and receiving narcotics.

Table 3.2 Therapeutic options in cerebral edema

Therapy	Clinical state	Dose/duration	Associated risks
Hyperventilation	Acute crisis or impending herniation	Temporizing measure only $PaCO_2$ 28–32	Vasoconstriction leading to ischemia
Head position	All states	Continuous	
Mannitol	Acute crisis, herniation, interstitial, cytotoxic, osmotic edema	Bolus 0.5–1 g/kg Redose 0.25–0.5 mg/kg Q6hr goal serum osmolality 310–320	Electrolyte disturbances, concern for worsening midline shift in large hemispheric lesions
Hypertonic saline	Acute crisis, herniation, interstitial, osmotic, cytotoxic, and vasogenic edema	Multiple formulations available	Rebound edema associated with withdrawal Damage to peripheral vessels Volume overload. Electrolyte abnormalities, renal insufficiency
Steroids	Vasogenic edema surrounding tumor	Dexamethasone 4-6 mg Q4-6h	No role in ischemia, trauma, hemorrhage
Pharmacologic coma	Salvage therapy from any pathology	Pentobarbital 10 mg/kg bolus, 1–4 mg/kg/h (Alternative propofol) Consider titration of agents to EEG burst suppression	Infection Lack of neurologic exam Hypotension, cardiac depression Prolonged half-life
Intraventricular catheter	Intracranial hypertension, hydrocephalus	Continuous	Infection
Hemicraniectomy	Refractory intracranial hypertension Large hemispheric stroke	Within 0–48 h	Surgical risks

Steroids

Steroids reduce the inflammatory disruption of the blood barrier in patients with vasogenic edema. In patients with significant edema associated with brain tumor, high-dose steroids can profoundly decrease vasogenic edema and improve functional status. Their use in ischemic brain injury is unsupported and in traumatic brain injury may worsen outcome.

Osmotic Therapy

Osmotherapy theoretically aims to maximize intravascular oncotic pressures thereby producing a gradient down which both intracellular and extracellular brain water may move into the vasculature and exit the cranial vault. Any osmotic agent therefore is only of utility if it can remain largely within the cerebral vessel and does not cross the blood–brain barrier. Where the blood–brain barrier is disrupted, an osmotic agent could potentially enter the interstitial spaces and lead to rebound cerebral edema.

Mannitol, a six-carbon sugar alcohol, is the most well-studied osmotic therapeutic in cerebral edema. Mannitol is typically prepared as a 20–25% solution and can be administered in 0.25–1 g/kg boluses in acute cerebral edema. Larger doses have been studied, and their effectiveness has been outweighed by the resultant electrolyte imbalances. Mannitol will produce a profound osmotic diuresis, and electrolytes and serum osmolality should be checked regularly. A hyperosmolar state on the order of 310–320 mOsm/L should be the target. Mannitol has been extensively studied for its extraosmotic properties which include increases in blood volume and decrease in blood viscosity leading to improved cerebral blood flow, antioxidant properties, decrease in CSF production, and inhibition of apoptosis. Mannitol will have a greater effect on cells within the uninjured hemisphere and could therefore theoretically lead to worsening midline shift.

Hypertonic saline has become increasingly popular as a resuscitative fluid in brain injury. Hypertonic saline is supplied in a variety of concentrations, ranging from 3% to 23.4%. Three percent solution can safely be administered peripherally, but higher concentrations should be administered centrally. For acute resuscitative efforts, 30 mL of 23.4% or 250 mL of 3% can be administered as a rapid bolus dose. Bolus dosing to reverse brain tissue volume in response to a clinical concern such as a fixed and dilated pupil is associated with reversal of that neurologic finding. Extraosmotic properties of hypertonic saline include increased tissue oxygen delivery, decreased CSF production, and increased CSF resorption.

Hypertonic saline may also be administered as a continuous infusion. The quality of evidence for bolus dosing is better than that for titration of an infusion to a particular sodium goal for prevention of ongoing edema formation. The osmotic gradient may dissipate over time as brain osmolarity equilibrates, and the duration that fixed sodium augmentation has an effect on edema prior to osmotic equilibration is unknown. Despite the lack of high-quality evidence, continuous infusion therapy with hypertonic saline is common. Initial therapy calls for hypernatremia for 24–72 h to a goal sodium set at some level higher than the patient's pretreatment level, usually augmentation of 5–10 mEq/L. After the period of concern for edema has elapsed, the infusion can be slowly tapered while monitoring level of edema, serum sodium

concentration, and neurologic exam. A slow taper to normonatremia over a period of days is ideal, and hyponatremia, or acute decreases in sodium more than 2–3 meq/L per day, should be avoided.

Large infusions of chloride ion present in 3% NaCl will produce a hyperchloremic metabolic acidosis, which is associated with renal dysfunction and coagulopathy. For continuous infusion, a 50:50 mix of sodium chloride with sodium acetate is preferable to avoid the chloride load. Sodium acetate 3% may also be used but will precipitate a metabolic alkalosis.

Whether mannitol is better than hypertonic saline for the management of cerebral edema depends on patient factors. Patients with underlying congestive heart failure may develop pulmonary edema initially after mannitol administration, while hypovolemic patients may not tolerate the diuresis associated with mannitol. Hypertonic saline may be a more appropriate osmotic therapy for hypovolemic patients in shock. No large randomized studies exist that directly compare the two agents, but recent meta-analyses suggest that hypertonic saline may be more effective in lowering elevated ICP than mannitol. Hypertonic saline may also be used as rescue therapy when ICP remains high after mannitol administration.

Finally, loop diuretics such as furosemide are sometimes used, but their utility is controversial and not recommended by all authors. Aggressive diuresis can lead to decreases in cardiac output and cerebral perfusion pressure, which is not ideal. Furosemide is an excellent agent for use in the diuresis of isotonic fluid, and if that loss can be replaced with hypertonic saline solution concomitantly, then dehydration may be avoided, and hypernatremia achieved more quickly.

Induced Coma/Paralysis

When the above therapies prove ineffective, more aggressive approaches aimed at salvage of brain tissue may be employed as a last resort. Pharmacologic coma is one such option; the goal here being to reduce neuronal activity which in turn will reduce cerebral metabolic rate of oxygen or CMRO2. Cerebral blood flow is coupled directly to cerebral metabolic rate and will also decrease under pharmacologic coma. Barbiturates are the drugs of choice for instituting a pharmacologic coma. Pentobarbital coma is initiated with a bolus dose of 5–10 mg/kg followed by an infusion rate of 1–4 mg/kg/h titrate to goal reduction in intracranial pressure less than 20 mmHg. Complications of barbiturate coma include cardiac depression, increased infection risk, and long half-life, which could delay the time to return of reasonably assessable neurologic function. Propofol, a shorter acting hypnotic, may also be used. Paralysis with nondepolarizing neuromuscular blockade may blunt ICP increases associated with ventilator intolerance, coughing, and straining and improve venous drainage of the head.

Surgical Options

A patient with unremitting intracranial hypertension despite maximal medical therapy is a possible candidate for decompressive hemicraniectomy. Hemicraniectomy, performed within the first 48 h of injury, improves mortality in patients with cytotoxic edema after ischemic stroke. For this therapy to be effective, it needs to be completed within 48 h and ideally sooner. Whether there is benefit to functional outcome with early surgical decompression remains unclear.

Key Points

- Four subtypes of cerebral edema exist, and their correct diagnosis can appropriately direct therapy.
- Monitoring, particularly the neurologic exam, is the key to early detection of clinically significant cerebral edema and thereby prevention of secondary injury.
- Therapy for cerebral edema should be approached in a stepwise fashion, employing least invasive measures first.
- Upon termination of any therapeutic measure, slow taper as opposed to sudden withdrawal is the recommended course.

Suggested Reading

Bardutzky J, Schwab S. Antiedema therapy in ischemic stroke. Stroke. 2007;38(11):3084–94.

Bradley WG. Neurology in clinical practice. 5th ed. Philadelphia: Butterworth Heinemann Elsevier; 2008. p. 1694–708.

Brouns R, De Deyn PP. Neurological complications in renal failure: a review. Clin Neurol Neurosurg. 2004;107(1):1–16.

Hofmeijer J, Kappelle LJ, Algra A, Amelink GJ, van Gijn J, van der Worp HB. HAMLET investigators. Surgical decompression for space-occupying cerebral infarction (the Hemicraniectomy After Middle Cerebral Artery infarction with Life-threatening Edema Trial [HAMLET]): a multicentre, open, randomised trial. Lancet Neurol. 2009;8(4):326–33.

Kahle KT, Simard JM, Staley KJ, Nahed BV, Jones PS, Sun D. Molecular mechanisms of ischemic cerebral edema: role of electroneutral ion transport. Physiology (Bethesda). 2009;24:257–65.

Kamel H, Navi BB, Nakagawa K, Hemphill JC 3rd, Ko NU. Hypertonic saline versus mannitol for the treatment of elevated intracranial pressure: a meta-analysis of randomized clinical trials. Crit Care Med. 2011;39(3):554–9.

Kramer DJ, Canabal JM, Arasi LC. Application of intensive care medicine principles in the management of the acute liver failure patient. Liver Transpl. 2008;14(Suppl 2):S85–9.

Mortazavi MM, Romeo AK, Deep A, Griessenauer CJ, Shoja MM, Tubbs RS, Fisher W. Hypertonic saline for treating raised intracranial pressure: literature review with meta-analysis. J Neurosurg. 2012;116(1):210–21.

Qureshi AI, Suarez JI. Use of hypertonic saline solutions in treatment of cerebral edema and intracranial hypertension. Crit Care Med. 2000;28(9):3301–13.

4 Management of Fluids, Electrolytes, and Blood Products in Neurosurgical Patients

Pratik V. Patel and Sadeq A. Quraishi

Overview

- The major fluid compartments of the body are the intracellular compartment and the extracellular compartment, which is subdivided into intravascular and interstitial spaces.
- The volume of the individual compartments may change in a disease state or as the body adapts to environmental stress.
- In peripheral tissues, the primary determinant of fluid movement across capillaries (i.e., between the intravascular and interstitial spaces) is the oncotic gradient produced by large plasma proteins such as albumin.
- Unlike the peripheral tissues, the brain and spinal cord are isolated from the intravascular compartment by the blood–brain barrier.
- The primary determinant of water movement across the intact blood–brain barrier is the osmotic pressure gradient produced by osmotically active particles including plasma sodium and other electrolytes.
- Intravenous infusion of solutions hyperosmolar to plasma (e.g., 3% sodium chloride, mannitol) will lead to a decrease in brain water content and intracranial pressure (ICP). Administration of excess free water (e.g., hypoosmolar or dextrose-containing electrolyte-free solutions) will lead to increased brain water content and ICP.
- Osmotically active particles as well as plasma proteins may "leak" into the cerebral tissue where the blood–brain barrier has been disrupted and thus contribute to worsening cerebral edema in such regions.
- Intravenous administration of hyperosmolar solutions results in a decrease in water content in the brain where the blood–brain barrier is intact to allow the injured brain to expand while attenuating the increase in intracranial pressure (i.e., Monro–Kellie hypothesis).

Implications for the Neurosurgical Patient

Perioperative fluid management in neurosurgical patients poses special challenges.

- The presence and treatment of elevated ICP, surgical bleeding, and a variety of pathophysiological derangements associated with neurologic injury may lead to significant hypovolemia, electrolyte abnormalities, anemia, and coagulopathy.

Care must be taken to:

- Maintain hemodynamic stability, optimal cerebral perfusion pressure, and oxygen delivery to the CNS.
- Minimize the impact of fluid resuscitation on the development or exacerbation of cerebral edema.

The goals of fluid resuscitation are (see Tables 4.1, 4.2, 4.3, 4.4, and 4.5):

- Restore intravascular volume and cerebral perfusion pressure.
- Achieve a slightly hyperosmolar state.

The clinician can choose from a variety of intravenous fluids including crystalloid, hypertonic saline, colloid, and blood products as dictated by the clinical scenario. The typical initial fluid choice for an elective craniotomy is normal saline or Plasma-Lyte A/Normosol™-R (Table 4.6).

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Table 4.1 Commonly used IV solutions

Commonly used intravenous solutions	Osmolarity (mOsm/L)
Plasma osmolarity	270–295
Crystalloid	
Lactated Ringer's	273[a]
Plasma-Lyte A (or Normosol™-R)	294 (or 295)
0.9% normal saline	308
D5 lactated Ringer's	525
20% mannitol	1098
3% hypertonic saline (HS)	1026
Colloids	
6% hetastarch[b]	310
Pentastarch[b]	326
6% dextran (70)[b]	300
5% albumin	300
25% albumin	1500
HS colloid mixture	
7.5% HS 6% dextran[c]	2568

[a]Calculated osmolarity, of note LR solutions actual osmolarity can be significantly lowered due to incomplete disassociation
[b]Rarely used in the USA since FDA "black box" warning on labeling due to increased risk for mortality and/or acute kidney injury requiring dialysis and European Medicines Agency recommendation to stop the use of these synthetic colloids in patients with sepsis, burns, or critical illness
[c]Available in Europe

Table 4.2 Common causes of hyponatremia

Dilution
Excess water intake
Administration of hypoosmolar fluids
Use of diuretics
Mannitol, thiazides
Adrenal insufficiency
Hypothyroidism
Hyperglycemia, hyperlipidemia, hyperproteinemia (psuedohyponatremia)
Cerebral salt-wasting syndrome
Common in subarachnoid hemorrhage
Associated with hypovolemia
SIADH
CNS disorders
Chronic infections
Medications (e.g., carbamazepine, opioids)
Organ failure
Cirrhosis, congestive heart failure, nephrotic syndrome
Associated with hypervolemia

SIADH syndrome of inappropriate antidiuretic hormone secretion

Table 4.3 Common causes of hypernatremia

Dehydration
Diabetes insipidus
Use of hypertonic saline

Table 4.4 Common causes of hypokalemia

Combined use of osmotic and loop diuretics
Hypomagnesemia
Intracellular potassium shift secondary to
Hyperventilation
Insulin infusion

Table 4.5 Considerations for assessing intravascular volume

History
Preoperative fasting and insensible losses
Presence of hemorrhage
Use of diuretics
Use of hyperosmotic intravenous contrast
Physical exam
Vital signs: presence of fever, tachycardia, hypotension
Orthostatic tachycardia and hypotension
Status of neck veins, skin turgor, mucous membranes
Oliguria
Pulmonary edema
Monitors
Trend in CVP or PAOP
Marked reduction in arterial pulse pressure or stroke volume with positive pressure ventilation signifying intravascular depletion

CVP central venous pressure, *PAOP* pulmonary artery occlusion pressure

Table 4.6 Indications for commonly used intravenous fluids and blood products

Indication	Fluid or blood product	Amount
Fluid maintenance	Plasma-Lyte A/ Normosol™-R or 0.9% saline (normal saline, NS)	1:1 Crystalloid/ fluid loss ratio; (usual rate: NS at 1.5 mL/kg/h)
Insensible and interstitial losses		
Brain relaxation for exposure during craniotomy	20% mannitol	0.25–1.25 g/kg
	3% sodium chloride (hypertonic saline, HS)	5 mL/kg
Treatment of elevated ICP	20% mannitol	0.25–1.25 g/kg
	3% saline (HS)	200 mL
Replacement of blood loss	Lactated Ringer's, NS	3:1 crystalloid/ blood loss ratio
	Colloid	1:1 colloid/blood loss ratio
	Hetastarch 6%	If used, limit to 20 mL/kg/24 h
	Red cells – ideally washed, leukoreduced, <15 days old	1 unit should raise Hgb by 1 g/dL or Hct by 3%
Disseminated intravascular coagulation (DIC)		
Elevated INR, PTT	Fresh frozen plasma	Start at 10–15 mL/ kg
Fibrinogen <100 mg/ dL	Cryoprecipitate	1 pool (6 bags) raises fibrinogen by 45 mg/dL
Thrombocytopenia <100,000 in a bleeding patient	Platelets phereses	1 bag (4–6 pooled units) raise platelets by 30,000/μL

Concerns and Risks (Table 4.7)

Anemia

- Has been associated with worse neurologic outcome in cardiopulmonary bypass surgery and with perioperative visual loss in prone spine surgery.

Table 4.7 Concerns and risks of fluid management in neurosurgical patients

Under-resuscitation	Hypotension, inadequate cerebral perfusion pressure, secondary brain injury
Over-resuscitation	Exacerbation of cerebral edema
Hyponatremia	<120–125 mEq/L – change in mental status, seizures
Hypernatremia	>160–170 mEq/L – change in mental status, seizures
Lactated Ringer's	Hypoosmolar state, hyponatremia
Plasma-Lyte A	Alkalinizing effect – increase renal clearance of acidic drugs and lithium, decrease renal clearance of alkaline drugs
Normosol™-R	
0.9% saline	Hyperchloremic metabolic acidosis
Dextrose solutions	Hypoosmolar state, hyperglycemia exacerbating cerebral injury
20% mannitol	Hyponatremia
	Loss of bicarbonate – metabolic acidosis
	Excessive diuresis – intravascular volume depletion, electrolyte losses
	Rebound cerebral edema
	Hyperkalemia with extremely high doses (2 g/kg)
Hypertonic saline	Hypernatremia
	Hyperchloremic metabolic acidosis
	Rebound cerebral edema when plasma sodium falls
	Tearing of bridging cortical veins – subdural hemorrhage
	Excessive diuresis – intravascular volume depletion, renal failure
	Central pontine myelinolysis – with rapid rise of plasma sodium from hyponatremic levels; malnourished and alcoholic patients at increased risk
	Sclerosis of veins
	Interference with coagulation and platelet aggregation
Synthetic colloids	Interference with coagulation, factor VIII complex; potential increased risk for intracranial hemorrhage
	No clear benefit compared with crystalloid as a resuscitative fluid
	Renal impairment
	Allergic reactions
	Pruritus
	Interference with blood crossmatching with dextran
	Increased risk of mortality and/or acute kidney injury
Albumin	Expensive
	No clear benefit compared with crystalloid as a resuscitative fluid; potential harm in patients with traumatic brain injury

- The ideal hematocrit for optimizing cerebral blood flow and oxygen delivery in focal ischemia model is currently believed to be 30–34%. Higher hematocrit results in increased blood viscosity; hematocrit ≤25% results in decreased oxygen-carrying capacity.
- Normovolemic hemoglobin levels of 7–9 g/dL appear to be safe for the general ICU patient population.
- There is insufficient evidence to allow recommendations regarding:
  - The "safe" level of anemia for patients with neurologic injury
  - Whether correction of anemia by transfusing red cells has beneficial or detrimental effects on neurologic outcome

Table 4.8 Examples of risks associated with transfusion of blood products

Risk	Risk per unit transfused
Infectious risks	
HIV	1:1.5–4.7 million
Hepatitis C	1:1.9–3.1 million
Hepatitis B	1:31,000–205,000
Hemolytic reactions	
Acute	1:13,000
Delayed	1:1600
Alloimmunization	1:1600
Immunosuppression	1:1
TRALI	1:5000

Adapted in part from reference by Marik and Corwin (2008)

Transfusion of Blood Products

Current concerns regarding blood product transfusion in the developed world focus more on the immunomodulating effects of transfusion rather than transmission of infectious agents (Table 4.8). Transfusion-related acute lung injury (TRALI) is thought to be the leading cause of transfusion-related mortality.

Special Circumstances (Table 4.9)

Table 4.9 Special circumstances

Traumatic brain injury	Subarachnoid hemorrhage
Risk of coagulopathy and DIC	Electrolyte abnormalities
Multitrauma	Hypocalcemia, hypomagnesemia
Massive hemorrhage	Hypokalemia
Dilutional coagulopathy	Hyponatremia
Neurogenic pulmonary edema	Cerebral salt-wasting syndrome
Hyponatremia	SIADH
Cerebral salt-wasting syndrome	Avoid hypovolemia
SIADH	Vasospasm – therapeutic goal: aggressive maintenance of euvolemia

Key Points

- Fluid management goal is a euvolemic, slightly hyperosmolar state.
- Avoid hypoosmolar fluids and dextrose-containing solutions unless needed to treat hypoglycemia.
- Consider using hypertonic saline, unless contraindicated, to treat elevated ICP in a hypovolemic, hemodynamically unstable patient.
- In anemic patients with neurologic injury, there is insufficient evidence regarding transfusion thresholds. Do not use an arbitrary hemoglobin number; weigh risks of transfusion (e.g., TRALI, immunosuppression) with benefits of oxygen delivery to injured CNS tissue.

Suggested Reading

Kumar MA. Red blood cell transfusion in the neurological ICU. Neurotherapeutics. 2012;9:56–64.

Lira A, Pinsky MR. Choices in fluid type and volume during resuscitation: impact on patient outcomes. Ann Intensive Care. 2014;4:38–50.

Marik PE, Corwin HL. Efficacy of red blood cell transfusion in the critically ill: a systematic review of the literature. Crit Care Med. 2008;36:2667–74.

Patel PM, Drummond JC, Lemkuil BP. Cerebral physiology and the effects of anesthetic drugs. In: Miller's anesthesia. 8th ed. Philadelphia: Elsevier; 2015. p. 387–422.

Perel P, Roberts I, Ker K. Colloids versus crystalloids for fluid resuscitation in critically ill patients. Cochrane Database Syst Rev. 2013;2:CD000567.

SAFE Study Investigators. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. NEJM. 2007;357:874–84.

Tomamsino C. Fluids and the neurosurgical patient. Anesthesiol Clin N Am. 2002;20:329–46.

Key Monitoring in Neuroanesthesia: Principles, Techniques, and Indications

5

Martin Smith

Overview

One of the primary roles of the neuroanesthesiologist is to maintain cerebral perfusion to meet the brain's metabolic demands and, under circumstances of reduced perfusion, to protect the brain. Disturbance of systemic and cerebral physiological variables can cause or exacerbate brain injury, but their optimization offers effective neuroprotection. Monitoring techniques must therefore include measurement of both systemic and cerebral physiologic variables. Intraoperative neurophysiological monitoring is widely used to minimize the risk of spinal cord injury during spine surgery.

Implications for the Neurosurgical Patient

Monitoring and managing systemic and central nervous system (CNS) physiology is fundamental to the perioperative and critical care management of patients with neurologic disease. Several techniques are available for global or regional monitoring of cerebral hemodynamics, oxygenation, metabolism, and electrophysiology (Table 5.1).

Clinical Monitoring

The clinical neurologic examination remains the cornerstone of neuromonitoring. The Glasgow Coma Scale (GCS) is a standardized method for evaluating global neurologic status by recording best eye opening and motor and verbal responses to physical and verbal stimuli. In association with identification and documentation of localizing signs, including pupil responses and limb weakness, the GCS remains fundamental to the clinical neurologic assessment more than 40 years since its first description. The GCS has some limitations – verbal responses cannot be assessed in intubated patients and brainstem function is not directly considered. The Full Outline of UnResponsiveness (FOUR) score provides a more complete assessment of brainstem function by measuring ocular (as well as limb) responses to command and pain, pupillary responses and respiratory pattern, but it is not as widely used as GCS. Clinical assessment, apart from pupillary responses, is unreliable or impossible in unconscious or uncooperative patients.

Monitoring Systemic Physiologic Variables

Monitoring and managing systemic physiologic variables allows optimization of cerebral perfusion and oxygenation. Routine monitoring during neuroanesthesia includes EKG, arterial oxygen saturation (pulse oximetry), arterial blood pressure (ABP), end-tidal carbon dioxide tension, and temperature. Noninvasive blood pressure monitoring is appropriate for minor cases, but an arterial catheter should be placed to allow beat-to-beat pressure monitoring and arterial blood gas analysis during intracranial and complex spine surgery and in patients with significant comorbidities. Central venous pressure is now considered an unreliable guide to cardiovascular management. Various minimally invasive cardiac output monitoring techniques provide more accurate assessment of intravascular volume and guide titration of vasopressors and inotropes. Urine output and fluid balance should be monitored when large fluid shifts are likely, particularly if osmotic diuretics will be administered or in the presence of neurogenic fluid disturbances such as cranial diabetes insipidus.

Monitoring the Brain and Spinal Cord

In 2014, the Neurocritical Care Society and European Society of Intensive Care Medicine published consensus guidance on multimodality neuromonitoring during neurocritical care.

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Table 5.1 Applications of neuromonitoring techniques

Monitoring technique	Established intraoperative applications	Established neurointensive care applications	Invasive/ noninvasive	Modalities monitored
Intracranial pressure	Yes	Yes	Invasive	ICP
				CPP
				Cerebrovascular reactivity
Transcranial Doppler	Yes	Yes	Noninvasive	FV as an estimate of CBF
				Cerebral vasospasm
				Cerebral autoregulation
Thermal diffusion flowmetry	Research	No	Invasive	Absolute regional CBF
Jugular venous oximetry	Yes	Yes	Invasive	Global cerebral oxygenation
				$AVDO_2$
Brain tissue oxygen tension	No	Yes	Invasive	Regional brain tissue oxygen tension
				Cerebrovascular reactivity
Near-infrared spectroscopy	Yes	Research	Noninvasive	Regional cerebral oxygenation
				Cerebral hemodynamics, including vasoreactivity
				Cerebral cellular energy status
Cerebral microdialysis	No	Research	Invasive	Glucose metabolism
				Hypoxia/ischemia
				Cellular energy failure
Electroencephalography	Yes	Yes	Noninvasive	Seizures
				Cortical spreading depolarizations
				Cerebral ischemia
				Cortical mapping
Evoked potentials	Yes	Yes	Minimally invasive	Sensory and motor pathways
				Cerebral ischemia

$AVDO_2$ Arteriovenous oxygen content difference, *CBF* cerebral blood flow, *CPP* cerebral perfusion pressure, *ECF* extracellular fluid, *ICP* intracranial pressure

However, many modalities are less suited to the operating room because of incompatibility or inadequate temporal resolution.

Intracranial Pressure

In addition to direct measurement of intracranial pressure (ICP), ICP monitoring allows calculation of cerebral perfusion pressure (CPP) as the difference between mean arterial pressure (MAP) and ICP, identification and analysis of pathological ICP waveforms, and derivation of indices of cerebrovascular pressure reactivity. Different methods of monitoring ICP are available, but invasive monitoring via an intraventricular catheter or intraparenchymal microtransducer device is most common in clinical practice (Table 5.2). Several noninvasive ICP monitoring techniques have been described but currently fail to measure ICP sufficiently accurately for routine clinical use.

The indications for ICP monitoring during the critical care management of traumatic brain injury (TBI) are well established, and the 2016 Brain Trauma Foundation (BTF) recommendations have recently been supplemented by a European expert statement (Table 5.3). The only randomized controlled trial of ICP-guided management after TBI (Benchmark Evidence from South American Trials: Treatment of Intracranial Pressure, BEST:TRIP) found similar 3- and 6-month outcomes in patients in whom treatment was guided by ICP monitoring compared to treatment guided by imaging and clinical examination in the absence of ICP monitoring. Subsequent assessments of this study, which was conducted in Bolivia and Ecuador, have questioned whether its findings are relevant to healthcare systems with more developed prehospital and rehabilitation services and also come to very varied conclusions about its broader relevance to current practice. In response to this dissonance, a group of international experts published a consensus-based interpretation of the BEST:TRIP study, calling for further research on ICP monitoring and interpretation while emphasizing that this study should not change current clinical practice. The evaluation and diagnosis of intracranial hypertension therefore remains fundamental to the management of severe TBI, and clinical guidelines recommend treating ICP above a certain threshold (usually >22 mmHg). ICP monitoring is increasingly being incorporated into protocols for the critical care management of subarachnoid (SAH) and intracerebral hemorrhage, although these indications are not as well-defined or well-studied as those for TBI.

Perioperative ICP monitoring should be considered in patients with TBI, large brain tumors with mass effect,

Table 5.2 Intracranial pressure monitoring devices

Method	Advantages	Disadvantages
Intraventricular catheter	Gold standard measure of ICP	Risk of hematoma
	Measures global ICP	Risk of catheter-related ventriculitis
	Allows therapeutic drainage of CSF	
	In vivo calibration	
Microtransducer sensor	Intraparenchymal/subdural placement	No in vivo calibration
	Low procedure complication rate	Measures local pressure
	Low infection risk	
	Low zero drift over time	
	Bedside insertion	
Noninvasive methods,	Noninvasive	Limited accuracy prevents clinical use
e.g., optic nerve sheath diameter measured by CT scan or ultrasound and TCD-derived PI	Applicable in a broad range of patient groups	Continuous monitoring not possible

CT Computed tomography, *ICP* intracranial pressure, *PI* pulsatility index, *TCD* transcranial Doppler ultrasonography

Table 5.3 Indications for intracranial pressure monitoring in traumatic brain injury

Brain trauma foundation guidelines
(*Neurosurgery* 2017; 80: 6–15)
Salvageable patients with severe TBI and an abnormal cranial CT scan
Salvageable patients with severe TBI and a normal scan and two or more of the following:
Age >40 years
Unilateral or bilateral motor posturing
Systolic blood pressure <90 mmHg
Milan consensus conference recommendations
(Stocchetti N et al. *Acta Neurochir (Wien)* 2014; 156: 1615–22)
Comatose TBI patients with minimal abnormality on initial CT scan and subsequent worsening (e.g., development of contusions or signs of raised ICP)
Comatose TBI patients with cerebral contusions when interruption of sedation to check neurologic status is dangerous, or clinical examination unreliable
Comatose TBI patients with large bifrontal contusions and/or hemorrhagic mass lesions close to the brainstem, irrespective of initial GCS
Following secondary decompressive craniectomy
Following evacuation of acute supratentorial intracranial hematoma in salvageable patients with:
GCS motor score ≤5
Pupillary abnormalities
Prolonged/severe hypoxemia and/or hypotension
Compressed or obliterated basal cisterns
Midline shift >5 mm or exceeding thickness of an extra-axial clot
New extra-axial hematomas, parenchymal contusions, or brain swelling
Intraoperative brain swelling

ICP Intracranial pressure, *CPP* cerebral perfusion pressure, *CT* computed tomography, *GCS* Glasgow Coma Scale, *TBI* traumatic brain injury

hydrocephalus, intracranial and subarachnoid hemorrhage, and in the presence of significant cerebral edema from whatever cause. Postoperative ICP monitoring after intracranial surgery is indicated in any patient who will remain sedated or if there is a risk of intracranial hypertension.

Cerebrovascular Reactivity

Cerebral autoregulation is an important mechanism that protects the brain from fluctuations in cerebral blood flow (CBF) in the face of changing CPP. It can be impaired after brain injury and by anesthetic and sedative agents, thereby putting the brain at risk of pathophysiologic derangements of regional blood flow and increased susceptibility to ischemia.

The pressure reactivity of cerebral vessels is a key component of autoregulation and determines the ICP response to changes in ABP. A pressure reactivity index (PRx), calculated as the moving correlation coefficient of consecutive time averaged data points of ICP and ABP, can be used as a continuous assessment of autoregulatory status. A negative value for PRx indicates an inverse correlation between ABP and ICP and therefore normal cerebrovascular reactivity, whereas a positive PRx defines nonreactive cerebrovascular responses when changes in ABP and ICP are in phase. PRx has been used to guide MAP and CPP management after TBI. Cerebrovascular reactivity can also be assessed using ABP-related changes in brain tissue partial pressure of oxygen ($PbtO_2$), transcranial Doppler (TCD)

ultrasonography-derived cerebral blood flow velocity (FV), and several near-infrared spectroscopy (NIRS)-derived hemoglobin variables.

Cerebral Blood Flow

Transcranial Doppler ultrasonography is a noninvasive technique that measures blood FV from the Doppler shift caused by moving red blood cells in basal cerebral vessels from which changes in (but not absolute) CBF can be estimated. The TCD FV waveform resembles an arterial pulse wave and may be quantified into peak systolic, end-diastolic and mean FVs, and pulsatility index. The latter provides an assessment of distal cerebrovascular resistance. Reductions in FV correlate with cerebral ischemia and have been used to determine the need for shunt placement during carotid surgery, where TCD can also identify intraoperative air and particulate emboli. TCD is most widely used in the diagnosis and monitoring of cerebral vasospasm after SAH, which is confirmed when FV exceeds 120–140 cm/s or the ratio between FV in the middle cerebral and internal carotid arteries (the Lindegaard ratio) exceeds 3. It also has a role in the identification of patients at high risk of critically low brain perfusion and to direct therapy, assess autoregulation, and identify the need for brain imaging and invasive neuromonitoring after acute brain injury (ABI).

Thermal diffusion flowmetry is a relatively new technique that provides a real-time measure of absolute regional CBF (rCBF). Clinical data using this technology are limited, but intraoperative rCBF monitoring might be useful where there is a risk of focal cerebral ischemia.

Cerebral Oxygenation

Assessment of perfusion alone is insufficient to identify potential cerebral ischemia because reductions in CBF might be associated with appropriately coupled changes in metabolism. Cerebral oxygenation monitoring assesses the balance between cerebral oxygen delivery and utilization and therefore the adequacy of cerebral perfusion and provides a more complete picture of the injured or "at-risk" brain and its response to treatment.

Jugular venous oxygen saturation ($SvjO_2$) monitoring was the first bedside method for assessing cerebral oxygenation. It is a flow-weighted, global measure providing a nonquantitative estimate of the adequacy of cerebral perfusion. $SvjO_2$ accurately reflects global changes only if the dominant jugular bulb is cannulated, although, in practice, the right side is usually chosen. The normal range of $SvjO_2$ is 55–70%. Low $SvjO_2$ values indicate cerebral hypoperfusion or increased oxygen demand that is not matched by increased supply, whereas high values indicate relative hyperemia or arteriovenous shunting. The arterial to jugular venous oxygen content concentration difference, and other derived variables, have been studied extensively as an assessment of the adequacy of CBF.

$SvjO_2$ has been used to guide intraoperative blood pressure and ventilation management and during the critical care management of TBI where maintenance of above $SvjO_2$ above 55% has been associated with improved outcomes. Its lack of sensitivity to regional ischemia is a major disadvantage, and $SjvO_2$ monitoring is being superseded by other techniques.

Brain tissue oxygen partial pressure has become the standard bedside monitor of cerebral oxygenation. $PbtO_2$ catheters incorporate a gold polarographic (Clark-type) cell which reduces oxygen as it diffuses across a semipermeable membrane from the brain into the catheter, generating an electrical current that is proportional to the tissue oxygen tension. $PbtO_2$ is a complex and dynamic variable representing the interaction between cerebral oxygen delivery and demand, as well as tissue oxygen diffusion gradients. It is also a highly focal measure, and probe placement in peri-lesional but viable brain tissue allows selective monitoring of critically perfused tissue in "at-risk" brain regions. An alternative approach recommends placement in normal appearing white matter, when $PbtO_2$ effectively acts as a global measure of cerebral oxygenation. Probe location must always be confirmed with a cranial CT scan to allow appropriate interpretation of $PbtO_2$ readings.

Brain hypoxia can occur despite ICP and CPP being within accepted thresholds for normality, and therapy directed toward maintenance of $PbtO_2$ in addition to ICP and CPP has been associated with improved outcomes after TBI. Treatment is recommended when $PbtO_2$ falls below 15 mmHg; values less than 10 mmHg are indicative of severe brain hypoxia. Several factors, including ABP, CPP, PaO_2, $PaCO_2$, and hemoglobin concentration, are known to influence $PbtO_2$, but which intervention (or combination of interventions) to reverse brain hypoxia is most effective in improving outcome remains unclear. The responsiveness of the hypoxic brain to a given intervention is the major determinant of outcome, with reversal of hypoxia being associated with reduced mortality.

$PbtO_2$ monitoring is sufficiently responsive for intraoperative applications, allowing rapid detection of cerebral ischemia, and the potential to manipulate systemic and intracranial variables before irreversible neuronal damage occurs. However, there are limited data on intraoperative indications which is in any case be limited by the 1 h "run-in" period required for $PbtO_2$ readings to stabilize following probe insertion.

Near-infrared spectroscopy is a noninvasive technique based on the transmission and absorption of near-infrared light (700–1000 nm) at multiple wavelengths as it passes through tissue. Oxygenated and deoxygenated hemoglobin have different and characteristic absorption spectra in the near-infrared range, and, using transcranial reflectance spectroscopy, cortical oxygenation and hemodynamic status can be determined by their relative absorption of near-infrared light. Commercially

available NIRS-based cerebral oximetry devices provide continuous and noninvasive monitoring of regional cerebral oxygen saturation ($rScO_2$), the relative proportions of oxy- and deoxyhemoglobin in the field of view, with high temporal and spatial resolution over multiple regions of interest. The "normal" range of $rScO_2$ is reported to lie between 60% and 75%, but there is substantial intra- and inter-individual variability. Claims for $rScO_2$ thresholds for the identification of ischemia often lack any form of validation, and cerebral oximetry is currently best considered a trend monitor.

There has been rapid expansion of the clinical use of NIRS-based cerebral oximetry to guide brain-protective strategies during cardiac surgery following studies suggesting an association between intraoperative cerebral desaturation and an increased risk of perioperative cognitive decline. During carotid surgery, NIRS has similar accuracy and reproducibility in the detection of cerebral ischemia compared with other monitoring modalities and some advantages in terms of simplicity and temporal resolution. However, an accurate $rScO_2$ threshold to guide shunt placement or detect cerebral ischemia is not defined. Hypotension-associated decreases in $rScO_2$ in anesthetized patients in the beach chair position are widely reported, but these do not appear to be associated with an increased incidence of postoperative cognitive dysfunction or serum biomarkers of brain injury. There are no data to support the wider application of NIRS to monitor cerebral oxygenation during routine anesthesia and surgery, including during neurosurgical procedures. The role of NIRS in the neurocritical care unit is also undefined. Small observational studies investigating cerebral desaturation during changes in CPP, impending brain herniation, cerebral vasospasm, and pharmacological interventions in brain-injured patients have produced conflicting results, and there is no evidence that therapy guided by changes in NIRS-derived variables influences outcome. There are several concerns during the clinical application of NIRS, particularly "contamination" of the signal by extracranial tissue and the potential for confounding by the optical complexity of the injured brain. Advances in NIRS technology are likely to overcome these issues.

Metabolic Monitoring

Cerebral microdialysis (MD) monitoring allows bedside analysis of biochemical substances in brain tissue extracellular fluid (ECF). Glucose, lactate, pyruvate, and glycerol are commonly measured in the clinical setting because each is a marker of a particular cellular process associated with glucose metabolism, hypoxia/ischemia, or cellular energy failure (Table 5.4). The ability to assess cerebral glucose metabolism is a particular strength of cerebral MD monitoring; the lactate:pyruvate (LP) ratio in combination with ECF glucose levels provides unique information about the brain's metabolic state. Because cerebral MD monitors both the supply of substrate and its cellular metabolism, it is not solely a monitor of cerebral ischemia but also of nonischemic causes of cellular energy dysfunction and the ensuing metabolic crisis. In the research setting, cerebral MD can be used to measure a multitude of other substances including cytokines. Cerebral MD is a focal technique, and it is recommended that the MD catheter is placed in "at-risk" tissue to allow assessment of biochemical changes in the area of the brain most susceptible to secondary injury.

Cerebral MD monitoring can be considered in any patient at risk of cerebral hypoxia/ischemia, cellular energy failure, and glucose deprivation but is most commonly used in the

Table 5.4 Cerebral microdialysis markers of secondary brain injury

Microdialysis variable	Thresholds for intervention	Processes monitored	Comments
Glucose	<0.2 – <0.8 mmol/L	Hypoxia/ischemia	MD glucose monitoring is recommended
		Reduced cerebral glucose supply	Interpret in relation to serum glucose concentration
		Cerebral hyperglycolysis	
Lactate:pyruvate ratio	>20 – >40	Hypoxia/ischemia	MD LP ratio monitoring is recommended
		Cellular redox state	High LP ratio is associated with unfavorable outcome
Lactate	> 0.4 mmol/L	Reduced cerebral glucose supply	Most reliable biomarker of ischemia
			Increased LP ratio may result from a failure of oxygen delivery(ischemic hypoxia) or from nonischemic causes
			Absolute lactate and pyruvate concentrations should be considered when interpreting a high LP ratio
Glycerol	Unquantified	Marker of cell membrane breakdown	MD glycerol is an option as a marker of cerebral injury
		Potential marker of oxidative stress	Limited specificity – increased glycerol may also occur because of production of glycerol from glucose
			No definitive evidence of a relationship between glycerol and outcome
Glutamate	Unquantified	Glutamate release observed in ischemia and seizures	MD glutamate monitoring is an option
		Excitotoxicity	Large inter- and intra-patient variability

LP ratio Lactate:pyruvate ratio, *MD* microdialysis

critical care management of TBI and SAH. Since MD measures changes at the cellular level, it has potential to identify cerebral compromise before it is detectable clinically or by other monitored variables. Early detection of impending hypoxia/ischemia would also benefit in the intraoperative setting, but there is limited and only low-quality evidence to support the use of MD as a diagnostic tool during neurosurgery. The hourly sampling rate in the commercially available clinical system is unlikely to be sufficient for intraoperative monitoring. A continuous rapid-sampling cerebral MD technique has been described for research use, but is currently not available for clinical applications.

Near-infrared spectroscopy-monitored changes in the oxidation status of oxidized cytochrome *c* oxidase (CCO) have been validated in research settings as a noninvasive assessment of cerebral cellular energy status. CCO is the final electron acceptor in the mitochondrial electron transport chain and responsible for over 95% of oxygen metabolism. In association with NIRS-derived hemoglobin variables, monitoring CCO may aid in the noninvasive determination of ischemic thresholds in the injured brain. Developments in technology are likely to allow the introduction of a single NIRS-based device for monitoring absolute cerebral oxygenation, hemodynamics, and metabolic status at the bedside.

Electrophysiologic Monitoring

Several methods are available for monitoring electrophysiological changes during neurosurgery and neurocritical care (Table 5.5).

Electroencephalography (EEG) is a voltage-time recording of spontaneous cortical electrical activity measured from electrodes placed at specific locations on the scalp. The electrical signal is amplified, filtered, and displayed in multiple channels (usually eight per hemisphere) to give a continuous EEG recording that is analyzed in terms of frequency, amplitude, and location. Interpretation of the EEG is complex, but several automated EEG processing systems are available that allow bedside interpretation by non-experts. Processed EEG techniques, such as the bispectral index or entropy, have been developed to monitor depth of anesthesia, but their indications and application are not unique to neurosurgical anesthesia and are not considered here.

Reduction in CBF below 20 ml/100 g/min results in decreases in the frequency and amplitude of the EEG, which becomes flattened when CBF falls below 10 ml/100 g/min. Quantitative analysis of these changes has been used to monitor intraoperative cerebral ischemia in a variety of circumstances, most commonly to identify cerebral hypoperfusion necessitating shunt placement during carotid surgery. The electrocorticogram (ECoG) is the EEG measured directly from the cortical surface and used to identify the site of an epileptogenic focus during epilepsy surgery and afterdischarges (that can precipitate seizures) during mapping of eloquent areas with electrical cortical stimulation during awake craniotomy. Intraoperative EEG monitoring has several limitations as well as advantages (Table 5.6).

Continuous EEG (cEEG) monitoring is becoming more widespread during neurocritical care because of an increased awareness that nonconvulsive seizures are common in brain-injured patients. EEG monitoring should be undertaken in all patients with unexplained and/or persistently altered consciousness to exclude seizures as the cause of the neurological state. cEEG is a resource intense technology, but the development of automated seizure detection software is likely to facilitate its wider introduction into clinical practice. Spreading cortical depolariza-

Table 5.5 Indications for electrophysiologic monitoring

Monitored variable	Indications
EEG	Depth of anesthesia monitoring
	Epilepsy surgery
	Carotid surgery
	Seizure detection and monitoring
cEEG	Diagnosis and monitoring of nonconvulsive seizures
	Identification of cortical spreading depolarizations
EMG	Acoustic neuroma surgery
	Posterior fossa surgery
	Spine surgery
SSEP	Spine surgery
	Parietal cortex lesions
MEP	Spine surgery
	Motor cortex lesions
BAEP	V, VII, and VIIth nerve surgery
	Posterior fossa surgery
	Diagnosis of brainstem death
VEP	Pituitary and suprasellar surgery
	Retro-orbital lesions
	Occipital cortex lesions

EEG Electroencephalography, *EMG* electromyography, *SSEP* somatosensory evoked potential, *MEP* motor evoked potential, *BAEP* brainstem auditory evoked potential, *VEP* visual evoked potential

Table 5.6 Intraoperative electroencephalography monitoring

Advantages
Noninvasive
Continuous
Regional information
Correlates with reductions in cerebral blood flow and oxygenation
Identification of seizures
Identification of cerebral ischemia
Disadvantages
Trained neurophysiologist required for interpretation
Influenced by anesthetic agents
Influenced by systemic physiologic changes, e.g., hypothermia
Subject to artifacts from electrical and diathermy “noise”
Insensitive to subcortical changes

tions (SDs) are pathological events characterized by near-complete, sustained depolarization of neurons and astrocytes that result in secondary brain injury. They have been reported in 50–60% of TBI patients and were previously detectable only via electrode strips placed directly on the cortical surface. Recent data suggest that standard scalp cEEG may be able to detect SDs, offering the potential for routine monitoring of this important pathophysiological manifestation of ABI.

Electromyography (EMG) allows assessment of cranial and peripheral nerves via needle electrodes placed in or near specific muscles (Table 5.5). Spontaneous EMG records continuous muscle activity and triggered EMG muscle activity in response to direct stimulation of the nerve. Spontaneous EMG activity is detected if the nerve is touched or stretched during surgery, thereby alerting the neurosurgeon to the risk of imminent nerve damage. Seventh nerve monitoring is widely used during acoustic neuroma surgery. While muscle relaxants are best avoided during EMG monitoring, they can be used if the dose is carefully adjusted to maintain two strong twitches during train-of-four monitoring.

Evoked potentials (EPs) are the electrical response from the nervous system to an external stimulus and evaluate conduction along, and therefore the integrity of, neural pathways. They are interpreted in relation to the latency and amplitudes of the waveform peaks and troughs. For monitoring in the operating room, EPs are compared to initial baselines, whereas for diagnostic purposes on the intensive care unit, they are compared to normal control recordings.

SSEPs monitor the whole sensory pathway from specific peripheral nerves through the large Ia fibers in the dorsal column and then via the sensory thalamus to the sensory cortex. Cortical SSEPs are recorded from the cerebral cortex using scalp electrodes following electrical stimulation of a peripheral nerve, and subcortical responses from electrodes placed adjacent to the upper cervical spine. MEPs monitor the efferent motor pathways from the motor cortex via fibers in the internal capsule to the muscle through the largest 2% of axons in corticospinal or corticobulbar tracts. MEPs are generated during spine surgery following transcranial stimulation of the motor cortex with a high-voltage electrical source or using direct cortical electrical stimulation during craniotomy. The motor evoked responses are usually recorded as compound motor action potentials (CMAPs) in peripheral muscles (myogenic MEPs). MEPs progressing along the spinal cord can also be recorded from epidural/intrathecal electrodes or an electrode placed directly on the exposed spinal cord. There are two components to such responses – a direct wave (D-wave) which is the action potential generated in the corticospinal axons and indirect waves which are action potentials resulting from cortical activation of internuncial neurons. D-wave monitoring is used when the spinal cord is exposed, such as during intramedullary surgery, and usually in conjunction with myogenic MEPs. MEPs are recorded following a single, brief stimulation volley, whereas SSEPs require multiple stimulations and signal averaging to extract the EP from the background EEG.

EP monitoring is used during intracranial and spine surgery (Table 5.5) to localize critical neural structures in order to avoid intraoperative damage to them, particularly if normal anatomic landmarks are distorted by pathology. Spinal cord injury may occur during spine surgery because of ischemia secondary to spinal distraction and disruption of perforating radicular vessels or because of direct trauma during placement of pedicle screws or resection of intrinsic spinal cord lesions. MEPs are more sensitive to spinal cord ischemia than SSEPs and correlate better with motor function after spine surgery. SSEPs and MEPs are sensitive to anesthetic agents and SSEPs additionally to physiologic changes, such as hypotension and alterations in $PaCO_2$. Total intravenous anesthesia techniques with a high-dose opioid component are recommended, with the avoidance of muscle relaxants during myogenic MEP monitoring. Unlike the CMAP, the D-wave MEP involves no synapses, and therefore, anesthetics at normal concentrations have very little effect on them.

Cortical SSEPs may also be used to monitor cerebral ischemia during intracranial and carotid surgery. Visual evoked potentials monitor the visual pathways but are technically difficult and exquisitely sensitive to anesthetic agents. Lesions at different parts of the auditory pathway can be identified by changes in the amplitude or latency of one of the five waves that make up the complex brainstem auditory evoked potentials which are relatively resistant to anesthetic agents (Table 5.5).

Concerns and Risks

Avoiding, detecting, and treating cerebral and spinal cord ischemia are key factors in the intraoperative management of the neurosurgical patient. Neuromonitoring detects changes early so that the neuroanesthesiologist and neurosurgeon can intervene and minimize the risk of irreversible CNS damage and poor neurologic outcome.

Given the physiologic complexity of the brain and spinal cord, a single variable or single device is unable to provide adequate monitoring during neurosurgery or neurocritical care. Multimodality electrophysiologic monitoring during spine surgery is well-established and guides interventions that can minimize the risk of permanent neurologic injury. Although intracranial monitoring, including measures of cerebral perfusion, oxygenation, and metabolic status, is recommended during the management of brain-injured patients on the neurocritical care unit, many modalities are less suited

to the operating room. Currently, every monitor of cerebral perfusion and oxygenation has its own specific shortcomings, and none is a standard of care in the intraoperative period.

Key Points

- The neuroanesthesiologist plays a key role in protecting the brain and spinal cord from intraoperative ischemic injury by maintaining brain and spinal cord perfusion and oxygenation.
- Various monitoring modalities can be used to guide optimization of cerebral physiology during surgery and neurocritical care.
- Invasive and noninvasive monitors of cerebral oxygenation, hemodynamics, and metabolism are widely used during the neurocritical care management of brain-injured patients, but many do not translate well into the operating room.
- Multimodal electrophysiological monitoring techniques are established during complex spine surgery and guide interventions to prevent permanent neurologic injury.
- The ideal cerebral monitor would allow noninvasive, simultaneous measurement of cerebral oxygenation, hemodynamic, and metabolic status over multiple regions of interest.

Suggested Reading

Ghosh A, Elwell C, Smith M. Cerebral near-infrared spectroscopy in adults: a work in progress. Anesth Analg. 2012;115:1373–83.

Hutchinson PJ, Jalloh I, Helmy A, et al. Consensus statement from the 2014 International Microdialysis Forum. Intensive Care Med. 2015;41:1517–28.

Kirkman M, Smith M. Multimodality neuromonitoring. Anesthesiol Clin. 2016;34:511–23.

Kirkman M, Smith M. Intracranial pressure monitoring, cerebral perfusion pressure estimation, and ICP-CPP guided therapy: a standard of care or an optional extra after brain injury? Brit J Anaesth. 2013;112:35–6.

Lazaridis C, Andrews CM. Brain tissue oxygenation, lactate-pyruvate ratio, and cerebrovascular pressure reactivity monitoring in severe traumatic brain injury: systematic review and viewpoint. Neurocrit Care. 2014;21:345–55.

Le Roux P, Menon DK, Citerio G, et al. Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care: a statement for healthcare professionals from the Neurocritical Care Society and the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40:1189–209.

Citerio G, Oddo M, Taccone FS. Recommendations for the use of multimodal monitoring in the neurointensive care unit. Curr Opin Crit Care. 2015;21:113–9.

Shils J, Sloan T. Intraoperative neuromonitoring. Int Anesthesiol Clin. 2015;53:53–73.

Smith M. Multimodality neuromonitoring in adult traumatic brain injury: a narrative review. Anesthesiology. 2018;128:401–15.

Teasdale G, Maas A, Lecky F, Manley G, Stocchetti N, Murray G. The Glasgow coma scale at 40 years: standing the test of time. Lancet Neurol. 2014;13:844–54.

Assessing the Anesthetized State with the Electroencephalogram

6

George A. Mashour

Introduction

Although the brain is the target organ of anesthesia during surgery, standardized monitors for assessing the effects of anesthesia on the brain are notably lacking. There is great interest in understanding the potential of EEG for monitoring the brain during anesthesia, extending its clinical utility beyond the field of neurology. Such monitoring has the potential to improve neurologic outcomes, including reducing the risk of intraoperative awareness with explicit recall (hereafter referred to as "awareness") and enhancing postoperative cognitive recovery. Although promising, additional research is needed to establish EEG markers that accurately mirror level of consciousness and to determine whether EEG improves perioperative neurologic outcomes. To create an effective approach, a foundational understanding of how EEG reflects the neurophysiologic effects of anesthetics is required.

EEG Data Acquisition and Interpretation

Raw EEG

Scalp electrodes applied in standard locations continuously collect EEG data by detecting spikes in cortical microvoltages at various frequencies. These microvoltage spikes reflect postsynaptic voltage potentials from pyramidal neurons activated by cortical and thalamic sources. Voltage oscillation frequencies are commonly separated into gamma (26–80 Hz), beta (13–25 Hz), alpha (9–12 Hz), theta (5–8 Hz), delta (1–4 Hz), and slow-wave (<1 Hz) bandwidths, with many bandwidths contributing to the overall EEG waveform in states of consciousness and unconsciousness. Fourier transformation—represented as an EEG spectrogram with time on the x-axis, frequency on the y-axis, and power on the z-axis (or through a colored "heat map")—can deconstruct complex waveforms into individual frequency components. Indeed, this transformation permits simple analysis of frequency bandwidth power for any EEG segment.

EEG patterns differ among classes of anesthetics. For example, propofol largely exhibits alpha, delta, and slow oscillations on the raw EEG (Fig. 6.1a) under conditions of general anesthesia, with high power noted in the frequency bandwidths on the corresponding spectrogram (Fig. 6.1b). Raw EEG patterns similar to propofol occur in response to ether-based volatile anesthetics, such as isoflurane, sevoflurane, and desflurane. The ether-based volatile anesthetic pattern is characterized by alpha, theta, delta, and slow oscillations (Fig. 6.1a), with the spectrogram showing high power in the bandwidths and increased theta power compared to propofol (Fig. 6.1b). Halogenated ethers and propofol share similar neurophysiologic traits with non-rapid eye movement (NREM) sleep. For example, sedation by propofol and NREM sleep are associated with coherent oscillatory spindle activity, which likely indicates disruption of thalamocortical processing, and with asynchronous slow-wave oscillations, suggesting fragmented cortical connectivity. In contrast to the lower-frequency patterns induced by propofol and ether-based volatile agents, ketamine anesthesia is associated with elevated beta and gamma oscillatory activity on the raw EEG (Fig. 6.1a), with increased power in the gamma range near 30 Hz (Fig. 6.1b). Finally, dexmedetomidine sedation increases slow oscillations in a way similar to sleep (Fig. 6.1b). EEG in both the time and spectral domain can be accessed through current neuromonitoring regimens employed during major neurosurgical interventions for the spine and brain. For cases without neuromonitoring and amenable to frontal EEG electrodes, many processed EEG modules display spectral properties.

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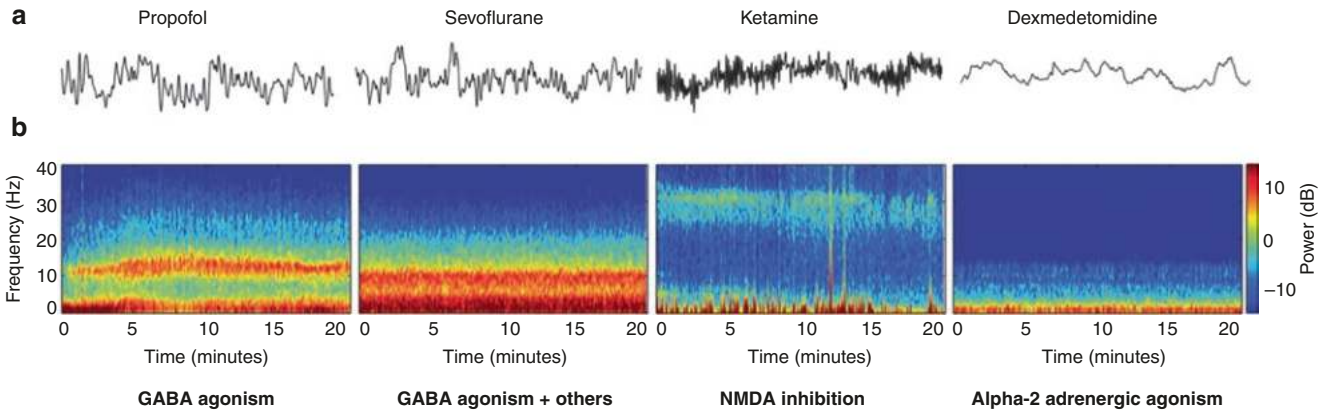

Fig. 6.1 Comparison of raw EEG and spectrogram patterns among different anesthetic classes. (**a**) Raw EEG patterns are displayed for each anesthetic class represented. Faster frequencies are appreciated with ketamine compared to other anesthetics. (**b**) Each anesthetic drug class corresponds to a specific spectrogram signature, which may reflect nuances in molecular and circuital properties in each class. (Reproduced with permission: Purdon et al. 2015)

Processed EEG

There are many portable systems that permit intraoperative EEG monitoring (Table 6.1), with Bispectral Index (BIS) and SEDLine monitors in common use. For these systems to capture and display raw and processed EEG data, electrode channels, or montages, are applied to the foreheads of patients. Processed EEG data, in this situation, utilizes a proprietary multivariable algorithm to acquire, integrate, analyze, and convert raw EEG data into a dimensionless number that reflects the depth of anesthesia. As one example of readout among systems, values ranging from 40–60 to 20–50 indicate a similar depth of general anesthesia in the BIS and SEDLine monitors, respectively. However, processed EEG data is not without limitations, which will be described below.

Table 6.1 Commercially available processed EEG systems

Monitor	Data and display features	Index range for general anesthesia
Bispectral index (BIS)	Raw EEG, processed values:	40–60
	BIS index	
	Spectral analysis	
SEDLine	Raw EEG, processed values:	25–50
	Patient state index (PSI)	
	Spectral analysis	
Narcotrend	Raw EEG, processed values:	D, E; 40–60
	EEG stage (A-F)	
	Narcotrend index	
	Spectral analysis	
Entropy module	State entropy (EEG-based), response entropy (EMG-based)	40–60
IoC-view	Raw EEG, processed values:	40–60
	IoC index	
	EEG suppression ratio	
SNAP II	High-frequency (80–240 Hz) and low-frequency (0–18 Hz) EEG analysis, processed SNAP index	50–65
NeuroSENSE	Raw EEG, processed values:	40–60
	Wavelet-based (WAV_{CNS}) index	
	Spectral analysis	

Number range reportedly consistent with general anesthesia for each device

EEG Electroencephalogram, *IoC* index of consciousness, *EMG* electromyogram

Clinical Utility of Raw and Processed EEG

Major randomized controlled trials on processed EEG have focused primarily on the role of the Bispectral Index monitor in preventing awareness. Comparative effectiveness trials have not revealed a reduced risk of awareness with processed EEG monitoring compared to end-tidal anesthetic concentration monitoring. However, processed EEG monitoring reduces the incidence of awareness compared to routine care and monitoring, and it may be beneficial in situations where anesthetic concentration is not an option, and there is increased risk of awareness, such as during total intravenous anesthesia. One potential reason is that, by using processed EEG, the depth of anesthesia was not informed by direct neurophysiologic assessment. A challenge with this approach is that index values do not capture the diverse neurophysiologic properties of anesthetics. For example, ketamine and nitrous oxide produce higher processed EEG values because they increase EEG oscillation frequency. Another potential factor preventing EEG from reducing awareness is the fact that the current generation of perioperative brain monitors was not developed with a sophisticated understanding of the neurobiology of consciousness. EEG-based markers, including disruption of corticortical and thalamocortical connectivity, might 1 day inform causally sufficient mechanisms that promote unconsciousness. However, the neuroscientific

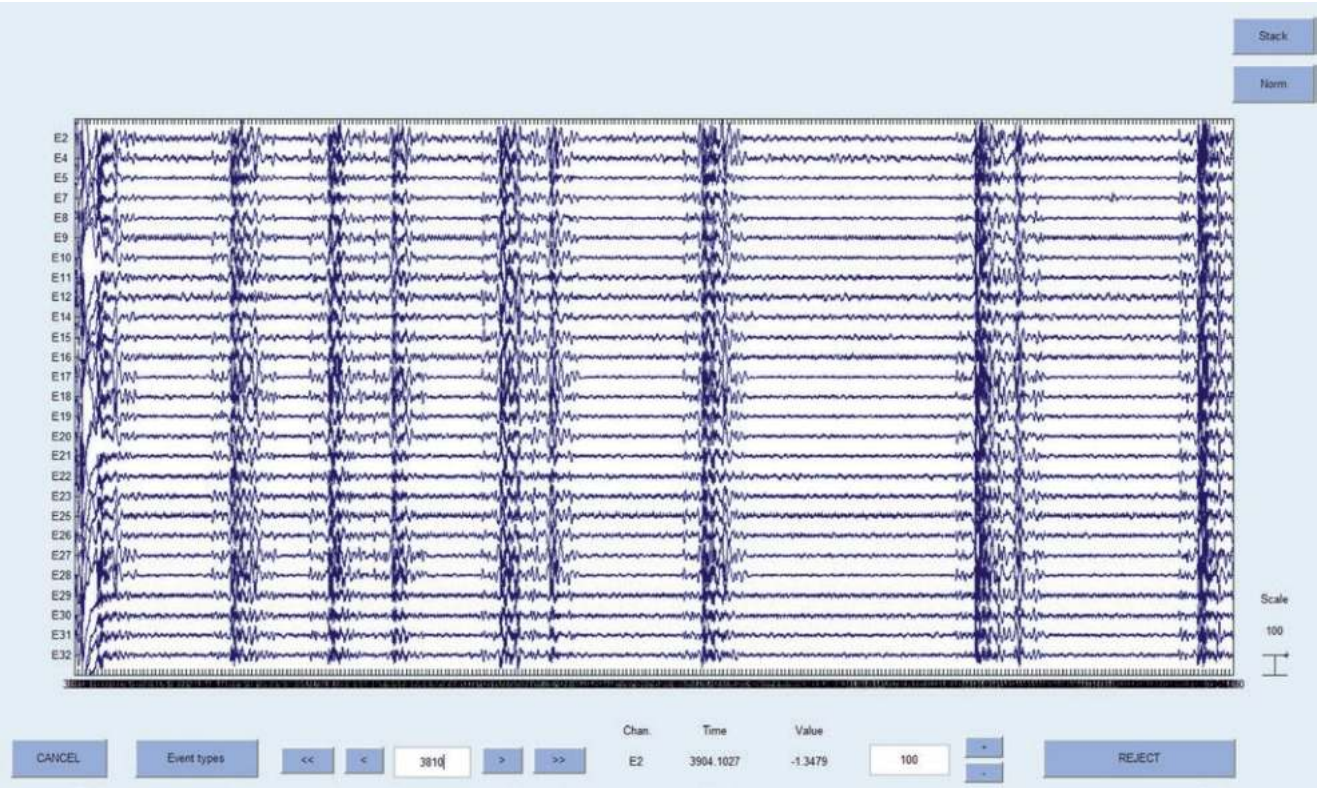

Fig. 6.2 Burst suppression illustrated on continuous EEG data. Note periods of high-frequency, high-amplitude activity followed by relative electrical quiescence. The "burst suppression" ratio is often used as a metric of this pattern and is defined by the percentage of total time in suppression/epoch length; a burst suppression ratio of 1, for example, would represent continuous suppression

framework underlying consciousness is not entirely understood, making it difficult to interpret a single number meant to represent a patient's state of arousal. The ability to accurately determine level of consciousness necessitates a deeper neurophysiologic understanding of consciousness and mechanisms of action of anesthesia.

In addition to its utility in preventing awareness, EEG may guide the titration of anesthetic depth by permitting detection of burst suppression, which is a pattern of electrical bursts interspersed with electrical silence (Fig. 6.2). Burst suppression patterns do not occur during normal sleep and likely indicate supratherapeutic levels of general anesthesia. Postoperative delirium correlates with extended periods of intraoperative and postoperative burst suppression, and a recent meta-analysis of prospective trials showed a reduced risk of postoperative delirium with BIS-guided protocols. There are specific clinical scenarios in which achieving burst suppression by titrating depth of anesthesia may be beneficial. One example is cerebral aneurysm clipping, where burst suppression may decrease the risk of ischemic injury by reducing cerebral metabolism (although this has not been definitively demonstrated).

An additional clinical use for both raw continuous (cEEG) and quantitative EEG (qEEG) findings is in assisting with the detection of cerebral ischemia in high-risk settings. When cerebral blood flow (CBF) declines below defined ischemic thresholds, cortical voltage oscillations decrease in frequency as the result of ischemic damage to neurons, which require high oxygen and glucose to maintain electrochemical gradients across cellular membranes. Unique EEG patterns represent frequency slowing, as evidenced intraoperatively during carotid endarterectomy (CEA) where irregular delta waveforms are elicited in response to asymmetric oscillatory slowing. In addition, qEEG markers, including spectral edge frequencies and relative delta band power, help identify ischemia after carotid clamping during CEA. Postoperatively, cEEG and qEEG can predict cerebral ischemia in some pathologic settings, including vasospasm after subarachnoid hemorrhage. Cerebral ischemia can be acutely diagnosed by cEEG when pathologic delta patterns and regional attenuation of faster frequencies, in the absence of delta waves, are noted. qEEG markers that predict cerebral ischemia include reduced total power and decreased relative alpha frequency variability. A benefit of these quantitative markers of EEG is that they can be interpreted in the absence of continuous EEG surveillance and specific expertise (Fig. 6.3).

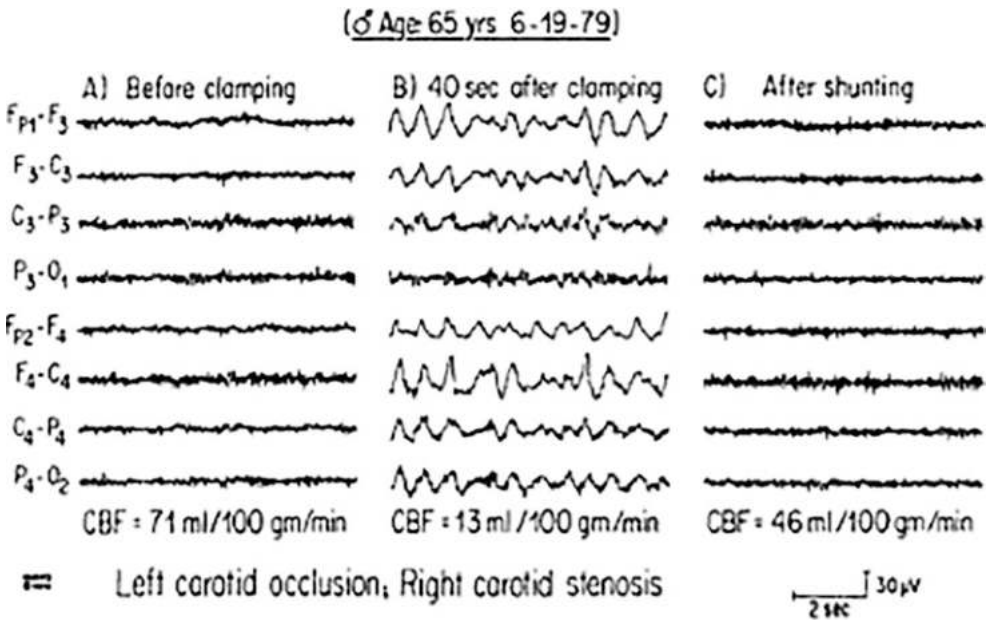

Fig. 6.3 Frequency slowing noted after clamping of the right carotid artery during endarterectomy. Irregular, delta-wave activity is appreciated with attenuation of faster frequencies. Changes are more pronounced on the right, which is the side of clamping. EEG waveforms return to baseline after shunt is placed. (Reproduced with permission from Dr. Don Schomer and Dr. Fernando Lopes da Silva, *Niedermeyer's Electroencephalography: Basic Principles, Clinical Applications, and Related Fields*, Fifth Edition)

Future Directions of EEG Monitoring

There is a need for a deeper understanding of both the neurobiology of consciousness and the mechanisms underlying the effects of anesthesia on the brain, both of which may be revealed using current EEG approaches. Current EEG monitors show indices that are empirically derived by comparing the awake and anesthetized EEG; however, it is unclear whether the differences are due to changes that are critical for the anesthetic suppression of consciousness.

One approach that is more principled seeks signatures on the EEG that are drug specific by linking neural systems-level effects of anesthetics to network-level oscillations. For instance, a strong alpha oscillation occurs in the frontal spectrogram when propofol is administered to healthy adults; this outcome may be due to a GABAergic effect in the nucleus reticularis of the thalamus, resulting in highly coherent thalamofrontocortical signaling loops. In contrast to propofol, frontal spectrograms following ketamine administration reveal slow oscillations and high-frequency gamma activity, with gamma activity potentially due to the antagonist effects of NMDA on GABAergic interneurons. These entrained oscillations might disrupt the typically flexible repertoire of connectivity and communication across the cortex. However, ketamine does not induce increased alpha oscillations, possibly due to weak GABAergic properties.

Despite the molecular and neurophysiologic differences among propofol, sevoflurane, and ketamine, all three drugs consistently inhibit communication between anterior and posterior brain regions. Disruption of information synthesis in the brain is a candidate as the proximal mechanism for anesthetic-induced unconsciousness. This heralds the possibility of another principled approach to EEG and intraoperative monitoring through the analysis of how neural correlates of consciousness are suppressed by general anesthetics. Current data suggest that conscious experience is dependent on integration of neural information that, if interrupted, disturbs or eliminates conscious processing. EEG can be used to assess surrogates of both connectivity and communication. For example, coherence and phase synchronization can gauge functional connectivity, which is the statistical interdependence between two areas of the brain, and transfer entropy and Granger causality can determine directed connectivity, which is statistical interdependence that unfolds over time. Additionally, dynamic casual modeling is used as a surrogate of the casual influence of one region of the brain on another, also known as effective connectivity. In the case of general anesthesia, these techniques reveal that long-range functional connections and surrogates of communication become degraded, an effect common across the major classes of anesthetics and a possible mechanism for the breakdown in consciousness. However, it should be noted that the literature assessing these models is not entirely straightforward. Thus, while identifying drug-specific signatures may link anesthetic mechanisms to EEG features, state-specific signatures common across drugs are based on and also may inform neural correlates of consciousness. The latter approach requires additional development and refinement before it will be useful for routine and real-time intraoperative monitoring. That being said, the implementation of a drug-invariant approach should help to effectively identify both the breakdown and return of consciousness in the operating room in addition to disruptions of consciousness in the

postoperative period, such as delirium. Importantly, the utility of these techniques in monitoring the sedative-hypnotic effects of general anesthetics will likely not extend to monitoring amnesic effects, which are mediated primarily by structures in the medial temporal lobe.

Discussion

EEG is a valuable tool for surgical patients in a variety of clinical settings. Currently, we need a better understanding of the neural correlates of consciousness in order to identify valid neurophysiologic markers of general anesthesia. This deficit in knowledge may be the reason why processed EEG monitors do not reduce the incidence of awareness compared to end-tidal anesthetic monitoring protocols. Regardless, EEG monitoring may have utility in other important clinical areas, including the prevention of harmful neurologic outcomes associated with surgery and anesthesia. For instance, using EEG to detect burst suppression and inform titration of anesthesia may reduce the risks of postoperative cognitive dysfunction and postoperative delirium, a theory that needs to be substantiated though larger, multicenter trials. Postoperative cognitive dysfunction correlates with the length of burst suppression and deeper planes of anesthesia, but it is unclear whether this has causal significance or whether burst suppression indicates a vulnerable brain. In addition, EEG monitoring detects cerebral ischemia in specific surgical and intensive care settings and, with further study, has the potential to recognize cerebral ischemia and prevent perioperative stroke in high-risk settings. Techniques for studying the brain are evolving, new discoveries continue to enhance our understanding of the central nervous system, and anesthesiologists are able to monitor and modulate the brain as our foundational scientific understanding increases.

Key Points

- Raw EEG waveforms and spectrogram patterns help reflect the neurophysiologic effects of various anesthetics.
- Compared to end-tidal anesthetic concentration monitoring protocols, processed EEG monitoring does not reduce the risk of awareness with explicit recall.
- The risk of cognitive dysfunction (such as delirium) following surgery may potentially be minimized by using EEG to inform depth of anesthesia; findings need to be confirmed with large pragmatic trials.
- Numerous EEG markers reflecting cerebral ischemia show frequency slowing, decreased power and variability of faster frequencies, and increased regional asymmetry.

Suggested Reading

Avidan MS, Mashour GA. Prevention of intraoperative awareness with explicit recall: making sense of the evidence. Anesthesiology. 2013;118:449–56.

Avidan MS, Jacobsohn E, Glick D, Burnside BA, Zhang L, Villafranca A, Karl L, Kamal S, Torres B, O'connor M, Evers AS, Gradwohl S, Lin N, Palanca BJ, Mashour GA. Prevention of intraoperative awareness in a high-risk surgical population. N Engl J Med. 2011;365:591–600.

Chan MT, Cheng BC, Lee TM, Gin T. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. J Neurosurg Anesthesiol. 2013;25:33–42.

Lee U, Ku S, Noh G, Baek S, Choi B, Mashour GA. Disruption of frontal-parietal communication by ketamine, propofol, and sevoflurane. Anesthesiology. 2013;118:1264–75.

Purdon PL, Sampson A, Pavone KJ, Brown EN. Clinical electroencephalography for anesthesiologists: part I: background and basic signatures. Anesthesiology. 2015;123:937–60.

Part II

Preoperative Concerns of the Neuroanesthesiologist

Cardiovascular Risk and Instability: Evaluation, Management, and Triage

7

Justin D. Ramos and Jeffrey R. Kirsch

Overview

The cardiovascular system interacts with the neurologic system on many levels. This has implications for disease states in both systems. Therefore, when treating patients with neurosurgical disease, the provider must consider and be prepared to address pathological changes and consequences of treatment in the cardiovascular system. In the USA alone, approximately one of five persons has been diagnosed with some form of cardiovascular disease, and 40% of these patients are 65 years of age or older. With the progressive increase in life expectancy, the percentage of patients with significant cardiovascular disease and a comorbid neurological condition is also expected to increase.

Implications for the Neurosurgical Patient

Neurologic Injury and Cardiac Dysfunction

Cardiac disease in the neurosurgical population increases the overall morbidity and mortality. In patients who have suffered a cerebrovascular accident or neurologic injury (e.g., traumatic brain injury, brain tumor, and subdural hematoma), cardiac manifestations may include EKG changes, cardiac arrhythmias, neurogenic cardiomyopathy, as well as neurogenic pulmonary edema.

EKG changes are very common in patients with neurologic injuries and occur in 49–100% of cases, with higher incidence in patients suffering from intracerebral or subarachnoid hemorrhage and lower incidence in patients with ischemic stroke. These changes may consist of sinus tachycardia, sinus bradycardia, large inverted T waves, prolonged QT intervals, ST segment changes, or large U waves. Arrhythmias ranging from bradycardia to fatal ventricular fibrillation are also seen in the acute period following onset of stroke symptoms.

Following subarachnoid hemorrhage (SAH), hypothalamic stress leads to a massive release of catecholamines. In addition to EKG changes and hypertension, left ventricular dysfunction is present in 10–20% of patients with SAH. Neurogenic cardiomyopathy is commonly described in SAH, which is also referred to as stress-induced or "Takotsubo" cardiomyopathy. Female gender, poor-grade SAH, and a history of stimulant drug use are risk factors for stress-induced cardiomyopathy, and the vast majority of patients will have elevation of troponins. EKG changes consistent with myocardial ischemia should prompt further evaluation, and if there is concern for STEMI or a high-risk NSTEMI, percutaneous coronary intervention (PCI) should be considered if not contraindicated (e.g., life-threatening hemorrhage). The typical patient with neurogenic cardiomyopathy will not have obstructive coronary lesions on angiography, and echocardiography would demonstrate an apical ballooning pattern or wall motion abnormalities in multiple vascular territories, which is considered a hallmark of neurogenic cardiomyopathy. Therapy is supportive, as the syndrome is self-resolving over several days to weeks. It is reasonable to avoid further exposure to exogenous catecholamines, and clinicians may consider alpha and beta blockade in patients who are not hypotensive or hemodynamically unstable.

Neurosurgical Patients and Anticoagulation

Pharmacological and Physiological Risks for Bleeding Patients with neurosurgical disorders are often older and, therefore, can have disease processes that require anticoagulation for management. These typically originate from the cardiovascular system and include atrial fibrillation, thromboembolism, or atherosclerotic manifestations like carotid artery disease. The use of antithrombotic agents has increased over the past decade and is expected to continue to rise.

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Anticoagulant therapy can cause spontaneous bleeding. Listed below are several classes of pharmacological agents with representative drugs that can cause bleeding.

- Antiplatelet agents: Acetylsalicylic acid (ASA), clopidogrel (Plavix), and abciximab (Rheopro)
- Heparins: Unfractionated (no trade name, usually from pork intestine); low-molecular-weight heparins (LMWHs) – enoxaparin (Lovenox), dalteparin (Fragmin)
- Inhibitors of vitamin K-dependent coagulation factors: warfarin (Coumadin) with a half-life of 36–42 h
- Direct thrombin inhibitors: Lepirudin, bivalirudin, argatroban, dabigatran (Pradaxa)
- Direct factor Xa inhibitors: Rivaroxaban (Xarelto), apixaban (Eliquis), edoxaban (Savaysa)
- Fibrinolytic agents: Tissue-type plasminogen activator (tPA).

In addition to these pharmacological risks, patients may present with congenital clotting defects (e.g., von Willebrand's disease, hemophilia). Further, patients with unrelated diseases may be prescribed pharmaceuticals with anticoagulant properties and/or have interactions with other drugs that act to change the patient's coagulation status (i.e., drug–drug, drug–food, and drug–genomic interactions). In addition, patients with severe liver disease may manifest increased bleeding tendency due to decreased synthetic function of the liver with reduced production of coagulation factors. Patients who have a malignancy may have antibodies to clotting factors and/or to platelets or have a consumptive coagulopathy and present with excessive bleeding (in addition to their neurologic disease).

Assessing Coagulation Status Coagulation status is most commonly determined by measuring the international normalized ratio (INR) of the prothrombin time (PT) test, which indicates function of vitamin K-dependent coagulation factors and the synthetic function of the liver. Generally, an INR value <1.2 is considered normal. If INR is >1.4 in the setting of serious hemorrhage, treatment of coagulopathy or reversal of anticoagulation may be indicated as outlined below. Fibrinogen levels can also be useful in assessing the coagulation status of the perioperative neurosurgical patient since fibrinogen is the main "building block" of clot. Normal fibrinogen levels range from 150 to 400 mg/dL, and a fibrinogen level <150 mg/dL in the setting of serious bleeding may warrant further evaluation of coagulopathy and transfusion of cryoprecipitate. The activated partial thromboplastin time (APTT) test helps to assess the effectiveness of unfractionated heparin (UFH). Normal values range from 25 to 35 seconds, and therapeutic ranges of APTT while anticoagulated with UFH may be 70–120 seconds, depending on the clinical situation. In addition, Factor Xa levels may help to assess the effectiveness of LMWHs, although this test is not commonly used.

Unfortunately, it is somewhat difficult to get a quick evaluation of platelet function in patients on antiplatelet agents. A normal platelet count does not ensure normal platelet function. Lancet-induced bleeding time is also not a good predictor of platelet function. There are specialized tests to evaluate platelet function, but these are generally not readily available. Examples are flow cytometry, thromboelastography (TEG), and Sonoclot evaluations.

D-Dimer is a test that helps to assess the presence of a hypercoagulable state, which may be present in some stroke patients. There are two main types of stroke: ischemic (85% of all strokes) and hemorrhagic (15%). Ischemic stroke occurs when an obstruction in the arterial system causes ischemia in the brain. Hemorrhagic stroke occurs when a vessel ruptures and bleeds into the brain or into the subarachnoid space (when a large vessel ruptures). In hemorrhagic stroke patients, coagulation increases when fibrinogen is converted to fibrin to form a clot. This process yields fibrin degradation products, and a positive D-dimer test signals a high level of these products in the plasma. (It should be noted that D-dimer is a nonspecific test and may also be elevated following surgery, liver disease, heart disease, and cancer.)

Many more specialized tests are available and may be ordered by a hematologist when caring for a complicated patient. For a patient who requires reversal of anticoagulation, the general approach is to first elucidate the level of anticoagulation and define the mechanism of anticoagulation. Normally, all common coagulation tests (INR, APTT, CBC including platelet count, fibrinogen, and D-dimer) are performed simultaneously to expedite the diagnosis. In the acute patient, more advanced coagulation investigations may not be available in a timely manner, since more sophisticated blood tests require longer processing times.

Treating Coagulation Disorders Treatment for coagulation defects in neurologically impaired patients targets specific deficiencies that persist after stopping anticoagulant therapy. For bleeding patients with platelet dysfunction, platelets should be transfused. This is also recommended for patients with a normal platelet count when platelet dysfunction is suspected. The target value for platelet count is 50,000 for patients scheduled for surgery or for patients with hemorrhage that could be life-threatening. The usual recommended dose is 1 U of platelets per 10 kg body weight. One unit of platelets will increase the platelet count by $5–10 \times 10^9$/L. One unit of platelets is 5×10^{10} platelets in 50–70 mL plasma; typically, 5–10 U (random donor platelets) are pooled in one component bag for ease of administration. Apheresis platelets (from a single donor) may also be used and contain $3–5 \times 10^{11}$ platelets in 200–400 mL plasma, equivalent to 4–6 U of platelets. Platelet transfusion is also the treatment of choice for reversal of antiplatelet agents such as clopidogrel.

Desmopressin (DDAVP) at a dose of 0.3 μg/kg intravenously can also be attempted to improve coagulation in patients on antiplatelet agents or those who are diagnosed with mild to moderate von Willebrand's disease or hemophilia A. DDAVP releases factor VIII and von Willebrand factor and is a manufactured analog of vasopressin without its vasoconstrictive effects. However, like vasopressin, DDAVP causes antidiuresis and could be associated with congestive heart failure in patients with poor cardiac function. Therefore, smaller doses of DDAVP (e.g., 0.15 μg/kg IV) should be considered for elderly patients and patients with cardiovascular diseases.

Unfractionated heparin has an antidote in protamine. The usual dose is 1 mg protamine (IV) for each 100 U of heparin given. This dose is reduced by 50% (i.e., 0.5 mg protamine for each 100 U of heparin) at 60–120 min after heparin has been discontinued. The recommended rate of administration is 5 mg protamine per minute. Intravenous protamine can cause hypotension via histamine release as well as more severe reactions such as anaphylaxis and, very rarely, catastrophic pulmonary vasoconstriction (resulting in pulmonary hypertension and vascular collapse). In patients with significant neurologic disease, treatment of these protamine reactions should be primarily supportive, with standard approaches ranging from small boluses of intravenous fluid and intravenous ephedrine (or phenylephrine) to treat hypotension up to full treatment of anaphylaxis with intravenous fluids, epinephrine, anti-histamines (H1 and H2), and possibly steroids and intubation, if indicated. Subcutaneous heparin for prophylaxis of deep vein thrombosis (DVT) is usually not reversed. LMWHs, unfortunately, cannot be fully reversed by protamine. However, some authors recommend 1 mg of protamine (IV) for each milligram of enoxaparin administered over the previous 4–8 h.

Anticoagulation by inhibitors of vitamin K-dependent pathways can be reversed by administering vitamin K, either intravenously (risk of anaphylaxis and hypotension) or subcutaneously. In non-life-threatening situations, the recommended dose of vitamin K is 1–2 mg. For life-threatening situations, the recommended dose is 10 mg vitamin K, which accelerates the onset of effect and also presents a higher risk of complication. The higher dose is also associated with some difficulty in subsequent titration of anticoagulation; however, in the case of brain hemorrhage, this becomes a secondary concern. Vitamin K should not be used as sole treatment to reverse anticoagulation in intracranial hemorrhage because it takes hours to normalize INR. In vitamin K antagonist-associated intracranial hemorrhage with INR >1.4, a 4-factor or 3-factor PCC (prothrombin complex concentrate) should be administered intravenously (IV) to rapidly reverse INR and improve coagulation. Dosing should be based on weight or actual INR with an INR goal. Typical doses are 15–50 U/kg. In randomized trials, treatment with prothrombin complex concentrates demonstrated equivalent hemostasis, more rapid correction of INR, and less volume overload when compared to reversal with fresh frozen plasma. When PCC is not available, fresh frozen plasma (FFP) should be infused at 15–20 mL/kg. However, administration of FFP increases the risk for anaphylaxis, bloodborne diseases (e.g., HIV, hepatitis), and fluid overload, with subsequent heart failure, because of the large amount of FFP that may be required to achieve the desired level of improved coagulation. Adverse thrombotic events are a risk of treatment with both PCC and FFP.

Direct factor Xa inhibitors (i.e., rivaroxaban, apixaban, edoxaban) prevent factor Xa-dependent conversion of prothrombin to thrombin. These medications are associated with increased risk of intracranial hemorrhage, although studies suggest that the risk of intracranial hemorrhage is lower with oral direct factor Xa inhibitors than with warfarin. In minor, non-life-threatening hemorrhage, discontinuation of the medication may be sufficient due to relatively short half-life. However, intracranial hemorrhage and major bleeding warrant pharmacologic reversal. After a careful history regarding the last dose of medication, reversal with 4-factor PCC (50 U/kg) or activated PCC (50 U/kg) is recommended when intracranial hemorrhage occurred three to five terminal half-lives of drug exposure or in liver failure. Activated charcoal (via a nasogastric or oral gastric tube) may be considered in patients who present within 2 h of last dose ingestion and are intubated with enteral access or considered low aspiration risk. Recombinant factor VIIa is not recommended due to potentially increased adverse thrombotic events.

Direct thrombin inhibitors (e.g., argatroban, dabigatran) can also be reversed by 4-factor PCC (50 U/kg, IV) or activated PCC (50 U/kg, IV) if last drug exposure was within three to four terminal half-lives or in renal failure. Idarucizumab (Praxbind) is a humanized antibody to dabigatran. Approved by the FDA in 2015, idarucizumab has been shown to be an effective and immediate antidote in dabigatran-associated hemorrhage. If idarucizumab is not available, hemodialysis is recommended in life-threatening hemorrhage associated with direct thrombin inhibitor (DTI) anticoagulation.

Recombinant-activated factor VII is currently being investigated as an IV treatment for coagulopathy. The FDA indication for clinical administration of recombinant-activated factor VII is bleeding associated with hemophilia and antibodies to factors VIII or IX. A wide range of doses has been tested, but the typical dose is approximately 90 μg/kg. Off-label recombinant-activated factor VII has been used in a variety of clinical bleeding scenarios, including neurosurgical bleeding, with varied results. It may have some efficacy in the reversal of LMWH.

Fibrinolytic agents such as tPA can be reversed by 6–8 U of platelets or cryoprecipitate (six to eight doses)

that contains factor VIII. Congenital clotting defects and bleeding are best managed with the help from an experienced hematologist.

Hypertension and Neurosurgical Disease

Many neurosurgical disease states such as intracerebral hemorrhage, ischemic neurological injury, and carotid artery disease are affected by the blood pressure. Finding an optimal level of blood pressure depends on many factors including severity of chronic hypertension, patient age, and impairment of intracranial compliance (e.g., patients with elevated ICP). Blood pressure control may be particularly critical in patients with (or at risk for) hemorrhage in areas that place neurologic tissue at risk for further injury (e.g., brain or spinal cord).

For individual patients with neurologic injury, the optimal blood pressure range is often difficult to establish. Ideally, the blood pressure range would allow for optimal cerebral perfusion without placing the patient at risk for cerebral hemorrhage or edema. This can be difficult to demonstrate since CT and MRI – the usual scanning methods – are static exams and are impractical for providing information over time. More advanced studies such as PET scanning can give more insight but are not readily available. One study in stroke patients shows a U-shaped blood pressure curve with increased mortality for patients presenting with blood pressures greater than 220/111 or less than 100/61. Hypotension is rare in patients in the acute setting of stroke. When hypotension is observed in this population, potential etiologies include aortic dissection, dehydration, blood loss, sepsis, and decreased cardiac output. If hypotension is noted, immediate steps should be taken to correct the hypotension and to identify and treat the underlying cause.

Hypertension is more commonly seen in the acute setting following stroke, and the possible etiologies include acute stress, pain, hypoxia, and increased ICP. For patients with intracerebral hemorrhage, the 2015 AHA/ASA guidelines suggest a target systolic blood pressure less than 140 is safe (class 1, level a) and can be effective for improving functional outcome (class 2a, level b). First-line antihypertensives should be agents that are unlikely to inadvertently raise ICP (e.g., labetalol, nicardipine, esmolol, and enalapril). Significantly increased ICP can manifest as severe impairment following acute stroke, severe hypertension, bradycardia, decreased level of consciousness, and abnormal respirations (i.e., Cushing's reflex). Since these findings are often premorbid, it is critical that the clinician define the nature of the intracranial pathology and treat appropriately. Great caution must be used in administering direct vasodilators to control blood pressure (e.g., nitroprusside and nitroglycerin) as these drugs may cause reduced cerebral perfusion and increased ICP with worsening of neurologic injury.

Acute Ischemic Stroke Treatments

Current treatments for acute ischemic stroke include intravenous recombinant tPA and intracranial endovascular neurointerventional treatments (i.e., intra-arterial thrombolysis or mechanical clot extraction) that can be performed under local or general anesthesia. Blood pressure management is key, and systolic BP must be lowered and stabilized to <185 mmHg and diastolic blood pressure to <110 mmHg for a patient to be eligible for IV rtPA or intra-arterial thrombolysis. While evaluating a patient prior to a neurointerventional procedure, important considerations include assessment of the patient's level of consciousness, cooperation, and noting any significant hypotension or hypertension. Both general anesthesia and local anesthesia with sedation are feasible. The advantages of general anesthesia include a motionless patient and control of oxygenation and ventilation with a protected airway. Potential disadvantages include possibly increased hypotension, higher frequency of hyperventilation (reduced $PaCO_2$ and reduced cerebral blood flow), increased risk of respiratory complications, and concerns about anesthetic neurotoxicity. A sedation approach may allow for ongoing neurologic examinations and potentially less hypotension; however, there is a risk of aspiration with an unprotected airway, and sedation may not be appropriate in patients with severe deficits. Retrospective studies have found an association between type of anesthesia and outcomes in patients undergoing treatment for acute ischemic stroke. General anesthesia was associated with poorer functional outcome and increased mortality when compared to local anesthesia with sedation. However, patients receiving general anesthesia tended to have more severe stroke symptoms, and to date there are no prospective, randomized trials.

Cerebral Vasospasm

Following subarachnoid hemorrhage or severe head injury, many patients develop acute cerebral vasospasm causing delayed cerebral ischemia in the period 4–14 days after aneurysm rupture. The current treatment principle is to keep the cerebral perfusion pressure (CPP) above 60–70 mmHg by managing the patient with fluids and vasopressors to ensure adequate perfusion. Following aneurysmal subarachnoid hemorrhage, many centers employ a strategy of pharmacologically induced hypertension and hypervolemia in hopes of facilitating improved cerebral perfusion and preventing delayed cerebral ischemia. The risks of hypertension-related bleeding must be balanced with maintenance of cerebral perfusion pressure. This approach may also place the patient at risk for myocardial dysfunction (an imbalance between myocardial oxygen consumption and supply) and congestive heart failure.

Concerns and Risks

Electrocardiographic changes may reflect myocardial processes caused by sympathetic stimulation associated with neurosurgical bleeding, even in patients with no organic ischemic cardiac disease. To ensure optimal oxygen delivery to the brain, support of circulation must be initiated when cardiac dysfunction leads to decreased cerebral oxygenation and perfusion. With appropriate hemodynamic monitoring (e.g., invasive arterial pressure, central venous pressure, and possibly pulmonary artery pressure) to guide therapy, standard treatment with inotropes may be necessary for low cardiac output states that have been confirmed by clinical exam and supporting investigations such as echocardiography. Anti-arrhythmics are indicated for hemodynamically significant arrhythmias. These treatments are started in all patients when indicated. A cardiac workup can then be performed to separate the patients with true underlying cardiac disease from patients with only temporary cardiovascular manifestations resulting from their acute neurological condition.

Anticoagulation therapies can worsen the outcome of the neurosurgical process and must often be discontinued after carefully weighing the risk/benefit ratio of continued anticoagulation vs. discontinuation. Patients are placed on anticoagulation treatment for a variety of reasons, and some indications may be weaker than others. For example, some biological cardiac valve prostheses may not need more aggressive anticoagulation than aspirin; on the other hand, cardiac stents require more intensive anticoagulation therapy, and discontinuation would place the patient at risk for catastrophic stent thrombosis – in BMS (bare metal stents) especially the first month and in DES (drug-eluding stents) especially the first year. These treatment decisions are best made in consultation with a cardiologist.

In acute ischemic strokes, acute lowering of the blood pressure may decrease the risk for hemorrhagic transformation (cerebral hemorrhage after an ischemic stroke) and cerebral edema; however, actively lowering the blood pressure can worsen neurological injury by increasing the ischemia in the penumbra (the zone of reversible ischemia surrounding the infarct) because of inadequate driving pressure through a stenosis. In contrast, a blood pressure that is too high can cause increased edema and increased bleeding, especially in patients with ruptured aneurysms or arteriovenous malformations who are at risk for rebleeding.

Consideration should be given to maintaining an adequate CPP, i.e., greater than 70 mmHg. CPP is the difference between mean arterial pressure and the downstream pressure, either the jugular venous pressure or the intracranial pressure, whichever is higher. For stable patients, noninvasive blood pressure monitoring is adequate; but in unstable patients who require continuous intravenous antihypertensives, and in deteriorating patients, an invasive arterial catheter should be considered to provide beat-to-beat monitoring and an easy way to measure metabolic status. Unfortunately, this metabolic information will only reflect the global status and not the focal values that would better guide therapy. For patients with cardiac disease, control of blood pressure is indicated to tip the myocardial oxygen balance in favor of reduced work and, therefore, lower the risk for ischemia.

Key Points

- Signs of myocardial damage without underlying cardiac disease can be present in patients with neurosurgical disease, and these manifestations must be evaluated and treated.
- Rapid and aggressive reversal of anticoagulation may be indicated in patients with critical bleeding in the central nervous system.
- Control of blood pressure is often necessary to mitigate the effects of hypertension on intracerebral hemorrhage. It reduces the risk of rebleeding in patients with hemorrhagic strokes and reduces the risks for cerebral edema and hemorrhagic transformation in patients with ischemic strokes.
- Consideration should be given to maintaining adequate cerebral perfusion pressure in acute intracranial processes, as both hypotension and hypertension are potentially harmful in patients presenting with ischemic or hemorrhagic strokes.
- The ideal anesthetic technique for endovascular neurointerventional procedures is not yet defined, though retrospective data suggest an association between general anesthesia and poorer outcomes.

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Suggested Reading

Boland TA, Lee VH, Bleck TP. Stress-induced cardiomyopathy. Crit Care Med. 2015;43(3):686–93.

Frontera JA, Lewin iii JJ, Rabinstein AA, et al. Guideline for reversal of antithrombotics in intracranial hemorrhage: a statement for healthcare professionals from the Neurocritical Care Society and Society of Critical Care Medicine. Neurocrit Care. 2015;24:6–46.

Hemphill JC, Greenberg SM, Anderson CS, et al. Guidelines for the management of spontaneous intracerebral hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2015;46(7):2032–60.

Powers W, Derdeyn C, Biller J, et al. 2015 American Heart Association/American Stroke Association focused update of the 2013 guidelines for the early management of patients with acute ischemic stroke regarding endovascular treatment. Stroke. 2015;46(10):3020–35.

8 Risk Assessment and Treatment of Critical Carotid Stenosis: Suggestions for Perioperative Management

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Overview

Carotid artery stenosis is the narrowing of the carotid arteries and is typically the result of atherosclerotic disease involving the intima of the vessel wall. Carotid atherosclerotic disease is generally most severe at the bifurcation of the common carotid artery, extending distally into the lumen of the internal carotid artery and often proximally into the common carotid artery. Carotid artery stenosis is classified as asymptomatic if there have been no ischemic events related to it or symptomatic if the patient has a history of prior stroke or transient ischemic attack (TIA) in the vascular distribution of the affected artery. Carotid artery stenosis is evaluated and quantified by carotid ultrasonography, magnetic resonance angiography (MRA) with or without contrast, computed tomography angiography (CTA), or digital subtraction angiography (DSA). Intervention in the form of either carotid endarterectomy (CEA) or carotid artery stenting (CAS) is indicated for those with symptomatic disease and 70–99% stenosis, but not for those with complete occlusion. It may also be beneficial for those with symptomatic disease and 50–69% stenosis in centers known to have a very low surgical morbidity and mortality. Intervention should also be considered in those with asymptomatic disease and 60–99% stenosis.

Both CEA and CAS confer a clear benefit in stroke prevention in patients with carotid artery stenosis, and either CEA or CAS can be offered to appropriate patients with carotid artery stenosis. The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST) established that CAS is equally efficacious to CEA in secondary prevention of ipsilateral stroke. Generally, CEA is preferred to CAS unless the patient has certain risk factors that may make them better candidates for CAS. These risk factors include:

- Severe cardiac disease
- Severe pulmonary disease
- Contralateral carotid occlusion
- History of neck surgery or neck radiation
- Contralateral laryngeal nerve palsy
- Recurrent stenosis after previous CEA
- Age >80

Both methods of carotid revascularization require a thorough preoperative evaluation and medical optimization strategy, as well as an understanding of the associated perioperative risks and management concerns.

Preoperative Evaluation and Management

Preoperative evaluation involves assessing cardiac function, the amount of central nervous system (CNS) impairment, if any, and the degree of CNS reserve.

A thorough neurologic exam should be performed and documented prior to surgery to establish an accurate clinical baseline of the patient. A preoperative CT or MRI of the brain is indicated for all symptomatic patients to evaluate the size and location of infarct, the presence of hemorrhagic transformation, and the severity of cerebral edema. Routine DSA is not indicated if other vessel imaging modalities have previously been obtained, as it rarely affects the surgical plan and is associated with a number of significant risks, including stroke (0.1–1.6%) and death (0.1%).

Cardiac Disease

Perioperative mortality associated with CEA is <0.5–3%, with a higher risk when performed at non-tertiary care centers. Cardiac events are the most common cause of perioperative mortality, and as such preoperative cardiac assessment and optimization are of paramount importance. A thorough

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cardiac history and 12-lead EKG should be performed on all patients prior to CEA or CAS. Additional cardiac assessment and optimization, in collaboration with a cardiologist, may be necessary for patients with severe cardiac disease.

Antiplatelet Therapy

Antiplatelet therapy with aspirin reduces the risk of stroke of any cause in patients undergoing CEA. The recommended dose is 81–325 mg daily. Consensus guidelines from the American Academy of Neurology (AAN) and the American College of Chest Physicians (ACCP) recommend starting aspirin prior to CEA and continuing indefinitely as long as there are no contraindications. Clopidogrel can be used with patients who have contraindications to aspirin. For patients undergoing CAS, we recommend dual antiplatelet therapy with aspirin and clopidogrel, which should be initiated prior to CAS and continued for at least 30 days after stenting. There is limited data to guide the dosing regimen and duration of dual antiplatelet therapy following CAS. The CREST trial used aspirin 325 twice daily and clopidogrel 75 mg twice daily, starting at least 48 hours prior to the procedure. Patients who underwent CAS within 48 hours received aspirin 650 mg and clopidogrel 450 mg at least 4 hours prior to the procedure. After the procedure, patients were maintained on aspirin 325 mg daily and clopidogrel 75 mg daily for at least 30 days, followed by aspirin monotherapy indefinitely. Alternatively, the ARMYDA-9 CAROTID trial demonstrated in a 2 × 2 trial design that a clopidogrel load of 600 mg 6 hours prior to the procedure, given concurrently with a statin reload regimen (atorvastatin 80 mg load 12 hours prior to the procedure and another 40 mg given 2 hours prior to stenting), was superior to a clopidogrel 600 mg load without statin reload as well as a clopidogrel 300 mg load with or without statin reload. Our practice includes a regimen of aspirin 325 mg daily, combined with a 600 mg loading dose of clopidogrel, given at least 6 hours prior to CAS, followed by clopidogrel 75 mg daily maintenance therapy for at least 4 weeks post-procedure and aspirin 325 mg daily indefinitely. Until more definitive data emerge to guide antiplatelet therapy in patients undergoing CAS, any of the above regimens is reasonable.

Statin Therapy

All patients with known coronary heart disease or risk equivalents, including those with symptomatic carotid artery stenosis, should be treated with a statin when tolerated. ACC/AHA guidelines recommend high-intensity statin therapy in all individuals 75 years old or less with known cardiovascular disease, and in the case of individuals older than 75 years, it is reasonable to weigh the risks and benefits of statin therapy. Patients already on statin therapy prior to CEA or CAS should continue it in the perioperative period. As described above, there is some evidence that those already receiving statin therapy prior to CAS may benefit from a reload regimen.

Operative Course

Carotid Endarterectomy

An arterial line is placed for intraoperative hemodynamic monitoring and should be maintained for the postoperative period. Fluid use in the neurosurgical patient is typically 0.9% saline without dextrose or Ringer's lactate.

Local versus general anesthesia is generally the choice of the surgeon in consultation with the anesthesiologist, and there does not appear to be any difference in mortality, MI, or stroke at 30 days between the two strategies. If the patient is a poor general anesthesia candidate, regional anesthesia in the form of a superficial cervical plexus block may be performed. Awake (local) anesthesia provides the advantages of being able to conduct frequent intraoperative neurologic examinations and avoids the typical hemodynamic stress that occurs with induction and emergence for general anesthesia. However, it creates the challenge of airway management under the drapes if the patient becomes unable to continue in the awake state throughout the procedure. The use of general anesthesia usually allows for better operating conditions but depending on the anesthetic technique may result in a delay in postoperative neurologic evaluation. In order to minimize this risk, many anesthesiologists choose a technique that includes the use of short-acting anesthetic agents (e.g., propofol, desflurane, remifentanil, sufentanil) in combination with a superficial cervical plexus block (placed at the beginning of the case). The block provides for intraoperative and postoperative analgesia, thus reducing the need to administer longer-acting intravenous opiates, which may delay the timing and quality of postoperative neurologic assessment.

The operation proceeds with a skin incision that is either made along the anterior border of the sternocleidomastoid muscle or transversely over the jugular bulb. This is followed by dissection of overlying tissues away from the common carotid to above the bifurcation. Systemic heparin is given intravenously, and the internal, common, and external arteries are clamped sequentially, after which a longitudinal incision is made through the adventitia of the carotid artery. A vascular shunt may be placed at this time (see below). A dissection plane between the intima and media is made with removal of the plaque. The edges are tapered carefully to avoid leaving a gap that could result in a dissection after blood flow is restored. The arteriotomy is closed with suture,

and the shunt, if used, is removed. If there is concern that direct closure of the arteriotomy may result in lumen narrowing, a graft using the saphenous vein or an artificial patch such as Dacron or polytetrafluoroethylene (PTFE) may be used. The distal internal carotid artery is then unclamped, allowing retrograde flow of debris. The internal carotid artery is then reclamped, and the common and external carotid arteries are unclamped. This allows a flushing of debris away from the internal carotid.

Thrombin-soaked gel may be placed over the suture site, and, once hemostasis is achieved, the wound is closed with or without a drain.

Carotid Artery Stenting

An arterial line is placed for intraoperative hemodynamic monitoring and should be maintained for the postoperative period. Moderate sedation is typically performed for carotid stenting and allows for an accurate intraprocedural neurologic exam.

The femoral artery is accessed percutaneously followed by the placement of a 5F short sheath. Heparin (50–80 U/kg) is then administered with a goal aPTT of 250–300 seconds. A guide wire is advanced to the brachiocephalic or left common carotid artery followed by catheter cannulation with subsequent imaging of the distal arterial anatomy of interest. The guide wire is then navigated across the internal carotid artery lesion. A neuroprotective device in the form of a distal filter, balloon, or proximal common and external carotid occlusive device is deployed prior to stent placement. In preparation for hemodynamic changes with carotid bulb expansion, atropine or glycopyrrolate should be readily available as well as an IV vasopressor and antihypertensive agent. A stent or angioplasty balloon plus stent is advanced via catheter to the site of the lesion. The stent may be self-expanding or may require a balloon assist device that is deployed at the site of the lesion. The sheath is removed and the femoral artery is closed with the proceduralist's preferred device.

Concerns and Risks

Complications Associated with Carotid Endarterectomy

- Carotid clamping with risk of cerebral ischemia
  - Assessing risk/tolerance of carotid clamping
  - Intraoperative monitoring
  - Selective shunting
- Hemodynamic lability
- Reperfusion syndrome
- Postoperative stroke
- Local versus general anesthesia
- Postoperative hematoma
- Nerve damage

Complications Associated with Carotid Artery Stenting

- Stroke
- Reperfusion/hyperperfusion syndrome
- Hemodynamic lability
- Carotid stent fracture
- Restenosis
- Dissection

Both CEA and CAS are associated with a risk of cardiac events. The CREST trial demonstrated no significant difference between CEA and CAS using a composite primary endpoint of any stroke, myocardial infarction (MI) or death in the perioperative period, or ipsilateral stroke during the 10-year follow-up period. CAS carried a significantly lower risk of MI when compared to CEA, but a significantly higher risk of stroke in the periprocedural period. Independent risk factors for poor outcome (stroke, myocardial infarction, or death) following CEA include age $\geq$80, severe heart disease, severe lung disease, renal failure or insufficiency, stroke as the indication for intervention, limited surgical access, prior cervical irradiation, prior ipsilateral CEA, and contralateral carotid occlusion. Risk factors for poor outcome after CAS are similar to those for CEA, with some important additional considerations including the presence of aortic stenosis, chronic kidney disease, and carotid plaque morphology.

Possible independent risk factors for stroke within 30 days of CEA include intraoperative transfusion, baseline hemiplegia, shorter height (likely representing smaller artery size), and increased intraoperative anesthesia time.

Assessing Risk/Tolerance of Carotid Clamping

The internal carotid artery is clamped during CEA, exposing the associated hemisphere to transient hypoperfusion. If there is inadequate cerebral perfusion via collateral blood flow, ischemia and infarct can occur. Approximately 80–85% of patients tolerate carotid artery clamping without experiencing ischemic complications. In patients who do not undergo routine carotid shunting, intraoperative neuro (electrophysiologic) monitoring for evidence of ischemia is often used to identify patients who may benefit from selective shunting.

Intraoperative Monitoring

A number of monitoring modalities may be employed to identify cerebral ischemia during carotid clamping, and these modalities can indicate patients for selective shunting:

- Frequent neurologic assessment in the patient undergoing CEA with local anesthesia only.
- Continuous intraoperative electroencephalography (EEG) – the emergence of delta or theta waves or amplitude attenuation is used as evidence of intraoperative ischemia.
- Somatosensory evoked potential (SSEP) – often used in conjunction with EEG, SSEP amplitude reductions of over 50% are used as evidence of intraoperative ischemia.
- Cerebral oximetry – employs near infrared spectrophotometry (NIRS) to determine regional cerebral oxygen saturation as a measure of cerebral ischemia.
- Stump pressure (SP) – SP is the internal carotid artery pressure distal to the carotid clamp, which reflects the cerebral perfusion pressure in the distal vessels. SP thresholds of less than 40–60 mmHg are generally used as an indication of inadequate collateral blood flow and the need for shunt placement.
- Transcranial Doppler (TCD) – a sustained and marked reduction in the mean middle cerebral artery (MCA) velocity during clamping may be used to identify ischemia and the need for selective shunting. The reliability of this method, and the optimal threshold of reduction in mean MCA velocity for defining ischemia, is unclear. However, unlike other intraoperative monitoring modalities, TCD can be used intraoperatively to detect embolic events.

Shunting

A shunt can be placed as a temporary bypass between the common carotid and the internal carotid arteries distal to the surgical site to decrease the length of time that blood flow to the internal carotid vascular distribution is interrupted during CEA. Shunts may be placed either routinely or selectively in patients in whom there is evidence of cerebral ischemia during clamping. It is unclear whether the use of a shunt, either routinely or selectively, results in improved patient outcomes after CEA, and the use and indication of shunting remains controversial. Presently, there is little evidence to suggest the superiority of one intraoperative monitoring method over another in the case of selective shunting.

Labile Hemodynamics

Baroreflex dysfunction is ubiquitous with CEA and can result in abrupt changes in arterial pressure and heart rate. Treatment may involve immediate cessation of surgery (with communication between the surgeon and anesthesiologist), local anesthetic infiltration at the bifurcation, and/or immediate intravenous administration of drugs to reverse the undesirable hemodynamic change. Hypotension increases the risk of ischemia and infarction, while hypertension may increase the risk of ICH, cerebral hyperperfusion syndrome, surgical site tearing, or neck hematoma formation. Baroreflex dysfunction may persist for hours to days after CEA, during which time arterial pressure and heart rate often remain labile and difficult to treat. Consequently, we recommend routine intra-arterial blood pressure monitoring in the postoperative period.

Cerebral Hyperperfusion Syndrome

Cerebral hyperperfusion syndrome occurs in 1–3% of patients following CEA and in 1% of patients following CAS. Patients generally present with a severe headache ipsilateral to the revascularized carotid artery, seizures, and focal neurologic deficits contralateral to the revascularized carotid artery. Cerebral hyperperfusion syndrome usually develops within 1–2 weeks of carotid revascularization, but it can occur up to 30 days following CEA or CAS. Risk factors for cerebral hyperperfusion syndrome include a preoperative carotid artery stenosis of greater than 80%, or when CEA has been performed after a recent cerebral infarct. Postoperative TCD to monitor MCA velocities has been investigated as a method of predicting cerebral hyperperfusion syndrome, but the accuracy and usefulness of TCD for this purpose remains unclear.

All patients in whom cerebral hyperperfusion syndrome is suspected should be evaluated with either CT or MRI to assess for intracerebral hemorrhage and edema. Management involves aggressive treatment of postoperative hypertension with nicardipine, labetalol, esmolol, or enalaprilat intravenously. Some vasodilators such as nitroglycerin or nitroprusside may increase cerebral blood flow and intracranial pressure and should therefore be avoided. There are no established guidelines for the optimal blood pressure to prevent or treat cerebral hyperperfusion syndrome with or without intracerebral hemorrhage. For prevention of cerebral hyperperfusion syndrome and ICH, a SBP goal of less than 150–160 mmHg is typical and reasonable postoperatively in all patients. For patients diagnosed with cerebral hyperperfusion syndrome with ICH, we recommend a more aggressive SBP goal of less than 140 mmHg, a goal extrapolated from current ASA/AHA guidelines for blood pressure management in spontaneous ICH.

Intracerebral hemorrhage occurs in about 0.6% of patients after CEA, and its occurrence portends a poor prognosis with a mortality of 36–63%. ICH should be managed by acutely lowering blood pressure to a goal systolic blood pressure of 140 mmHg or less as described above. Protamine sulfate should be used to reverse the effects of heparin in applicable patients. Platelet transfusion for patients who have been taking antiplatelet medications is controversial, and the role of platelet function assays and platelet transfusion in uncertain. According to current ASA/AHA guidelines for spontaneous

ICH, there is not enough evidence to recommend platelet transfusions in patients receiving antiplatelet therapy, and extrapolating that recommendation to patients with ICH after CEA seems reasonable.

Seizures are common in cerebral hyperperfusion syndrome and should be managed with antiepileptic medications such as fosphenytoin or levetiracetam. Prophylactic antiepileptic medications are not recommended for cerebral hyperperfusion syndrome, with or without ICH.

Postoperative Stroke

Postoperative stroke occurs in less than 3% and 5% of asymptomatic and symptomatic patients undergoing CEA, respectively. Etiologies include endarterectomy site thrombosis, arterial dissection, intracerebral hemorrhage, distal arterial emboli, and watershed infarction. The specific approach to postoperative stroke is variable depending on the clinical context but generally includes carotid ultrasonography to rule out CEA site thrombus or dissection, CT of the head to rule out hemorrhage, and potentially an immediate return to the OR for suspected CEA site thrombus. Additionally, CTA or DSA may be obtained to assess for arterial emboli or dissection that could be amenable to endovascular interventions. Starting a heparin infusion in these patients may be done immediately, but a CT scan of the head is recommended prior to initiating anticoagulation therapy to rule out intracranial hemorrhage.

Crisis Management

Postoperative Hematoma

Postoperative hematoma is more common in those on anticoagulation medications. This is often managed conservatively but may require a return to the OR for surgical control of the bleeding source. Venous oozing may be managed with heparin reversal using protamine and careful direct pressure for several minutes. Rarely, a neck hematoma following CEA may result in airway compromise. Under these circumstances, opening the wound at the bedside, prior to gaining definitive control in the OR, may be lifesaving.

Nerve Damage

A number of nerves may be damaged during CEA surgery:

1. Vagus nerve – lies in the carotid sheath with the carotid artery and jugular vein and is at risk of injury, resulting in hoarseness.
2. Recurrent laryngeal nerve – injury to this nerve may result in unilateral vocal cord paralysis.
3. Facial nerve – injury to the marginal mandibular branch innervating the lateral orbicularis oris muscle may result in lower facial asymmetry.
4. Hypoglossal nerve – injury results in tongue deviation ipsilateral to the CEA site.
5. Ansa hypoglossus – innervates the strap muscles of the neck and may be sacrificed during surgery.
6. Sympathetic chain – injury results in ipsilateral complete or partial Horner's syndrome.

The majority of cranial nerve injuries are temporary, with persistent cranial nerve injuries occurring in less than 1% of patients. The only risk factor for cranial nerve injury is surgery longer than 2 hours.

Parotitis

Perioperative parotitis can occur secondary to manipulation during surgery, but this is uncommon.

Oxygen Concentration

For CEA patients, oxygen concentration should be kept as low as possible while maintaining good oxygen saturation in patients who do not have an endotracheal tube or laryngeal mask airway to decrease the risk of intraoperative fire during a surgery that involves the use of electrocautery in the head or neck region.

Bilateral CEA

The risk of neck hematoma, laryngeal nerve damage, and bilateral cerebral ischemia has led to a staged procedure with each CEA being performed a week or more apart.

Restenosis

This can occur early (within 3 years) or late (greater than 3 years) and may warrant revascularization with either CEA or CAS. Early restenosis risk factors are age <65, female gender, and smoking. Repeat surgery is associated with an increased risk of stroke or death at 30 days compared to the initial surgery. This risk is less if stenosis recurs within 2 years, as this is most likely due to intimal hyperplasia rather than recurrent atherosclerotic plaque formation.

Acute or subacute restenosis can occur in 0.5–2% of carotid stent placements. Stenosis beyond 30 days is typically due to neointimal hyperplasia. Drug-eluting stents are

rarely used for CAS, and the use of bare metal stents warrants the use of aspirin indefinitely and of clopidogrel for at least 4–6 weeks after placement.

Key Points

- The highest risk of mortality following CEA is from cardiac causes. Investigation and medical optimization of these patients is crucial.
- Tight blood pressure control must be instituted as soon as flow is returned to the internal carotid artery during surgery and must be maintained for 1–14 days – the first 24 hours are the most labile and critical.
- Patients are at risk for cerebral hyperperfusion syndrome with ICH and seizures, which must be treated with reversal of anticoagulation, aggressive blood pressure management, and antiepileptics, as indicated.
- Close monitoring of hemodynamic and neurologic status in an ICU setting is recommended for 24 hours following CEA.

Suggested Reading

Adhiyaman V, Alexander S. Cerebral hyperperfusion syndrome following carotid endarterectomy. QJM. 2007;100(4):239–44.

Anderson CS, Heeley E, Huang Y, Wang J, Stapf C, Delcourt C, Lindley R, Robinson T, Lavados P, Neal B, Hata J, Arima H, Parsons M, Li Y, Wang J, Heritier S, Li Q, Woodward M, Simes RJ, Davis SM, Chalmers J, INTERACT2 Investigators. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. N Engl J Med. 2013;368:2355–65.

Bouri S, Thapar A, Shalhoub J, Jayasooriya G, Fernando A, Franklin IJ, Davies AH. Hypertension and the post-carotid endarterectomy cerebral hyperperfusion syndrome. Eur J Vasc Endovasc Surg. 2011;41:229–37.

Brott TG, Hobson RW II, Howard G, Roubin GS, Clark WM, Brooks W, Mackey A, Hill MD, Leimgruber PP, Sheffet AJ, Howard VJ, Moore WS, Voeks JH, Hopkins LN, Cutlip DE, Cohen DJ, Popma JJ, Ferguson RD, Cohen SN, Blackshear JL, Silver FL, Mohr JP, Lal BK, Meschia JF, the CREST Investigators. Stenting versus endarterectomy for treatment of carotid-artery stenosis. N Engl J Med. 2010;363:11–23.

Brott TG, Halperin JL, Abbara S, Bacharach JM, Barr JD, Bush RL, Cates CU, Creager MA, Fowler SB, Friday G, Hertzberg VS, McIff EB, Moore WS, Panagos PD, Riles TS, Rosenwasser RH, Taylor AJ, Jacobs AK, Smith SC, Anderson JL, Adams CD, Albert N, Buller CE, Creager MA, Ettinger SM, Guyton RA, Halperin JL, Hochman JS, Hunt SA, Krumholz HM, Kushner FG, Lytle BW, Nishimura RA, Ohman EM, Page RL, Riegel B, Stevenson WG, Tarkington LG, Yancy CW. 2011 ASA/ACCF/AHA/AANN/AANS/ACR/ASNR/CNS/SAIP/SCAI/SIR/SNIS/SVM/SVS guideline on the management of patients with extracranial carotid and vertebral artery disease: executive summary. Cathet Cardiovasc Intervent. 2013;81:E76–E123.

Fisher JE, editor. Mastery of surgery. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2007.

Hans J, Wilke II, Ellis JE, McKinsey JF. Carotid endarterectomy: perioperative and anesthetic considerations. J Cardiothorac Vasc Anesth. 1996;10(7):928–49.

Mulholland MW, Lillemoe KD, et al. Greenfield's surgery: scientific principles and practice. 4th ed. Philadelphia: Lippincott Williams & Wilkins; 2006.

Qureshi AI, Palesch YY. Antihypertensive Treatment of Acute Cerebral Hemorrhage (ATACH) II: design, methods, and rationale. Neurocrit Care. 2011;15(3):559–76.

9 Aneurysmal Subarachnoid Hemorrhage: Risk Assessment and Perioperative Complications

Chanhung Z. Lee, Pekka Talke, and Nerissa U. Ko

Overview

Blood in the subarachnoid space is most commonly a result of a ruptured cerebral arterial aneurysm, but it can also be due to a ruptured arteriovenous malformation, tumor, embolic stroke, or trauma. In this chapter, we will focus on subarachnoid hemorrhage (SAH) from rupture of a cerebral aneurysm. An estimated 1–5% of adults worldwide harbor intracranial aneurysms. In the United States alone, each year there are at least 30,000 patients who have SAH due to rupture of a cerebral aneurysm.

Implications for Neurosurgical Patients

Morbidity and mortality are very high in aneurysmal SAH patients throughout the world. Although incidence of SAH varies among different regions and populations, about 15% of patients die before reaching a hospital, and overall, 25% subsequently die from the initial hemorrhage or its complications. Up to 50% of survivors will have long-term neurological deficits.

Institutional factors have been shown to influence outcome after aneurysmal SAH. Treatment of a ruptured cerebral aneurysm consists of surgical clipping or endovascular coil embolization. The largest multicenter randomized trial, conducted by the International Subarachnoid Aneurysm Trial (ISAT), comparing the outcome of these two treatment modalities showed a delicate balance of safety and durability at different time durations of follow-up, indicating the importance of tailored treatment choice based on patient and aneurysm characteristics. Proper perioperative care is vital in facilitating therapeutic interventions and in reducing morbidity and mortality in this high-risk patient population. This chapter will focus on management of aneurysmal SAH-related perioperative complications and concerns relating to neuroanesthesia.

Concerns and Risks

Typical initial medical measures after aneurysmal SAH include mild sedation and analgesics for anxiety and headache, prevention of arterial blood pressure elevation, and avoidance of antiplatelet agents. Blood pressure frequently rises precipitously as a result of the initial intracranial hemorrhage, presumably as a result of acute elevation of intracranial pressure (e.g., Cushing response). Unbearable headache and anxiety may also be contributing factors. Placement of an intra-arterial catheter enables continuous blood pressure monitoring and helps in guiding blood pressure management in patients requiring frequent intervention. The parameters of blood pressure control have not yet been defined, but it is generally reasonable to maintain systolic blood pressure below 160 mmHg. Beta-blockers and short-acting calcium channel blockers are commonly used to control hypertension. Some studies have shown smoother control of blood pressure using intravenous nicardipine, but there is no reported difference in clinical outcome. Coexisting intracranial hypertension may impair cerebral perfusion, and therefore systemic hypotension should be avoided.

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Airway and Ventilation Management

Most patients with aneurysmal SAH will be intubated during the surgery or procedure for treating the aneurysm. However, earlier endotracheal intubation and mechanical ventilation may be required in some patients with significant decline of consciousness, as well as in those experiencing seizures. For these patients, inability to protect the airway may lead to aspiration, often resulting in pneumonitis or pneumonia. Mechanical ventilation may also be needed for patients who have neurogenic or cardiogenic pulmonary edema. To keep the patient comfortable and facilitate frequent neurological exam, propofol or dexmedetomidine infusions can be used for sedation during mechanical ventilation.

Current goals of mechanical ventilation in SAH patients are to support adequate oxygenation and maintain normocarbia. Hypoventilation or hyperventilation should be avoided unless specifically indicated. Hypoventilation can lead to cerebral vasodilation and increase in intracranial pressure (ICP), while hyperventilation may cause cerebral vasoconstriction and worsen cerebral ischemia. Transmural pressure, defined as the difference between mean arterial pressure (MAP) and ICP, is an indication of aneurysm wall tension. Inadvertent hyperventilation may decrease ICP and, as a consequence, increase transmural pressure across the aneurysm; this can theoretically lead to re-rupture of the aneurysm. In the event of dangerously high ICP, transient hyperventilation may be indicated to reduce ICP. This should help to prevent global hypoperfusion, while other more definitive interventions are considered**.**

Aneurysm Re-rupture

Recurrence of aneurysmal hemorrhage is a major acute complication after SAH and carries significant catastrophic risks. The incidence of rebleeding from a ruptured aneurysm is around 30% in the first month following SAH, with the occurrence of 4–13.6% in the first 24 hours. Re-rupture is associated with high mortality and poor outcome. Early obliteration of the aneurysm reduces the risk of rebleeding from the natural course. In patients with significant risk of rebleeding but with unavoidable delay of definitive treatment, short-term antifibrinolytic therapy with tranexamic acid or aminocaproic acid may be considered as a temporary measure to reduce the incidence of aneurysm rebleeding. However, neither drug is approved by US Food and Drug Administration for this indication.

Rebleeding is also common in patients undergoing treatment interventions of ruptured aneurysms. The multicenter study of Cerebral Aneurysm Rupture After Treatment (CARAT) reported an intraprocedure rupture rate of 19% with clipping and 5% with endovascular coiling. Intraoperative rupture of the aneurysm results in high morbidity and mortality. Although intraoperative aneurysm re-rupture is most commonly due to surgical manipulation of the aneurysm, prevention of aneurysm re-rupture by aggressively limiting the degree and duration of systemic hypertension has been one of the major goals for the anesthesiologist. Maintaining stable transmural pressure and adequate cerebral perfusion pressure should be central to anesthesia management. Significant increase in MAP or decrease in ICP will increase transmural pressure, which may precipitate the rupture of the aneurysmal vessel wall.

A deep plane of anesthesia should be ensured to prevent acute increases in blood pressure during stressful events, such as laryngoscopy and endotracheal intubation, head pinning, tissue dissection, and dural opening. Careful and incremental administration of medications, such as propofol and short-acting narcotics, can be used for the induction of anesthesia to ensure stability of cerebral perfusion. Meticulous care is needed to control ventilation. For patients without intracranial hypertension, the goal is to keep the patient normocarbic, avoiding decreases in ICP before the dura is opened, while employing subsequent mild hyperventilation and mannitol to relax the brain, facilitate surgical exploration, and reduce the potential damage from tissue retraction. Generous application of local anesthetics can help to avoid acute cardiovascular effects secondary to head pinning and extradural tissue dissection.

During surgical clipping, maintaining adequate blood pressure is important to ensure adequate cerebral perfusion to reduce injury from ischemic insults. Intraoperative blood pressure is typically controlled to maintain cerebral perfusion pressure between 70 and 90 mmHg. Intraoperative hypotension may increase the risk of retractor-induced cerebral ischemia and injury. Transient-induced hypotension may infrequently be requested by the surgeon immediately prior to clipping the aneurysm to allow for more secure placement of the permanent clip on the neck of the aneurysm. In addition, if intraoperative aneurysm rupture occurs, induced hypotension will decrease the rate of bleeding into the surgical field, thereby helping the surgeon gain better control. In contrast, induced hypertension may be needed to raise blood pressure above baseline levels to augment collateral blood flow, if the surgeon applies temporary clipping of the feeding arteries to reduce the rupture risk of the aneurysm during surgical manipulation of the aneurysm dome. Although the use of temporary clips decreases the risk of rebleeding during surgical manipulation, this practice results in an area of cerebral ischemia, which can be minimized by using controlled hypertension. Blood pressure management can also be guided by intraoperative neurophysiological monitoring, such as electroencephalography

and somatosensory-evoked potential and motor-evoked potential monitoring. Adenosine-induced transient cardiac pause has been used at some centers to assist in the control of bleeding from intraoperative rupture or to decompress large aneurysms for clipping; controlled studies are needed to validate the efficacy and safety of these applications. An extensive review of endovascular treatment of ruptured aneurysms is discussed elsewhere in this book.

Postoperative hypertension, while not uncommon after aneurysm clipping, should be treated cautiously using intermittent boluses of beta-blockers and/or intravenous infusions of short-acting vasodilators. Excessive hypertension may result in the formation of brain edema and hematoma, while hypotension may increase the risk for cerebral ischemia secondary to postsurgical traction edema, perforator vessel occlusion, and regional cerebral vasospasm.

Elevation of Intracranial Pressure

Cerebral aneurysmal rupture can cause a sudden rise in ICP, which accounts for the sudden onset of a severe headache and transient loss of consciousness occurring in 50% of patients with aneurysmal SAH. The development of acute hydrocephalus, occurring in 15–87% of patients, can also cause a rapid rise in ICP. Patients with increased ICP may develop stupor and coma. Increased ICP can be gradually lowered by using osmotic diuretics or hyperosmolar therapy (e.g., mannitol or hypertonic saline) and by ventriculostomy placement. Elevation of the head to 30° will improve venous outflow and thereby facilitate the control of ICP. Perioperatively, patients with intracranial hypertension can be slightly hyperventilated.

Subacute hydrocephalus may also increase ICP and can develop over days or weeks, presumably due to occlusion of arachnoid granulations. Subacute hydrocephalus can be associated with impaired mentation and incontinence and should be differentiated from vasospasm-induced neurologic changes. Temporary external ventricular drain or permanent CSF diversion is recommended in symptomatic patients to treat subacute hydrocephalus.

Cardiac Complications

Various SAH-related cardiac abnormalities are fairly common. Among SAH patients, 40–70% exhibit abnormal ECG tracings, ranging from ST segment changes, T-wave abnormalities, QT prolongation, and new U waves to life-threatening arrhythmias. SAH-initiated neurocardiogenic injury may result in myocardiac cell damage and ventricular dysfunction, which, in turn, are also associated with adverse neurological outcome. The degree of cardiac morbidity is often related to the severity of the SAH. Echocardiogram should be considered in these patients especially in the setting of hypotension.

The mainstay of treatment should be supportive. Electrolyte abnormalities should be corrected, and drugs that can potentially prolong QT interval should be avoided. In the event of clinically significant cardiac arrhythmia and myocardial injury, an urgent cardiology consultation is recommended for further evaluation.

Vasospasm and Delayed Cerebral Ischemia

Vasospasm refers to the narrowing of the cerebral arteries following SAH, secondary to thickening of the blood vessel walls. It usually develops 4–10 days after the initial hemorrhage, with the prevalence as high as 30–70%. Despite extensive research efforts, there is no effective preventive therapy to date, which may be partially due to the fact that vasospasm can occur at multiple levels of the arterial circulation. Large artery narrowing, detectable by current angiography technology, is not always proportional to ischemia insults. Delayed cerebral ischemia (DCI), especially in association with vasospasm, is a major threat to life in patients surviving the initial treatment after SAH. Signs of new onset of neurological deterioration from cerebral ischemia and/or infarction could be the warning presentations of cerebral vasospasm. Diagnosis of cerebral vasospasm can be made with transcranial Doppler or cerebral angiography. There are emerging data that perfusion imaging with CT or magnetic resonance may be more accurate in identifying DCI from hypoperfusion in the brain.

The goal for the management of cerebral vasospasm and DCI is to reduce the threat of ischemic neuronal damage by controlling intracranial pressure, decreasing metabolic rate of cerebral oxygen consumption, and improving cerebral blood flow. Early oral nimodipine therapy has been shown to reduce poor outcome related to SAH. Some evidence also points to a role for nicardipine, an intravenous calcium channel blocker, in reducing vasospasm and brain ischemia after SAH.

A change in treatment for acute symptomatic vasospasm and DCI has shifted from the traditional combination of triple "Hs" (hypertension, mainly after the aneurysm has been treated, hypervolemia, and hemodilution) to the maintenance of euvolemia and induced hypertension. The treatment target is to raise the systolic blood pressure 20% above a patient's baseline blood pressure using vasopressors (e.g., phenylephrine, norepinephrine), to reach a central venous pressure of 8–12 cm H_2O using intravenous fluids, and to allow hematocrit to remain in the low 30s. It is imperative to monitor and manage the potential risks of the abovementioned hemody-

namic therapy, including cardiac failure, electrolyte abnormality, cerebral edema, and bleeding diathesis resulting from dilution of clotting factors.

At some centers, endovascular treatment of vasospasm using balloon angioplasty and/or super-selective injection of intra-arterial vasodilators is becoming common. The anesthesiologist should be prepared to manage possible systemic hypotension resulting from intra-arterial injection of vasodilators.

Seizures

Seizure-like episodes occur in 10–20% of SAH patients, with majority of the reported onset occurring before medical attention is provided. Delayed seizures happen in 3–7% of patients. The mode of treatment may influence the occurrence of later seizure activities, based on ISAT results that show a significant lower incidence of seizures in patients treated with endovascular coiling in the long-term follow-up. The American Stroke Association recommends consideration of 7 days of prophylactic anticonvulsant treatment in the immediate post-hemorrhagic period; however, this is based on very little data and remains controversial. The routine long-term use of anticonvulsants for SAH patients is not recommended, but may be considered for patients with risk factors including prior seizures, parenchymal hematoma and/or infarction, or middle cerebral artery aneurysms.

Hyponatremia

Both hypernatremia and hyponatremia are common after acute SAH. Hyponatremia occurs in about 10–30% of patients after SAH and can develop in the first 2 weeks after SAH. The majority of the cases occur as a result of cerebral salt-wasting syndrome (CSW), although a smaller portion of patients may develop a syndrome of inappropriate antidiuretic hormone (SIADH) after SAH. It is important to distinguish these two underlying causes of hyponatremia since intravascular volume is usually contracted in the former, but normal or elevated in the latter. For most SAH patients, therefore, hyponatremia should not be routinely treated with the conventional free-water-restriction approach since it may increase the risk for ischemia-induced injuries from intravascular volume contraction. It is reasonable to monitor intravascular volume status, frequently check serum electrolytes, and treat the volume contraction with isotonic fluids. Medical therapies such as hypertonic saline and fludrocortisone acetate may be useful to correct severe hyponatremia.

Summary

Proper perioperative monitoring and management of SAH-induced complications is critical in helping improve patients' outcome. Although there are only a few areas in the management of SAH for which there is conclusive evidence from randomized, controlled clinical studies, this chapter has summarized the principles currently used to manage patients with aneurysmal SAH during the perioperative period.

Key Points

- Securing the airway and proper ventilation control may be required prior to the treatment of the ruptured cerebral aneurysm in patients with severe decline of consciousness and/or seizures.
- Close monitoring and adequate control of intracranial pressure and blood pressure are critical in the prevention of aneurysm re-rupture pre- and intraoperatively.
- Intracranial hypertension should be diagnosed and treated promptly.
- Caution against vasospasm and DCI should remain high in patients after SAH. It can be treated using induced hypertension therapy and/or endovascular interventions. It is important to monitor and be ready to manage treatment-related complications.
- Hyponatremia most likely develops as a result of cerebral salt-wasting syndrome after SAH. Appropriate treatment is important to avoid the risk of worsening brain ischemia after SAH.

Suggested Reading

Connolly ES, Rabinstein AA, Carhuapoma JR, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2012;43:1711–37.

Drummond JC, Patel PM. Part V: Chapter 70: Neurosurgical anesthesia. In: Miller RD, editor. Miller's anesthesia, vol. II. 8th ed. Philadelphia: Churchill Livingstone; 2015.

Elijovich L, Higashida RT, Lawton MT, et al. Predictors and outcomes of intraprocedural rupture inpatients treated for ruptured intracranial aneurysms: the CARAT study. Stroke. 2008;39:1501–6.

Molyneux AJ, Birks J, Clarke A, et al. The durability of endovascular coiling versus neurosurgical clipping of ruptured cerebral aneurysms: 18 year follow-up of the UK cohort of the International Subarachnoid Aneurysm Trial (ISAT). Lancet. 2015;385(9969):691–7.

Pong RP, Lam AM. Chapter 13: Anesthetic management of cerebral aneurysm surgery. In: Cottrell JE, Young WL, editors. Cottrell and Young's neuroanesthesia. 5th ed. Philadelphia: MOSBY Elsevier; 2010.

Traumatic Brain Injury: Risk Assessment and Perioperative Management

10

Jonathan Z. Pan and Lingzhong Meng

Overview of Neurotrauma

Approximately 1.4 million cases of traumatic brain injury (TBI) are reported in the USA each year, among which roughly 50,000 patients die and 235,000 are hospitalized. The incidence of spinal cord injury (SCI) has remained stable over the past 30 years in North America, ranging between 27 and 47 cases per million, 55% of which are cervical spine (C-spine) injuries. TBI and SCI are often associated with other traumatic injuries. Approximately one-third of the fatalities after multisystem traumatic injury (150,000 deaths) each year is due to fatal head injuries; C-spine injuries occur in 1.5–3% of all major trauma patients.

Implications for the Neurosurgical Patients

Early diagnosis and management of TBI or SCI are of paramount importance to prevent further (secondary) injury immediately after initial injury and preserving neurologic function. In life-threatening situations, resuscitation, including airway, breathing, and circulation (ABC) management, must take priority. Protecting the injured brain or spinal cord during the resuscitation is important. For example, avoid nasal intubation in patients with basilar skull fracture or use in-line manual stabilization in patients with unstable C-spine.

Concerns and Risks

The management of TBI and SCI, especially in a serious polytrauma situation, is challenging. The most pertinent and urgent perioperative concerns and risks in managing neurotrauma patients are as follows:

- Jeopardized airway may be caused by impaired consciousness, direct injury to the face and neck, and/or full stomach and aspiration. Airway management is always the top priority.
- Inadequate ventilation and oxygenation may be caused by obstructed airway, depressed central drive, neuromuscular weakness caused by high C-spine injury, or thoracic injuries such as pulmonary contusion, pneumothorax, hemothorax, or multiple rib fractures. Avoiding hypercapnia will facilitate intracranial pressure management; however, hyperventilation-related hypocapnia may impair cerebral perfusion and should be used with caution. Avoiding hypoxemia is crucial in preventing secondary injury to both the brain and spinal cord.
- Hypovolemia and hypotension often occur in a patient with multiple traumatic injuries. Rarely do isolated brain and/or spinal cord injury cause massive bleeding, unless the patient is pharmacologically anticoagulated before the injury. Fluid and blood product administration may be required immediately at the time of presentation to maintain adequate brain perfusion. Treating hypotension via fluid resuscitation and vasopressors is the standard of care in neurotrauma patients. Hypotension that does not respond to volume resuscitation or requires high doses of vasopressors should prompt the clinician to consider neurogenic or vasoplegic shock. SCI above the midthoracic level may be associated with bradyarrhythmias.
- Anemia and coagulopathy: Acute and massive hemorrhage may result in a decrease in hematocrit below the acceptable level for oxygen content and delivery. Coagulopathy may occur directly as a result of TBI or may be associated with massive transfusion of blood

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products and exhaustion of factors necessary for adequate clot formation. Early and goal-directed blood product therapy is important for severely injured neurotrauma patients, but the endpoint targets are controversial.

- Intracranial hemorrhage and cerebral edema can cause intracranial hypertension. The impaired cerebral perfusion pressure (CPP = MAP [mean arterial pressure] – ICP) causes decreased cerebral blood flow (CBF), which is detrimental to the already injured brain. Patients with suspected ICP elevation should receive interventions in escalating levels of invasiveness such as head of bed up 30°, hyperosmolar therapy (e.g., mannitol, hypertonic saline), loop diuretics, cerebrospinal fluid drainage, or anesthetic (e.g., propofol or barbiturate), anti-seizure prophylaxis, etc. that need to be instituted as soon as possible based on the severity of intracranial hypertension. Hyperventilation may be employed briefly, as a bridge to other ICP-reducing therapies such as decompressive craniectomy. In patients with TBI and admission Glasgow Coma Scale less than 7, ICP monitoring is appropriate. The correction of intracranial hypertension should always be balanced against the potential hazards, for example, compromising cerebral perfusion with hypocapnia-induced cerebral vasoconstriction.
- The unstable C-spine is associated with difficult airway management and mandates spinal cord protection when transporting and positioning patients to prevent further injury.

The multiple relevant issues are summarized in the following discussion.

Glasgow Coma Scale and TBI Severity

The Glasgow Coma Scale (GCS), first proposed by Teasdale and Jennett in 1974, is currently the most widely used clinical measure for severity of TBI. The GCS must be obtained through interaction with the patient and should be measured after initial resuscitation has been performed and prior to the administration of sedative or neuromuscular blocking agents. A score of 14–15 is defined as mild TBI, 9–13 as moderate, 5–8 as severe, and 3–4 as critical (Table 10.1).

Table 10.1 Glasgow Coma Scale

Eyes opening	Spontaneous	4
	Speech	3
	Pain	2
	None	1
Verbal response	Oriented	5
	Confused	4
	Inappropriate	3
	Incomprehensible	2
	None	1
Motor response	Obeys commands	6
	Localize pain	5
	Flexor withdrawal	4
	Flexor posturing (decorticate rigidity)	3
	Extensor posturing (decerebrate rigidity)	2
	None	1
Total		3–15

Primary Survey in Polytrauma Patients with Coexisting TBI and SCI

The advanced trauma life support (ATLS) primary survey should be used as the guideline for managing a patient after traumatic injury and consists of simultaneous diagnostic and therapeutic activities intended to identify and treat life- and limb-threatening injuries, beginning with the most emergent problem. The ABCDE acronym of primary survey is shown in Fig. 10.1.

Airway Management After Traumatic Injury

A successful early resuscitation and a promising long-term outcome depend on expert airway management. This is especially true when TBI is present in the context of SCI in a multisystem trauma patient. The airway management algorithm after traumatic injury is presented in Fig. 10.2; however, variation can exist from institution to institution and provider to provider as long as the fundamentals are followed. Note that this algorithm differs from ASA algorithm in that (1) reawakening the patient is seldom an option in a truly emergent situation, (2) awake fiberoptic intubation is often counterproductive in an uncooperative trauma patient, and (3) glidescope is advantageous due to the fact that it may require less neck flexion/extension and improved first-attempt success, which are desirable in a patient with an uncleared C-spine.

Resuscitation After Traumatic Injury with Coexisting TBI and SCI

Resuscitation, in a broad sense, refers to the restoration of normal physiology after injury. Resuscitation commences immediately after injury, beginning with the patient's own compensatory mechanisms, and continues for hours and even days thereafter. The cornerstone of clinical resuscitation after traumatic injury is fluid resuscitation to replete the depleted intravascular volume caused by acute hemorrhage. The early phase of resuscitation refers to the efforts of

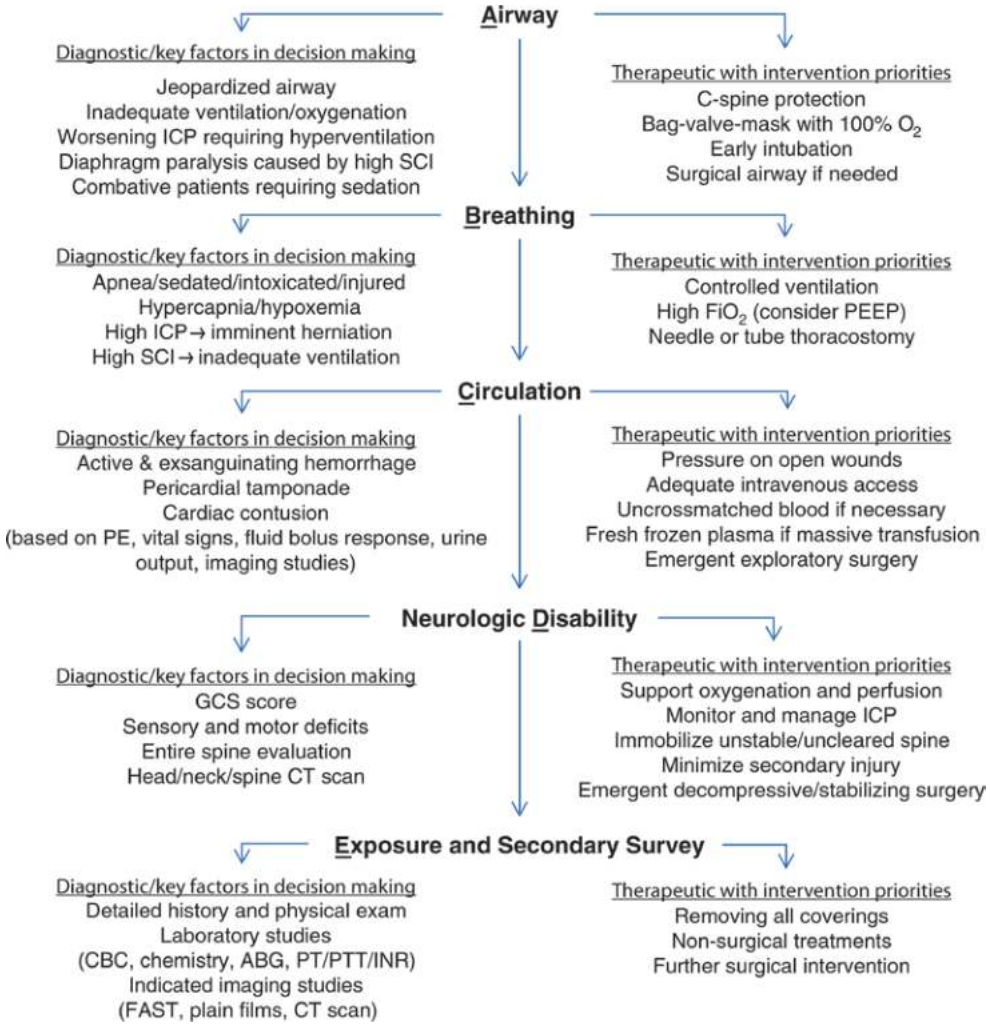

Fig. 10.1 Diagnostic and therapeutic principles of ATLS primary survey (ABCDE) in polytrauma patients with coexisting TBI and/or SCI. *ICP* intracranial pressure, *FiO_2* inspired oxygen fraction, *PEEP* positive end-expiratory pressure, *PE* physical exam, *GCS* Glasgow Coma Scale, *CT* computed tomography, *CBC* complete blood count, *ABG* arterial blood gas, *PT* prothrombin time, *PTT* partial thromboplastin time, *INR* international normalized ratio, *FAST* focused assessment by sonography for trauma. (Adapted from the Advanced Trauma Life Support curriculum of the American College of Surgeons)

replacing intravascular volume and controlling active bleeding in a parallel or simultaneous manner, while the late phase of resuscitation deals with post-hemorrhage fluid and/or blood product administration to optimize oxygen delivery and tissue perfusion.

The targets of early resuscitation are a matter of controversy due to the side effects of aggressive volume replacement, which include decreased blood viscosity, low hematocrit, and dilution/destabilization of clotting factors. Deliberate hypotension via restraining resuscitation volume is proposed in an effort to reduce the physiologic derangements caused by aggressive resuscitative approach; however, this approach is not encouraged in a polytrauma patient with coexisting TBI and/or SCI. Maintaining normal or patient's baseline blood pressure, to maintain brain and/or spinal cord perfusion pressure, is the current standard of care in a patient with injured brain and/or spinal cord. Simplified resuscitation principles for a patient in acute hemorrhagic shock after polytrauma with coexisting TBI and/or SCI are presented in Fig. 10.3.

Development of Secondary Injury of Brain

Conventionally, primary injury refers to the brain damage incurred at the moment of impact and secondary injury to the damage that evolves over the ensuing minutes, hours, and days. The deleterious post-TBI multisystem sequelae, such as hypoxemia and hypotension, are the major contributing factors in secondary injury. The pathophysiologic mechanisms of secondary injury are illustrated in Fig. 10.4.

Multisystem Sequelae After TBI and Their Management

Once primary injury of the brain incurred, management should focus on early diagnosis and treatment of deleterious multisystem sequelae in order to decrease the mortality, morbidity, and additional damage caused by secondary injury. The two strongest predictors of mortality in patients

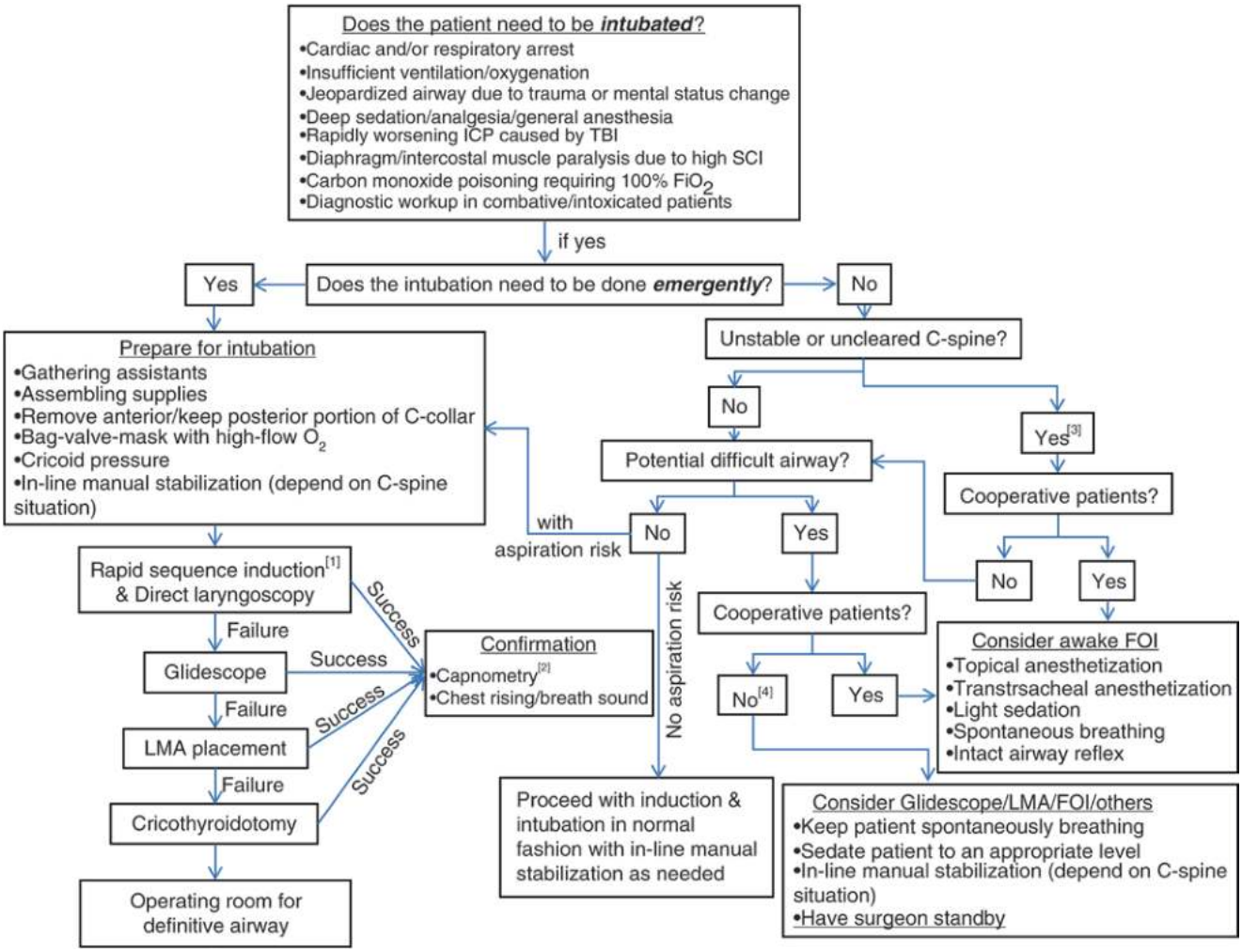

Fig. 10.2 Airway management algorithm in patients with traumatic injury (Carney et al. 2017). The dose of anesthetic must be decreased in the face of hemorrhage, even down to none at all in patients with severe hypovolemia; scopolamine or midazolam can be considered in order to reduce awareness when none or very small dose of quick-offset anesthetics is being administered; etomidate is advocated due to its better cardiovascular stability profile; succinylcholine can be safely used in the first 24 h after traumatic injuries; as sugammadex for quick reversal of neuromuscular blockers becomes available, use of rocuronium for rapid sequence induction may become more common even with potential difficult airway; ketamine is not advocated in patients with TBI who are not mechanically ventilated (Dutton et al. 2010). Capnometry may show low CO_2 level in low cardiac output situations (Furlan and Fehlings 2008). In-line manual stabilization is the standard of care in the ATLS curriculum for unstable or uncleared C-spine (Harris & Sethi 2006). If difficult airway is anticipated in an uncooperative patient, it is prudent to sedate the patient to an appropriate level while keeping him/her spontaneously breathing due to the dilemma that awake intubation is often counterproductive in a combative patient and making the patient apneic is risky; having alternative plans ready to be instituted is well-advised, which include glidescope, LMA, fiberoptic scope, and surgical airway by having a surgeon standby. *ICP* intracranial pressure, *FiO_2* inspired oxygen fraction, *LMA* laryngeal mask airway, *FOI* fiberoptic intubation

presenting to the emergency room with TBI are hypoxia and hypotension. A systemic approach is summarized in Table 10.2.

Nonsurgical Approaches of Spinal Cord Protection

Transfer of the patient with SCI to a level I trauma center as soon as possible is recommended. Considerable emphasis has been placed on the early immobilization of the entire spine of all patients with a potential SCI starting at the scene of injury. The combination of a rigid cervical collar and supportive blocks on a backboard with straps or similar device to secure the entire spine is the current standard of care. An adequate number of personnel should be deployed to "log-roll" the patient with a potential unstable spine as a unit when repositioning, turning, or preparing for transfers.

Like TBI, SCI can cause multisystem sequelae (e.g., spinal shock with profound arterial hypotension), which are the major contributing factors in secondary injury of the spinal cord. Early diagnosis and treatment of those deleterious

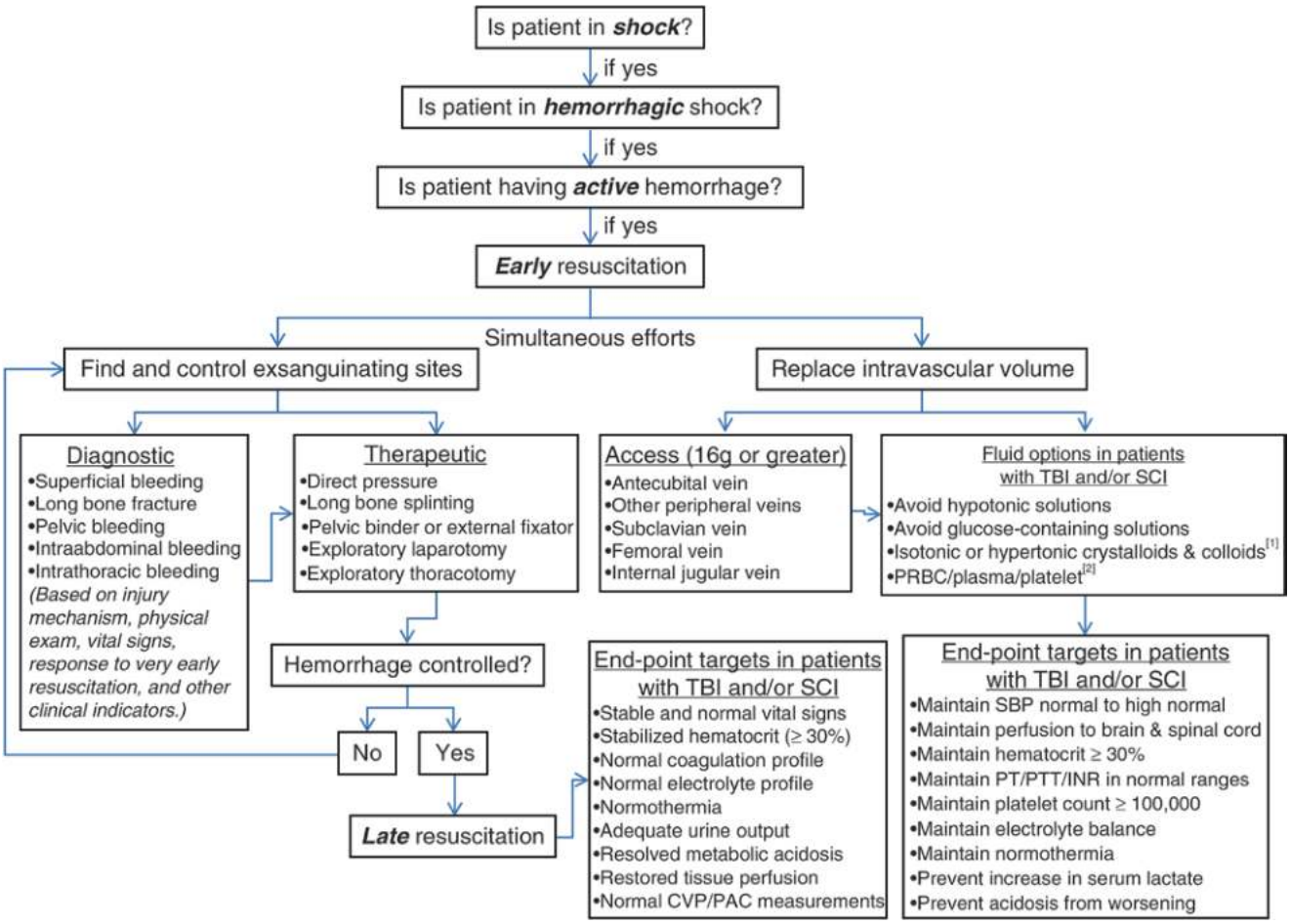

Fig. 10.3 Simplified resuscitation principles for a patient in acute hemorrhagic shock after polytrauma with coexisting TBI and/or SCI (Carney et al. 2017). Both crystalloids and colloids are lacking oxygen-carrying capacity and coagulation capability. Colloids have a longer intravascular half-life and can restore intravascular volume more rapidly at a lower administered volume than crystalloids (Dutton et al. 2010). PRBC is the mainstay of treatment in hemorrhagic shock. Plasma is indicated for the treatment of coagulopathy that arises during resuscitation. One unit of plasma for each unit of PRBC is generally required in a massive transfusion situation (one blood volume or about ten units of PRBCs); plasma is not usually necessary with the transfusion requirement of one to four units of PRBCs; the need for plasma is variable and better guided by coagulation studies when five to nine units of PRBCs are given. Transfused platelets have a very short serum half-life and should generally be administered only to patients with visible coagulopathy or to TBI patients whose platelet counts are lower than 100,000. *IV* intravenous, *PRBC* packed red blood cell, *SBP* systolic blood pressure, *CVP* central venous pressure, *PAC* pulmonary artery catheter, *PT* prothrombin time, *PTT* partial thromboplastin time, *INR* international normalized ratio

consequences are the centerpieces in the post-SCI management. Airway management in a patient with potential SCI is confounded by multiple factors, including unstable or uncleared C-spine, combative/uncooperative patient, full stomach, and potential difficult airway. The airway management algorithm presented above is appropriate for SCI, as well as TBI.

There is no existing clinical evidence to definitively recommend the use of any neuroprotective pharmacologic agent, including steroids, in the treatment of acute SCI in order to improve functional recovery. Currently, administration of glucocorticoid for the treatment of acute SCI is not recommended. Accumulating evidence suggests that high-dose steroids are associated with harmful side effects.

Multisystem Sequelae After SCI and Their Management

The management of the deleterious post-SCI multisystem sequelae is summarized in Table 10.3.

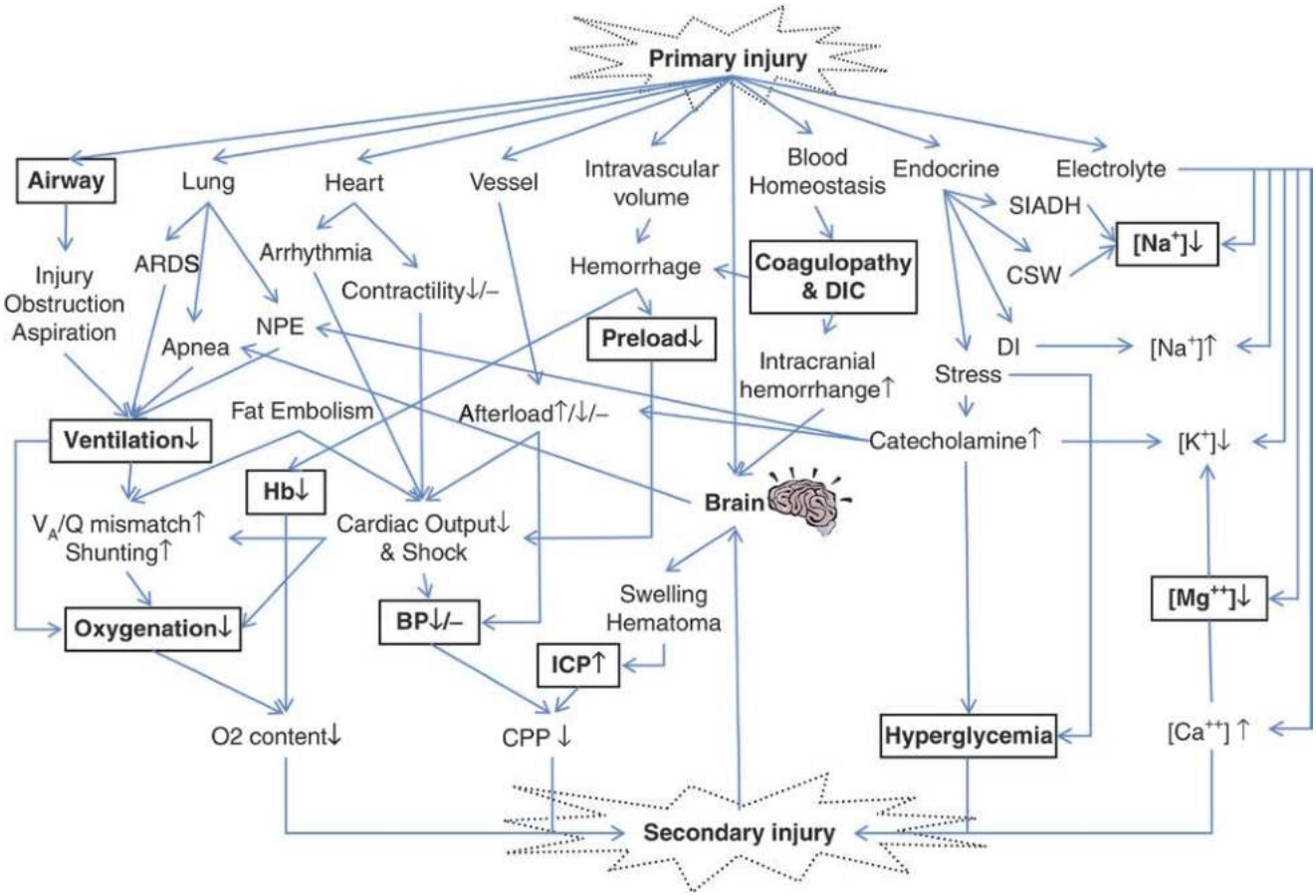

Fig. 10.4 Schematic illustration of the pathophysiologic processes after TBI with emphasis on the development of secondary injury. The open squares highlight the targets of clinical interventions. *ARDS* adult respiratory distress syndrome, *NPE* neurogenic pulmonary edema, *Hb* hemoglobin, V_A/Q ventilation over perfusion, *BP* blood pressure, *ICP* intracranial pressure, *CPP* cerebral perfusion pressure, *SIADH* syndrome of inappropriate antidiuretic hormone release, *CSW* cerebral salt-wasting syndrome, *DI* diabetes insipidus, *DIC* disseminated intravascular coagulopathy, [N_a^+] sodium, [K^+] potassium, [Mg^{++}] magnesium, [C_a^{++}] calcium; ↑, increase; ↓, decrease; –, no change

Table 10.2 Multisystem sequelae and their managements after traumatic brain injury

System	Sequelae	Management	Guideline recommendations for severe TBI[a]
Airway	Apnea	Early endotracheal intubation	Level II: pneumonia prophylaxis
	Obstruction		Level II: early tracheostomy when feasible
	Injury		
	Aspiration		
Pulmonary	ARDS	Supportive	Level II: prophylactic hyperventilation not recommended
	NPE	Mechanical ventilation	Level III: temporary hyperventilation for worsening ICP
	Contusion	High FiO2	Level III: avoid hypoxia (PaO_2 <60 mmHg or SaO_2 <90%)
	Pneumothorax	Consider PEEP	Level III: avoid jugular venous saturation <50% or brain tissue oxygen tension <15 mmHg
		Thoracostomy	
Cardiovascular	Hypovolemia	Maintain normal to high normal BP	Level II: avoid hypotension (systolic BP <90 mmHg)
	Arrhythmia	Replace intravascular volume	
	Contusion	Vasopressors	Level II: avoid aggressively maintaining CPP >70 mmHg due to ARDS risk
	Tamponade	Pericardial window	Level III: avoid low CPP (<50 mmHg)
Brain	Primary injury	Monitor and control ICP	Monitor ICP via ventricular catheter connected to an external strain gauge
	Secondary injury	Prevent secondary injury	Level II: monitor ICP in all salvageable patients with a severe TBI (GCS score of 3–8 after resuscitation) and an abnormal CT scan
			Level II: avoid ICP >20 mmHg
	↑ICP	Decrease $CMRO_2$	Level II: prophylactic barbiturates coma not recommended; barbiturate coma recommended for elevated ICP refractory to maximum standard medical and surgical treatment
	↓CPP	Hypothermia[b]	
		Hyperventilation	
		Hyperosmolar therapy	
		Avoid hypotonic solutions	
		Avoid glucose-containing solutions	
		CSF drainage	
		Decompressive craniectomy	
		Barbiturate coma	Level II: prophylactic anticonvulsants indicated to decrease the incidence of early (within 7 days) but not late posttraumatic seizures
		IV anesthetic agents	
		Avoid inhalational agents	Level III: restrict mannitol use prior to ICP monitoring to patients with signs of transtentorial herniation or progressive neurological deterioration not attributable to extracranial causes
Blood and homeostasis	Acute hemorrhage	PRBC → keep Hct ≥30	Level III: graduated compression stockings or intermittent pneumatic compression (IPC) stockings is recommended and should be combined with LMWH or low-dose unfractionated heparin for DVT prophylaxis; however, there is an increased risk for expansion of intracranial hemorrhage
	Coagulopathy	FFP and Factor VIIa	
	DIC	DIC treatment	
	Thrombocytopenia	Platelet	
	DVT	Prophylaxis	
	Hyponatremia	NS or 3% NS slowly	
	Hypomagnesemia	Magnesium replacement	
Endocrine	Hyperglycemia	Insulin → keep BG <200 ml/dl	Level I: the use of steroids is not recommended for improving outcome or reducing ICP. In patients with moderate and severe TBI, high-dose methylprednisolone is associated with increased mortality and is contraindicated
	SIADH	Water restriction	
	CSW	Sodium replacement	
	DI	DDAVP	

ARDS adult respiratory distress syndrome, *NPE* neurogenic pulmonary edema, *FiO_2* inspired oxygen fraction, *PEEP* positive end-expiratory pressure, *ICP* intracranial pressure, *PaO_2* arterial oxygen partial pressure, *SaO_2* arterial oxygen saturation, *BP* blood pressure, *CPP* cerebral perfusion pressure, *$CMRO_2$* cerebral metabolic rate of oxygen, *PRBC* packed red blood cell, *FFP* fresh frozen plasma, *DVT* deep venous thrombosis, *LMWH* low molecular weight heparin; *Hct* hematocrit, *BG* blood glucose, *SIADH* syndrome of inappropriate antidiuretic hormone release, *CSW* cerebral salt-wasting syndrome, *DI* diabetes insipidus, ↑ increase, ↓ decrease

[a]Based on "Guidelines for the Management of Severe Traumatic Brain Injury, 3rd Edition. Journal of Neurotrauma. 2007: 24 (Supplement 1)." Level I recommendations are based on the strongest evidence for effectiveness and represent principles of patient management that reflect a high degree of clinical certainty; level II recommendations reflect a moderate degree of clinical certainty; for level III recommendations, the degree of clinical certainty is not established

[b]Temperature management is still a matter of controversy

Table 10.3 Multisystem sequelae and their managements after spinal cord injury

Systems	Sequelae	Managements[a]
Pulmonary	Weak or paralyzed respiratory muscles (depend on the level of injury); reduced lung volumes except for residual volume, atelectasis; high risks for infection and aspiration; pulmonary edema (cardiogenic, noncardiogenic); coexisting blunt chest trauma (pulmonary contusions, hemothorax, pneumothorax); respiratory failure (hypoxemia, hypercapnia)	Aggressive pulmonary hygiene; bronchodilator therapy; early use of fiberoptic bronchoscopy in cases of lobar atelectasis secondary to retained secretions; early endotracheal intubation or tracheostomy when feasible[b]; early institution of mechanical ventilation; admit patients with complete tetraplegia and injury level at C5 or rostral to ICU; ventilator-associated pneumonia prophylaxis
Cardiovascular	*Orthostatic hypotension* due to vasodilation caused by functional sympathectomy	Intravascular volume repletion (overzealous fluid administration can cause or worsen pulmonary edema); vasopressor therapy; maintain BP with a balance of infusion and inotropes
	Spinal shock (characterized by hypotension, bradycardia, hypothermia, loss of somatic motor and sensory function, loss of voluntary rectal contraction, and a typical resolution over a period of days to a few weeks) caused by the imbalance of autonomic nervous system due to functional sympathectomy and unopposed parasympathetic activity	Exclude other injuries before assigning the cause of hypotension to neurogenic shock, determine the initial base deficit or lactate level to assess severity of shock and need for ongoing fluid resuscitation; invasive hemodynamic monitors; intravascular volume repletion and vasopressor therapy; treat persistent bradycardia
	Bradycardia due to loss of cardiac accelerator nerves (T1–T4) and unopposed parasympathetic nerves; profound bradycardia, even cardiac arrest, when stimulating the patient; supraventricular dysrhythmia; ventricular dysrhythmia	Anticipate bradycardia and hypotension during intubation of the tetraplegic patient; sedate the patient before stimulation such as tracheal suctioning; administer atropine; consider temporary pacemaker if atropine not working
Autonomic nervous system	Autonomic dysreflexia (or hyperreflexia) is a massive sympathetic response due to the loss of the modulation by the normal inhibitory impulses arising from brain stem and hypothalamus, characterized by vasoconstriction below the lesion and vasodilation above the lesion and often accompanied by bradycardia, ventricular dysrhythmias, and even heart block. It occurs in 85% of patients with spinal cord transections above T5 and usually begins to appear about 2–3 weeks after injury	Change patient's position from supine to sitting; loosen any clothing or constrictive devices; quickly survey the individual for the instigating causes, place an indwelling urinary catheter if not in place or troubleshoot the catheter if in place, consider the possibility of fecal impaction and check the rectum for stool; consider antihypertensive treatment; consider deep general, epidural, or spinal anesthesia
Blood and homeostasis	DVT (40% of patients with complete SCI); PE (4–13% and primarily in the 1st month after SCI)	Prophylactic treatment for a minimum of 3 months; combination of mechanical compression devices and adjusted-dose of heparin, LMWH, or warfarin in all patients once primary hemostasis achieved[c]; consider placing an inferior vena cava filter[d]
Gastrointestinal	Ileus; gastroparesis; peptic ulcer disease; pancreatitis; acalculous cholecystitis; occult acute abdomen	Aspiration precaution; gastric decompression via nasogastric tube; antacids/H_2 blockers/sucralfate; provide appropriate nutrition
Genitourinary	Bladder flaccidity (early phase), bladder spasticity (late phase); recurrent UTI/urosepsis; nephrocalcinosis	Place an indwelling urinary catheter early and leave it in place at least until a stable hemodynamics achieved and strict attention to fluid status no longer needed
Muscle	Hyperkalemia from succinylcholine	Avoid the use of succinylcholine after the first 48 h post-SCI
Bone	Osteoporosis; hypercalcemia; heterotopic ossification and muscle calcification	Early physical therapy
Skin	Decubitus ulcers	Frequently assess areas at risk and provide meticulous care
Thermoregulation	Prone to hypothermia due to inability to conserve heat	Monitor and regulate temperature
Immunologic	Pneumonia; urosepsis; skin infection	Relevant prophylaxis and appropriate antibiotics

DVT deep venous thrombosis, *PE* pulmonary embolism, *LMWH* low molecular weight heparin, *UTI* urinary tract infection

[a]Based on "Consortium for Spinal Cord Medicine: Early acute management in adults with spinal cord injury: a clinical practice guideline for health-care professionals. 2008"

[b]For those patients who are likely to remain ventilator dependent or to wean slowly from mechanical ventilation over an extended period of time

[c]Intracranial bleeding, perispinal hematoma, or hemothorax are potential contraindications to the administration of anticoagulants, but anticoagulants may be appropriate once bleeding has stabilized

[d]Only in those patients with active bleeding anticipated to persist for more than 72 h and begin anticoagulants as soon as possible

Key Points

- Life-threatening situations, including airway, breathing, and circulation, are always the priorities in managing patients after traumatic injury.
- The early diagnosis and management of the coexisting TBI and/or SCI in a polytrauma patient is of paramount importance in terms of preventing further injury immediately after injury and preserving neurologic function.
- The early diagnosis and treatment of multisystem sequelae after traumatic injury, such as hypoxemia and hypotension, are crucial in preventing secondary injury after TBI or SCI, which should be the focus of attention after initial successful resuscitation.

Suggested Reading

Carney N, Totten AM, O'Reilly C, Ullman JS, Hawryluk GW, Bell MJ, Bratton SL, Chesnut R, Harris OA, Kissoon N, Rubiano AM, Shutter L, Tasker RC, Vavilala MS, Wilberger J, Wright DW, Ghajar J. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery. 2017;80(1):6–15.

Dutton RP, McCunn M, Grissom TE. Anesthesia for trauma. In: Miller R, editor. Miller's anesthesia. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010. p. 2277–311.

Furlan JC, Fehlings MG. Cardiovascular complications after acute spinal cord injury: pathophysiology, diagnosis, and management. Neurosurg Focus. 2008;25:1–15.

Harris MB, Sethi RK. The initial assessment and management of the multiple-trauma patient with an associated spine injury. Spine. 2006;31:S9–15.

Hurlbert RJ, Hadley MN, Walters BC, Aarabi B, Dhall SS, Gelb DE, Rozzelle CJ, Ryken TC, Theodore N. Chapter 8: pharmacological therapy for acute spinal cord injury. Guideline for the management of acute cervical spine and spinal cord injuries. Neurosurgery. 2013;72:93–105.

Lim HB, Smith M. Systemic complications after head injury: a clinical review. Anaesthesia. 2007;62:474–82.

Matjasko MJ, Stier GR, Schell RM, Cole DJ. Multisystem sequelae of severe head injury. Spinal cord injury. In: Cottrell JE, Smith DS, editors. Anesthesia and neurosurgery. 4th ed. St. Louis: Mosby; 2001. p. 693–747.

Moppett IK. Traumatic brain injury: assessment, resuscitation and early management. Br J Anaesth. 2007;99:18–31.

11 Rare Neurologic Disorders and Neuromuscular Diseases: Risk Assessment and Perioperative Management

Nicholas Hirsch and Ugan Reddy

Neurodegenerative diseases
Parkinson's disease
Amyotrophic lateral sclerosis
Demyelinating disease
Multiple sclerosis
Neuromuscular diseases
Guillain–Barré syndrome
Myasthenia gravis
Lambert–Eaton myasthenic syndrome
Critical illness neuropathy and myopathy
Muscle diseases
Muscular dystrophies
Myotonic dystrophy

Neurodegenerative Diseases

Parkinson's Disease

Overview

- Parkinson's disease (PD) is characterized by triad of bradykinesia (difficulty initiating movement), increased muscle tone (cogwheel rigidity), and tremor (pill-rolling).
- Seen in 3% of population >65 years old, it is due to an imbalance of dopamine and acetylcholine (ACh) in the substantia nigra of the basal ganglia.
- Etiology is usually unknown although it may follow traumatic brain injury, cerebrovascular disease, carbon monoxide poisoning, and encephalitis. Drugs causing parkinsonism include phenothiazines, butyrophenones, and metoclopramide.
- Drug treatment of PD aims to increase levels of dopamine in basal ganglia and includes levodopa, dopamine agonists (e.g., bromocriptine, pergolide), and monoamine oxidase type B inhibitors (e.g., selegiline). Surgical treatment centers on deep brain stimulation (especially of subthalamic nucleus).

Implications for the Neurosurgical Patient

A number of physiological systems are affected in PD (Table 11.1).

Concerns and Risks

- Antiparkinsonian drug therapy must be continued throughout the perioperative period (via a nasogastric tube if necessary) as untreated severe PD can result in respiratory and bulbar failure.
- Drugs which worsen PD (e.g., metoclopramide, high-dose opioid agents) should be avoided.
- Thiopental, propofol, and suxamethonium are safe in PD patients.

Key Points

- Patients with Parkinson's disease require thorough preoperative assessment of their CNS and their respiratory and cardiovascular systems.
- Antiparkinsonian medication must be continued throughout the perioperative period.
- Drugs which exacerbate parkinsonism must be avoided.
- Careful cardiovascular monitoring is essential as autonomic nervous system involvement may be present.

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Table 11.1 Physiological derangements seen in Parkinson's disease

System	Abnormalities
Respiratory	Upper airway/vocal cord dysfunction may result in postoperative laryngospasm
	Respiratory muscle impairment due to rigidity and bradykinesia
	Poor lung function due to repeated aspiration
Cardiovascular	Arrhythmias if on high doses of levodopa
	Orthostatic hypotension due to PD itself or chronic therapy with levodopa (causes reduction in blood volume and a decrease in norepinephrine production and stores)
	Autonomic instability especially if parkinsonism is associated with other neurodegenerative diseases (e.g., multisystem atrophy)
Gastrointestinal	Poor swallow in majority of patients with abnormal handling of saliva and increased risk of tracheal aspiration
	Increased incidence of reflux and constipation
	Poor nutritional status
Central nervous system	Bradykinesia, muscle rigidity, and tremor
	Depression
	Confusion, hallucinations

Amyotrophic Lateral Sclerosis (Motor Neuron Disease)

Overview

- Amyotrophic lateral sclerosis (ALS) is characterized by degeneration of motor neurons throughout the central nervous system from motor cortex to anterior horn cell.
- Onset most common in late middle age and death usually occurs within 3 years.
- Patients may present with bulbar and pseudobulbar symptoms and signs (dysphagia, dysarthria, poor tongue movement, and emotional lability), with cervical symptoms (weakness and wasting of arm and hand muscles, fasciculation, and brisk reflexes) and lumbar symptoms (e.g., foot drop, difficulty climbing stairs).
- Death usually caused by pneumonia is secondary to respiratory muscle weakness and aspiration pneumonia. Riluzole, a glutamate antagonist, prolongs life expectancy by 3 months.

Implications for the Neurosurgical Patient

The anesthesiologist usually encounters the patient with ALS when anesthesia and surgery are required for an unrelated condition; the intensivist encounters the patient when the question of intensive care treatment of respiratory failure arises. This clearly brings profound ethical issues to the forefront.

Concerns and Risks

- Respiratory muscle weakness is invariable in the latter stages of ALS, and many patients will be receiving intermittent mechanical ventilation either via a nasal mask or tracheostomy.
- Postoperative weaning from mechanical ventilation may prove to be impossible due to respiratory muscle weakness.
- Bulbar dysfunction predisposes to perioperative pulmonary aspiration and airway obstruction.
- Suxamethonium may result in severe hyperkalemia and must be avoided. Patients with ALS require reduced doses of nondepolarizing neuromuscular blocking agents.

Key Points

- Patients with ALS often have profound bulbar dysfunction increasing the perioperative risk of pulmonary aspiration.
- Respiratory muscle function is almost invariably affected, and patients may be receiving respiratory support preoperatively. Postoperatively it may be impossible to wean the patient from mechanical ventilation, and it is important that this possibility is discussed carefully with the patient and their relatives.
- Suxamethonium must be avoided as it may cause fatal hyperkalemia.

Demyelinating Disease

Multiple Sclerosis

Overview

- Multiple sclerosis (MS) is the most common of the demyelinating diseases and is characterized by a wide spectrum of neurological symptoms and signs that are "disseminated in time and space."
- Symptoms and signs include visual disturbance (typically caused by optic neuritis; frequently first manifestation), sensory and motor disturbances (causing pain, numbness, weakness, spasticity, etc.), autonomic dysfunction, and behavioral changes.
- Most commonly affects women between ages of 20–40 years. Eighty-five percent suffer from intermittent partial or complete relapses and remissions ("relapsing-

Table 11.2 Physiological derangements seen in multiple sclerosis

Abnormality	Comments
Disordered control of breathing, especially during sleep	Seen with brainstem involvement
Poor pharyngeal and laryngeal control predisposing to aspiration	Seen with lower cranial nerve involvement
Diaphragmatic weakness	Seen with cervical cord involvement
Generalized respiratory muscle weakness	May occur with baclofen treatment of spasticity
Postural hypotension	Seen with high thoracic cord lesions

remitting MS"), while others exhibit a slowly progressive picture (primary progressive MS).
- Diagnosis is confirmed using magnetic resonance imaging and examination of cerebrospinal fluid.
- Acute relapses of MS are treated with high-dose corticosteroids and/or plasma exchange. Treatments shown to reduce recurrence rates of relapses include interferon beta-1a and beta-1b, azathioprine, and cyclophosphamide.

Implications for the Neurosurgical Patient

MS can affect all parts of the CNS resulting in respiratory and cardiovascular instability (Table 11.2).

Concerns and Risks

- Neurological deficits should be recorded carefully preoperatively.
- Bulbar and respiratory function must be assessed.
- Spinal anesthesia has resulted in worsening of neurological deficit although epidural anesthesia has been successfully used, often avoided for medicolegal reasons.
- Suxamethonium may result in fatal hyperkalemia; nondepolarizing neuromuscular blocking agents have variable effects and require intraoperative monitoring.
- Increases in body temperature can result in exacerbation of MS and must be avoided.

Key Points
- MS may affect bulbar and respiratory function.
- Drug therapy of MS may influence anesthesia.
- Suxamethonium must be avoided and nondepolarizing neuromuscular blocking agents used with careful neuromuscular monitoring.
- Rises in body temperature should be avoided.

Neuromuscular Diseases

Guillain–Barré Syndrome

Overview

- Guillain–Barré syndrome (GBS) is the most common cause of acute neuromuscular paralysis in the Western world and is usually the result of a postinfectious demyelinating polyneuropathy.
- In its classical form, it is characterized by ascending limb weakness, areflexia, and mild sensory symptoms (usually glove and stocking paresthesia).
- Thirty percent of GBS patients require tracheal intubation and mechanical ventilation because of respiratory and/or bulbar muscle paralysis.
- Diagnosis is based on history, examination, nerve conduction studies, and CSF examination.

Implications for the Neurocritical Care Patient

Patients often require prolonged periods of mechanical ventilation, and tracheostomy is usually performed early. Suxamethonium may result in hyperkalemia and must be avoided. Autonomic involvement may result in labile blood pressure and tachy- and bradyarrhythmias. General management consists of meticulous nursing care, management of pain, early nutrition, and thromboembolic prophylaxis. Specific treatment consists of plasma exchange or intravenous immunoglobulin (IVIg) which are equally efficacious.

Key Points
- GBS is the most common cause of acute neuromuscular paralysis.
- Thirty percent of patients will require mechanical ventilation, often for prolonged periods; tracheostomy should be performed early.
- Autonomic involvement may result in cardiovascular instability.
- Specific treatment involves plasma exchange or intravenous immunoglobulin which accelerate recovery.

Myasthenia Gravis

Overview

- Myasthenia gravis (MG) is a disease of the neuromuscular junction (NMJ) in which IgG autoantibodies are directed toward the postsynaptic ACh receptor at the NMJ. The decreased ACh receptor density causes weakness and fatigability of skeletal muscle.
- Fifteen percent of patients with MG will require mechanical ventilation during the course of their disease; when this occurs it is called a *myasthenic crisis*. Deterioration may also be associated with overtreatment with anticholinesterase agents; this is referred to as *cholinergic crisis.* However, clinical presentation is often similar between crisis types.

Treatment of MG includes anticholinesterase drugs (e.g., neostigmine, pyridostigmine), immunosuppressive agents (e.g., prednisolone, azathioprine), and thymectomy. IVIg and plasma exchange are useful in the treatment of myasthenic crisis.

Implications for the Neurosurgical Patient

Patients with MG either present for thymectomy or for surgery unrelated to their condition; intensivists encounter MG patients when they present with myasthenic or cholinergic crises.

Concerns and Risks

- Patients with MG undergoing anesthesia require careful assessment of their respiratory reserve. A forced vital capacity of <2.9 L, bulbar dysfunction, and a long history of MG are associated with increased risk of needing postoperative mechanical ventilation.
- Drug treatment must be optimized preoperatively. Hydrocortisone should be given at induction if patients have been receiving corticosteroid therapy.
- Patients are relatively resistant to suxamethonium and are very sensitive to nondepolarizing neuromuscular blocking agents. Careful neuromuscular monitoring is mandatory.
- Patients in myasthenic crisis often require prolonged periods of mechanical ventilation, while their MG is controlled with a combination of anticholinesterase and immunosuppressant drugs and intravenous immunoglobulin treatment.

Key Points

- Patients with MG often have poor respiratory reserve and require careful preoperative assessment and optimization of respiratory muscle function and drug treatment.
- Patients with MG are resistant to suxamethonium and sensitive to nondepolarizing neuromuscular blocking drugs. Their use should be titrated against effect using neuromuscular monitoring.

Lambert–Eaton Myasthenic Syndrome

Overview

- Lambert–Eaton myasthenic syndrome (LEMS) is a disease of the NMJ in which IgG autoantibodies are directed toward the presynaptic voltage-gated calcium channel receptor. Blockage of these channels results in decreased release of ACh at the NMJ leading to muscle weakness.
- Ocular and proximal leg muscles are most commonly affected; respiratory muscle failure is rare.
- Autonomic involvement is common.
- Fifty to 70% of patients have an underlying malignancy (most commonly small-cell carcinoma of the lung).

Implications for the Neurosurgical Patient

Patients most commonly present for resection of their bronchial tumor but may also be admitted for investigation of unexplained muscular weakness.

Concerns and Risks

- Patients often have symptoms and signs of underlying malignancy and smoking related illness.
- Patients with LEMS are extremely sensitive to both suxamethonium and the nondepolarizing neuromuscular blocking drugs, and anticholinesterase agents may be ineffective at reversing the latter's actions.

Critical Illness Polyneuropathy and Myopathy

Overview

- Critical illness polyneuropathy (CIP) is an acute axonal motor and sensory neuropathy that occurs in 50% of ITU

patients; its incidence rises to almost 100% of patients with the severe sepsis.
- Clinical features of CIP include generalized muscle weakness and wasting with absent or reduced reflexes. Diagnosis requires exclusion of other causes of weakness and nerve conduction studies.
- Prevention of CIP includes rapid treatment of sepsis and possibly tight glycemic control.
- Critical illness myopathy (CIM) is seen in a similar population to CIP.
- There may be an association between CIM and the use of corticosteroids and neuromuscular blocking drugs.
- Definitive diagnosis requires muscle biopsy.

Implications for the Neurointensive Care Patient

- CIP and CIM may coexist and are potent causes of failure to wean from mechanical ventilation.
- It may be difficult to differentiate between CIP and CIM, and the term *polyneuromyopathy* has been suggested to encompass both entities.
- Treatment is largely supportive while awaiting recovery.

Muscle Diseases

Muscular Dystrophies

Overview

- The muscular dystrophies (MD) are a group of inherited muscle disorders characterized by progressive muscle weakness often ultimately resulting in respiratory failure.
- Duchenne muscular dystrophy (DMD) is the commonest (1 in 3500 live male births) muscular dystrophy and is due to a deficiency of dystrophin, a protein necessary for sarcolemmal stability.
- Respiratory muscle failure and dilated cardiomyopathy in DMD often lead to death from cardiopulmonary causes. Associated scoliosis exacerbates respiratory dysfunction. Mean survival is 25 years.
- Patients are often receiving noninvasive nasal positive pressure ventilation (NPPV) especially during sleep.

Concerns and Risks

- Patients with DMD with impaired respiratory function are at high risk for death when exposed to sedation or general anesthesia.
- Patients with DMD have an *increased risk of a malignant hyperthermia* type reaction with associated rhabdomyolysis, hyperkalemia, and cardiac arrest when anesthetized with volatile anesthetic agents and suxamethonium.
- There is an increased need for cardiopulmonary support following surgery.
- Gastrointestinal pathology may lead to acute gastric dilatation.

Key Points

- Patients with DMD require thorough assessment of respiratory and cardiac function. An FVC < 30% of predicted is associated with an increased need for postoperative respiratory support.
- Total intravenous anesthetic techniques should be considered for induction and maintenance of anesthesia. *Volatile anesthetic agents and suxamethonium must be avoided.*
- Following extubation, a period of NPPV may be necessary.
- Postoperatively, patients must be cared for in a high-dependency setting. Supplemental oxygen therapy must be used with caution.
- A nasogastric tube should be in situ to treat gastric distension and immobility.

Table 11.3 Systems affected by DM1

System	Abnormalities
Cardiac	Conduction defects which may result in sudden death. Cardiomyopathy, septal defects, and valvular disease
Respiratory	Respiratory muscle weakness with alveolar hypoventilation and poor cough. Reduced ventilatory to carbon dioxide. Central and obstructive sleep apnoea. Undue sensitivity to sedative and anesthetic agents
Gastrointestinal	Dysphagia, reduced rate of gastric emptying
Endocrine	Hypothyroidism, diabetes mellitus

Myotonic Dystrophy

Overview

- Myotonic dystrophy (DM1) is an autosomal dominant disease of muscle characterized by myotonia (persistent contraction following exercise of a muscle). Prevalence is 1 in 20,000 of population.
- DM1 is a multisystem disease (Table 11.3).

Concerns and Risks

- Patients with DM1 are sensitive to the respiratory depressant effects of premedication, induction agents, and opioid drugs.
- Suxamethonium may result in an increased myotonia making laryngoscopy and ventilation impossible. Hyperkalemia following suxamethonium has been reported.
- If muscle wasting is present, nondepolarizing neuromuscular blocking drugs may have a prolonged action. Anticholinesterase drugs may precipitate increased myotonia.
- Surgical stimulation, cold, and shivering may increase myotonia.

Key Points

- Patients with DM1 require careful cardiorespiratory assessment.
- Reduced doses of sedative, induction, and analgesia agents are required.
- Suxamethonium should be avoided.
- Nondepolarizing neuromuscular agents should be carefully titrated using neuromuscular monitoring.
- Normothermia must be maintained perioperatively.

Suggested Reading

Parkinson's Disease

Clarke CE. Parkinson's disease. Br Med J. 2007;335:441–5.
Nicholson G, Pereira AC, Hall GM. Parkinson's disease and anaesthesia. Br J Anaesth. 2002;89:904–16.

Amyotrophic Lateral Sclerosis (Motor Neuron Disease)

Bradley MD, Orrell RW, Clarke J, et al. Outcome of ventilatory support for acute respiratory failure in motor neurone disease. J Neurol Neurosurg Psychiatry. 2002;72:752–6.
Mitchell JD, Borasio GD. Amyotrophic lateral sclerosis. Lancet. 2007;369:2031–41.

Multiple Sclerosis

Dorotta IR, Schubert A. Multiple sclerosis and anesthetic implications. Curr Opin Anaesthesiol. 2002;15:365–70.

Guillain–Barré Syndrome

Hughes RAC, Cornblath DR. Guillain-Barré syndrome. Lancet. 2005;366:1653–66.
Ng KKP, Howard RS, Fish DR, Hirsch NP, Wiles CM, Miller DH. Management and outcome of severe Guillain-Barré syndrome. Q J Med. 1995;88:243–50.

Myasthenia Gravis

Meriggioli MN, Sanders DB. Autoimmune myasthenia gravis: emerging clinical and biological heterogeneity. Lancet Neurol. 2009;8:475–90.
O'Riordan JI, Miller DH, Mottershead JP, Hirsch NP, Howard RS. The management and outcome of patients treated acutely in a neurological intensive care unit. Eur J Neurol. 1998;5:137–42.

Lambert–Eaton Myasthenic Syndrome

Hirsch NP. Neuromuscular junction in health and disease. Br J Anaesth. 2007;99:132–8.

Critical Illness Polyneuropathy and Myopathy

Zink W, Kollmar R, Schwab S. Critical illness polyneuropathy and myopathy in the intensive care unit. Nat Rev Neurol. 2009;5:372–9.

Muscular Dystrophies

Birnkrant DJ, Panitch HB, Benditt JO, et al. American College of Chest Physicians consensus statement on the respiratory and related management of patients with Duchenne muscular dystrophy undergoing anesthesia or sedation. Chest. 2007;132:1977–86.

Myotonic Dystrophy

Russell SH, Hirsch NP. Anaesthesia and myotonia. Br J Anaesth. 1994;72:210–6.

Perioperative Pharmacotherapy in Neurosurgery: Risk Assessment and Planning

12

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Inhaled Anesthetics

Overview

These drugs are widely used as fundamental components of general anesthesia.

Implications for the Neurosurgical Patient

In addition to their marked cerebrovascular effects, inhaled anesthetics produce important hemodynamic and respiratory changes in a dose-dependent manner that can have a significant impact on the neurologic patient.

Concerns and Risks

All inhalational anesthetics are potent cerebral vasodilators in a dose-dependent fashion; therefore, they have the potential to increase intracranial pressure (ICP).

Halothane is the most powerful cerebral vasodilator; however, currently it has limited use. It produces an increase in cerebral blood flow in association with a decrease in cerebrovascular resistance that can result in significant increases in ICP. Controlled hyperventilation can help to limit this effect.

Isoflurane, sevoflurane, and desflurane produce cerebral vasodilation and an increase in ICP, but the effects are clinically significant with doses higher than 1 MAC. Desflurane might produce more vasodilation than the others and has been proposed to be the inhaled agent of choice for brain protection in patients undergoing temporary cerebral artery occlusion during cerebrovascular surgery.

Nitrous oxide has a variable effect from zero to marked cerebral vasodilation and the potential to increase ICP depending on the initial $PaCO_2$ and the presence of adjuvant anesthetic drugs. Experimental evidence suggests that inhaled anesthetics cause neuro-apoptosis in the very young and the brain of the elderly. Nitrous oxide is the only inhaled agent that appears to worsen short-term outcome following transient focal cerebral ischemia.

Key Points

- Inhaled anesthetics as a group cause cerebral vascular dilation and increased ICP in high doses.
- Avoid halothane if possible.
- Use isoflurane, sevoflurane, or desflurane at a concentration ≤1 MAC.
- Use nitrous oxide cautiously.

Intravenous Anesthetics

Overview

They are used virtually in every general anesthetic, either only at induction or also during maintenance. These drugs are responsible for the hypnosis, while opioids provide the analgesic component of general anesthesia (balanced anesthesia).

Implications for the Neurosurgical Patient

In general, intravenous anesthetics reduce the cerebral metabolic rate and oxygen consumption, and because they have no vasodilatory effects, both cerebral blood flow and ICP are proportionally reduced.

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Concerns and Risks

The optimal anesthetic should maintain normal coupling between cerebral blood flow and metabolism, keep cerebrovascular autoregulation intact, and not increase cerebral blood volume and ICP and ideally, (potentially combined with other drugs) provide neuroprotective effects.

Barbiturates and propofol are used during temporary clipping of intracerebral arteries in cerebral vascular surgery (i.e., aneurysm and extra- to intracranial bypass surgery) because of their allegedly neuroprotective effects in focal ischemia. When barbiturates are used as the primary anesthetic (usually by infusion), emergence may be delayed. In addition, propofol infusion (short- or long-term) infrequently can be associated with impaired free fatty acid utilization and mitochondria activity (propofol infusion syndrome) often presenting as acidosis, cardiac dysrhythmias, and myocardial dysfunction.

Alpha2-adrenoceptor agonists (e.g., dexmedetomidine) are now being used as a component of a balanced anesthesia and for sedation in the ICU. Although dexmedetomidine is associated with an easily managed level of sedation, rapid administration may be associated with hypertension and slow rate infusion with hypotension. In addition, there is the concern that dexmedetomidine might prevent normal cerebral vasodilation during hypoxemia.

Although etomidate is a reasonable choice for the induction of anesthesia in cardiovascularly compromised patients, it does not confer significant neuroprotection. A single dose of etomidate for the induction of anesthesia produces adrenal suppression that can be relevant in trauma and septic patients. As many neurologically impaired patients are receiving high-dose steroids as part of their underlying therapy, the adrenal suppression effects of etomidate might have less clinical significance in these patients. Etomidate during temporary clipping was associated with a reduction in brain oxygenation and should, therefore, be avoided in this context.

Opioids are necessary components for most surgical procedures to afford the patient with appropriate intra- and postoperative analgesia. Although they inhibit the respiratory drive, the use of short-acting opioids (fentanyl, alfentanil, and remifentanil) is common in neurosurgical patients. Using the right dose and dosing frequency, even opioids with a long duration of action can be used safely (e.g., hydromorphone). The use of opioids and benzodiazepines requires caution, particularly toward the end of surgery, as they will impair respiratory drive leading to significant increments in $PaCO_2$ and ICP.

Table 12.1 shows the effect of different drugs on some important parameters.

Table 12.1 Effect of different intravenous anesthetics on some cerebral physiologic parameters and arterial pressure

	CBF	CMR	ICP	CO_2 reactivity	Arterial pressure
Halothane	⇑	⇓	⇑	⇓⇓	⇓⇓
Isoflurane	⇑	⇓	⇑	⇓	0 or ⇓
Sevoflurane	⇑	⇓	⇑	⇓	0 or ⇓
Barbiturate	⇓ ⇓	⇓ ⇓	⇓⇓	0	⇓
Propofol	⇓⇓⇓	⇓ ⇓	⇓	0	⇓⇓
Etomidate	⇓ ⇓	⇓⇓	⇓⇓	0	0
Benzodiazepines	⇓	⇓	⇓ or 0	⇓⇓	0
Ketamine	⇑	⇑ or 0	⇑	?	⇑
Opioids	0	0	0	⇓	⇓ or 0

CBF Cerebral blood flow, *CRM* cerebral metabolic rate, *ICP* intracranial pressure, ⇑/⇓ slight increase/reduction, ⇓⇓ significant reduction, ⇓⇓⇓ marked reduction, 0 without significant effect, ? uncertain effect

Key Points

- Consider intracranial distensibility and hemodynamic parameters to choose the appropriate intravenous anesthetics.
- The use of benzodiazepines and opioids to sedate and treat pain in awake patients with closed head trauma must be done very carefully.

Neuromuscular Blocking Drugs

Overview

Neuromuscular blocking drugs (NMBs) are used to facilitate tracheal intubation, to assure lack of movement during surgery and sometimes to facilitate mechanical ventilation in the ICU.

Implications for the Neurosurgical Patient

NMBs are used in virtually all the neurosurgical patients; however, they have several adverse effects that can be harmful for these patients.

Concerns and Risks

NMBs can be classified into two groups according to their mechanism of action.

(a) ***Depolarizing** NMBs*: succinylcholine is the only drug of this group in clinical use. Its rapid onset of action makes

it particularly useful to obtain a rapid control of the airway. Some of its problems in neurologic patients include:

- *Transient increase in* ICP that might be dangerous when it is already elevated. Adequate depth of anesthesia, normal arterial pressure, and controlled $PaCO_2$ are required to reduce this adverse effect.
- ***Hyperkalemia****:* a single dose of succinylcholine (1–2 mg/kg) usually increases potassium plasma levels by approximately 0.5–1.0 mEq/L; however, in some patients with severe skeletal muscle trauma, denervation injury with skeletal muscle atrophy, upper motor neuron lesions, paraplegia, spinal cord injury or transection, stroke, and closed head trauma, severe hyperkalemia leading to cardiac arrest has been described. The mechanism for hyperkalemia appears to be linked to the increased expression of extra-junctional acetylcholine receptors on the muscle surface secondary to the abovementioned diseases.

(b) ***Nondepolarizing*** *NMBs* include pancuronium, vecuronium, rocuronium, cisatracurium, and several others. With the advent of intraoperative electrophysiologic monitoring, use of nondepolarizing NMBs has become more limited. The use of these drugs is contraindicated during EMG monitoring (e.g., acoustic neuroma surgery and facial nerve monitoring) or motor evoked potentials (e.g., for spine surgery). Great caution must be used when administering nondepolarizing NMBs in patients who have previously experienced a cerebral vascular accident (i.e., ischemic stroke). In addition to the higher risk of hyperkalemia from depolarizing NMBs (see above), these patients are at high risk of being overmedicated with nondepolarizing NMBs, particularly if neuromuscular monitoring is done on the paretic extremity (because of the higher concentration of postsynaptic receptors in that extremity secondary to upregulation).

- ***Residual paralysis*** secondary to their use is not a real adverse effect but undesired clinical practice and can lead to upper airway obstruction, hypoxemia, and hypercarbia within minutes. In addition, it has been associated with a higher rate of postoperative respiratory complications. To avoid this complication, the routine use of neuromuscular monitoring and careful clinical assessment before extubation is mandatory. Clinical manifestations include respiratory difficulty, problems swallowing secretions, and muscular weakness. Residual paralysis must be rapidly treated with anti-acetylcholinesterases. Alternatively, sugammadex has the advantage of reliably reversing profound blockade without the side effects of acetylcholinesterase inhibitors. Sugammadex is effective to reverse residual neuromuscular blockade in the neurosurgical setting, particularly when rocuronium has been used.

Key Points

- Succinylcholine should be used with great caution and only if it cannot be substituted with a nondepolarizing neuromuscular blocking agent.
- Residual paralysis must be ruled out and properly treated before extubation to be sure that the patient is safe while spontaneously breathing.

Inotropic and Vasoactive Drugs

Overview

The recognition that cerebral hypoperfusion is associated with adverse outcome in acute brain syndromes and during neurosurgery has led to an increase in the use of vasoactive drugs. Thus, some of the inotropes (adrenaline, dopamine, dobutamine, etc.) and vasoactive drugs (phenylephrine and noradrenaline) are extensively used in neurologic patients during surgery and ICU care. In some cases, vasodilators (sodium nitroprusside, nitroglycerin, calcium channel blockers, etc.) are also used.

Implications for the Neurosurgical Patient

Normally inotropic drugs have minimal or no direct effect on cerebral vessels; therefore, their effects on cerebral perfusion pressure (CPP), cerebral blood flow, intracranial volume, and ICP mostly depend on their effects on systemic hemodynamics. In patients with areas of brain with poor or lack of autoregulation (e.g., tumor, ischemia, or trauma), the maintenance of arterial pressure within a very tight range is critical. Sodium nitroprusside and nitroglycerin may worsen neurologic injury. While they do not have direct cerebrovascular vasodilatory effects, the reduction in arterial pressure may lead to vasodilation in areas of preserved autoregulation and, secondarily, to an increase in ICP: This will result in a reduction of CPP.

Concerns and Risks

Aggressive use of vasopressor drugs and fluids to raise arterial pressure can lead to systemic (pulmonary edema, cardiac failure, and myocardial ischemia) and neurologic (brain bleeding and edema) complications.

Intravenous, and to a lesser extent also by oral route, nimodipine as a prophylaxis of cerebral vasospasm after subarachnoid hemorrhage, can result in arterial hypotension. However, this does not contraindicate its use.

Key Points

- Treat and exclude reversible causes of hypotension before using vasopressor drugs to improve CPP.
- Limited experimental and clinical evidence suggests that norepinephrine might be the most appropriate catecholamine to augment cerebral perfusion in traumatic brain injury.
- Recommended therapy for severely elevated arterial pressure after acute stroke include labetalol, nicardipine, and nitroprusside (used with great caution in patients with elevated ICP). Hemodynamic goals are greatly different between hemorrhagic stroke (tight control to prevent rebleeding) and ischemic stroke (permissive hypertension to improve collateral flow).
- Any pharmacologic intervention to reduce elevated arterial pressure in neurologic patients has to be very slowly and should be intensively monitored. With continuous treatment regimes, careful and repeated reassessments are paramount with particular considerations of the treatment effects on CPP.

Diuretics and Hypertonic Saline

Overview

Diuretics, particularly mannitol and furosemide, and hypertonic saline are used in neurosurgical patients to reduce ICP and/or to obtain intraoperative brain relaxation.

Implications for the Neurosurgical Patient

Adverse effects are predictable and usually dose dependent. Therefore, these drugs can be applied safely to the neurosurgical patient if the clinician treats these known adverse effects in a preemptive fashion.

Concerns and Risks

Hypovolemia: secondary to diuretics can result in hypotension and reduced CPP.

Hypervolemia: secondary to the use of mannitol and/or hypertonic saline. Although this is rather a theoretical problem, it is transient and would only theoretically occur after rapid administration. The consequences of transient hypervolemia would be most significant in patients with a history of congestive heart failure.

Electrolyte disorders: secondary to a high urine output (hyponatremia and hypokalemia) or massive load of crystalloid solutions, particularly hypertonic saline. Mannitol causes sodium diuresis, which should be replaced to prevent hyponatremia. Loop diuretics (e.g., furosemide) cause hypokalemia, hypocalcemia, and hypomagnesaemia, which can cause cardiac arrhythmias and hypotension. When hypertonic saline is used for hyperosmolar treatment, it can produce hypernatremia and hyperchloremic metabolic acidosis. When using hypertonic saline (e.g., as a 3% solution) in the neurosurgical patient, many clinicians limit administration to a serum sodium not higher than 150 mEq/L. Hyperchloremic metabolic acidosis can be prevented by administering the 3% sodium as a 50% mix of chloride and 50% as acetate.

Key Point

- Monitor electrolyte status after a period of high urine output and/or hypertonic saline administration.

Antiemetic Drugs

Overview

Post-craniotomy patients (this excludes transsphenoidal hypophysectomy) are at high risk of postoperative nausea and vomiting (PONV). Despite the lack of a documented case of harm caused by retching or vomiting in these patients, an important number of patients undergoing general surgery fear the occurrence of PONV more than postoperative pain. However, the potential risk caused by vomiting, the associated arterial hypertension, and high intra-abdominal/intrathoracic pressure leading to high ICP suggests that avoiding/treating PONV in these patients is warranted.

Implications for the Neurosurgical Patient

Antiemetic drugs for PONV prophylaxis/treatment include several groups of drugs with an excellent safety profile in general surgery patients. However, some agents (e.g., droperidol and haloperidol) are associated with sedation. Droperidol is also an alpha-1 receptor agonist and may be associated with transient hypotension.

Concerns and Risks

Some adverse effects might be more relevant in neurosurgical patients.

Hyperglycemia: It is the most frequent known adverse effect after dexamethasone 8–10 mg IV. Steroid-induced hyperglycemia peaks between 8 and 10 h after IV administration and can exceed 200 mg/dL. Significant hyperglyce-

mia has been demonstrated to impair neurologic outcomes and increases the risks for infection and impairs wound healing. The use of dexamethasone for PONV in patients undergoing intracranial surgery should possibly not be considered the first-line therapy.

Sedation: A decrease in level of consciousness can occur secondary to many antiemetics including droperidol and haloperidol, with both time- and dose-dependent effects. Though symptoms may be mild at low-dose ranges, these drugs should be avoided in patients having craniotomy because the differential diagnosis of decreased level of consciousness may be unnecessarily complicated in the immediate post-craniotomy period.

Extrapyramidal side effects*:* They can be secondary to droperidol/haloperidol and metoclopramide, usually after higher than recommended doses. Rarely, administration of haloperidol, droperidol, promethazine, and metoclopramide may cause neuroleptic malignant syndrome. In the postoperative period of neurosurgical patient, this diagnosis must be considered in the presence of rigidity, autonomic dysfunction, hyperthermia, and mental status changes. If unrecognized and improperly treated, the outcome could be fatal.

Headache: Occurs in 3–5% of patients given 5-HT(3) antagonists at the usual doses (such us ondansetron and granisetron) and must be taken into consideration for the differential diagnosis of headache in the neurological patient.

Endocrine effects: Patients who were treated with dexamethasone PONV prophylaxis showed changes in cortisol levels. This can be important information on the analysis of potential pituitary sufficiency after transsphenoidal surgery. On this matter, TIVA (total intravenous anesthesia) can be a possible alternative in patients with high PONV risk.

Key Points

- Monitor blood glucose levels after dexamethasone administration. Treat hyperglycemia in neurological patients to a goal of 130–180 mg/dL (current recommendations).
- Neurological and surgical causes of sedation, extrapyramidal signs, and headache must be ruled out before assuming that they are secondary to AEDs.

Anticonvulsants

Overview

Seizures can appear at anytime in a neurosurgical patient. Up to 60% of people with a diagnosis of brain tumor can present it, and the onset can be before, during, or after surgery. The risk of seizure depends on the type of pathology. However, prophylactic use of anticonvulsants is not free of adverse effects, and its indication is still a debatable issue. Supporting evidence in favor or against the use of antiepileptic drugs as a primary prophylaxis in patients with brain tumor has been erratic, and some centers recommend its use only after the first convulsive episode.

Phenytoin is probably still the most commonly used agent, although the emergence of new agents such as levetiracetam appears like an eligible choice with fewer side effects.

Implications for the Neurosurgical Patient

Perioperative fluctuations in antiepileptic medication plasmatic levels may occur, contributing to the development of seizures. Adverse effects are predictable and usually dose dependent. It must be remembered that during the postoperative period, patients may have reduced protein binding (particularly affecting phenytoin) due to altered albumin and other drug-binding proteins making it imperative to monitor free drug concentrations in the perioperative period.

Concerns and Risks

Patients with brain tumors appear to present more frequently the typical anticonvulsant-induced side effects, such as cognitive impairment, myelosuppression, liver dysfunction, and dermatologic reactions compared with non-oncological patients.

Second-generation antiepileptic drugs such as levetiracetam shows similar efficacy in seizure controlling but greater tolerability and even fewer drug interaction as they are not metabolized by the hepatic P450 system.

Cognitive impairment: some problems, such us drowsiness, dizziness, and behavioral changes, are usually dose related. They are less frequent with second-generation anticonvulsant where doses as high as 5 g of levetiracetam are well tolerated without requiring level monitoring.

Hypotension: secondary to almost all these drugs especially when administered quickly by the intravenous route. Hypotension is often accentuated when these drugs are administered during surgery, as they may act synergistically with anesthetic agents having the same cardiovascular effects.

Bradycardia/arrhythmia: phenytoin when injected fast can produce arrhythmia including asystole. This risk is accentuated when the drug is administered during the period of general anesthesia.

Sedation/respiratory depression: secondary to benzodiazepines and barbiturates. Respiratory depression can result in an increased arterial tension of CO_2 and hypoxemia in

patients breathing spontaneously and thereby potentially in severe secondary brain injury.

*Interaction*s:

- Chronic treatment with phenytoin and carbamazepine is associated with modest increase in acetylcholine receptor numbers, induced liver metabolism, and increased release of acute-phase reactant proteins that bind the NMDs, all causing reduced duration of neuromuscular blockade.
- Phenytoin, carbamazepine, and phenobarbital reduce the efficacy of corticosteroids and stimulate the cytochrome P450 enzyme resulting in an accelerated metabolism of a large spectrum of chemotherapeutic agents.

Key Points

- The use of primary antiepileptic drugs in patients with brain tumor must be studied case by case, considering the type of tumor among other risk of seizure. Because of the lack of efficacy and their potential side effects primarily prophylaxis must not be use routinely with newly diagnosed patients. When used and in absence of seizure, anticonvulsant must be discontinued a week after surgery.
- Patients with previous antiepileptic treatment must receive it during the perioperative period.
- Anticonvulsant monitoring plasma levels drugs is recommended during the perioperative period.
- Anticonvulsant must be administered slowly when active seizures are not currently present. Never inject phenytoin at a rate >50 mg min^{-1}.
- When barbiturates and benzodiazepines are administered at a fast rate, check frequently hemodynamic and respiratory status until patient's recovery; consider admission to the intensive care unit.
- Monitor intraoperative neuromuscular blockade more frequently in patients under treatment with phenytoin and carbamazepine.
- In the presence of severe cutaneous reactions in patients receiving anticonvulsants other than benzodiazepines, consider changing to a different family of drugs.

Suggested Reading

Burkhardt T, Rotermund R. Dexamethasone PONV prophylaxis alters the hypothalamic-pituitary-adrenal axis after transsphenoidal pituitary surgery. J Neurosurg Anesthesiol. 2014;26:216–9.

Glantz MJ. Practice parameter: anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. Minneapolis: American Academy of Neurology; 2000.

Jackson WL. Should we use etomidate as an induction agent for endotracheal intubation in patients with septic shock?: a critical appraisal. Chest. 2005;127(3):707–9.

Lukins MB, Manninen PH. Hyperglycemia in patients administered dexamethasone for craniotomy. Anesth Analg. 2005;100:1129–33.

Martyn JA. Neuromuscular physiology and pharmacology. In: Miller R, editor. Miller's anesthesia. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010. p. 341–60.

McNamara J. Drugs effective in the therapy of epilepsies. In: Hardman JG, Limbird LE, editors. Goodman and Gilman's the pharmacological basis of therapeutics. 10th ed. New York: McGraw-Hill; 2001.

Minton MD, Grosslight K, Stirt JA, et al. Increases in intracranial pressure from succinylcholine: prevention by prior nondepolarizing blockade. Anesthesiology. 1986;65(2):165–9.

Murphy GS, Szokol JW, Marymont JH, et al. Intraoperative acceleromyographic monitoring reduces the risk of residual neuromuscular blockade and adverse respiratory events in the post anesthesia care unit. Anesthesiology. 2008;109(3):389–98.

Pasternak J, McGregor D, Lanier W, et al. Effect of nitrous oxide use on long-term neurologic and neuropsychological outcome in patients who received temporary proximal artery occlusion during cerebral aneurysm clipping surgery. Anesthesiology. 2009;110:563–73.

Patel MP, Drummond JC. Cerebral physiology and the effects of anesthetic drugs. In: Miller RD, editor. Miller's anesthesia. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010. p. 305–40.

Pfister D, Strebel SP, Steiner LA. Effects of catecholamines on cerebral blood vessels in patients with traumatic brain injury. Eur J Anaesthesiol. 2008;42(Suppl):98–103.

Reves J, Glass P, et al. Intravenous anesthetics. In: Miller R, editor. Miller's anesthesia. 7th ed. Philadelphia: Elsevier Churchill Livingstone; 2010. p. 719–68.

Rozet I, Tontisirin N, Saipin M, et al. Effect of equiosmolar solutions of mannitol versus hypertonic saline on intraoperative brain relaxation and electrolyte balance. Anesthesiology. 2007;107:697–704.

Talbert RL. The challenge of blood pressure management in neurologic emergencies. Pharmacotherapy. 2006;26(8 Pt 2):123S–30S.

The NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. N Engl J Med. 2009;360(13):1283–9.

Trement IW. Antiepileptic drugs for preventing seizures in people with brain tumors. Cochrane Database Syst Rev. 2008;(2):CD004424.

White H, Cook D, Venkatesh B. The role of hypertonic saline in neurotrauma. Eur J Anaesthesiol. 2008;42(Suppl):104–9.

13 Specific Considerations Regarding Consent and Communication with Patients and Family Prior to Neurosurgery

Kenneth Abbey and Chloe Allen-Maycock

Overview

For any medical procedure, informed consent consists of four basic elements: (1) voluntariness, (2) competence, (3) informed, and (4) comprehended (capacity). For neuroanesthesia, satisfaction of the elements may be more difficult due to both the underlying pathology and the difficult choices facing patients undergoing neurosurgery. As a result of the unique nature of neurosurgical cases, anesthesiologists need to allow more time and need to take more care in obtaining consent for the anesthetics used in those cases.

A review of the elements for valid consent is useful for understanding the challenges faced in obtaining valid consent in neurosurgical cases. The classic criteria for voluntariness was set forth in the Nuremberg Code which stated that the patient should be "able to exercise free power of choice, without the intervention of any element of force, fraud, deceit, duress, overreaching, or other ulterior form of constraint or coercion." Several factors may impair the voluntary nature of informed consent. First, sedation is commonly encountered among preoperative patients and may constitute a form of constraint on a patient's ability to fully evaluate and participate in informed consent. Sedation may be obvious in the case of a sleepy patient who has received a large dose of anxiolytic or may be more subtle, such as in a patient who has received a smaller dose of analgesic medication. The environment in which informed consent is obtained may also undermine voluntariness. Addressing informed consent in the operating room may make a patient more likely to feel pressured to agree to a procedure. The anesthesia provider may also limit voluntariness by deliberately limiting anesthetic choices for the patient, based on the anesthesia provider's preference.

Patient competency is a legal term and designation. All adults are deemed competent unless designated otherwise by a court, and a declaration of incompetence is universally followed by appointment of a legal guardian. Patients that have been declared incompetent cannot consent, and consent must be obtained from their designated guardian.

Capacity is distinct from competency and is a determination made by the physician. The subject of informed consent should have "sufficient knowledge and comprehension of the elements of the subject matter involved as to enable him to make an understanding and enlightened decision." This requires that the patient have the capacity to provide informed consent and "implies that a patient has the ability to understand and weigh medical information and make decisions." The patient must be able to understand the medical problem and proposed treatment alternatives. For some procedures, this may be relatively simple. However, as the complexity of the medical problem and treatment increases, the patient's decision-making capacity may be exceeded. Likewise, as the complexity of the medical decision increases, so does the obligation of the physician to ensure that the patient has the capacity to understand the medical decisions and its implications.

Meeting the "informed" element of consent can be obtained by addressing the four key components of the PARQ discussion: (1) procedures, (2) alternatives, (3) risks, and (4) questions. The PARQ discussion can be utilized not only to provide information to the patient but also in determining the patient's ability to understand the concomitant risks and alternatives.

Implications for Neurosurgical Procedures

Obtaining informed consent from neurosurgical patients can be complex, due to the nature of the patient's diagnosis, the treatment options, and the increased likelihood for dimin-

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ished decision-making capacity related to the neurosurgical procedure. First, voluntariness may be problematic for several reasons. Neurosurgical problems often present treatment choices without a "good" choice. For example, a patient with a brain mass must decide between surgery, which may leave the patient with a significant neurologic deficit or even death, or not having surgery and risk the tumor growing causing neurologic deficits and again possibly death. Family members may strongly support or oppose some options and may place pressure on the patient to choose a particular course.

Neurosurgical problems often compromise a patient's decision-making capacity, and any diagnosis or treatment that alters mentation may be associated with diminished capacity. Neurosurgical conditions most likely to decrease capacity include stroke and dementia. In cases of delirium, waxing and waning mental status creates a moving target for the assessment of medical decision-making capacity. Additionally, based on the degree of delirium, sedative medications may be required to maintain the patient's safety. The intensive care unit setting itself is associated with a high proportion of patients with diminished medical decision-making capacity. Conditions among patients in the ICU can range from postoperative sedation to ICU psychosis, which interfere to varying degrees with a patient's ability to evaluate medical decisions, but interfere nonetheless. Psychiatric diagnoses can also impair capacity. Unfortunately, many physicians caring for impaired patients may not appropriately identify them as such.

Much variability can exist within a given diagnosis or even between physicians evaluating whether a patient has capacity to provide informed consent. Other instruments that may be valuable in assessing capacity include the Mini-Mental State Examination (MMSE), which has been found to correlate with clinical judgments of incapacity. A score of <19 is associated with lack of capacity. The MacArthur Competence Assessment Tool for Treatment may also be utilized and specifically incorporates information related to a patient's decision-making situation. Unfortunately, these assessments can be time-consuming; the Mac-CAT takes about 20 min to perform.

Often, obtaining surgical consent implies consent for anesthesia, although the PARQ process for each should be distinct. It is possible, however, that a patient may be able to provide surgical consent without the capacity to consent to anesthesia. Again, it is incumbent on the anesthesia provider to weigh whether the patient has medical decision-making capacity, even if surgical consent has already been obtained from the patient.

Concerns and Risks

Neurosurgical patients comprise a group at risk for incomplete and/or inadequate informed consent. Taking the necessary time to assess a patient's ability to engage in and understand informed consent is fundamental to ensure the patient's ability to provide informed consent. Failure to obtain proper consent may subject the provider to a claim of battery (the tort of an inappropriate and unconsented touching).

Key Points

- Address each element of informed consent, including voluntariness, competence, informed, and comprehended (capacity).
- It is incumbent upon physicians taking care of neurosurgical patients to ensure that informed consent is obtained.
- Neurosurgical patients comprise a high-risk group of patients who may have diminished medical decision-making capacity and may require additional time.
- Maintain a heightened awareness of factors potentially interfering with obtaining informed consent.

Suggested Reading

Appelbaum PS. Assessment of patients' competence to consent to treatment. N Engl J Med. 2007;357:1834–40.

Grisso T, Appelbaum PS. MacArthur competence assessment tool for treatment (MAC-CAT-T). Sarasota: Professional Resource Press; 1998.

Kim SYH, Caine ED. Utility and limits of the mini mental state examination evaluating consent capacity in Alzheimer disease. Psychiatr Serv. 2002;53:1322–4.

Kim SYH, Karlawish JST, Caine ED. Current state of research on decision-making competence of cognitively impaired elderly persons. Am J Geriatr Psychiatry. 2002;10:151–65.

Marcucci C, Seagull FJ, Loreck D, Bourke DL, Sandson NB. Capacity to give surgical consent does not imply capacity to give anesthesia consent: implications for anesthesiologists. Anesth Analg. 2010;110(2):596–600.

Raymont V, Bingley W, Buchanen A, et al. Prevalence of mental incapacity in medical inpatients and associated risk factors: cross-sectional study. Lancet. 2004;364:1421–7.

Terry PB. Informed consent in clinical medicine. Chest. 2007;131:563–8.

Trials of War Criminals before the Nuremberg Military Tribunals under Control Council Law No. 10. vol. 2. Washington, D.C.: U.S. Government Printing Office; 1949. p. 181–2.

Neurotoxicity of General Anesthetics

14

Margaret K. Menzel Ellis and Ansgar M. Brambrink

Introduction

Rapid evolution in the safety and sophistication of general anesthesia has paved the way for revolutionary advances in medicine and surgery. However, a growing body of both preclinical and observational clinical evidence has fostered both scientific and public concerns regarding anesthetic neurotoxicity, particularly in young children. Volatile anesthetic, nitrous oxide, and propofol exposure have all been studied in animal models, revealing similarly concerning toxic effects as well as negative effects on cognition and behavior.

The severity and consistency of this injury prompted several large, retrospective database studies, the majority of which suggest an association between early anesthetic exposure in young children and difficulties with behavior or cognition later in life. Ongoing prospective investigations are underway to further explore these implications. While the current data does not support a change in our current clinical practice, those who provide anesthesia to pediatric patients should consider these concerns when discussing the risks and benefits of anesthesia with parents. In December 2016 the Federal Drug Administration (FDA) issued a statement that requires the currently used anesthetics and several sedative drugs to be labeled with a warning that drug exposure exceeding 3 hours may harm the developing brain. The available evidence, its current controversial discussion, and recent action of regulatory institutions have already influenced medical practice for millions of children exposed to such drugs each year. While three long-awaited longitudinal studies of neurodevelopmental outcomes after pediatric anesthesia (the GAS, PANDA, and MASK studies) have shown reassuring results with regards to IQ testing, there is still a great need for further research that clarify risk and benefits of anesthetics and sedatives for young children with respect to other aspect of neurologic and behavioral developments. This chapter aims to provide structured brief summaries of the currently available knowledge to support the reader in following the ongoing discussion in the field and guide the discussion between healthcare providers and families when planning procedures that require sedation or anesthesia in young children.

Current Clinical Evidence

Historically, the use of anesthesia for surgical procedures in very young infants raised concerns about hemodynamic safety and monitoring. As anesthetic monitoring and medication safety have dramatically improved over the past several decades, the risk of life-threatening cardiopulmonary complications during general anesthesia has decreased. Furthermore, as our understanding of the physiology of neonatal pain and the infant brain has evolved, the previously accepted belief that neonates did not feel and could not remember the pain of surgery has now given way to a clear understanding of the detriment to young patients who undergo surgical procedures without anesthesia or analgesia. However, now that anesthesia can be safely provided to an increasing number of very young surgical patients, new concerns have emerged regarding the long-term cognitive and behavioral effects of anesthetic exposure during brain development, particularly in patients who are exposed to anesthesia before 3 years of age.

Numerous retrospective, observational studies have been undertaken to assess the association of exposure to anesthesia in infancy and early childhood with long-term alterations in behavior, development, learning, memory, cognition, and

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Table 14.1 Summary of design, population, and findings of population-based studies of neurocognitive and behavioral outcomes following childhood exposure to general anesthesia

Study	Design	Population (surgery type)	Number (history of anesthesia exposure)	Outcome	Exposure	Inclusion	Exclusion (n)	Findings
Kalkman et al. (2009)	Retrospective pilot study	University Medical Center, Utrecht, Netherlands (urologic surgery)	$n = 243$ ($n = 243$)	Performance on Child Behavior Checklist completed by parent or surrogate	GA <6 years	Underwent pediatric urologic surgery in 1987, 1991, 1993, or 1995	Congenital dx other than the one requiring surgery	Trend toward more behavioral issues observed in population exposed at younger ages
							Other risk factors for cognitive impairment	No statistically significant difference
							Urgent or day surgery	
							Moved outside Netherlands	
							Adopted	
							>19 years old at time of analysis	
Bartels et al. (2009)	Retrospective monozygotic twin cohort	Netherlands twin registry (any surgery)	$n = 2286$ ($n = 425 < 3$ years; $911 < 12$ years)	Standardized test scores age 12	GA <3 years or	Born 1986–1995 Monozygotic twins	Severe illness or handicap ($n = 50$)	Lower standardized test scores in population exposed <3 years
				Teacher ratings age 12	GA <12 years		Gestational age <32 weeks ($n = 132$)	More cognitive problems in population exposed <3 years
							Low birth weight ($n = 670$)	No differences within twin pairs between exposed and unexposed
DiMaggio et al. (2009)	Retrospective cohort	New York State Medicaid (inguinal hernia repair)	$n = 5433$ ($n = 383$)	Behavioral or developmental d/o dx	GA <3 years	Born in NY state 1999–2001 IHR <age 3	Behavioral or developmental dx preceded IHR (n not reported)	Doubled likelihood of developmental or behavioral d/o in exposed pts
Wilder et al. (2009)	Retrospective birth cohort	Olmsted County, MN (any surgery)	$n = 5357$ ($n = 593$)	Reading, written language, or math LD by age 19	GA <4 years	Born 1976–1982	Left Olmsted County or died <5 years old ($n = 2830$)	Single exposure not associated with risk of LD
							Severe MR ($n = 19$)	Increased risk of LD with multiple exposures
							Non-consent ($n = 342$)	Increased risk of LD with longer duration of exposure

DiMaggio et al. (2011)	Retrospective sibling cohort	New York State Medicaid (any surgery)	n = 10,450 (n = 304)	Behavioral or developmental d/o dx	GA <3 years	Born in NY state 1999–2005	Behavioral or developmental dx preceded exposure or was <10 months in unexposed (n = 1200)	Increased likelihood of developmental or behavioral d/o in exposed pts
							Cardiac, ENT, or neurosurgery (n = 59)	Increased likelihood of developmental or behavioral d/o with increased number and duration of exposure
								No difference within twin pairs between exposed and unexposed
Flick et al. (2011)	Retrospective matched cohort	Olmsted County, MN (any surgery)	n = 5357 (n = 350)	Need for IEP for emotional or behavioral d/o	GA <2 years	Born 1976–1982	Left Olmsted County or died <5 years old (n = 2830)	Increase in LD if multiple surgeries
				Reading, written language, or math LD by age 19			Severe MR (n = 19)	Decrease in school group achievement and cognition test scores in exposed pts
				Score on school administered achievement test and cognition exam			Non-consent (n = 342)	No difference in need for IEP for emotional or behavioral d/o
Hansen et al. (2011)	Retrospective birth cohort	Denmark national civil registry (inguinal hernia repair)	n = 17,234 (n = 2689)	Average 9th grade test scores (age 15–16)	GA <1 year	Born 1986–1990 IHR <age 1	Died or migrated before June 1, 2006 (n = 1078)	No significant difference in test scores in exposed pts
				Proportion of children not attaining test scores (special needs, alternative school, dropouts)				Bigger effect seen from male gender, birth weight, parental education than from anesthetic exposure
								Higher risk of test score nonattainment in exposed group

(continued)

Table 14.1 (continued)

Study	Design	Population (surgery type)	Number (history of anesthesia exposure)	Outcome	Exposure	Inclusion	Exclusion (n)	Findings
Block et al. (2012)	Retrospective cohort	University of Iowa (IHR/orchiopexy, pyloromyotomy, circumcision)	$n = 287$ ($n = 287$)	Iowa state achievement test scores	GA <1 year	At least one of three included surgeries	Died ($n = 18$)	Disproportionate number of exposed pts had very low state achievement test scores (<5%ile) vs. population average
							Unable to locate ($n = 93$)	
						Otherwise healthy	Did not return study mailing questionnaire ($n = 215$)	Association between poor score and exposure duration
						Between 7 and 17.9 years old at time of search	No Iowa test scores ($n = 85$)	No difference in mean test scores
							Non-consent ($n = 22$)	
Ing et al. (2012)	Retrospective analysis of prospectively collected pregnancy/birth cohort data	Australian Pregnancy Cohort (Raine) Study (any surgery)	$n = 2608$ ($n = 321$)	Testing at age 10	GA <3 years	Born to mothers enrolled in pregnancy cohort 1989–1992	Lost to follow-up ($n = 260$)	Lower scores on receptive and expressive language testing in exposed pts
				Language				
				Cognitive function				Lower scores on testing of abstract reasoning in exposed pts
				Motor skills				
				Behavioral d/o				No difference on motor or behavioral testing
Sprung et al. (2012)	Retrospective cohort	Olmsted County, MN (any surgery)	$n = 5357$ ($n = 350$)	ADHD by age 19	GA <2 years	Born 1976–1982	Left Olmsted County or died <5 years old ($n = 2830$)	Association between multiple exposures and ADHD
							Severe MR ($n = 19$)	
							Non-consent ($n = 342$)	
Bong et al. (2013)	Retrospective cohort	Singapore (minor surgery including IHR, circumcision, cystoscopy, pyloromyotomy)	$n = 206$ ($n = 100$)	Aggregate score on standardized test at age 12	Sevo GA <1 year	Born 1998–1999	Prematurity	No difference in standardized testing scores
						ASA I or II	Genetic d/o	
						Minor surgery	CNS d/o	Increase in formal LD in exposed pts
				Formal LD dx		30–120 min	Congenital cardiac defect	
							Severe renal d/o	
							Family hx of DD or LD (combined $n = 29$)	
							Declined participation ($n = 49$)	

Garcia Guerra et al. (2013)	Retrospective cohort	A University-affiliated pediatric hospital, Alberta, Canada (CHD surgery)	$n = 91$ ($n = 91$)	Testing in kindergarten:	GA ≤6 weeks for CHD surgery	Admitted to pediatric ICU following CHD surgery with CPB between 4/2003 and 12/2006	Died before kindergarten age ($n = 19$)	Number of days on chloral hydrate associated with lower score on performance IQ testing
				IQ testing				
				Visual motor integration developmental testing			Chromosomal abnormalities ($n = 16$)	Cumulative dose of benzodiazepine associated with lower score on visual motor integration testing
							Lost to follow-up (n = 8)	
				Adaptive behavior assessment testing			Encephalitis ($n = 1$)	
Andropoulos et al. (2014)	Retrospective cohort	A university-affiliated pediatric hospital, Houston, TX (CHD surgery)	59 ($n = 59$)	Bayley scale of infant and toddler development testing at 12 months	GA <30 days for CHD surgery	Pre-op and 7-day postop MRI available	Died before 12 months ($n = 10$)	Increased cumulative volatile anesthesia exposure associated with lower composite scores on cognitive testing
						Survival to 12 months	Did not return for testing ($n = 24$)	Increased cumulative volatile anesthesia exposure associated with trend toward lower language section scores
						Completion of neurocognitive tests	Did not meet inclusion criteria or met exclusion criteria (n not reported)	New postoperative brain injury on MRI associated with lower composite scores and trend toward lower language section scores
						Hypothermic (<30 °C) CPB >60 min	Prematurity <35 weeks	
						Anatomic cardiac lesion	Low birth weight	
							Known dysmorphic syndrome	Length of ICU stay was most consistent factor associated with lower cognitive testing scores
							Surgery not requiring CPB	
							Preoperative hx of cardiac arrest	
							Intraoperative factors	
							No aortic cross-clamping	
							CPB <60 min	
							Temperature nadir >30 °C	

(continued)

Table 14.1 (continued)

Study	Design	Population (surgery type)	Number (history of anesthesia exposure)	Outcome	Exposure	Inclusion	Exclusion (n)	Findings
Chemaly et al. (2014)	Retrospective cohort	A university-affiliated pediatric hospital, Lebanon (any surgery)	$n = 592$ ($n = 292$)	Behavioral change on Eyberg Child Behavior Inventory questionnaire	GA <4 years	Anesthesia between 1/2004 and 12/2005	Chronic illness ($n = 40$)	Increased rate of behavioral abnormalities in exposed group
						Age	Complicated neonatal course ($n = 35$)	Increased rate of behavioral abnormalities in pts who had surgery vs. a diagnostic procedure
							>1 anesthetic exposure ($n = 52$)	Increased rate of behavioral abnormalities with increased duration of anesthesia
							Behavioral assessment data unavailable ($n = 74$)	Highest rate of behavioral abnormalities in pts who received anesthesia between 0 and 6 months
								Increased rate of behavioral abnormalities in pts who received multiple vs. a single anesthetic agent
Ing et al. (2014)	Retrospective cohort	Pregnancy cohort (Raine) study (any surgery)	$n = 2547$ ($n = 375$)	Direct neuropsychological testing	GA 3–10 years	Born to mothers enrolled in pregnancy cohort 1989–1992	Exposure before 3 years of age ($n = 321$)	Decreased motor function in exposed vs. unexposed pts
				McCarron assessment of neuromuscular development			Lost to follow-up ($n = 220$)	No difference in language or cognitive function between exposed and unexposed pts
Ing et al. (2014)	Retrospective cohort	Pregnancy cohort (Raine) Study (any surgery)	$n = 781$ ($n = 112$)	Direct neuropsychological testing results	GA <3 years	Born to mothers enrolled in pregnancy cohort 1989–1992	Lost to follow-up ($n = 260$)	Increased of language deficit on neuropsych testing in exposed pts
				ICD-9 code for mental, behavioral, neurodevelopmental disorder			Incomplete data ($n = 1825$)	Increased risk of ICD-9 coded language, cognitive and/or behavioral disorder
				Standardized testing academic achievement scores				No difference in standardized testing benchmark score achievement between groups

Stratmann et al. (2014)	Retrospective case matched cohort	Northern California: UCSF, UC Davis (any surgery other than neurosurgery or CHD surgery)	$n = 56$ ($n = 28$)	Object recognition memory test	GA <2 years	Age 6–11 at time of testing	Did not meet inclusion criteria or met exclusion criteria ($n = 484$)	Decreased recollection on object memory test in exposed pts
				IQ test score		ASA PS 1 or 2	ASA PS ≥3	No difference in familiarity on object memory test
				Child behavior checklist scores		Anesthetic dose of >120 MAC minutes	Attention or learning impairment	No difference in IQ
						Induction with volatile ± propofol	CNS dx or trauma	No difference in child behavior checklist score
						Maintenance with volatile ± N_2O	Cancer	
							Prematurity	
							Low birth weight	
							Genetic syndrome	
							Intraoperative hemodynamic or respiratory instability	
							Colorblindness	
							English nonfluency	
							Unable to contact ($n = 292$)	
							Declined participation ($n = 28$)	
							Inability to comply with instructions ($n = 2$)	

(continued)

Table 14.1 (continued)

Study	Design	Population (surgery type)	Number (history of anesthesia exposure)	Outcome	Exposure	Inclusion	Exclusion (n)	Findings
Backeljauw et al. (2015)	Retrospective case matched cohort	Existing language development and MRI database: Cincinnati, OH (any surgery)	$n = 106$ ($n = 53$)	MRI findings	GA <4 years	5–18 year old volunteers	Did not meet inclusion criteria	Lower IQ test scores in exposed pts
				Oral and written language test score		No hx neuropsych illness, head trauma, LD, prematurity	Unsatisfactory MRI quality ($n = 1$ pair)	Lower listening comprehension scores in exposed pts
				IQ test score				No gray matter differences in thalamus or retrosplenial cortex
								Decreased IQ associated with decreased gray matter volume in anterior cerebellum, parts of frontal lobe, lingual gyrus, occipital lobes
								Decreased oral and written language test score associated with decreased gray matter volume in right lingual gyrus, occipital lobe, temporal lobe, parahippocampal gyrus
Glatz et al. (2015)	Retrospective cohort analysis	Swedish national healthcare and population registers (any surgery)	$n = 2$ million ($n = 107{,}640$ exposed, $n = 34{,}480$ single exposure <4 years)	Average school marks at 16 years old	GA <4 years	Born in Sweden 1973–1993	Neurosurgery	Minimal difference in average school marks with one exposure
					Subgroups	At least one surgical procedure before 4 years	Cardiac surgery	No difference within any age subgroup
					0–6 months		Cancer dx	
					7–12 months		Dx of malformation (abstract, n not reported)	
					13–24 months			

Taghon et al. (2015)	Retrospective cohort	Nationwide Children's Hospital: Columbus, OH (any surgery)	$n = 30$ ($n = 15$)	Accuracy and response time on go/no-go task testing	GA <2 years	10–17 years old	Did not meet inclusion or met exclusion criteria	No difference in response time or task accuracy between exposed pts and unexposed controls
				Whole-brain activation pattern on fMRI		Surgery at least 1 h duration	Known or possible pregnancy	Differences in activation of cingulate gyrus, cerebellum, paracentral lobule between groups
						Cognitive capacity to complete go/no-go task and participate in fMRI	Documented respiratory or hemodynamic instability on anesthesia record	
						Right hand dominance	Prenatal ethanol exposure	
						English fluency	Exposure to antiepileptic medication	
							ADHD	
							Traumatic brain injury	
							Psychiatric dx	
							Substance abuse	
							Psychoactive medications	
							(Screening criteria, n not reported)	

ADHD attention deficit hyperactivity disorder, *ASA PS* American Society of Anesthesiologists Physical Status, *CHD* congenital heart disease, *CPB* cardiopulmonary bypass, *DD* developmental delay, *d/o* disorder, *dx* diagnosis, *GA* general anesthesia, *hx* history, *ICU* intensive care unit, *IEP* individualized educational plan, *IHR* inguinal hernia repair, *IQ* intelligence quotient, *LD* learning disability, *MR* mental retardation, *pts* patients, *sevo* sevoflurane, *MAC* minimal alveolar concentration

language (Table 14.1). One retrospective birth cohort study of over 5000 children assessed the risk of learning disabilities later in life in those who received general anesthesia before the age of 4. When compared to children who did not receive anesthesia at a young age, children who received two or more anesthetics were found to have a twofold increased risk of developing a learning disability; there was also a concomitant risk increase associated with a longer duration of anesthesia. Similar results from subsequent studies support these findings; cumulative exposures to volatile anesthetics, chloral hydrate, and midazolam in congenital cardiac surgery patients have been found to be independent predictors of poor performance on neurocognitive testing, despite the multiple comorbidities and risk factors for neurologic injury in that population. When a cohort of patients was analyzed specifically for the development for attention deficit hyperactivity disorder (ADHD) by the age of 19, a significant association with repeated anesthetic exposures was again noted. In a study comparing school-aged children who were exposed to general anesthesia for surgical procedures in the 1st year of life with unexposed children, there was no difference in mean standardized test scores, but an inverse relationship was observed between test score and duration of anesthetic exposure, and a higher proportion of the exposed children had very poor test performance.

Other very large studies of academic performance have produced negative results. Contrary to the majority of prior studies, one Swedish study of approximately two million children found little to no association between anesthetic exposure in early childhood and impairment in academic function. In fact, they found that several other factors, including being male, being born in December vs. January, and low parental education levels, were associated with a risk of poor academic performance that was several orders of magnitude higher than the very small risk associated with anesthetic exposure. It seems there may be variability of the phenotype of anesthetic neurotoxicity between populations.

The association between early anesthetic exposure and later diagnosis of a developmental or behavioral disorder has also been investigated. Multiple large retrospective cohort studies have demonstrated an increase in the likelihood of developmental or behavioral disorders in children who have received anesthesia, including an association of increased risk with cumulative anesthetic exposure. Other retrospective evidence suggests that deficits of language are more common in children exposed to anesthesia at an early age, even with a single exposure.

Recently, magnetic resonance imaging (MRI) has been explored as a potential modality for evaluating changes in brain structure in function in young adults with a history of exposure to anesthesia. In retrospective trials, anesthetic exposure in children and young adults has been associated with decreased grey matter volume, impaired neurocognitive testing and white matter lesions on postop MRI, and differences in the functional MRI measured activation of several brain areas during task performance. These findings have been demonstrated at multiple time points,

While these findings are compelling, the retrospective nature of the existing data prevents clear conclusions from being drawn. As with any retrospective study, the presence of confounders such as patient characteristics necessitating surgery, the homogeneity of any national population, possible effects of surgery itself, each patient's social and economic environment, and other comorbidities cannot be excluded. Many of the patients in these studies were exposed to anesthesia decades ago; newer agents/improved monitoring make these results difficult to interpret. Moreover, the various outcome measures studied in these retrospective analyses (neurocognitive testing, diagnostic codes found in medical records, standardized test results, school performance) may not be comparable.

Three large, prospective studies are in progress at this time. The General Anesthesia and Apoptosis (GAS) study, a randomized, multicenter trial comparing neurocognitive outcomes at 5 years of age following general and regional anesthesia for neonates undergoing inguinal hernia repair is ongoing. Preliminary results from the first 2 years of follow-up have shown no difference in neurodevelopmental outcome. The Pediatric Anesthesia and Neurodevelopment Assessment (PANDA) study is a multicenter cohort study, comparing healthy children undergoing inguinal hernia repair under any type of anesthesia to unexposed siblings. Enrollment is ongoing, and neurocognitive and behavioral testing will take place at 8 and 15 years of age. Finally, the Mayo Anesthesia Safety in Kids (MASK) study, which will evaluate a large cohort of Minnesota children with multiple, single, or no anesthetic exposures through extensive prospective neurocognitive testing, began recruitment in 2013.

Proposed Mechanisms of Anesthetic Neurotoxicity

While it is challenging to perform prospective experiments in human subjects, there are several well-established in vitro and in vivo animal models for studying the cellular and molecular effects of exposure to anesthetic agents. Since brain development involves a complex confluence of events, anesthesia may cause damage through various related mechanisms. Multiple animal studies have strongly associated exposure to a variety of anesthetic agents with cognitive and developmental disorders in rodents and nonhuman primates. The consistent association of anesthesia with neurotoxicity and the theory that anesthetics exert their main actions through a relatively small number of receptor interactions ($GABA_A$ potentiation, NMDA antagonism) have prompted further investigation of these specific pathways and their related mechanisms.

Synaptogenesis

In humans, synaptogenesis begins in the third trimester of pregnancy and continues throughout life. The developing brain is most vulnerable to anesthetic toxicity during the period of highly active synaptogenesis known as the "brain growth spurt," which is a rapid period of connection building that peaks at birth, a pattern that is seen both in humans and in other species. When animal models are used in studies of neurotoxicity, the developmental age of the animal model is chosen to correspond closely to that of the infant human brain.

Synaptogenesis is not a homogeneous process. Different areas of the brain may be most vulnerable to anesthetic neurotoxicity at variable times during the brain growth spurt. In fact, there is evidence that vulnerability to anesthetic-induced neuroapoptosis may vary with the age of each individual cell. Further complicating this picture is the fact that different anesthetic agents may actually have more potent toxicity during different stages of brain development. Although it is known that maturation of some brain areas, e.g., the frontal lobe, continues into young adulthood, there has been no investigation of the effects of anesthetic toxicity on this phase of brain development.

Apoptosis

Ketamine, propofol, thiopental, isoflurane, sevoflurane, benzodiazepines, and nitrous oxide have all been shown to induce neuronal apoptosis in fetal or neonatal rodent, porcine, and nonhuman primate models. Ketamine, isoflurane, and propofol have also been shown to induce apoptosis of oligodendrocytes, which are critical for axonal myelination.

Apoptosis is seen in glutaminergic, GABAergic, and dopaminergic neurons throughout the hippocampus, cingulate cortex, and substantia nigra in rats exposed to volatile anesthesia. However, when the basal forebrain was examined (in which cholinergic neurons predominate in rats and humans), there was no significant difference between exposed and unexposed rats. Suppression of cholinergic signaling by anesthesia may contribute to apoptosis of glutaminergic, GABAergic, and dopaminergic neurons that rely upon cholinergic stimulation to prevent atrophy and apoptosis.

Reactive oxygen species have also been implicated in anesthetic-induced neuroapoptosis. Antioxidants such as L-carnitine and pramipexole, which counteract the effects of reactive oxygen species, attenuate ketamine-induced neurotoxicity in rat forebrain culture and prevent both neuroapoptosis and cognitive impairment in rats when co-administered with isoflurane/nitrous oxide.

Anesthetic agents also lead to apoptosis through inflammatory processes that activate the extrinsic pathway. While many anesthetics have anti-inflammatory properties in the adult brain, they have been shown to promote inflammation in the developing rodent brain. Multiple inflammatory cytokines including TNF-alpha and IL-6 are increased in animals after anesthetic exposure. These inflammatory mediators may exert a synergistic neurotoxic effect when combined the widespread inflammatory response seen after surgical stimulation.

Excitotoxicity may be another potential mechanism of anesthetic-induced neurotoxicity. Although GABAergic agents exert sedative-hypnotic effects in adults, $GABA_A$ receptor activation is an excitatory phenomenon during early development of the mammalian brain. Volatile anesthetics may produce excitotoxicity via potassium-chloride cotransporter KCC-2. Activation of KCC-2 through GABAergic signaling in the mature brain leads to neuronal inhibition; however, in the immature brain, an immature form of KCC-2, known as NKCC1, is present. GABAergic activation of NKCC1 causes an excitatory response. Thus, while GABAergic medications are commonly used to treat excitatory conditions such as status epilepticus in the mature brain, it is possible that sustained paradoxical $GABA_A$-mediated excitation may contribute to anesthetic-induced neurotoxicity in the developing brain.

Micro-RNA

Small ribonucleic acid (RNA) molecules, known as micro-RNA (mi-RNA), are noncoding RNA molecules that bind in complexes to messenger RNA (mRNA), downregulating translation or increasing degradation of mRNA strands. Downregulation of anti-apoptotic pathways through mi-RNA signaling, in particular, miR-21 has been demonstrated after volatile, propofol, and ketamine anesthesia. Additional investigation into the interaction of anesthetic exposure and mi-RNA activity is ongoing.

Impaired Neurogenesis

Reduction in neurogenesis following early exposure to general anesthesia may lead to memory deficits. When postnatal day 14 rats and mice were exposed to daily isoflurane anesthesia for 4 days, they showed significant memory impairments on subsequent testing. On histologic examination, no increase in cell death was observed; however, the hippocampal stem cell pool was significantly smaller, and the number of hippocampal neurons was lower in the young rodents who were exposed to isoflurane. The underlying mechanism and significance of these findings is unclear.

Alteration in the Neuronal Network Structure

During neuron development, several outgrowths, known as neurites, begin to extend from the neuronal cell body. One of these is destined to extend, grow, and develop into a signal-transmitting axon, while the others will arborize into a network of signal-receiving dendrites. Dendrite development, arborization, and the density of small dendrite projections known as dendritic spines, which increase the specificity of dendrite signal reception, are all important parts of synapse building. Exposure to anesthetic agents has been demonstrated to increase synaptic spine density in some phases of brain development but not others. This suggests that the effects of propofol on this aspect of synapse generation may be dependent upon the developmental stage of the brain. This effect was not observed with midazolam. Ketamine exposure is associated with a *decrease* in dendritic spine length and complexity. Since GABAergic neurons often function as interneurons, which form modulatory connections between other neurons, an alteration in their behavior during development could disrupt the formation and function of important neural networks.

During axonal development, the establishment of axon-dendrite polarity, in which the axon becomes differentiated from the dendrites, is a crucial step in the development of a functional neuron. Isoflurane exposure delays this polarization process in mice; higher concentrations of isoflurane and a longer exposure time were associated with a dose-dependent retardation of neuronal polarization. Similar results were seen with exposure of the same model to propofol, but interestingly were not seen with the pure $GABA_A$ agonist muscimol, arguing against a purely $GABA_A$-mediated process.

Once polarity is established, the axonal neurite forms a growth cone, which is comprised of the flattened end of the extending neurite and several small, spiky extensions of actin and microtubules known as filopodia. The filopodia respond to attractive and repulsive external guidance cues, which influence the growth cone to extend and collapse, respectively. The balance of these alternating influences and resulting morphologic changes guides the growing axon down a specific path. This process requires precise timing, as the elongation of axons toward their eventual targets requires the presence of a series of time-limited signals. When a model of embryonic mouse neocortical neurons were exposed to isoflurane, impaired collapse of the axonal growth cone in response to a repulsive cue was observed; once the cells were allowed to recover from isoflurane, a normal collapse response was restored. Although these effects on the sensitivity of the growth cone to repulsive cues are short-lived, even a temporary alteration in axon migration may be associated with a long-term change in brain development or may contribute to eventual neuroapoptosis.

Role of Glial Cells

Glial cells, which include microglia, astrocytes, oligodendrocytes, ependymal cells, and Schwann cells, are the support system for neurons. They provide nutrients and oxygen, degrade and remove dead neuronal cells, and provide physical structural support to maintain the spatial relationships between neurons.

In astrocytes, which are responsible for a diverse set of functions including nutrient provision, maintenance of ionic balance, and support of the blood-brain-barrier endothelium, cytostructural changes have been clearly observed when rat cells were exposed to isoflurane in vivo. Interestingly, these changes did not seem to affect cell function or survival, suggesting that astrocytes may be relatively resistant to toxicity from anesthetics. In fact, astrocytes may actually be instrumental to attenuate propofol-induced neuroapoptosis.

Microglial cells act as macrophages in the central nervous system, removing dead and injured cells and infectious agents. Given the observed increase in pro-inflammatory mediators after exposure to general anesthetics, it has been theorized that microglial activation may be the source of these inflammatory mediators and may lead to accelerated destruction of other neuronal cells. Indeed, when 6-day-old mouse pups were exposed to sevoflurane anesthetics on three consecutive days, the number of cells that stained positive a marker of microglial cell activation, was significantly increased compared with unexposed controls. This suggests that stimulation of microglial cells may be an important step in the neuroinflammatory cascade associated with anesthetic toxicity in the developing brain.

Oligodendrocytes, which are necessary for myelination in the central nervous system white matter, have been shown to be subject to isoflurane-, ketamine- and propofol-induced apoptosis in fetal and neonatal rhesus macaques. This apoptosis occurs at the point of maturation when the oligodendrocytes developed the ability to myelinate axons, suggesting that a deficit in myelination could partially explain anesthetic-associated problems with neurobehavioral development. Further investigation is needed to determine whether or not oligodendrocytes remain vulnerable to the toxic effects of anesthesia as well during later stages of brain development.

The Role of Surgery

Since the vast majority of anesthetic exposures occur simultaneously with a surgical procedure, the effect of surgery itself on the developing brain must also be considered. Exposure to pain is associated with long-term behavioral changes in both animals and humans and that analgesia is necessary to address pain resulting from surgical procedures and other conditions. Neonates with a history of circumcision

without local anesthesia had a stronger pain response to subsequent routine vaccination than neonates who were either uncircumcised or who had been pre-treated with a local anesthetic prior to undergoing circumcision. In one retrospective study of children who underwent surgery or diagnostic procedures under general anesthesia before the age of 4, the children who had surgery had a significantly higher rate of behavioral abnormalities on testing at age 10–12 than the children who underwent diagnostic procedures. This data, while conflicting, suggests that the relationship between pain stimulus, anesthetic exposure, and neurotoxicity warrants systematic investigation.

Reducing Neurotoxicity

Several therapeutic agents have been shown to be potentially protective against anesthetic-induced neurotoxicity. In animal models, alpha-2 agonists have been shown to be protective against neuroapoptosis and cognitive impairment induced by isoflurane, ketamine, and propofol. Dexmedetomidine, a selective alpha-2 receptor agonist with sedative and analgesic properties, has been shown to attenuate both neuroapoptosis and long-term memory impairment when co-administered with isoflurane anesthesia in rats. Multiple other agents have been studied in animals with mixed evidence in reducing markers of apoptosis: erythropoietin, bumetanide, lithium, estradiol receptor antagonists, etc.

Pramipexole, which restores mitochondrial integrity and has antioxidant properties, was protective against cognitive impairment when administered to 7-day-old rats alongside an anesthetic of midazolam, nitrous oxide, and isoflurane; similar results have been seen with several other antioxidant medications and substances, including melatonin, curcumin, L-carnitine, and bone marrow stromal cells.

Inhaled substances have also been studied as neuroprotectants. Hydrogen and xenon gases are both able to quickly neutralize reactive oxygen species and have been shown to reduce neuroapoptosis and oxidative stress, as well as memory and behavioral deficits. Preconditioning with isoflurane itself, when administered for a short period of time on the day prior to a 6-h general anesthetic with 1.5% isoflurane, has been shown to ameliorate isoflurane-mediated apoptosis in young rats. Early evidence suggests that low concentrations of carbon monoxide administered as a carrier gas component may also be protective, possibly through modulation of cytochrome oxidase activity and reduction of oxidative stress. More research is needed in this area, as identification of a successful, feasible mitigation strategy could have profound clinical impact.

Finally, there is evidence in experimental studies that providing environmental enrichment may actually reverse the neurocognitive deficits seen after exposure to anesthesia. Rat studies have found that an enriched environment may improve clinical tests of memory impairment over several months, while memory deficits persisted in the rats living in the standard (deprived) environment. It is unclear how this will translate to human infants; the overwhelming majority of whom already grow up in an "enriched environment" and are intensely tended to following anesthesia and surgery.

Conclusions

The majority of anesthetic medications, including the volatile anesthetics, propofol, NMDA antagonists (nitrous oxide, ketamine), $GABA_A$ agonists (including barbiturates and benzodiazepines), nitrous oxide, and synergistic combinations thereof have been strongly associated with neurotoxicity and cognitive disorders in the developing brains of several animal species, including nonhuman primates. Many mechanisms of neurotoxicity have been described in preclinical experiments, and new mechanisms continue to emerge. These data support the observed association of impaired cognitive and behavioral development when anesthetic exposure occurred during the vulnerable period. Results from both, prospective animal and retrospective human cohort studies have fueled concerns about the long-term effects of anesthesia as the body of evidence grows. Indeed, neurocognitive dysfunction has now been shown to persist for years in a cohort of nonhuman primates following even a single, albeit prolonged (24 h) neonatal ketamine anesthetic. Nevertheless, while the laboratory evidence is robust, there is still no defining evidence available that these effects are translatable to humans. Furthermore, the bulk of available human data is almost exclusively retrospective in nature. Results from the large, prospective GAS, PANDA, and MASK studies have found no difference in IQ in children who received a short general anesthetic as infants compared to those who did not; however, the effect of early childhood exposure to anesthesia upon other neurobehavioral outcome measures is still uncertain. Thus, at the moment anesthesiologists and parents alike are still faced with the dilemma, as we still cannot say whether or not anesthetic exposure in infancy and childhood results in any human neurocognitive or behavioral phenotype later in life.

The SmartTots initiative, which is a collaborative public-private partnership between the International Anesthesia Research Society (IARS) and the FDA, works to address gaps in science regarding pediatric anesthetic safety and neurotoxicity. The current consensus of this expert group of anesthesiologists and scientists is that mounting concerns about the potential for cognitive or behavioral impairment in the future should not prevent urgent or emergent pediatric

surgery, as withholding a necessary surgical procedure is likely to cause patient immediate harm. If the need for surgery is less clear, discussion of the risks, benefits, and timing of surgery should take place between the anesthesiologist, the surgeon, and the parents.

It is important to note that at this time, there is no recommendation to support a change in clinical practice based upon the current state of the evidence. However, some anesthesiologists choose to employ putative mitigation strategies, such as regional anesthesia or the use of an opioid-heavy anesthetic, to reduce the amount of anesthetic exposure; while there is no evidence to support this as a neuroprotective strategy, it may be acceptable based on clinical judgment and the individual characteristics of each patient. The use of a combination of regional anesthesia, dexmedetomidine, and opioid as a substitute for volatile anesthetics, ketamine, or benzodiazepines is currently being investigated; at this time, it is unknown whether the elimination of the offending agents in pediatric practice will be feasible or will affect the potential long-term neurologic sequelae of anesthesia and surgery.

Ongoing prospective studies may help to link these laboratory observations to outcomes in humans. Until that time, anesthesiologists should counsel patients and families regarding the current state of our understanding of the neurologic risks of anesthesia.

Suggested Reading

Bong CL, Allen JC, Kim JT. The effects of exposure to general anesthesia in infancy on academic performance at age 12. Anesth Analg. 2013;117(6):1419–28.

Coleman K, Robertson ND, Dissen GA, Neuringer MD, Martin LD, Cuzon Carlson VC, Kroenke C, Fair D, Brambrink AM. Isoflurane anesthesia has long-term consequences on motor and behavioral development in infant rhesus macaques. Anesthesiology. 2017;126:74–84.

Creeley C, Dikranian K, Dissen G, Martin L, Olney J, Brambrink A. Propofol-induced apoptosis of neurones and oligodendrocytes in fetal and neonatal rhesus macaque brain. Br J Anaesth. 2013;110(Suppl 1):i29–38.

Creeley CE, Dikranian KT, Dissen GA, Back SA, Olney JW, Brambrink AM. Isoflurane-induced apoptosis of neurons and oligodendrocytes in the fetal rhesus macaque brain. Anesthesiology. 2014;120(3):626–38.

Flick RP, Katusic SK, Colligan RC, et al. Cognitive and behavioral outcomes after early exposure to anesthesia and surgery. Pediatrics. 2011;128(5):e1053–61.

Fredriksson A, Pontén E, Gordh T, Eriksson P. Neonatal exposure to a combination of N-methyl-D-aspartate and gamma-aminobutyric acid type a receptor anesthetic agents potentiates apoptotic neurodegeneration and persistent behavioral deficits. Anesthesiology. 2007;107(3):427–36.

Glatz P, Sandin RH, Pedersen NL, Edstedt Bonamy A, Eriksson LI, Granath FN. Academic performance after anesthesia and surgery during childhood: a large-scale nation-wide study. Anesth Analg. 2015;120:S-289.

Ing C, Brambrink AM. Mayo anesthesia safety in kids continued: two new studies and a potential redirection of the field. Br J Anaesth. 2019;122(6):716–9.

Ing CH, DiMaggio C, Whitehouse AJO, et al. Neurodevelopmental outcomes after initial childhood anesthetic exposure between ages 3 and 10 years. J Neurosurg Anesthesiol. 2014;26(4):377–86.

Jevtovic-Todorovic V. Pediatric anesthesia neurotoxicity: an overview of the 2011 SmartTots panel. Anesth Analg. 2011;113(5):965–8.

Jevtovic-Todorovic V, Hartman RE, Izumi Y, et al. Early exposure to common anesthetic agents causes widespread neurodegeneration in the developing rat brain and persistent learning deficits. J Neurosci. 2003;23(3):876–82.

Jevtovic-Todorovic V, Absalom AR, Blomgren K, et al. Anaesthetic neurotoxicity and neuroplasticity: an expert group report and statement based on the BJA Salzburg Seminar. Br J Anaesth. 2013;111(2):143–51.

McCann ME, de Graff JC, Dorris L, Disma N, Withington D, Bell G, et al. Neurodevelopmental outcome at 5 years of age after general anaesthesia or awake-regional anaesthesia in infancy (GAS): an international, multicentre, randomised, controlled equivalence trial. Lancet. 2019;393(10172):664–77.

Olsen EA, Brambrink AM. Anesthetic neurotoxicity in the newborn and infant. Curr Opin Anaesthesiol. 2013;26(5):535–42.

Sanders RD, Hassell J, Davidson AJ, Robertson NJ, Ma D. Impact of anaesthetics and surgery on neurodevelopment: an update. Br J Anaesth. 2013;110(Suppl 1):i53–72.

Sun LS, Li G, Miller TLK, Salorio C, Byrne MW, Bellinger DC, et al. Association between a single general anesthesia exposure before age 36 months and neurocognitive outcomes in later childhood. JAMA. 2016;315(21):2312–20.

Warner DO, Zaccariello MJ, Katusic SK, Schroeder DR, Hanson AC, Schulte PJ, et al. Neuropsychological and behavioral outcomes after exposure of young children to procedures requiring general anesthesia: the Mayo Anesthesia Safety in Kids (MASK) study. Anesthesiology. 2018;129(1):89–105.

Wilder RT, Flick RP, Sprung J, et al. Early exposure to anesthesia and learning disabilities in an population-based birth cohort. Anesthesiology. 2009;110(4):796–804.

Postoperative Neurocognitive Disorders in the Geriatric Patient

15

Katie J. Schenning and Miles Berger

Overview

Adults 65 and older represent the fastest-growing age group in the United States, and these older adults already account for one third of all surgical patients. Accordingly, there has been an increase in the number of older patients with spinal pathology such as symptomatic degenerative spine disease, tumors, and fractures. Multilevel fusions on these older patients are a relatively common occurrence as are other neurosurgical procedures such as decompressions, discectomies, and deformity corrections. Geriatric patients have decreased functional reserve, not only cardiac and pulmonary function but neurologic function as well. Individuals over the age of 65 are particularly at risk for neurocognitive changes after surgery. In fact, 30–80% of older adults become delirious after major surgery, 30–40% experience early postoperative cognitive dysfunction (POCD), and 10–15% develop late POCD.

Preoperative Cognitive Function

The prevalence of cognitive impairment in patients presenting for surgery has been reported from 25% to 45% of patients before elective cardiac surgery and in over 30% of patients before non-cardiac surgery. This is not surprising when considering that 35–50% of older adults in the United States have a diagnosis of mild cognitive impairment (MCI) or dementia. It is likely that preoperative cognitive impairment is frequently unrecognized due to lack of formal screening.

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The presence of preoperative impaired cognition is a risk factor for postoperative morbidity and mortality. Postoperative delirium is one of the most common postoperative complications associated with preoperative impaired cognition. Additionally, when compared to patients without pre-existing deficits, patients with baseline cognitive impairment prior to surgery have an increased risk for developing cognitive dysfunction that is present at both 3 and 12 months postoperatively.

Current Status of Preoperative Cognitive Screening

Though it has been well established that preoperative cognitive impairment is a leading risk factor for postoperative delirium and POCD, preoperative cognitive function is not routinely or formally assessed in the majority of institutions in the United States. It is not uncommon for the only patients that are identified as having pre-existing cognitive dysfunction are those that either carry a diagnosis of dementia or those that report subjective memory complaints. The optimal preoperative neurocognitive assessment of geriatric patients as outlined by the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) and the American Geriatrics Society (AGS) 2012 guidelines includes assessing the patient's cognitive ability, depression screening, identifying risk factors for developing postoperative delirium, and screening for alcohol and other substance abuse/dependence. More recently, the AGS published a best practice statement regarding postoperative delirium. This statement includes a recommendation to "assess and clearly document preoperative cognitive function in older adults at risk of postoperative delirium."

There are several reasons to evaluate and carefully document the geriatric patient's cognitive status. First, a thorough understanding of the preoperative neurocognitive state is required in order to determine whether a change has occurred postoperatively. There is perhaps greater impor-

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tance for the use of neuropsychological testing before and after surgery in patients with gliomas in eloquent areas, because several tasks in the domains of language, memory, and executive functions have been shown to deteriorate after tumor resection surgery. Next, preoperative neurocognitive screening can direct the informed consent process and guide optimal perioperative medical management as described below.

While it is unrealistic to administer an extensive neuropsychological test battery to all geriatric patients before elective surgery, it is likely possible to administer a brief screening test preoperatively. Tests that have been used in this context include the following:

- Animal fluency test
- Mini-Cog
- Cognitive Disorder Examination (CODEX)
- Clock-in-the-Box test
- Montreal Cognitive Assessment (MoCA)
- Mini Mental Status Exam (MMSE)

Informed Consent Considerations

In 2016, the American Society of Anesthesiologists launched a patient safety initiative focused on improving brain health, fostering understanding, developing best practices, and increasing awareness of postoperative delirium and POCD with the goal of laying groundwork for research into minimizing the incidence and effects of these postoperative neurocognitive disorders. The initiative will first focus on reducing delirium through patient education, provider education, and research advocacy. The goal of the initiative is to accelerate the adoption of best practices and ensure patients are aware of risks when making decisions regarding surgical interventions.

The preoperative informed consent process is a dual responsibility between surgeons and anesthesiologists. The possibility of postoperative delirium and/or cognitive dysfunction should be discussed with at-risk patients, since these are two of the most common postoperative complications in older adults. Risk factors are listed in Table 15.1. There is a wide range of postoperative neurocognitive trajectories. Some older patients clearly show postoperative cognitive improvement, particularly if the surgery improves cerebral blood flow (as in the case of an endarterectomy for carotid artery stenosis) or if the surgery ameliorates disease processes that are detrimental to brain function (such as the resection of an intracranial tumor). Many patients will show no significant change in overall cognitive trajectory; nonetheless, a sizable minority of older patients will experience either postoperative delirium or cognitive dysfunction after perioperative care. For this reason, discussing the risks of postoperative delirium or cognitive dysfunction is an essential component of helping patients and their families set realistic expectations about their postoperative recovery process. Patients may experience confusion or other cognitive problems for days to months after anesthesia and surgery. While anesthesia is unlikely to be the sole "cause" of POCD or delirium, there is clear level 1 evidence that perioperative anesthetic management modulates the risk of postoperative neurocognitive disorders. Likewise, a large body of literature suggests that both surgical and anesthetic management influence the risk of developing postoperative neurocognitive disturbances. Considering this, and since we already consider much more rare risks on anesthetic consent forms (such as the real but miniscule risk of intraoperative death or awareness with explicit recall), we believe it is appropriate to include the risks of POCD and delirium as part of the consent process.

Whether anesthesia and surgery actually contribute to longer-term cognitive decline that lasts for more than months is unclear; further prospective studies are necessary to address this issue. Indeed, whether anesthesia and surgery can precipitate, accelerate or help cause dementia (such as Alzheimer's disease), and the frequency with which this happens is currently one of the most controversial questions in perioperative medicine.

Table 15.1 Patient risk factors for postoperative neurocognitive disorders

Increasing age
Low educational attainment
Pre-existing cognitive impairment
Frailty
Alcohol abuse
ASA status

Implications of Postoperative Neurocognitive Disorders and Recommendations

Although postoperative delirium or cognitive dysfunction may appear to be "soft" diagnoses or subjective assessments, as opposed to the more "hard" physiologic measures such as blood pressure or PaO2 to which anesthesiologists are accustomed to handling, there should be zero doubt that both postoperative delirium and cognitive dysfunction are extremely important problems both from the perspectives of individual patients and the larger healthcare system. Both postoperative delirium and cognitive dysfunction are associated with increased mortality, decreased quality of life, increased healthcare costs, early exit from the work force, and long-

Table 15.2 Recommended interventions to prevent delirium or POCD

Intervention	Level of evidence
If BIS monitor is available, titrate anesthetic administration to maintain 45–60 range during general anesthesia	1b
In MAC cases, if BIS monitor is available, titrate to a BIS range of ~80 or higher	1B
If EEG monitoring of any type is available, avoid burst suppression	3b
Consider avoidance of elective surgery	5
Minimize centrally acting anticholinergics and benzodiazepines	1b

Key Points

- Postoperative delirium and cognitive dysfunction are two of the most common postoperative complications or adverse events experienced by older patients
- Preoperative cognitive impairment is a risk factor for subsequent postoperative delirium and postoperative cognitive dysfunction
- The geriatric patient's preoperative cognitive status should be evaluated and carefully documented
- Perioperative physicians should include a discussion of postoperative delirium and cognitive dysfunction in the informed consent conversation with at-risk patients
- Careful intraoperative anesthetic management can decrease the risk of postoperative delirium and possibly of longer-term cognitive dysfunction

term cognitive decline. Whether this long-term cognitive decline is "caused" by postoperative delirium or cognitive dysfunction or whether both the short-term dysfunction (i.e., delirium and POCD) and the long-term decline are both symptoms of a common underlying causal process (such as poor preoperative neurocognitive reserve) is a major question that will need to be resolved by future prospective studies. Nonetheless, postoperative delirium and cognitive dysfunction both clearly matter to our patients and affect their quality of life. Thus, both postoperative delirium and cognitive dysfunction should matter to us as anesthesiologists, and it is incumbent upon us to discuss the risks of these disorders with patients and to do everything we can to help prevent them (Table 15.2). This is a core part of the ASA brain health initiative, and for good reason, our patients deserve nothing less.

Suggested Reading

Avidan MS, Evers AS. Review of clinical evidence for persistent cognitive decline or incident dementia attributable to surgery or general anesthesia. J Alzheimers Dis. 2011;24(2):201–16.

Avidan MS, Evers AS. Persistent postoperative cognitive decline?: The pyramid of evidence. Anesthesiology. 2016;124(2):A23.

Avidan MS, Searleman AC, Storandt M, et al. Long-term cognitive decline in older subjects was not attributable to noncardiac surgery or major illness. Anesthesiology. 2009;111(5):964–70.

Berger M, Burke J, Eckenhoff R, Mathew J. Alzheimer's disease, anesthesia, and surgery: a clinically focused review. J Cardiothorac Vasc Anesth. 2014;28:1609–23.

Berger M, Nadler JW, Browndyke J, et al. Postoperative cognitive dysfunction: minding the gaps in our knowledge of a common postoperative complication in the elderly. Anesthesiol Clin. 2015;33(3):517–50.

Cavallari M, Dai W, Guttmann CR, et al. Neural substrates of vulnerability to postsurgical delirium as revealed by presurgical diffusion MRI. Brain. 2016;139(Pt 4):1282–94.

Chan MT, Cheng BC, Lee TM, Gin T, Group CT. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. J Neurosurg Anesthesiol. 2013;25(1):33–42.

Culley DJ, Flaherty D, Reddy S, Fahey MC, Rudolph J, Huang CC, et al. Preoperative cognitive stratification of older elective surgical patients: a cross-sectional study. Anesth Analg. 2016;123:186–92.

Inouye SK, Robinson T, Blaum C, Busby-Whitehead J, Boustani M, Chalian A, et al. Postoperative delirium in older adults: best practice statement from the American Geriatrics Society. J Am Coll Surg. 2015;220(2):136–48.

Inouye SK, Marcantonio ER, Kosar CM, et al. The short-term and long-term relationship between delirium and cognitive trajectory in older surgical patients. Alzheimers Dement. 2016;12:766–75.

Kline RP, Pirraglia E, Cheng H, et al. Surgery and brain atrophy in cognitively normal elderly subjects and subjects diagnosed with mild cognitive impairment. Anesthesiology. 2012;116(3):603–12.

McDonagh DL, Berger M, Mathew JP, Graffagnino C, Milano CA, Newman MF. Neurological complications of cardiac surgery. Lancet Neurol. 2014;13(5):490–502.

Moller JT, Cluitmans P, Rasmussen LS, et al. Long-term postoperative cognitive dysfunction in the elderly ISPOCD1 study. ISPOCD investigators. International Study of Post-Operative Cognitive Dysfunction. Lancet. 1998;351(9106):857–61.

Monk TG, Weldon BC, Garvan CW, et al. Predictors of cognitive dysfunction after major noncardiac surgery. Anesthesiology. 2008;108(1):18–30.

Purdon PL, Sampson A, Pavone KJ, Brown EN. Clinical electroencephalography for anesthesiologists: Part I: background and basic signatures. Anesthesiology. 2015;123(4):937–60.

Radtke FM, Franck M, Lendner J, Kruger S, Wernecke KD, Spies CD. Monitoring depth of anaesthesia in a randomized trial decreases the rate of postoperative delirium but not postoperative cognitive dysfunction. Br J Anaesth. 2013;110(Suppl 1):i98–105.

Saczynski JS, Marcantonio ER, Quach L, et al. Cognitive trajectories after postoperative delirium. N Engl J Med. 2012;367(1):30–9.

Schenning KJ, Murchison CF, Mattek NC, Silbert LC, Kaye JA, Quinn JF. Surgery is associated with ventricular enlargement as well as cognitive and functional decline. Alzheimers Dement. 2015;12:590–7.

Silbert B, Evered L, Scott DA, McMahon S, Choong P, Ames D, et al. Preexisting cognitive impairment is associated with postoperative cognitive dysfunction after hip joint replacement surgery. Anesthesiology. 2015;122(6):1224–34.

The Chronic Pain Patient Scheduled for Neurosurgery

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Implications for the Neurosurgical Patient

The neurosurgical patient has distinctive characteristics important for his/her perioperative management. The underlying pathology of several neurologic diseases has the potential to cause severe hemodynamic and/or physiologic derangements, and this must be taken into great consideration when planning a patient's anesthetic. Likewise, chronic pain patients have unique considerations and alterations of physiology important to assess in the perioperative period. These factors in combination make it imperative that, whenever possible, providers recognize chronic pain patients having neurosurgery so a multidisciplinary approach may be taken to devise an optimal perioperative analgesic and anesthetic plan.

Optimizing a chronic pain patient for any type of surgery begins with early consultation by the surgeon to a pain management specialist. A thorough focused preoperative assessment should be done. The anesthesiologist should specifically review any manifestations of neurological disease in detail with the patient. If a patient is a known chronic pain patient, information should be obtained about the patient's current pharmacotherapy regimen. Names, class, dosage, and duration of use should be noted as well as perceived efficacy and side effects. Additional details such as underlying pain type, location, quality, intensity, and modifiers are also important to review. In neurosurgical patients, neuropathic conditions such as hyperalgesia, allodynia, or motor weakness should also be discussed and documented ahead of time.

Taking the extra time to focus on the details of a patient's chronic pain history allows for the lines of communication to open up between the care teams and the patient. It also allows the anesthesiologist to educate the patient, establish trust, alleviate anxiety, and set expectations for the upcoming neurosurgery. This is important as anxiety and psychological distress in the perioperative period have been associated with higher postoperative pain scores, less early physical therapy participation, and more cases of chronic pain postoperatively. Psychological preparation of the patient should be conducted for all neurosurgical cases but is especially important for chronic pain patients having neurosurgery.

A multidisciplinary approach (behavioral therapy, speech therapy, and physical therapy) may be necessary for optimal recovery, depending on the individual patient, type of neurosurgery, and what recovery is expected to entail. Many chronic pain patients depend on complementary and alternative medicine (CAM) approaches, such as massage or accupuncture, to improve daily function. Thus, it is helpful to understand which CAM strategies the patient gains benefit from, so that they can be reinstated postoperatively, as soon as possible. Establishing a provider-patient relationship ahead of time may also be helpful in providing coping mechanisms for the patient.

The following common pain-related clinical scenarios arising in neurosurgical patients warrant specific attention.

Scalp Pain from Craniotomies

The incidence of scalp pain has decreased substantially with the use of modern bone fixation systems (as opposed to wire bone closures). Scalp pain following a craniotomy does, however, remain a concern for some patients. Occipital nerve blocks can provide profound anesthesia of the back of the head and scalp, and are done under ultrasound guidance at the C2 tubercle. Supraorbital and oricular-temporal blocks are other blocks that can help prevent or treat pain from craniotomies affecting the frontal and temporal cranial regions. Blocks can

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help with opioid sparing, which is very desirable in the neurosurgical patient population because using less opioids reduces the risk opioid-induced cognitive dysfunction.

Chronic Pain Patients Having Spine Surgery

Patients presenting for spine surgery often have a history of chronic pain. There are several strategies that can be implemented along the perioperative course to optimize postsurgical outcome.

Obesity and cigarette smoking are each independent risk factors for low back pain and are associated with worse postsurgical outcomes. Patients should be made aware of these risk factors so that they have an opportunity to play an active role in reducing modifiable risk factors. Pre-surgical depression is another risk associated with worse postsurgical outcome. If appropriate, referrals can be made to dieticians (for management of obesity), for smoking cessation help, or for psychological evaluation prior to scheduling surgery.

It is especially important to identify chronic pain patients presenting for back surgery who are on chronic opioid therapy. Optimizing these patients may involve reducing opioid consumption leading up to surgery in order to maximize the opioid analgesic benefit a patient can achieve both during and post-surgery. While opioid reduction can work wonders for a chronic pain patient undergoing surgery, it is important to note that an opioid reduction strategy that is too quick can result in opioid withdrawal, and derail physiologic homeostasis resulting in worsening overall surgical risk. There is a delicate balance in preparing chronic pain patients for surgery. Perioperative recommendations are as follows:

Prior to surgery, a detailed discussion with the patient should be had, addressing:

- Current opioid regimen
- Surgical and postsurgical pain management history
- Increased potential for postoperative pain
- Concerns and expectations related to surgical pain management
- A post-surgery pain management plan
- Discuss that once the patient is healing from surgery, opioid medications will be tapered back down to preoperative doses

Day of surgery and intraoperatively:

- Consider adjuvant medications, examples include:
  - Acetaminophen 1000 mg PO or IV q8
  - Gabapentin 300–600 mg PO up to three times daily
  - Ketorolac 15–30 mg IV q6 h
  - Celecoxib 200–400 mg PO q 24 h
  - Ketamine IV 0.5 mg/kg bolus or 4–10 mcg/kg/min infusion
  - Lidocaine IV 1.5 mg/kg bolus plus 1–2 mg/kg/h infusion
- Administer opioids to meet patient requirements based on:
  - Pre-surgical daily consumption
  - Type of surgery
  - Anticipated acute postoperative requirements
- Local wound infiltration by surgeon.

Immediate postoperative phase:

- Titration of opioids to acceptable level of pain (maintaining respiration rate of 12–14 if patient is spontaneously breathing)
- Note that opioid-tolerant patients may have requirements up to 4x the amount that opioid-naïve patients require for the same surgery
- Close monitoring for oversedation as well as opioid withdrawal
- Titration of adjuvant medications.
- Consider initiation or continuation of infusions (ketamine, lidocaine)
- Consider initiation of PCA; avoid basal rates
- Consider continuous pulse oximetry (SpO2%); chronic opioid patients are at high risk for oversedation

Postoperative transition phase:

- Continue adjuvants that are or can be converted to PO (acetaminophen, gabapentin)
- Check in, remind/re-establish expectations and goals with patient
- Calculate 24 h opioid requirement, ideally, this should be done at least 24–48 h postop
- Divide daily opioid requirement into PRN use of short-acting PO opioid available every 3 or 4 h
- If patient is on very high requirements and is not getting adequate coverage with the above, consider delivering ¼ to ½ of the 24 h opioid dose as a long-acting formulation
- Once appropriate, begin tapering opioids to preoperative doses
- Outline clear taper plan in notes so that it can be documented in discharge summary if taper is to be continued out of hospital
- Consider follow-up with pain management specialist if not already established with one

Patients with Opioid Addiction

The pain management of patients recovering from opioid addiction, who are on medications such as Suboxone or other variants of buprenorphine to treat opioid addiction, can be challenging. Buprenorphine is a mixed agonist (weak) and

antagonist at mu-opioid receptors and has a relatively long half-life, of approximately 5 days. Ideally, for patient's on buprenorphine, treatment of intraoperative and immediate postoperative pain is achieved with non-opioid strategies such as regional anesthesia, ketamine infusions or lidocaine infusions. If surgery is minor and not many opioid medications are expected to be needed for the postoperative pain period, we often recommend just increasing the buprenorphine dose by a small amount for a few weeks (taking advantage of its weak agonist effects). This is typically enough to cover the postoperative pain period.

If the procedure is expected to be moderately painful and require more pain control postoperatively, and is elective, we recommend discontinuing the buprenorphine 1 week before hospital admittance. This will allow buprenorphine to be displaced from the opioid receptors so that pure opioid agonists will be able to bind and work.

In emergent situations, with no time for weaning off buprenorphine, and pain control using opioids is required, we recommend using lipid soluble opioids both intraoperatively and postoperatively. At high doses, lipid soluble opioids, such as fentanyl, alfentanil, remifentanil, or sufentanil, will antagonize the effects of buprenorphine and produce an analgesic effect.

Another medication commonly used to treat opioid addiction is Methadone. Methadone has a very long half-life, and because of this, we recommend that methadone doses not be increased more than every 2–3 days, especially when titrating upward. Methadone's popularity as a treatment for opioid addiction is declining, and most pain management specialists are working on transitioning patients off of long-acting agents like methadone. Nonetheless, perioperative patient's on Methadone are not rare and it is important to know how to treat these patients who present for any type of surgery including neurosurgeries.

Fibromyalgia

Fibromyalgia (FM) is another common complex chronic pain disorder in which advanced preparation is key to a successful postoperative outcome. Fibromyalgia is characterized by widespread musculoskeletal pain. Patients typically have complaints of tenderness and soreness of mostly soft tissue structures such as muscles, tendons, and ligaments. Pain is often accompanied by fatigue, anxiety, depression, and cognitive disturbances. Physical exam may reveal minor motor and sensory abnormalities but lacks signs of muscle or joint inflammation.

Cognitive behavioral therapy and physical activity play a key role in decreasing functional disability and mood disturbances in patients with FM. Since patients with FM are at risk for FM flares and prolonged recoveries after surgery, it is prudent to start preoperative preparation well in advance of the day of surgery. If possible, prior to surgery, patients with FM should have an established relationship with a cognitive-behavioral therapist and be actively trained in pain coping skills, including thought stopping, relaxation, and distraction.

There is potential for prolonged immobilization during and after neurosurgery. Since physical activity is an imperative part of pain control in patients with FM, a clear plan to keep immobility to a minimum should be discussed in advance. Painful areas not involved in the surgical field should be well padded with foam or towels. The patient's positioning should be checked routinely during surgery and adjusted off points of excess pressure. Physical activity should be resumed as soon as possible post surgery. Patients with FM having neurosurgery may require more physical therapy than those without FM. Arrangements for postsurgical physical and/or occupational therapy should be made well in advance.

If a patient is already taking medications for FM such as antidepressants, gabapentin, or pregabalin, they should be continued perioperatively. It is not advisable, however, to start a new medication for FM treatment immediately prior to surgical intervention. As with most chronic pain patients, optimizing medical/pain management of patients with FM for neurosurgery can be a challenge. Ideally, having an interdisciplinary team that offers a combination of cognitive-behavioral, educational, and physical interventions and is involved early on in the patient's care will provide optimal management of the patient with FM having neurosurgery.

Post-laminectomy Syndrome

Post-laminectomy syndrome (PLS), also known as failed back surgery syndrome, refers to patients who, despite having undergone a technically successful surgical repair, have suboptimal long-term clinical results. PLS patients often suffer from back pain and/or leg pain, and this may be unchanged or new post-surgery. PLS patients will also often have persistent functional and quality of life limitations.

Patients with PLS refractory to conservative therapies such as medications, physical therapy, and complimentary therapies may have implanted devices such as spinal cord stimulators or intrathecal pumps. Patients with these implants presenting for surgery require evaluation and special attention.

Spinal Cord Stimulator Patients

Spinal cord stimulators modulate pain through electrical impulses. There is not any medication delivered through a spinal cord stimulator (SCS), so medication requirements of these patients are not affected or changed by the SCS implant.

There is, however, the potential of electromagnetic interference with these devices. Strong interference can occur from an electrocautery, MRI (most devices are *not* MRI compatible), or cardiac defibrillation resulting in devastating complications such as severe burns, arrhythmias, or even death. Complications can occur even if the SCS is turned off. If a patient with an SCS undergoes a procedure in which electrocautery is to be used, bipolar electrocautery is preferable. If monopolar electrocautery must be used, ensure that a grounding pad is applied and placed as far away from the SCS generator as possible.

Intrathecal Pump Patients

Intrathecal pumps are implanted pumps that deliver opioids and or adjuvant medication to the intrathecal space. Perioperative recommendations for patients with intrathecal pumps presenting for surgery are similar to those for chronic opioid patients presenting for back surgery as outlined above. Understanding the patient's current pump medication regimen and settings is imperative. Any time a patient with an intrathecal pump (ITP) presents to an inpatient setting, the pump should be interrogated, and the provider who manages the pump should be contacted. In terms of perioperative planning, detailed decisions and planning regarding ITP perioperative management should be made with the patient, the ITP outpatient provider, and the surgeon. If the pump is to be turned off, or needs to be emergently explanted, careful attention must be paid to account for potential withdrawal. ITP medication withdrawal, especially opioid or baclofen withdrawal, can be fatal. It is essential a plan is in place prior to turning off or explanting an ITP if the pump is active at the time of implantation.

Concerns and Risks

Preoperative Opioid Tolerance

For years, opioids have been our first choice when managing postsurgical pain, but a multimodal approach has been proven to work better. There is now a call in outpatient pain management to move away from using opioids for managing pain. In particular, if opioids have not been reduced, there is likely opioid tolerance prior to surgery.

Altered opioid pharmacology can also have major implications in the perioperative setting and should not be taken lightly. We know that reducing opioids preoperatively leads to less opioid use postoperatively. In addition, weaning opioids preoperatively often results in less postoperative opioid use.

Preoperative Neuropathic Pain

Both gabapentin and pregabalin have clear efficacy in treating preoperative neuropathic pain. In addition, these drugs have efficacy for reducing postoperative pain, when administered immediately prior to surgery. In addition, preoperative gabapentin and/or pregabalin treatment has been shown to decrease postoperative delirium, improve patient satisfaction, decrease opioid consumption, decrease anxiety, decrease postoperative pain, decrease nausea, and decrease chronic pain.

The most effective strategy for reducing postoperative neuropathic pain and for treating preoperative neuropathic pain is to start the medication preoperatively or immediately postoperatively and continue it for a few days. These anti-neuropathic agents can work in conjunction with epidural analgesia, NSAIDS, and other multimodal approaches.

Significance of Postoperative Pain/Clinician Education

A multimodal treatment strategy is beneficial for controlling the postoperative neurosurgical pain. Liberal use of opioid medications will prevent early neurologic evaluation and may obscure neurologic deterioration so we administer opioid medications only as absolutely necessary. The recommended guidelines by many institutions and state medical boards are no more than 90 morphine equivalents daily. This refers to a 90 morphine equivalent amount when both the short and long-acting opioid medications dosages are added together. High levels of postoperative pain are associated with sympathetic surge, an increased risk of pulmonary, and cardiovascular complications, which are the most common reason for delayed discharges and are responsible for prolonged convalescence after a patient undergoes in-patient surgery.

Key Points

- Chronic pain patients have unique considerations and alterations of physiology important to assess in the perioperative period.
- Optimizing chronic pain patients for any type of surgery should begin with the consultation of a pain management specialist.
- Planning for neurosurgery for the chronic pain patient ideally involves a multidisciplinary team including a pain management specialist, surgeon, anesthesiologist, and the patient.
- Addressing modifiable risk factors such as obesity, smoking, and depression may lead to better postsurgical outcomes.

- Preoperative administration of anti-neuropathic pain agents such as gabapentin and pregabalin has been shown to reduce postoperative opioid use.
- There is evidence that gabapentin and pregabalin combined with opioids are more effective for analgesia than opioids alone and can be opioid sparing.
- If a chronic pain patient with an implantable pain device such as an SCS or ITP presents for neurosurgery, careful consideration and understanding of these devices is necessary for delivering a safe anesthetic and achieving adequate pain management.
- Uncontrolled postoperative pain is associated with sympathetic surges and can increase pulmonary, cardiovascular, and neurologic complications.
- A multimodal treatment strategy is beneficial for controlling pain in the postoperative neurosurgical patient, especially if they have chronic pain.

Suggested Reading

Amirdelfan K, Webster L, Poree L, et al. Treatment options for failed back surgery syndrome patients with refractory chronic pain: an evidence based approach. Spine. 2017;42:S41–52.

Carroll IR, Angst MS, Clark JD. Management of perioperative pain in patients chronically consuming opioids. Reg Anesth Pain Med. 2004;29(6):576–91.

Contrell JE, Patel P. Neuroanesthesia. 6th ed. New York: Elsevier; 2017.

Dowell D. CDC guideline for prescribing opioids for chronic pain – United States, 2016. Recomm Rep. 2016;65(1):1–49.

Gan TJ. MD., M.H.S., FRCA, Professor and Chairman, Department of Anesthesiology. Stony Brook: Stony Brook University.

Gilron I, et al. Morphine, gabapentin, or their combination for neuropathic pain. NEJM. 2005;352(13):1324–34.

Gore M, et al. A retrospective evaluation of the use of gabapentin and pregabalin in patients with postherpetic neuralgia in usual-care settings. Clin Ther. 2007;29:1655–70.

Oderda GM, Gan TJ, Johnson BH, Robinson SB. Effect of opioid-related adverse events on outcomes in selected surgical patients. J Pain Palliat Care Pharmacother. 2013;27:62–70.

Pyati S, Gan TJ. Perioperative pain management. CNS Drugs. 2007;21(3):185–211. Review.

Voutsalath MA, Bichakjian CK, Pelosi F, Blum D, Johnson TM, Farrehi PM. Electrosurgery and implantable electronic devices: review and implications for office-based procedures. Dermatol Surg. 2011;37:889–99.

Watve SV, Sivan M, Raza WA, Jamil FF. Management of acute overdose or withdrawal state in intrathecal baclofen therapy. Spinal Cord. 2012;50:107–11.

Willems P, de Bie R, Öner C, et al. Clinical decision making in spinal fusion for chronic low back pain. Results of a nationwide survey among spine surgeons. BMJ Open. 2011;1:e000391.

Anesthesia for Patients Scheduled for Intraoperative Electrophysiological Monitoring

17

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Introduction

A variety of anesthesia methods can be used during surgery where intraoperative neurophysiological monitoring is used. Clearly, the anesthesia must be titrated to each patient and adjusted for the various comorbidities, including the degree of neural compromise that may impact monitoring. In general, the choice of anesthesia depends on the particular monitoring modalities being used. The major limitations are when techniques are sensitive to inhalational agents (IH) and/or when they are sensitive to neuromuscular blocking agents (NMB). Some modalities are insensitive to both (e.g., auditory brainstem responses [ABR]), others are sensitive to NMB only (e.g., electromyography [EMG]) or IH only (e.g., cortical somatosensory evoked potentials [SSEP]), and some are sensitive to both IH and NMB (e.g., transcranial motor evoked potentials (MEP)). Although each monitoring modality used contributes to limitations to the choice of anesthetic agents, the modality with the most restrictions often defines the major anesthetic considerations.

The protocols below are usually successful with various types of monitoring. In these listings the doses are approximate for adults and need to be individualized for any given patient. Unless specifically mentioned, inhalational anesthetics mentioned here refer to desflurane (Des) or sevoflurane (Sevo). These are preferable to nitrous oxide because of their more desirable cortical and spinal effects. In general, desflurane or sevoflurane can be substituted for each other at MAC equivalent concentrations. Also in these techniques, infusions of sufentanil, fentanyl, and remifentanil can generally be substituted for each other at clinically equivalent infusion rates. Similarly, intermediate-acting non-depolarizing NMB can usually be substituted at equivalent doses. Induction boluses ideally should be the same agent as used subsequently by infusion (e.g., propofol) since induction will "load" the patient in preparation for the infusion which follows.

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Monitoring During Posterior Fossa Surgery

Auditory Brainstem Response

Monitoring during posterior fossa surgery frequently involves the auditory brainstem response (ABR) and electromyography (EMG) of muscles to assess the function of cranial nerves at risk. In addition, somatosensory evoked potentials (SSEP) and motor evoked potentials (MEP) may also be monitored along with the ABR to assess the brainstem by monitoring the transmission of their activity through the brainstem.

The ABR is produced by stimulation of the cochlea using "clicks" delivered into the ear canals. The sound elicits responses from the brainstem which can be recorded from electrodes near the ear and on the top of the head. Usually five major waves can be recorded in the 10 ms after stimulation, but only three major waves are usually monitored. These are produced by the extracranial portion of the eighth cranial nerve (wave I), nuclei in the medulla (wave III), and nuclei in the pons (wave V). When monitoring involves only the ABR, there are no anesthetic restrictions since this is neither sensitive to IH nor sensitive to NMB. Any anesthetic technique can be chosen and should be guided by considerations of the patient and surgery. In the unlikely event that the Eustachian tube is blocked, the use of nitrous oxide should be avoided because it could cause a middle ear tension that interferes with sound transmission through the middle ear and thereby alter the ABR.

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Anesthesia for Posterior Fossa Surgery with ABR only

- *Induction as usual*
- *Maintenance as usual (IH and NMB as desired)*

Cranial Nerve Electromyography

The most common addition to ABR during posterior fossa surgery is monitoring the various cranial nerves at risk, especially the facial nerve. This monitoring is usually accomplished using the muscles which are innervated by the cranial nerves. Termed electromyography (EMG), this activity is usually recorded using pairs of needle electrodes placed in the chosen muscles. Normally silent under anesthesia, EMG activity can be seen as a result of inadvertent mechanical stimulation of the nerve (brief burst activity) or potentially more damaging stretch or nerve ischemia (prolonged neurotonic "trains"). Finally, the surgeon can use an electrified probe to locate the nerve or nuclei or to test nerve integrity by evoking an EMG response with the probe (triggered EMG).

Because this monitoring assesses muscle responses, it is sensitive to NMB. They reduce the EMG amplitude and may obscure responses indicative of neural injury. For this reason, NMB is not usually recommended during EMG monitoring. Several studies have shown that partial neuromuscular blockade has been used with electrically evoked EMG when the responses are robust and the partial blockade is carefully controlled. However, when neural pathology is present, or when spontaneous activity is monitored, partial neuromuscular blockade may prevent adequate monitoring.

During microvascular decompression for hemifacial spasm, the lateral spread response may be monitored. In this case stimulation of one branch of the facial nerve may abnormally activate muscles in other branches of the nerve. Thought to be related to the pathologic process giving rise to the spasm, the loss of this response is thought to signal a successful decompression of the nerve. This response is particularly sensitive to non-depolarizing agents such that their use should be avoided if possible. In surgeries where ABR is combined with EMG, a balanced anesthetic is often chosen (e.g., opioids and inhalational agents) with NMB used with intubation to wear off.

Anesthesia for Posterior Fossa Surgery with ABR and EMG

- *Induction as usual*
- *Maintenance as usual (IH as desired)*
- *Let NMB wear off after induction and avoid additional neuromuscular blockade (avoid non-depolarizing agents if lateral spread is being monitored)*

Corticobulbar Responses

Occasionally corticobulbar responses are utilized during posterior fossa surgery to monitor cranial nerves VII (facial) or X (vagus). This monitoring is done using stimulation of the cerebral cortex using the techniques of motor evoked potentials (see below) with EMG recording of the orbicularis oris and orbicularis oculi (c.n. VII) or vocalis (c.n. X) muscles. If the MEP is not otherwise being monitored, anesthetic considerations listed for their use below need to be added to those of the other techniques being employed.

Monitoring Cerebral Ischemia

Electroencephalography

A variety of procedures utilize monitoring for potential ischemia in the cerebral cortex. A good example is carotid endarterectomy. The techniques usually used to monitor for cerebral ischemia include electroencephalography (EEG), SSEP, MEP, and a variety of non-electrophysiological techniques (transcranial Doppler ultrasound, cerebral oximetry, and jugular bulb oxygen saturation). If the only monitoring modality used is electroencephalography (EEG), the anesthesia is straightforward since it is insensitive to NMB (i.e., use as much as appropriate for other needs) and only sensitive to high doses of IH and large doses of intravenous sedatives (e.g., propofol).

The EEG is produced by the spontaneous inhibitory and excitatory synaptic potentials of the pyramidal cells in the superficial layers of the cerebral cortex. It is usually recorded from pairs of scalp electrodes, each of which records the summated potentials generated by a small volume of cortex beneath the electrode. It can also be recorded directly from the surface of the cortex after a craniotomy (e.g., awake craniotomy). Anesthetic agents generally produce rhythmic activity of 8–10 Hertz (Hz), but at higher doses where these agents markedly reduce synaptic activity the EEG is markedly reduced in amplitude and frequency mimicking the effect of cerebral ischemia.

The choice of anesthesia is usually designed to produce a rhythmic EEG that is associated with light to moderate anesthesia with IH (usually be limited to 1 minimal alveolar concentration (MAC) or lower) and can be titrated to the EEG. Of note, the EEG effects of the IH vary with the specific agent, particularly with nitrous oxide. Similarly, high doses of sedative-hypnotic agents (e.g., propofol) can also produce burst suppression or electrical silence such as that used for metabolic suppression. Opioids are usually used to supplement the inhalational agents and can produce EEG slowing without amplitude loss.

Anesthesia for Monitoring Cerebral Ischemia with EEG only

- *Induction as usual*
- *Maintenance balanced anesthesia (~1 MAC inhalational agent)*
- *Opioids and NMB as needed*

Of note, for the recommendations in this chapter, inhalational agents refer to the halogenated anesthetics (e.g., desflurane and sevoflurane) and not nitrous oxide. Although nitrous oxide can generally be substituted for the halogenated agents at MAC equivalent doses, these recommendations favor the halogenated agents because they have better anesthetic utility (unconsciousness, amnesia, and reduce reflex movement). In addition, nitrous oxide may need to be abruptly stopped to increase the oxygen concentration in a period of concern causing a shift in anesthetic effect at a time when monitoring is particularly important. Also of note, nitrous oxide and the halogenated agents are synergistic such that a combination of these agents is particularly depressant on the responses such that the combination is not recommended.

Somatosensory Evoked Potentials

Additional anesthesia considerations apply if somatosensory evoked potentials (SSEP) are used with the EEG during monitoring for cerebral ischemia. The SSEP is produced by electrical stimulation of peripheral nerves such as the median, ulnar, or posterior tibial nerve. Activation of the nerve produces a volley of activity which travels along the neural pathway of proprioception and vibration entering the spinal cord via the dorsal nerve root and ascending the ipsilateral posterior column to the cervical-medullary junction. The volley travels on to the contralateral medial lemniscus pathway after synapsing near the nucleus cuneatus or gracilis. Following transmission at a second synapse in the ventroposterolateral nucleus of the thalamus, the volley travels to the primary sensory cortex through thalamocortical radiations. The sensory response can be monitored by electrodes placed along peripheral nerves, near the spinal cord (especially along the cervical spine), but is most commonly recorded by scalp electrodes over the sensory cortex. These scalp electrodes indicate transmission through the entire pathway and are used to detect cortical ischemia. The prominent anesthetic effect appears to be blocking of transmission through the thalamus and the depression of synaptic activity in the cerebral cortex (similar to the effects on the EEG).

In these cases an IH must be kept low enough to keep the cortical SSEP responses large enough to be monitored. In general, cortical SSEP amplitudes are often acceptable with IH concentrations between 0.5 and 1 MAC. However, the effect is nonlinear; there is usually a concentration "threshold" such that above that level the cortical SSEP response is markedly reduced in amplitude. Each patient may have a different threshold so the IH must be titrated to effect. The use of an infusion of a short-acting opioid decreases the need for higher doses of inhalation agents, and a propofol infusion may be added if additional cerebral effects are needed.

Anesthesia for Monitoring for Cerebral Ischemia with SSEP

- *Induction as usual (*e.g., *propofol)*
- *Maintenance balanced anesthesia (0.5–1 MAC IH)*
- *Propofol infusion (25–75 μg/kg/min)*
- *Opioid infusion as needed*
- *NMB as needed*

Motor Evoked Potentials with SSEP

Additional anesthetic restrictions apply if motor evoked potentials (MEP) are also monitored to evaluate for ischemia in the motor cortex or motor pathway. Motor evoked potentials are produced by electrical stimulation of the motor cortex using scalp electrodes or direct cortical stimulation (e.g., during awake craniotomy). This produces a volley of activity which traverses the corticospinal pathway to the anterior horn cells in the spinal cord where a lower motor neuron can be activated to produce muscle responses. The MEP can be monitored by epidural electrodes (the D wave) but are most commonly recorded as compound muscle action potentials using electrode pairs placed in muscles (typically flexors of the hand and foot). The primary anesthetic effects on these myogenic MEP responses appear to involve synaptic inhibition in the spinal cord and considerations regarding NMB (similar to considerations for EMG). There are no apparent anesthetic restrictions for epidural recording of the D wave.

As mentioned above with the discussion of EMG, NMB are not recommended or must be severely restricted to partial blockade with tightly controlled infusions. In addition, the myogenic MEP response is more sensitive to IH than the SSEP. As such inhalational agents must usually be restricted to less than 0.5 MAC and may have to be completely avoided. If used, relatively insoluble agents such as desflurane or sevoflurane are recommended in case these low doses are not compatible with MEP responses such that they need to be eliminated. As such with MEP, intravenous agents (e.g., propofol, opioids) are frequently used to supplement the low doses of inhalational agents or as a total intravenous anesthetic (TIVA) when inhalation agents must be avoided. It is important to add that a key anesthesia component with MEP is a bite block since lip and tongue bite injuries are common

(especially if the bite block falls out when prone). Usually recommended is rolled gauze between the lateral incisors and molars.

Anesthesia for Monitoring Cerebral Ischemia with SSEP and MEP

- *Induction as usual*
- *Maintenance balanced anesthesia with 1/2 MAC or less*
- *Propofol infusion (25–75 μg/kg/min)*
- *Short acting Opioid infusion (remifentanil 0.1–0.4 μg/kg/min)*

Monitoring During Supratentorial Masses and Cerebral Vascular Surgery

SSEP and MEP

Monitoring during surgery for supratentorial masses and intracranial vascular lesions (e.g., aneurysms) usually involves the SSEP and MEP to map the brain to locate the sensory and motor cortex and to monitor for ischemia from retraction, temporary clipping, trapping, or accidental vascular occlusion. In these cases, opioids (e.g., remifentanil) and propofol infusions are used. The addition of a low concentration of IH helps keep the propofol infusion at low levels, protect against movement or recall in case of accidental interruption of the infusions, and to enable early wake up. To enable early neurological exam, the use of long-acting opioids is avoided, and the propofol infusion should be stopped about an hour before the end of surgery or longer if burst suppression was used. EEG monitoring can often be used to assess the cortical anesthetic effect, particularly if burst suppression is used for metabolic suppression.

Anesthesia for Monitoring Intracranial Tumors and Neurovascular Surgery with SSEP, MEP, and EEG

- *Induction as usual*
- *Maintenance with Inhalation agent ≤0.5MAC*
- *Propofol infusion 25–75 μg/kg/min*
- *Opioid infusion (*e.g., *remifentanil 0.1–0.4 μg/kg/min)*
- *NMB intermediate-acting agent for induction then none*
- *If burst suppression is needed propofol infusion is raised to150 μg/kg/min to achieve suppression within 10 min. If faster suppression is needed a bolos dose of 50 mg (0.7–1 mg/kg) can be used*

Monitoring During Awake Craniotomy

Awake craniotomy is frequently utilized when seizure foci, tumors, or arterial-venous malformations are near the cortical areas of motor or language function. Sedation and supplementary analgesia may be used with a scalp block or field infiltration of local anesthesia. During the monitoring to identify the motor or speech regions, supplementary anesthetics are stopped to allow a fully cooperative patient. They can identify muscle activity indicative of motor cortex stimulation and demonstrate language "pauses" when the surgeon electrically stimulates the language areas. Monitoring is usually done to identify native seizure activity or seizure activity resulting from cortical stimulation in addition to its use to locate the sensory, motor, and speech cortex. Supplementary sedation can be accomplished using infusions of propofol or dexmedetomidine and supplementary analgesia using remifentanil. Recent experience supports the possibility of achieving speech and motor mapping with little effects from small doses of remifentanil (≤0.5 μg/kg/min).

Anesthesia for Cerebral Procedures during Awake Craniotomy

- *Scalp block with long acting local anesthetic*
- *Sedation with propofol infusion (10–50 μg/kg/min) or dexmedetomidine (0.2–0.5 μg/kg/h)*
- *Supplementary analgesia with remifentanil infusion (0.02–0.18 μg/kg/min) as needed (keeping respiratory rate 8–12/min)*
- *Stop supplementary agents during testing*
- *Restart sedation and supplementary analgesia after the completion of testing*

Monitoring During Spinal Corrective Surgery

Spine Surgery with SSEP

Monitoring during spinal corrective surgery usually involves the SSEP and MEP to monitor the spinal cord pathways, cauda equina, and peripheral nerves. It usually involves monitoring of EMG from muscles innervated by the cauda equina and nerve roots at risk.

When providing anesthesia for spinal surgery where only the SSEP is used, a balanced anesthetic using opioids, muscle relaxation as needed, and 0.5–1 MAC inhalational agent is usually acceptable. Propofol is often utilized (e.g., 80–120 μg/kg/min) in addition to opioid (sufentanil [0.2–1 μg/kg/h], fentanyl [3–6 μg/kg/h], or remifentanil [0.2–0.4 μg/kg/min]). The sufentanil and fentanyl infusions need to be turned off about 30–45 min before the end of surgery. Remifentanil may be particularly helpful in short cases and when large opioid doses are needed (e.g., with chronic opioid use). When EMG and MEP are not being used, NMB should be acceptable. Since wake-up tests are still occasionally used, plans for such a procedure should be incorporated into the anesthesia planning.

Anesthesia for Spinal Corrective Surgery with SSEP only

- *Induction as usual (e.g., propofol)*
- *Maintenance balanced anesthesia (0.5–1 MAC inhalational agent)*

- *Propofol infusion (80–120 μg/kg/min)*
- *Opioids – sufentanil bolus as needed then 0.2–1.0 μg/kg/h turn off 30–45 min before end*
- *NMB as needed*

Anesthesia with Dexmedetomidine

An alternative approach is to use dexmedetomidine (0.2–0.5 μg/kg/h) instead of, or supplementary to, the propofol. An infusion of propofol (e.g., 50 μg/kg/min) or a low-dose inhalational agent (e.g., 0.5 MAC) is usually used since dexmedetomidine is not reliably amnestic. Because the mechanism of dexmedetomidine action is not opioid like (i.e., central alpha-2 stimulation), it may be helpful in opioid-tolerant patients.

Alternate Anesthesia for Spinal Corrective Surgery with only SSEP using Dexmedetomidine

- *Induction as usual (*e.g., *propofol)*
- *Maintenance balanced anesthesia (0.5–1 MAC inhalational agent)*
- *Dexmedetomidine infusion (0.2–0.5 μg/kg/h) turn off 30–45 min before end*
- *Propofol infusion (25–50 μg/kg/min) if IH not used*
- *Opioids – sufentanil bolus as needed than 0.2–0.5 μg/kg/h, turn off 30–45 min before end*
- *NMB as needed*

Spine Surgery with SSEP and Peripheral Nerve Electromyography

The most frequent addition to SSEP in spine surgery is EMG of muscles innervated by peripheral nerve roots at risk (particularly when portions of the cauda equina are included in the operative field). Similar to the use of EMG in posterior fossa surgery, NMB must be restricted. Of note, after induction of anesthesia and the baseline monitoring responses are acquired, surgeons may request relaxation for muscle dissection in an extensive, multilevel spinal surgery or to assist in the exposure of the spine during an anterior abdominal approach. With profound neuromuscular blockade, the EMG will not be monitorable; however, when the blockade resolves to two to three responses in a train of four (TOF), the EMG will often be monitorable. Small and mechanically elicited responses may, however, be obscured. If possible, it is usually recommended to avoid NMB during the portion of the surgical procedure involving EMG monitoring.

If muscle relaxation must be used during the portion of surgery when EMG monitoring is used, tightly controlled infusions of intermediate-acting drugs such as rocuronium (5–10 μg/kg/min) or vecuronium (0.5–0.8 μg/kg/min) are usually used to produce two to three responses in the TOF. In this case the EMG can usually detect muscle activity from electrically stimulated responses such as differentiating functional nerve tissue from non-neural tissue subsequent to stimulation of tissue in the cauda equina. This also includes the stimulation of pedicle screw pilot holes or pedicle screws to identify low stimulation thresholds consistent with medial screw placement that may place a nearby nerve root at risk for injury. With pedicle screw stimulation, data suggests that a deeper neuromuscular block (only one response in a train of four) may artificially increase the pedicle screw threshold which could reduce the ability to signal the need for repositioning the screws.

Since pathology in the nerve roots, peripheral nerves, or muscles (including chronic compression) may hamper EMG recording, partial paralysis may mask some small EMG responses. In addition, the detection of nerve root compromise from mechanical means might be reduced similar to facial nerve monitoring above, such that avoidance of NMB is desirable. In general, since the sensitivity of muscle groups to muscle relaxants varies, optimal TOF monitoring is done in the muscles being used for monitoring.

Anesthesia for Spinal Surgery with SSEP and EMG

- *Induction as usual (e.g., propofol)*
- *Maintenance balanced anesthesia (0.5–1 MAC inhalational agent)*
- *Propofol infusion (80–150 μg/kg/min)*
- *Opioids – sufentanil bolus as needed than 0.2–1.0 μg/kg/h turn off 30–45 min before end*
- *Higher doses of opioids and lower doses of propofol can be used*
- *NMB as needed for induction, possibly for muscle dissection then none*
  - *(Rarely acceptable 2+/4 twitches in TOF in muscles monitored for monitoring nerve stimulation but not spontaneous or mechanical nerve irritation)*

Anesthesia When SSEP Cannot Be Recorded

In general, the ability to use IH and partial muscle relaxation is very helpful in anesthetizing spine surgery patients. However, an increasing number of patients are presenting for spinal corrective surgery who have significant neurological compromise with numbness, weakness, and tingling such as with myelopathy or neuropathy. In these patients, anesthesia is more challenging due to poor SSEP responses; hence the IH concentration must be reduced or eliminated to facilitate monitoring. In this case the anesthesia becomes a total intravenous anesthetic (TIVA) usually with infusions of propofol (100–200 μg/kg/min) and opioids (e.g., sufentanil, fentanyl, or remifentanil as above). Since these responses may be very small, it is recommended that NMB not be utilized during the monitoring.

Anesthesia for Spinal Corrective Surgery in Patients where SSEP Cannot be Recorded at Low Dose IH

- *Induction as usual (e.g., propofol)*
- *Pure TIVA – no IH, no nitrous oxide*
- *Propofol infusion (100–200 μg/kg/min)*
- *Opioid infusion – sufentanil bolus or preferably as infusion of 0.2–1.0 μg/kg/h, turn off 30–45 min before end*
- *In long cases an early sufentanil infusion 1 μg/kg/h tapered down after 1 h to 0.8 μg/kg/h for the second hour and so on to 0.2–0.5 μg/kg/h, for the rest of the operation and stopped 1 h before the end of surgery. Higher sufentanil doses will allow lower propofol infusion rates*
- *NMB as needed for induction, possibly for muscle dissection then none (with EMG monitoring)*

Spine Surgery with SSEP, EMG, and MEP

Monitoring spinal corrective surgery in regions of the spine above the cauda equina usually utilizes EMG, SSEP, and MEP monitoring. Because of the sensitivity of MEP to anesthetic agents, anesthesia with MEP monitoring is one of the most challenging anesthetics because both IH and NMB must be severely restricted or avoided. For a medically healthy patient who is without neurological compromise, the use of 0.5 MAC of inhalational agent (e.g., 3% Des or 0.5% Sevo) is useful, especially with patients who are opioid-tolerant. Hence, after a standard induction with propofol and a short- or intermediate-acting muscle relaxant 0.5, MAC inhalation agent can often be used with an opioid infusion (such as sufentanil [0.2–1 μg/kg/h in long cases] or remifentanil [0.1–0.4 μg/kg/min in short procedures]) and a propofol infusion (50–150 μg/kg/min).

Anesthesia for Spinal Surgery with SSEP, MEP, and EMG

- *Induction as usual (*e.g., *propofol)*
- *Propofol infusion (50–150 μg/kg/min)*
- *Low dose IH (less than or 0.5 MAC)*
- *Opioid infusion – sufentanil bolus as needed than 0.2–1.0 μg/kg/h, turn off 30–45 min before end. Or remifentanil (0.1–0.4 μg/kg/min) and fentanyl (3–5 μg/kg/h) infusion.*
- *NMB as needed for induction, possibly for muscle dissection then none*
  - *(Rarely acceptable 2+/4 twitches in TOF in muscles monitored for monitoring nerve stimulation but not spontaneous or mechanical nerve irritation)*
- *For long cases, sufentanil 1 μg/kg/h for first hour followed by 0.8 μg/kg/h for the second hour and 0.5 μg/kg/h for the third hour and down more in the following hours to stop 1 h during closing*

Of note, experience with dexmedetomidine and MEP has been problematic and may not be successful. Hence propofol is recommended.

Spine Surgery When MEP Cannot Be Recorded

This technique using 0.5 MAC of desflurane or sevoflurane usually works well with patients with robust neural function and excellent responses. But occasionally the MEP responses are too small which necessitates turning off the IH and adjusting the propofol and sufentanil infusions. In this case a pure TIVA technique is recommended. Since it would be preferable to begin the maintenance anesthetic with the technique ultimately used (so as to not change the anesthetic during the monitoring), some practitioners start with TIVA when there is any question about neural functioning. If the addition of a low concentration of IH is subsequently desired, then with the demonstration of adequate baseline monitoring responses, the addition of 0.5 MAC of desflurane or sevoflurane can be tried with observation of the effect.

Anesthesia for Spinal Surgery in Patients Where MEP is Difficult to Record

- *Induction as usual (e.g.*, *propofol)*
- *Pure TIVA – no IH or nitrous oxide*
- *Propofol infusion (100–200 μg/kg/min)*
- *Opioid infusion – sufentanil infusion of 0.2–1.0 μg/kg/h turn off 30–45 min before end*
- *NMB as needed for induction, possibly for muscle dissection then avoid as possible*
  - *(Rarely acceptable 2+/4 twitches in TOF in muscles monitored for monitoring nerve stimulation but not spontaneous or mechanical nerve irritation)*

Anesthesia with Opioid-Tolerant Patients (Ketamine and Lidocaine)

Also challenging are the increasing number of patients for spinal corrective surgery with chronic pain and opioid tolerance where the usual opioid infusion doses are inadequate. If the surgery is limited to spinal levels below the conus of the spinal cord (usually L1-L2), frequently only EMG and SSEP are monitored allowing the use of some IH (e.g., 0.5 MAC) or dexmedetomidine. However, if MEP is monitored, these agents are often inconsistent with monitoring, so a TIVA technique becomes essential and supplementation utilized to address the opioid tolerance. Without supplementation the propofol infusion rate is often excessive (e.g., 180–200 μg/kg/min) resulting in response depression and loss, or the opioid infusion is simply inadequate to provide adequate anesthesia.

One of the most common supplements to assist in opioid-tolerant patients is ketamine. Ketamine can be given as an intermittent bolus (0.5–1 mg/kg/h), or as an infusion (0.25–0.5 mg/kg/h) (3–5 μg/kg/min). An infusion can also be made

by mixing the ketamine into the propofol infusion. Typically the initial mixture is 2 mg ketamine per cc of propofol. This addition is tapered down with each new 50 cc of propofol (1 ½, 1, ½, none – depending on length of case) used for infusion as the ketamine is metabolized more slowly than propofol. In addition, it is desirable to reduce the presence of ketamine near awakening avoid hallucinations in postoperative recovery. Note that the ketamine will increase the SSEP amplitude so you may see a slow decline in SSEP amplitude as the ketamine is tapered. Midazolam may be added to reduce the undesirable effects of ketamine.

Ketamine is also an excellent agent for anesthesia in very young children with an immature nervous system. For example, young children (less than 6 years) have incompletely developed motor pathways and may be very difficult to monitor with MEP. In these patients a ketamine-based anesthetic may be required, and an enhancing MEP stimulation technique using spatial enhancement or double pulse stimulation may be needed.

Alternatively, or along with the ketamine, a lidocaine infusion can be used (1.5 mg/kg/h, 25 μg/kg/min, maximum rate 2 mg/min). It is not clear if it is enhancing, but the mechanism of analgesia is not based on opioid action so it can be helpful in the opioid-tolerant patient. It usually allows a reduced propofol and opioid infusion rates.

Anesthesia for Spinal Corrective Surgery in Patients with Opioid Tolerance

- *Induction as usual (*e.g., *propofol)*
- *Pure TIVA – no IH or nitrous oxide*
- *Propofol infusion (80–150 μg/kg/min)*
- *Opioid infusion – sufentanil infusion 0.3–1.0 μg/kg/h, turn off 30–45 min before end*
- *Ketamine as a separate infusion (0.25–0.5 mg/kg/h) or mixed in the propofol (see text)*
- *Lidocaine as a separate infusion (25 μg/kg/min, maximum 2 mg/min)*
- *NMB as needed for induction, possibly for muscle dissection then none*
  - *(Rarely acceptable 2+/4 twitches in TOF in muscles monitored for monitoring nerve stimulation but not spontaneous or mechanical nerve irritation)*

Intramedullary Spinal Cord Surgery

During surgery for intramedullary spinal cord surgery, the considerations for spinal corrective surgery with EMG and MEP apply as above. The one addition to the monitoring is the monitoring of the D wave of the motor evoked response using epidural electrodes. This addition does not change the anesthetic requirements listed above because the D wave is not affected by IH or NMB.

Tethered Cord or Cauda Equina Pathology

During spinal surgery to release a tethered cord or to correct pathology in the cauda equina, the considerations listed above for spinal corrective with EMG apply. In these cases, the surgeon utilizes an electrified stimulation probe to test tissue in the operative field to determine if the tissue is functional or can be resected. Innervation related to bowel and bladder function is extremely important to the patient outcome, and additional techniques may be employed (e.g., bulbocavernosus reflex). It is highly recommended that NMB not be utilized during monitoring in these cases because of the importance of this stimulated EMG technique. If SSEP or MEP is also monitored, then the respective considerations mentioned above in spinal surgery apply.

General Comments

Mask Induction in Patients

It is worth mentioning that in patients where an intravenous line is not available for induction (such as in a child or a rare adult), a mask induction with sevoflurane with or without nitrous oxide works fine. Usually there is time for the concentration of these agents to decline after transition to the techniques mentioned above in time for the need for intraoperative monitoring.

Alternatives to Propofol

If propofol is unacceptable or unavailable, studies have shown that dexmedetomidine (see above), methohexital, etomidate, and midazolam have been used. Experience with these with MEP is limited; however, methohexital and etomidate have been used. Concerns about adrenal suppression and outcome suggest etomidate use may be less ideal.

Anesthesia Contribution to EP Monitoring

In addition to contributing to the effectiveness of the monitoring through anesthetic agent choice, the anesthesiologist provides assistance during the differential diagnosis of a monitoring change. When changes occur, the search for physiological (e.g., hypotension, hypothermia), unfavorable positioning (especially the upper extremity), and anesthetic causes involve the anesthesiologist. Finally, when changes suggest the neural structures are at increased risk, the anesthesiologist can help support neurological system. This may be particularly important during neural ischemia such as during the use of temporary clips, accidental arterial occlusions,

and other surgical maneuvers. In these circumstances the anesthesiologist can often raise the blood pressure to enhance collateral circulation (particularly if relative hypotension is occurring) and may be able to decrease oxygen requirements by decreasing metabolic oxygen consumption.

Conclusion

In general, the anesthetic technique is initially chosen based on the patient comorbidities, the degree of patient neural dysfunction or pathology, the actual surgery to be performed, and the specific monitoring modalities to be used. Once the baseline monitoring responses are acquired, the anesthetic technique may need to be adjusted if the chosen technique is inadequate for anesthesia or key monitoring responses cannot be consistently recorded. In all cases, it is desired to reach and maintain a steady state of anesthesia before and during the monitoring. This constant anesthetic effect allows the monitoring to focus on potentially deleterious effects on the nervous system. Then, when changes in the monitoring occur, the anesthesiologist can assist in determining if changes in physiology (e.g., blood pressure, oxygenation) or changes as a consequence of unfavorable positioning have contributed to the change in the monitoring. In addition, if a deleterious effect is occurring from a procedure-related effect, then the anesthesiologist may be able to reduce that effect by improving the physiological environment (e.g., increasing blood pressure).

Suggested Reading

Balvin MJ, Song KM, Slimp JC. Effects of anesthetic regimens and other confounding factors affecting the interpretation of motor evoked potentials during pediatric spine surgery. Am J Electroneurodiagnostic Technol. 2010;50(3):219–44.

Jameson LC, Janik DJ, Sloan TB. Electrophysiologic monitoring in neurosurgery. Anesthesiol Clin. 2007;25(3):605–30.

Jäntti V, Sloan T. Anesthesia and intraoperative electroencephalographic monitoring. In: Nuwer M, editor. Intraoperative monitoring of neural function, handbook of clinical neurophysiology, vol. 8. New York: Elsevier B.V.; 2008. p. 77–93.

Kalkman CJ, Drummond JC, Ribberink AA, Patel PM, Sano T, Bickford RG. Effects of propofol, etomidate, midazolam, and fentanyl on motor evoked responses to transcranial electrical or magnetic stimulation in humans. Anesthesiology. 1992;76(4):502–9.

Kawaguchi M, Furuya H, Kawaguchi M, Furuya H. Intraoperative spinal cord monitoring of motor function with myogenic motor evoked potentials: a consideration in anesthesia. J Anesth. 2004;18(1):18–28.

Koht A, Schutz W, Schmidt G, Schramm J, Watanabe E. Effects of etomidate, midazolam, and thiopental on median nerve somatosensory evoked potentials and the additive effects of fentanyl and nitrous oxide. Anesth Analg. 1988;67(5):435–41.

Koht A, Sloan TB, Hemmer LB. Neuromonitoring in surgery and anesthesia. In: Crowley M, editor. UpToDate. Waltham: UpToDate; 2015.

Macdonald DB, Skinner S, Shils J, Yingling C. Intraoperative motor evoked potential monitoring – a position statement by the American Society of Neurophysiological Monitoring. Clin Neurophysiol. 2013;124(12):2291–316.

Mahmoud M, Sadhasivam S, Salisbury S, Nick TG, Schnell B, Sestokas AK, et al. Susceptibility of transcranial electric motor-evoked potentials to varying targeted blood levels of dexmedetomidine during spine surgery. Anesthesiology. 2010;112(6):1364–73.

Pajewski TN, Arlet V, Phillips LH, Pajewski TN, Arlet V, Phillips LH. Current approach on spinal cord monitoring: the point of view of the neurologist, the anesthesiologist and the spine surgeon. Eur Spine J. 2007;16(Suppl 2):S115–29.

Pelosi L, Lamb J, Grevitt M, Mehdian SM, Webb JK, Blumhardt LD, et al. Combined monitoring of motor and somatosensory evoked potentials in orthopaedic spinal surgery. Clin Neurophysiol. 2002;113(7):1082–91.

Sloan T. Anesthesia and intraoperative neurophysiological monitoring in children. Childs Nerv Syst. 2010;26(2):227–35.

Sloan T. General anesthesia for monitoring. In: Koht A, Sloan T, Toleikis JR, editors. Monitoring for the anesthesiologist and other health professionals. New York: Springer; 2012. p. 319–35.

Sloan TB. Muscle relaxant use during intraoperative neurophysiologic monitoring. J Clin Monit Comput. 2013;27(1):35–46.

Sloan TB, Jäntti V. Anesthesia and physiology and intraoperative neurophysiological monitoring of evoked potentials. In: Nuwer M, editor. Handbook of clinical neurophysiology. Intraoperative monitoring of neural function, vol. 8. New York: Elsevier B.V.; 2008. p. 94–126.

Sloan TB, Mongan P, Lyda C, Koht A. Lidocaine infusion adjunct to total intravenous anesthesia reduces the total dose of propofol during intraoperative neurophysiological monitoring. J Clin Monit Comput. 2014;28(2):139–47.

Sloan TB, Toleikis JR, Toleikis SC, Koht A. Intraoperative neurophysiological monitoring during spine surgery with total intravenous anesthesia or balanced anesthesia with 3% desflurane. J Clin Monit Comput. 2015;29(1):77–85.

Taniguchi M, Nadstawek J, Langenbach U, Bremer F, Schramm J. Effects of four intravenous anesthetic agents on motor evoked potentials elicited by magnetic transcranial stimulation. Neurosurgery. 1993;33(3):407–15; discussion 15.

Toleikis JR. Intraoperative monitoring using somatosensory evoked potentials. A position statement by the American Society of Neurophysiological Monitoring. J Clin Monit Comput. 2005;19(3):241–58.

Factors Influencing Outcome in Neurosurgical Anesthesia

18

R. Ryan Field

General Risk

Overview

Some risks for neurosurgical patients concern the neuroanesthesiologist independent of their surgical intervention.

Education

Neurosurgical patients should not be concerned regarding obtaining intervention at an academic training center. Sufficient evidence suggests in both general and specific terms that not only does additional human capital catch errors more frequently and provide more frequent in-house supervision but also that the surgical outcome is not worsened by the presence of trainees.

Surgical Site Infections

Both preoperative corticosteroid and chemotherapy demonstrate higher incidences of organ-space, but not incisional, surgical site infection. Neoadjuvant chemotherapy unfortunately increases the risk of organ-space surgical site infection by as much as five times, while corticosteroid use preoperatively nearly doubles organ-space surgical site infection risk.

In spine surgery, surgical site infection independently associates with female sex, inpatient status, insulin-dependent diabetes mellitus, preoperative steroid use greater than 10 days, hematocrit under 35, body mass index above 30, wound classification, ASA classification, and operative duration.

Patient Risk Factors for Operative Complication

Age greater than 60, elevated C-reactive protein above 3 mg/L, and high Helsinki class score of four independently correlate with increased risk for postoperative complication in general, leading to increased length of stay, cost of care, and 30-day morbidity and mortality.

Key Points

- Neurosurgical encounters in the academic center do not consistently increase risk to the neurosurgical patient.
- Steroid use, particularly prolonged preoperative steroid use, increases the risk of surgical site infection in the neurosurgical patient.
- Neoadjuvant chemotherapy also increases this risk.
- Patient risk factors at baseline significantly predict the likelihood of perioperative surgical morbidity and mortality.

Epilepsy Surgery

Overview

Patients with epilepsy receive one of the most thorough preoperative workups available secondary to the multiphasic process of epilepsy surgery; however, they also frequently present with significant comorbidity and risks unique to their epilepsy itself.

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Implications for the Neurosurgical Patient

Epilepsy surgery remains a life-changing surgical intervention. Patients receive surface EEG and often proceed to strip, grid, and depth electrode placement or stereoelectroencephalography (SEEG) probes. Most continue the process and navigate further surgery for foci resection or vagal nerve stimulator placement.

Temporal lobe epilepsy probably represents the most common epilepsy amenable to frank surgical resection. Surgical intervention leaves the patient seizure-free in almost half of cases, while roughly two-thirds exhibit a highly desirable outcome. Length of epilepsy if predominantly tonic-clonic, particularly epilepsy for longer than 1 year prior to surgical resection, increases the risk of seizure recurrence by almost 250%. However, many investigated factors do not contribute to the risk of a negative surgical outcome: gender, race, family history of epilepsy, febrile seizure history, status epilepticus history, non-tonic-clonic temporal lobe epilepsy duration, IQ, and seizure frequency.

For epilepsy not confined to the temporal lobe, or for incompletely effective temporal lobe epilepsy surgery, vagal nerve stimulator insertion surgery may improve seizure frequency, quality, duration, and life impact. Vagal nerve stimulator surgery does not provide as much benefit to patients who already underwent temporal lobe resection. They show median improvements ranging from 42.5% at 3-month duration of stimulation to 50.5% at 24-month stimulation. For non-resected epilepsy, patients obtain improved results. Over 60% of patients receiving vagal nerve stimulator implantation report an at least 50% improvement in their epilepsy, over 40% also report at least a 75% improvement, over 25% report a greater than 90% improvement, and almost 10% are seizure-free.

Key Points

- Temporal lobe surgical intervention correlates with good surgical and seizure outcomes.
- Tonic-clonic seizure activity shows less improvement after temporal lobectomy if the activity presents greater than 1 year prior to surgery.
- Many other patient factors, though investigated, do not change seizure surgery outcome.
- Extra-temporal epilepsy and surgically refractory temporal lobe epilepsy may indicate candidacy for vagal nerve stimulator implantation surgery.
- Vagal nerve stimulator implantations show good outcome results, but not as good if the patient previously received temporal lobectomy.

Brain Tumor

Overview

Brain tumor outcomes constantly evolve as treatments, both surgical and medical, change. Many factors including tumor type and location may affect clinical course, morbidity, and mortality.

Implications for the Neurosurgical Patient

For both primary and metastatic brain tumor, presence of pre-, intra-, and/or postoperative seizure can influence outcomes and medical decision-making. Age less than 60 (OR 1.66), grade I or II glioma (OR 4), low total tumor volume (OR 2.18), and frontal tumor location (OR 2.28) all increased the risk of preoperative seizure. Presence of isocitrate-dehydrogenase mutation (OR 2.52) increased risk in a glioma subgroup. Age greater than 60 (OR 3.32), low tumor volume (OR 3.17), complete surgical resection (OR 15.5), diencephalic location (OR 12.2), and high-grade (OR 5.67) increased risk for intraoperative seizure. Interestingly, antiepileptic therapy did not affect seizure occurrence rates. Further work must be done to identify if seizure prophylaxis measurably improves perioperative seizure risk in subgroups; clarification may help maximize the value of this therapy while reducing the exposure of the patient to side effects.

In primary tumor, histologic classification helps determine recurrence rates. In cases of gross total resection, recurrence rates for ependymoma were 7.3%, astrocytoma 47.6%, and no recurrences occurred for hemangioblastoma. Tumor location did not affect neurological outcome. Ependymoma patients improved 20% of the time, 69% had no improvement, and 10.9% worsened. With astrocytoma, 4.8% improved, 47.6% experienced no change, and 47.6% worsened. With hemangioblastoma, 8.3% improved, while 91.7% experienced no change in neurologic condition post-resection.

For atypical meningioma, the overall postoperative complication rate is roughly 26%. Gross total resection, chemotherapy, and radiation failed to affect 5-year survival. High-grade meningioma, III compared to II, survived 5 years less often. Preoperative weakness dramatically worsened 5-year survival.

For glioblastoma, after second surgical resection, median survival was 11.4 months. MGMT methylation, young age, and completeness of resection correlated with improved median survival. Preoperative identification of younger patients and MGMT methylation presence may be useful

tools in identifying the value of a second surgical resection, possibly improving preoperative counseling.

With metastatic disease, postoperative stereotactic radiosurgery finds frequent use. Patients with less than four metastases and controlled systemic disease can have postoperative stereotactic radiosurgery with low risk of distant brain failure and safe improvement of local control.

Key Points

- The data on brain tumor medical and surgical outcomes are limited.
- Although it is now possible to identify high-risk groups for the development of pre- and intraoperative seizure, the use of antiepileptic prophylaxis does not appear to improve outcomes definitively.
- Histologic classification can predict how likely a primary complete tumor resection is to improve or maintain neurological outcomes.
- The global complication rate of atypical meningioma resection is higher than that for benign meningioma at 26% of all cases. Preoperative weakness and high tumor grade identification help council patients regarding 5-year survival.
- Metastases to brain remain safely amenable to postoperative stereotactic radiosurgery when the total number of metastases is less than four and systemic disease is well controlled.

Vascular Neurosurgical Intervention

Overview

Whether endovascular or open, vascular neurosurgical intervention makes great impact on the quality of life, morbidity, and mortality of neurosurgical patients.

Implications for the Neurosurgical Patient

Aneurysm

For aneurysm intervention, young age less than 50 reduces postoperative complication by roughly half (95% CI 0.3–0.7) and reduces mortality by roughly 60% (95% CI 0.2–0.9) when measured against those 60 and older. Patients between ages 50 and 60 showed similar impact on outcomes based on their age at presentation independently. These findings suggest the neuroanesthesiologist should risk-adjust for patient age greater than 60 at presentation.

In open intervention patients, preoperative anemia and transfusion both showed independent increases in adverse outcomes. Preoperative anemia correlated with increased hospital length of stay (OR 2.5), more frequent perioperative complication (OR 1.9), and increased rates of return to the operating room (OR 2.1). Transfusion history showed an overall increase in perioperative complication rates (OR 2.4).

Unruptured aneurysm remains an important patient population pathology requiring careful thought to the risk of surgery versus the risk of rupture. A new comorbidity index helps objectively assess the risk of perioperative complication. Twenty comorbidities ranging from neurological disorder to weight loss, acute myocardial infarction, GI bleeding, coagulopathy, hypothyroidism, depression, and hyperlipidemia create a composite risk score. This risk score improved prediction of morbidity and mortality, length of stay, and total economic patient charges and outperformed the previous two gold standard indices.

Beyond preoperative risk secondary to patient condition, unruptured cerebral aneurysm size plays a significant role in outcome. For very small unruptured aneurysm intervention, mortality rate was 0%, and early postoperative neurological deficit was 6.6%, which improved to 2.7% after 30 days. Posterior location predicted the highest risk of early neurological deficit, while middle cerebral artery aneurysm predicted the lowest rate of postoperative deficit at only 1.5%.

Other Vascular Outcomes and Risk Factors

Over 17 years, 72 patients were included in a review of risk factors for AVM recurrence. Only three cases exhibited recurrence; however, deep venous drainage of the AVM and presence of a diffuse AVM nidus both correlated with increased likelihood of recurrence. Preoperative embolization did not correlate by statistical analysis, but a differently designed study may show significance in the future since radiographic evidence suggested preoperative embolization played a role in recurrence in all three positive cases.

In cases of Moyamoya disease, a review of 31 cases identified only two risk factors: presence of any acute infarct in any location, even small ones, and impaired reserve on imaging. Both findings significantly predicted ischemic injury postoperatively.

Key Points

- For aneurysm surgery, age greater than 60 plays a significant role in perioperative outcomes.
- While transfusion worsens morbidity and mortality, preoperative anemia predicts a higher likelihood of perioperative complication.

- For unruptured aneurysms, a new index improves the quality of counsel and can improve patient selection for intervention.
- When aneurysms are very small, intervention itself presents very little risk to medical and surgical outcomes.
- AVMs with deep venous drainage and diffuse nidus are more likely to recur.
- Preoperative embolization may contribute to recurrence rates for completely resected AVMs, but further work must be done to confirm this hypothesis.
- Any history of acute infarct or evidence of poor cerebral circulatory reserve predicts postoperative ischemic events reliably.

Brain Trauma

Overview

Brain trauma presents a significant challenge to the neuroanesthesiologist and neurosurgeon. Outcomes are often poor, it is often difficult to predict who will do well, and cerebral trauma often does not present in isolation. More often, these patients suffer complex problem lists of polytrauma all requiring different methodologies and competing ideals of management.

Implications for the Neurosurgical Patient

Patient risk factors for mortality after subdural hematoma include age older than 60, presence of gangrene, presence of ascites, ASA class 4 or higher, coma, or bleeding disorder. Reoperation increased when patients exhibited symptoms of pneumonia, were of male sex, or became delirious during their hospitalization. Serious adverse events increased when patients were ventilator dependent, required dialysis, tested positive for delirium, possessed ASA class 4 or higher, or were of male sex. Length of stay increased similarly for patients except in cases requiring dialysis. Eighteen percent of patients died within 30 days when presenting with subdural hematoma; 64% of cases were male, and the average age at presentation was 71.

In cases of epidural hematoma, decompressive surgery should begin swiftly in patients experiencing a secondary massive cerebral infarction. Hematoma location, volume, GCS, duration, and extent of herniation, as well as preoperative shock, guide prediction of who will benefit from rapid decompression. Furthermore, they collectively create an epidural hemorrhage–massive cerebral infarction index (EDH-MCI) ranging from 0 to 18 points, consistently outperforming empiric decision alone. Hematoma evacuation surgery for patients scoring 9 points or less had excellent outcomes. Adding duraplasty improved outcomes in patients who scored 13 points or more. In cases between these two limits, patients needed to exhibit some extremes to undertake more extensive surgery, including unstable shock, severe brain stem injury, and/or unresponsive dilated pupils after burr hole evacuation. These patients also had a higher rate of postoperative massive cerebral infarction.

Key Points

- Patients with subdural hematoma fare differently based on their preoperative risk which may guide medical decision-making.
- For patients with epidural hematoma, a recent index can outperform empirical judgment alone in patient selection for simple hematoma evacuation, duraplasty, radical intervention, and possibly medical therapy only.

Spine Trauma

Overview

Spinal trauma remains a devastating injury where outcomes data are guiding medical and surgical therapy.

Implications for the Neurosurgical Patient

Of the decisions to be made with regard to the traumatic spine injury patient, the most important may be whether surgical decompression will benefit the patient or not. Waiting to make this decision may be the most impactful factor in neurological outcome. Of patients who received early surgical intervention within 24 h of injury, patients showed improved motor scores, better neurologic improvement rate, shortened length of hospital stay, and reduced requirement for ICU stay, and complication rates were reduced by almost 40%. Sadly, mortality remained the same independent of early or late surgical intervention. While mortality may not have improved, of those who could survive, neurological recovery improves faster and to a greater extent when receiving surgery within 24 h of injury.

The second most controversial intervention may be whether systemic steroids improve patient perioperative outcomes. In pharmacotherapy meta-analysis, methylprednisolone showed no significant improvement in neurological outcome. No class 1 evidence reported a positive correlation between methylprednisolone administration and improved neurological outcome. Of evidence other than class 1, meta-analysis grading showed significant methodological flaws in positive study outcomes. Given the outcome of the meta-analysis, the results of these nonclass 1 contributions were statistically more likely secondary to chance.

In the future, we may explore further the role of induced hypothermia to prevent damage from the secondary cascade in patients who acutely suffer spinal cord injury. As of now, there is more animal evidence than human evidence for neuroprotection in hypothermic subjects. Of the human evidence, there are few randomized controlled trials, and furthermore, there is little guidance on therapeutic parameters such as core temperature ranges and duration of therapy that will ultimately improve neurological outcome. Therefore, it is currently too early to make firm recommendations on induced hypothermia in spinal cord injury secondary to immature guidelines, but hopefully a clear protocol will emerge soon that shows benefit to neurological outcome and informs care.

Key Points

- The most important intervention we may be able to make, as neuroanesthesiologists, is to make an operating room and ourselves available to the patient as early as possible after injury.
- Perioperative steroids show no evidence of impact on neurological improvement in the spinal cord injury patient.
- Induced hypothermia shows promise, but no current evidence guides protocol for maximizing impact on neurological outcome.

Other Spine Surgery

Overview

Spine surgery presents a collection of diverse risks common to neurosurgery and unique to spinal surgery. Patient factors, surgical site, and surgical approach all affect neurosurgical outcomes.

Implications for the Neurosurgical Patient

A significant percentage of the patient population presenting for spinal surgery suffers from obesity. Spinal pathology may arise from excess bodyweight in some situations, but the general population has shifted to a higher prevalence of obesity regardless. This obesity creates longer surgical times, increased complication rates, and increased total cost of care, even when controlling for comorbidity. However, patients with obesity still report similar benefits from surgery for adult spinal deformity, even if their overall quality of life does not improve as much as the lives of patients who do not co-present with obesity at the time of surgery.

In degenerative cervical disease, the most important predictors of outcome were preoperative symptom severity and duration of symptoms; however, patient age at presentation had no significant correlation. The number of patient comorbidities and/or presence of diabetes, surprisingly, only show mixed effects in a number of studies of excellent graded methodology. Smoking only changed outcome in those with diabetes, while severity of psychological disease did worsen outcome. Only lower extremity weakness and/or co-presentation of upper and lower extremity symptoms showed correlation with poorer outcome, while bowel and bladder dysfunction did not. Positive Babinski sign does not consistently predict poor outcome, while leg spasticity and spastic gate do. Hand atrophy at presentation, sexual dysfunction, and possibly male sex predict poor outcome. Gradual onset of symptoms predicts worse outcome, yet slow disease progression predicts good outcome.

Patients receiving lumbar or thoracic minimally invasive surgery, for adult spinal deformity or tumor, do not necessarily show significant surgical outcome improvement compared to more invasive techniques. The rates of medical complication and increased hospital length of stay postoperatively may be less. Unfortunately, the outcomes data quality for these assertions currently lacks robust evidence and may contain bias. Overall, posterior lumbar interbody fusion patients report over 70% would recommend and repeat their experience, while 88% felt significant improvement.

Key Points

- The most detailed outcomes data for spinal surgery describe the population presenting for posterior cervical intervention.
- While male sex and smoking in the presence of diabetes may worsen surgical outcome, it is perhaps surprising that medical comorbidity does not more significantly affect outcome.
- This may be secondary to patient selection, effectively screening the most comorbid.
- Currently, the best predictors of surgical outcome are the patient's medical condition upon presentation for surgery rather than his or her intraoperative and postoperative medical management or surgical technique.
- Minimally invasive techniques may improve the rate of medical complication and length of hospital stay, but not the surgical outcome.
- The evidence for minimally invasive techniques requires further development and rigorous methodology to determine the true difference, if any.
- Obesity significantly determines cost outcomes, but surgical outcomes remain good.
- Despite all comorbidities, and the invasiveness of intervention, most patients report good outcomes, that they are satisfied, would have surgery again, and would recommend surgery to others.

Suggested Reading

General Risk

Lieber BA, Bruce JN, et al. Preoperative chemotherapy and corticosteroids: independent predictors of cranial surgical-site infections. J Neurosurg 11/6/2015. https://doi.org/10.3171/2015.4.JNS142719.

Lieber B, Tabbosha M, et al. Preoperative predictors of spinal infection within the National Surgical Quality Inpatient Database. World Neurosurg. 2016; https://doi.org/10.1016/j.wneu.2015.12.085.

Lim S, Kim JYS, et al. Impact of resident involvement in neurosurgery: an analysis of 8748 patients from the 2011 American College of Surgeons National Surgical Quality Improvement Program database. J Neurosurg. 2015;122:962–70.

Reponen E, Tuominen H, et al. Preoperative identification of neurosurgery patients with a high risk of in-hospital complications: a prospective cohort of 418 consecutive elective craniotomy patients. J Neurosurg. 2015;123:594–604.

Epilepsy Surgery

Amar AP, Liu CY. Vagus nerve stimulation therapy after failed cranial surgery for intractable epilepsy: results from the vagus nerve stimulation therapy patient outcome registry. Neurosurgery. 2004;55(5):1086–93. https://doi.org/10.1227/01.NEU.0000141073.08427.76.

Asadi-Pooya AA, Nei M, Sharan A, Sperling MR. Historical risk factors associated with seizure outcome after surgery for drug-resistant mesial temporal lobe epilepsy. World Neurosurg. 2016; https://doi.org/10.1016/j.wneu.2016.02.023.

Brain Tumor

Karikari I, Isaacs R, et al. Impact of tumor histology on resectability and neurological outcome in primary intramedullary spinal cord tumors: a single-center experience with 102 patients. Neurosurgery. 2011;68:188–97. https://doi.org/10.1227/NEU.0b013e3181fe3794.

Ling D, Heron D. et al. postoperative stereotactic radiosurgery to the resection cavity for large brain metastases: clinical outcomes, predictors of intracranial failure, and implications for optimal patient selection. Neurosurgery. 2015;76:150–7. https://doi.org/10.1227/NEU.0000000000000584.

Skardelly M, Tabatabai G, et al. Predictors of preoperative and early postoperative seizures in patients with intra-axial primary and metastatic brain tumors: a retrospective observational single center study. Ann Neurol. 2015;78:917–28. https://doi.org/10.1002/ana.24522.

Vascular Neurosurgical Intervention

Alan N, et al. Impact of age on 30-day postoperative outcome of surgery for ruptured and unruptured intracranial aneurysms. J Neurointerventional Surg. 2015;7(6):431–7.

Antonucci MU, et al. Acute preoperative infarcts and poor cerebrovascular reserve are independent risk factors for severe ischemic complications following direct extracranial-intracranial bypass for Moyamoya disease. Am J Neuroradiol. 2016;37(2):228–35.

Ivanov AA, et al. Recurrence of cerebral arteriovenous malformations following resection in adults: does preoperative embolization increase the risk? Neurosurgery. 2016;78(4):562–71.

Newman WC, Neal DW, Hoh BL. A new comorbidities index for risk stratification for treatment of unruptured cerebral aneurysms. J Neurosurg. 2016;125(3):713–9.

Seicean A, et al. Risks associated with preoperative anemia and perioperative blood transfusion in open surgery for intracranial aneurysms. J Neurosurg. 2015;123(1):91–100.

Brain Trauma

Lin H, et al. Novel clinical scale for evaluating pre-operative risk of cerebral herniation from traumatic epidural hematoma. J Neurotrauma. 2016;33(11):1023–33.

Lukasiewicz AM, et al. Patient factors associated with 30-day morbidity, mortality, and length of stay after surgery for subdural hematoma: a study of the American College of Surgeons National Surgical Quality Improvement Program. J Neurosurg. 2016;124(3):760–6.

Spine Trauma

Alkabie S, Boileau AJ. The role of therapeutic hypothermia after traumatic spinal cord injury-a systematic review (P3. 284). Neurology. 2016;86(16 Supplement):P3–284.

Fehlings MG, et al. Early versus delayed decompression for traumatic cervical spinal cord injury: results of the Surgical Timing in Acute Spinal Cord Injury Study (STASCIS). PLoS One. 2012;7(2):e32037.

Hurlbert RJ, et al. Pharmacological therapy for acute spinal cord injury. Neurosurgery. 2015;76:S71–83.

Liu J-M, et al. Is urgent decompression superior to delayed surgery for traumatic spinal cord injury? A meta-analysis. World Neurosurg. 2016;87:124–31.

Other Spine Surgery

Goldstein C, Rampersaud YR. Perioperative outcomes and adverse events of minimally invasive versus open posterior lumbar fusion: meta-analysis and systematic review. J Neurosurg Spine. 2016;24:416–27.

Higgins D, Clarke M. Understanding the impact of obesity on short-term outcomes and in-hospital costs after instrumented spinal fusion. Neurosurgery. 2016;78:127–32. https://doi.org/10.1227/NEU.0000000000001018.

Tetreault L, Fehlings M. Predictors of outcome in patients with degenerative cervical spondylotic myelopathy undergoing surgical treatment: results of a systematic review. Eur Spine J. 2015;24(Suppl 2):S236–51. https://doi.org/10.1007/s00586-013-2658-z.

A Comparison of Inhaled Anesthesia and Total Intravenous Anesthesia with Target-Controlled Infusion for Neuroanesthesia

19

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Overview

The ideal anesthetic drug or combination of drugs for neurosurgical procedures is often debated. Disregarding the actual characteristics of the drugs in question, an ideal regimen should have the following properties: favorable pharmacokinetics with fast onset and fast offset, insensitive decrement times, maintenance of hemodynamic stability, favorable effect on the physiology of the central nervous system (decreasing cerebral blood volume, decreasing intracranial pressure (ICP), maintaining CO_2 reactivity and cerebral autoregulation, not increasing cerebral metabolic rate (CMR), not affecting cerebrospinal fluid physiology), allowing neurophysiological monitoring with minimal interference, be anticonvulsant or at least not induce seizure activity, decrease edema, and finally should, with its own intrinsic properties, protect the brain from ischemia. Also, such a drug or regimen should have an adequate dose-response relationship for use in the awake neurosurgical patient with minimal ventilatory effects, with fast and easy titration to adjust individual requirements and adequate for easy measurement of its clinical effects. *Such a drug does not exist*, and in our daily clinical practice, we must instead choose from the existing armamentarium, those drugs that best fulfill the listed properties.

Whether a primarily intravenous or an inhalational technique is superior remains a subject of debate. One common approach has been to appraise the merits of both techniques with respect to several clinical endpoints like emergence times, neurosurgeon satisfaction, discharge from PACU, or incidence of early complications like nausea, vomiting, and pain. However, clinical comparisons of IV and inhaled-based anesthesia are difficult to interpret considering the likely different mechanisms of action of the anesthetic drugs and the issues of equipotency. A recently published systematic review and meta-analysis concluded that mean ICP values were lower and cerebral perfusion pressure (CPP) values were higher with propofol-maintained anesthesia.

Physiologic Properties of Anesthetic Drugs

Table 19.1 summarizes the effects of intravenous anesthetics and volatile agents on CBF, CMR, and ICP.

Changes in CBF with rising volatile anesthetic concentrations from 1 MAC to 2 MAC are patient-related and depend on the baseline metabolism. As volatile MAC increases above 1 MAC, cerebral blood flow will increase, while cerebral metabolic rate decreases. This uncoupling of metabolic rate and blood flow in the cerebral circulation is relatively unique to volatile anesthesia. Propofol, on the other hand, tends to maintain the CBF-CMR coupling.

Table 19.1 Cerebral blood flow (CBF), cerebral metabolic rate (CMR), and intracranial pressure response for different anesthetic drugs

	CBF	CMR	ICP
Dexmedetomidine	↓	→ or ↓	→
Barbiturates	↓↓	↓↓	↓↓
Etomidate	↓↓	↓↓	↓↓
Propofol	↓↓	↓↓	↓↓
Benzodiazepines	↓	↓	↓
Opioids	→ or ↓ or ↑	→ or ↓	→ or ↑
Ketamine	↑↑	↑ or →	↑ or ↑↑
N2O	↑↑	↑ or →	↑↑
Xenon	↓(gray) ↑(white)	↓	↑ or →
Isoflurane	↑ or →	↓↓	→ or ↑ or ↑
Sevoflurane	↓ or → or ↑	↓ or ↓ ↓	→ or ↑ or ↑
Desflurane	↓ or ↑	↓↓	↑ or →

↑: slight increase; ↑ increase; ↑↑ marked increase; → no change
↓: slight decrease; ↓decrease; ↓↓ marked decrease
Adapted from Cottrell and Young's Neuroanesthesia 5th Ed, Mosby

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Another goal of anesthetic drugs used during brain and spine surgery is the allowance of neurophysiological monitoring – electroencephalogram and evoked potentials. Volatile agents provoke abnormal and dissociated EEG waveform morphology and frequency and decrease amplitude and prolong latency of somatosensory evoked potentials (SSEP) in a dose-dependent manner. Propofol anesthesia will achieve a better preservation of evoked responses and produce a dose-dependent EEG burst suppression. Other intravenous anesthetic agents such as ketamine may increase gamma-beta wave activity on EEG and enhance SSEPs, whereas dexmedetomidine produces an EEG most similar to normal sleep.

Neuroinflammation and ischemic damage may occur during and after brain and spine surgery, as well as in cases of traumatic brain injury. The neuroprotective role of many anesthetics has been thoroughly investigated but results are inconclusive. In fact, it is looking more likely that anesthetics themselves may contribute to the presence of neuroinflammation. Very recently, sevoflurane and isoflurane were shown to induce structural changes in brain endothelial cells, increasing blood brain barrier permeability and leading to disturbed neuronal function. For spinal surgery, intravenous anesthesia has been shown to provide smoother emergence, less coughing, and less dramatic hemodynamic responses while maintaining reliable neuromonitoring.

Other intravenous drugs may be added to achieve important clinical endpoints. Esmolol blunts postoperative systemic and cerebral hemodynamic changes after intracranial surgery is associated with better postoperative pain control and is potentially neuroprotective. Ketamine, although classically contraindicated in the neurosurgical patient, might be considered as one important pharmacological option in the management of the neurosurgical patient due to the reduction in neuroinflammation, cognitive impairment, and pain signal modulation.

Parecoxib, a cyclooxygenase-2 inhibitor, also seems to reduce the incidence of postoperative cognitive dysfunction in the elderly, probably through anti-neuroinflammatory pathways, and thus can be included in the postoperative pain management.

Negative Neurologic Effects of Anesthetic Drugs

Assessment of the effects of intravenous and volatile agents in in vitro, animal, and human models of brain injury or anesthetic exposure is required to gain further insight regarding potential roles of intravenous versus inhalational techniques in neurosurgical patients.

Neurotoxicity

Anesthesia has been associated with developmental disturbance with worse long-term neurologic/cognitive outcomes in the young mammalian brain. In the last decade, research has produced contradicting evidence, implicating volatile agents, nitrous oxide, ketamine, and, in a lesser extent, propofol. In children undergoing magnetic resonance imaging during sevoflurane or propofol anesthesia, higher levels of cerebral lactate and glucose were observed in children under sevoflurane anesthesia and a strong association between these metabolites and the occurrence of emergence delirium. Additionally, propofol significantly decreases the severity and incidence of emergence agitation and delirium in pediatric patients. There is still no clarity about the significance of these findings, but they do generate questions about pediatric exposure to volatile agents.

Cognitive Impairment

The effects of the different anesthetic drugs in the aging brain constitute another field for research and collection of evidence for the preference of TIVA in the neurosurgical patient. The brain suffers significant changes with age, and exposure to anesthetic drugs may accelerate a declining cognitive trajectory with a possible link between anesthesia and long-term cognitive decline. The role of the anesthetic technique is currently unknown and uncertain, but there is some evidence which suggests benefits of intravenous propofol-based anesthesia. In patients at high-risk for postoperative cognitive changes who carry the Apolipoprotein E4 allele, there is a strong association between an inhalation-based general anesthesia regimen and postoperative cognitive dysfunction. In patients with preoperative amnestic mild cognitive impairment undergoing spine surgery, sevoflurane anesthesia accelerated the progression of mild cognitive impairment, whereas propofol or epidural anesthesia did not. TIVA with propofol has also been reported to be associated with lower CSF levels of interleukin-6, a known biomarker of neuroinflammation, up to 48 h after surgery, suggesting that the anesthetic technique may affect the neuroinflammatory response.

The latest published evidence shows that patients between 65 and 75 years of age undergoing high-risk esophageal surgery had a better postoperative cognitive performance when receiving propofol-based anesthesia compared to those receiving sevoflurane anesthesia, with lower levels of the neuroinflammatory mediator's TNF-α, IL-6, and S-100β protein in the propofol regimen.

Monitoring Anesthetic Depth

Some anesthesiologists prefer to monitor depth of TIVA using the bispectral index (BIS) or other forms of processed EEG. The current "consciousness monitors" or "depth of anaesthesia monitors" have been designed to reduce the risk of intraoperative awareness based on an index of frontal electroencephalographic activity. After years of inconsistent results, there remains a need for monitors that more closely reflect the electrophysiology of (un)consciousness. Several methodological and technological problems with current consciousness monitors exist and include the following:

A. Current consciousness monitors correlate a clinical state to a numerical index. The index does not give information about the effect of the progressive increase in drug concentration on brain areas that are not involved in the maintenance of consciousness.
B. Generalization of the intra- and inter-patient variability remains poor. The patients lose or recover consciousness in a broad range of values of the consciousness monitors' indices.
C. It is possible that an index varies in an individual patient in spite of using the same anesthetic agent at the same concentration and also independent of the noxious stimulus. The use of neuromuscular relaxants has been shown to interfere on the electromyographic response, which in turn interferes on the value of the consciousness monitor index.
D. The concentration-effect relationship for the index is highly variable. In some cases, the index may decrease its predictive value when anesthetic concentrations increase, while in other cases there is no relevant change in the predictive value in spite of important changes in anesthetic concentration.
E. The behavior of the monitors in the change from "not responding" to "responding" status is variable: some indexes may rapidly change their values, while others may be slower to respond.

Given these limitations, it seems that intravenous anesthesia may be reasonably administered without a processed EEG, which is a philosophy supported by evidence. Numerous studies show that the frequency of awareness is no greater with TIVA-TCI compared to inhaled anesthesia. On the other hand, BIS correlates poorly with the expired gas fraction, is frequently insensitive to significant changes in the expired gas fraction, and is vulnerable to interindividual variability. There are also conditions in which halogenated anesthetic gases generate distorsions in the assessment of the pEEG. For example, sevoflurane induces EEG beta activity at concentrations over 3%. Processed EEGs (BIS, SEDLINE, CSI, NARCOTREND, etc.) only partially represent the hypnotic condition and therefore should be used both in intravenous and inhaled anesthesia in the context of multiparameter analysis, ideally including monitors that display the EEG spectrogram.

Titration and Variability

The variability of anesthetic drug requirements is a known, but poorly systematized fact in clinical practice. For example, the use of MAC50 or EC50 values only correspond to a statistical figure which is useful for a single patient and could result in under- or overdosing of many patients. On the other hand, the MAC95 or EC95 mostly produce overdosing. A preferable approach is to identify the individualized requirements for each patient, therefore overcoming the multiple covariates that impact variability, such as age, BMI, gender, concomitant drug use, baseline neurologic condition, etc., adding objective clinical parameters (i.e., loss of response to call).

The main objectives of titration have historically centered on the risk of intraoperative awareness and awakening, but recently the discussion has migrated to the negative effect of the excess of anesthetic agents, such as postoperative delirium and cognitive alterations occurring at all ages.

Ease of Use of TIVA (TCI) Versus Inhaled Anesthetics for Titration of Loss of Consciousness

TCI (target-controlled infusion) technology is widely used globally, with the exception of the United States. TCI is a software package included with infusion pumps and includes a population pharmacokinetic model for different drugs (propofol, remifentanil, fentanyl, ketamine, etc.) in which the anesthetist can use to introduce a required calculated concentration for a desired effect. The best model of each drug includes the most important co-variable (age, height, weight, BMI, etc.) to describe the model. Each model adjusts the dose using the biometric data from the individual patient, based on drug distribution and/or clearance pharmacokinetics data. The TCI pumps include an algorithm that iterate very frequently to adjust the infusion to maintain the proposed plasma or effect concentration stable. The pump reassumes the target when we change the syringe and calculates the decremental time when we stop the infusion, helping the awake time prediction.

TCI allows the anesthesiologist to titrate using a step-by-step approach, or a flash induction, as required. It includes an effect-site model as a guide when the plasma and effect site are not equilibrated. The pharmacokinetic models included

in the TCI pumps can represent different populations including obese patients, elderly patients, or children, but in every case the anesthetist can adjust the required concentration for the clinical condition. TCI has given the anesthetist the chance to abandon mental calculation to reach and maintain calculated plasma concentration for a clinical endpoint.

TCI has been implemented commercially for propofol and remifentanil. Propofol TCI can be used in two PKPD model: Marsh model for patients between 16 and 65 years. This model uses only the co-variable of weight to describe the pharmacokinetic of the drug. The Schnider model is more adequate to be used in older patients.

The use of alfa-2 agonist like dexmedetomidine has been relatively well established in the TCI context employed in a three-compartment model. Dexmedetomidine TCI has been shown to have several beneficial effects, including reduced anesthetic requirement, less postoperative pain, and reduced ICU length of stay, mechanical ventilation, and occurrence of delirium helping to reduce the postoperative neuroinflammation.

The ideal titration of an anesthetic drug may be achieved through small increasing steps in plasma concentration (Cp) followed by plateaus that allow the anesthesiologist time to assess the effect produced by the drug. When the patient loses response to command, Cp is kept stable when using TCI, allowing unconsciousness to have been specifically titrated. All of this is only possible using TCI infusors (Fig. 19.1).

TIVA Versus TCI

The TIVA technique based on mental calculation is imprecise. It is based on empirical mental adjustments of speed of administration, using data from regular patients, and does not consider the pharmacokinetic complexity of the process.

Recent pooling of global TCI data has allowed researchers to construct a more comprehensive model that is able to explain the great kinetic variability through the use of multiple covariates. For example, TCI compensates for distributive transfer to deep tissues as well as metabolic clearance by adjustment of flow speed by the software to maintain the Cp proposed by the anesthesiologist. "Manual TIVA" does not consider the hysteresis (or delay) of the temporal course of the effect compared to the plasma drug concentration and also cannot generate tendencies during the titration phase or any other moments in which there is a change in Cp.

Although there has been a debate about the predictive capacity of TCI systems that include models representing effect, predictability is certainly improved by allowing a reasonable amount of time for plasma effect-site equilibrium. The equilibrium time (based in data using BIS index) in children and young adults is approximately 2 min, while in older patients it is approximately 4 min for propofol Probably this data will be readjusted using new EEG markers as alpha band or slow wave saturation time.

Fig. 19.1 Stepwise induction with propofol. When the patient loses consciousness, remifentanil infusion is started and is increased at the moment of skin incision. Anestfusor simulator (www.smb.cl/anestfusor_serie2_st.html). TCI is used for all drugs. The theoretical projection of drop in blood drug concentrations can be observed at the extreme right

The effector site models also allow for the prediction of emergence, thus optimizing surgical planning. The anesthetic technique also requires changing the drug Cp to adjust to the dynamics of surgery. In case a change in Cp is required, it is impossible to mentally calculate the distribution phase the drugs are in at that particular point in time, especially in the case of liposoluble drugs such as propofol. TCI permits changes in Cp targets during surgery without the need to calculate the distribution or elimination condition of the drug, with the possibility of returning to the initial titration target later.

The Titration of Nociception

The control of surgical stress, also known as nociceptive response, is one of the central tasks of anesthesiology distinct from maintenance of unconsciousness. The instruments used to measure this nociceptive response are still under development.

The utility of the hypertensive response or the heart rate response has shown to be insufficient to perform an assessment of surgical stress. When comparing BIS, to the assessment of motor response, or to the drug plasma concentration, the predictability is close to chance, and thus not particularly helpful.

The most flexible drug for adjustments in nociceptive control is remifentanil. It can also be used as a TCI, given that its pharmacokinetic profile is very different in young compared to older patients. Remifentanil is preferentially initiated after titration of propofol effect in TCI. Other opioids with long half-lives, such as sufentanil or fentanyl, may be used in high-dose boluses during surgeries that require postoperative mechanical ventilation, meaning a neurologic evaluation or an awake test will be difficult to achieve. An additional benefit of remifentanil TCI is the synergistic effect when administered with propofol.

BIS monitoring used in combination with TCI systems during anesthesia leads to a significant reduction of applied hypnotics and opioids in spinal surgery. Similar study using TCI systems monitors of auditory evoked potentials of mean latency led to less patient movement and better sedation conditions. TCI systems used in slow induction approach may be particularly useful for inexperienced personnel (e.g., non-anesthetist sedation providers) or in settings where neuromonitoring is not available or not implemented.

The new option of neuromonitoring with spectrogram and frontal oximetry and the fine-tuning titration approach using TCI are showing interesting results reducing the POCD and delirium (Table 19.2).

Table 19.2 Advantages of TCI

(a) Allows the anesthesiologist to perform dynamic and individualized titration
(b) Levels of Cp can be modified in a continuous manner without the need of calculating speed of perfusion
(c) The model used to control the infusion considers the hysteresis (delay) between plasma concentrations (Cp) and the effect-site concentrations (Ce)
(d) Can recover the calculated Cp after changing the infusion syringe
(e) TCI allows performing slow, stepwise titrated inductions, avoiding Cp plasma peaks, which are frequent when using the intermittent bolus manual technique
(f) It decreases the risk of underdosing the patient
(g) The prediction of the effect allows for shortening the transition to extubation and return of consciousness
(h) The titration of the Cps helps to maintain hemodynamic stability and better control anesthetic depth
(i) The Cps calculated by the pharmacokinetic can include multiple population covariates
(j) Aids in the transfer of patients to imaging suites, with the capacity to reinstall the initial Cp target upon return to the operating room

Recommendations for the Use of TIVA Without TCI

(a) Consider use of guiding simulator to correct infusion rates (available simulators: Anestfusor: www.smb.cl/anestfusor_serie2_st.html; TivaTrainer www.eurosiva.org).
(b) Use a pEEG which includes spectrography in the context of multiparametric analysis (pharmacological, biometric, and hemodynamic data, comorbid conditions, and expertise in the "calibration" of the patient during a titrated induction). Idealy including monitors that display raw EEG and the spectrogram with the properties of scaling adjustment of EEG amplitude, speed and power.
(c) Consider the complexity of the PK/PD interaction of the drugs. This is an option to have a rational approach reducing drug consumption, cost, and poor hemodynamic outcomes.

Key Points

- Inhalational and intravenous anesthetic exposure may be associated with neuroinflammation and cognitive impairment but also may have neuroprotective properties in specific clinical situations.
- Currently available intravenous anesthetics have numerous beneficial neurophysiologic properties including decreased cerebral metabolic rate and intracranial pressure
- Inhalational anesthetics may increase cerebral blood flow and intracranial pressure
- "Depth of anesthesia monitors" utilize frontal processed EEG to guide anesthetic dosing but are imprecise measures of anesthetic depth. These monitors may limit anesthetic overdose and delirium, but the common limits used (BIS 40–60) are an arbitrary value not proved to be valid in old, frailty, very young children, etc. Thus, we require monitors that represent better the complex phenomenon of anesthetic unconsciousness.
- Target-controlled infusion technology for intravenous anesthesia and analgesia is widely used and provides the ability for individual titration-based pharmacokinetics, patient-level biometric data, and effect sites.

Suggested Reading

Bilotta F, Stazi E, Zlotnik A, Gruenbaum SE, Rosa G. Neuroprotective effects of intravenous anesthetics: a new critical perspective. Curr Pharm Des. 2014;20(34):5469–75.

Chui J, Mariappan R, Mehta J, Manninen P, Venkatraghavan L. Comparison of propofol and volatile agents for maintenance of anaesthesia during elective craniotomy procedures: systematic review and meta-analysis. Can J Anaesth. 2014;61(4):347–56. https://doi.org/10.1007/s12630-014-0118-9. Epub 2014 Jan 31

Fritz B, Kalarickal PL, Maybrier HR, Muench MR, Dearth D, Chen Y, Escallier K, Avidan MS. Intraoperative electroencephalogram suppression predicts postoperative delirium. Anesth Analg. 2016;1:234–42.

Hannivoort LN, Eleveld DJ, Proost JH, Reyntjens KMEM, Absalom AR, Vereecke HEM, Struys MMRF. Development of an optimized pharmacokinetic model of dexmedetomidine using target-controlled infusion in healthy volunteers. Anesthesiology. 2015;123:357–67.

Hu C, Horstman D, Shafer S. Variability of target-controlled infusion is less than the variability after bolus inyection. Anesthesiology. 2005;102:639–45.

Iannuzzi M, Iannuzzi E, Rossi F, et al. Relationship between bispectral index, electroencephalographic state entropy and effect-site EC for propofol at different clinical endpoints. Br J Anaesth. 2005;94:613–6.

Jevtovic-Todorovic V, Absalom AR, Blomgren K, Brambrink A, Crosby G, Culley DJ, Fiskum G, Giffard RG, Herold KF, Loepke AW, Ma D, Orser BA, Planel E, Slikker W Jr, Soriano SG, Stratmann G, Vutskits L, Xie Z, Hemmings HC Jr. Anaesthetic neurotoxicity and neuroplasticity: an expert group report and statement based on the BJA Salzburg Seminar. Br J Anaesth. 2013;111(2):143–51.

Karwacki Z, Niewiadomski S, Rzaska M, Witkowska M. The effect of bispectral index monitoring on anaesthetic requirements in target-controlled infusion for lumbar microdiscectomy. Anaesthesiol Intensive Ther. 2014;46(102):284–8.

Lin B-F, Huang Y-S, Kuo C-P, Ju D-T, Lu C-H, Cherng C-H, Wu C-T. Comparison of A-line autoregressive index and observer assessment of alertness/sedation scale for monitored anesthesia care with target-controlled infusion of propofol in patients undergoing percutaneous vertebroplasty. J Neurosurg Anesthesiol. 2011;23:6–11.

Qiao Y, Feng H, Zhao T, Yan H, Zhang H, Zhao X. Postoperative cognitive dysfunction after inhalational anaesthesia in elderly patients undergoing major surgery: the influence of anesthetic technique, cerebral injury and systemic inflammation. BMC Anesthesiol. 2015;15:154.

Servin FS. TCI compared with manually controlled infusión of propofol: a multicentre study. Anaesthesia. 1998;53(Suppl, 1):82–6.

Whitlock EL, Villafranca AJ, Lin N, Palanca BJ, Jacobsohn E, Finkel KJ, Zhang L, Burnside BA, Kaiser HA, Evers AS, Avidan MS. Relationship between Bispectral Index values and volatile anesthetic concentrations during the maintenance phase of anesthesia in the B-Unaware trial. Anesthesiology. 2011;115:1209–18.

Absalom AR, Glen JB (Iain), Zwart GJC, Schnider TW, Struys MMRF. Target-controlled infusion. Anesth Analg. 122(1):70–8.

Sepúlveda PO, Tapia LF, Monsalves S. Neural inertia and differences between loss of and recovery from consciousness during total intravenous anaesthesia: a narrative review. Anaesthesia. 2019;74(6):801–9.

Part III

Fundamentals of Adult Neurosurgery/ Neuroanesthesia

Preparing for Anesthesia in Neurosurgical Patients

20

Melissa Brockerville and Pirjo Manninen

Introduction

Preparation for the surgical treatment of patients with neurological disease involves multiple elements related to the patient, the procedure, the anesthetic, and the location where the procedure will be performed. These patients often present with a wide range of pathological processes that may place additional demands on their management. The neurosurgical operating rooms and neuroradiological suites are highly complex as well as technical environments where healthcare professionals from various disciplines interact. Individuals from neurosurgery, anesthesia, nursing, neurophysiology, and radiology each bring unique perspectives, demands, and contributions to the care of the patient. Effective communication among individuals and disciplines is essential to the safe and efficient function of the entire team. Communication failure can lead to catastrophic medical errors. Careful planning is required with respect to the anesthetic techniques, as well as the equipment requirements for anesthesia, surgery, and neurological monitoring. Infectious complications following neurosurgical procedures can significantly impact on patient outcome and require careful adherence to established protocols.

Communication

Communication is essential in the operating room. Prior to the commencement of anesthesia, communication among the anesthesiologist, surgeon, nursing staff, and neurophysiology team must take place to ensure that each understands the medical concerns of the individual patient and the requirements for the specific procedure. Miscommunication has been identified as a major source of medical error leading to significant patient morbidity and mortality. Communication between the neurophysiology team and anesthesiology team is necessary to ensure that the form of anesthesia used allows for appropriate neuromonitoring.

All preoperative checks should include confirmation that informed consent has been obtained for the procedure to be performed, as well as adjunctive investigations and treatments such as medical imaging, invasive monitoring, and possible blood transfusion. The World Health Organization (WHO) aimed to improve surgical safety by developing a checklist entitled the WHO Surgical Safety Checklist. This checklist identifies a simple set of surgical safety standards that can be applied in all countries to provide a framework for safe intraoperative care. This list ensures that key critical safety elements are incorporated to minimize avoidable risks at various stages throughout the procedure – prior to induction of anesthesia, after induction of anesthesia and before surgical incision, and the period during or immediately after wound closure. All hospitals should follow the WHO Surgical Safety Checklist or adopt a hospital specific safety checklist.

Preoperative Assessment

The planning for the anesthetic management and for the prevention of complications related to anesthesia begins with the preoperative assessment of the patient. This includes the review of the concerns of the specific neurological disease as well as other medical comorbidities, the current neurological status of the patient, and presence of any acute symptoms such as those of elevated intracranial pressure (ICP) (nausea, vomiting, headache, seizure, focal neurological symptoms). The preoperative assessment should include an anesthetic directed physical examination. A thorough preoperative assessment of the patient's airway is critical in preparation and in prevention of devastating complications. Patients may present with acute or chronic cervical spine disease or trauma, placing them at increased risk of spinal cord injury with excessive neck motion. Appropriate investigations are

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undertaken with consideration of the patients' medical comorbidities and neurosurgical procedure**.** Depending on the urgency of the procedure, the anesthesiologist should ensure that there are no optimizable factors prior to proceeding with non-emergent surgery. Some neurosurgical procedures are performed on an urgent or emergent basis, thus limiting time for preoperative preparation.

The preoperative assessment should include an explanation of the anesthetic and a discussion of anesthetic risks. A detailed discussion and psychological preparation is especially necessary in surgical procedures requiring patient participation, such as an awake craniotomy with cortical mapping, where lack of preparation may result in failure of the procedure. Patients should be advised to continue most routine medications and especially neurological medications (such as dexamethasone and anti-epileptic agents). However, for some procedures such as insertion of deep brain stimulators or epilepsy surgery, patients may need to hold their regular medications. The anesthesiologist should consult with the surgeon in these specific cases.

Preparation for Anesthesia

The Operating Room

Many neurosurgical procedures are now performed in complex operating rooms that are combined with other modalities of therapy and investigation. These include the magnetic resonance imaging (MRI)-operating room, interventional neuroradiology-operating room, or the placement of a computerized tomography, or MRI scanner in a regular operating room. Advanced planning is absolutely necessary to ensure that the layout of the room allows space for all necessary anesthetic, surgical, and imaging equipment. All the safety aspects must be considered for the imaging, especially when MRI is used with respect to MRI compatible equipment (anesthesia machine, monitors). The protection of all personnel from radiation exposure is required during x-ray and CT imaging.

Positioning

Surgical positions can include supine, prone, semi-sitting, sitting, lateral, and park bench. Each of these positions has their own unique anesthetic considerations, and the anesthesiologist should be familiar with possible complications related to these positions. Some of these positions will require additional positioning tables and adjuncts such as padding, arm boards, and headframes. The anesthesiologist should also consider the final position of the patient for surgery when placing intravenous, arterial, and central lines and monitors. In cases of spinal instability or cervical myelopathy, special table/frames may be used to turn the patient to the prone position. A soft bite block should be used during neurosurgical procedures. In the dependent position, this keeps the mouth in a slightly open position and prevents tongue protrusion and subsequent compression by the teeth. During motor evoked potentials (MEP), the bite block helps to prevent laceration to the tongue during stimulation. Direct pressure on the eyes should be avoided in the prone position to prevent corneal abrasions and central retinal artery occlusion.

Neurosurgical procedures can be long procedures, and patients are at risk for perioperative peripheral nerve injuries. The anesthesiologist should follow the ASA Practice Advisory for the Prevention of Perioperative Peripheral Neuropathies for positioning strategies and protective padding. If possible, the anesthesiologist should ascertain that the patient can comfortably tolerate the operative position prior to induction of anesthesia such as neck extension or flexion.

Monitors

A comprehensive review of standard equipment should be carried out prior to the commencement of anesthesia. A checklist is a useful tool to ensure a proper safety check of the anesthetic machine. Standard monitors required during general anesthesia include electrocardiogram, blood pressure, oximetry, capnography, and an agent-specific anesthetic gas analyzer. Temperature and neuromuscular blockade monitoring are highly recommended. Recommendations for monitoring during sedation vary, but during conscious sedation neurosurgical procedures, such as awake craniotomy, monitoring of respiratory function with end-tidal CO_2 and respiratory rate is critical.

Many other additional monitoring devices may be used during neurosurgical procedures. Invasive monitoring such as intra-arterial lines and central venous catheters can assist hemodynamic monitoring and allow ease of intraoperative blood sampling. Other methods used to monitor volume status are available such as systolic pressure variation, pulse pressure variation, and stroke volume variation; however, their use in clinical practice has not become a standard of care. A precordial Doppler or transesophageal echocardiogram should be considered when there is a risk of venous air embolism. Urinary catheters should also be placed in longer procedures for assessment of fluid balance and monitoring of disorders such as diabetes insipidus. Brain function monitoring (bispectral index, entropy) is used to monitor depth of anesthesia. Specific brain monitors such as jugular venous oximetry, brain tissue oxygen tension, near infrared spectroscopy, and cerebral microdialysis may be used when there are concerns with cerebral oxygenation.

Cardiac arrest carts equipped with defibrillators and drugs for emergency resuscitation must be located nearby and maintained regularly. Some neurosurgical procedures can be associated with massive blood loss. Pressure bags or a rapid transfuser should be readily available. In multilevel spinal surgeries, a blood salvage system may be of assistance.

Anesthesia Considerations

Medications

Anesthetic medications should be prepared and labeled with appropriately colored labels, generic drug names, and concentration. All medications must be positively identified by label checking prior to administration. Potent vasoactive agents are infused through appropriate infusion pumps. Several medications, such as heparin and insulin, are commonly administered using the wrong concentration; therefore, some advocate that these drugs should only be administered after a double check of dose is conducted by another independent provider (nurse or surgeon).

The role of neurological protection by selective use of anesthetic agents is controversial but should be considered in high-risk procedures. Most anesthetic agents, including barbiturates, propofol, sevoflurane, desflurane, and isoflurane, have been shown to offer some element of neuroprotection. The actual technique of the anesthetic, inhalation versus total intravenous anesthesia, and the actual anesthetic agents chosen are probably not of the greatest concern.

Neuromonitoring (somatosensory evoked potentials, MEP, electromyography) may influence the type of anesthetic planned. Total intravenous anesthesia is often used in patients with MEP monitoring, while electromyography recordings also preclude the ongoing use of muscle relaxants. This should be discussed with the surgeon and neurophysiologist prior to the commencement of anesthesia.

Large complex surgeries (spine, vascular lesions) can be associated with significant blood loss. Tranexamic acid has been shown to reduce blood loss and the need for blood transfusion in spine surgery cases, and its use should be considered on a case-by-case basis.

Neurosurgical anesthesia frequently entails caring for a patient with significant comorbidities during long, complex operative procedures. During this time, the responsibility of medication dosing falls to the anesthesiologist. Depending on the patients' medical comorbidities and/or the surgical procedure, medications such as antibiotics, insulin, antifibrinolytics, anti-epileptic agents, and antiparkinson's drugs may need to be re-dosed. Some anti-epileptic and antiparkinson's drugs can only be given orally, and consideration should be given to administration through a naso- or orogastric tube. An alternative parenteral anti-epileptic drug could also be chosen in consultation with a neurologist.

Airway

The anesthesiologist should prepare various airway adjuncts and have skilled assistance readily available to aid whenever there is potential for difficult airway management. Once intubation of the trachea has been confirmed, the endotracheal tube must be definitively secured to prevent the loss of the airway during positioning of the patient. Controversy exists surrounding the optimal approach to airway management in the patient with unstable cervical spine. No single airway management technique has been shown to be superior. The choice will be guided largely by the skill set of the anesthesia provider and available equipment. If the patient has an unstable c-spine, inline stabilization should be performed, but the practitioner must recognize that that this may make airway management more difficult**.** The plans for emergence and extubation or for delay of extubation of the patient's airway at the end of the procedure should also be considered and planned for preoperatively. However, complications such as excessive bleeding during the surgical procedure may also require a change in the original plans.

Hemodynamic and Fluid Goals

Hemodynamic goals during the procedure will depend on the indication for the procedure and the patients' medical comorbidities. Blood pressure targets vary for intraoperative and postoperative management and should be discussed with the surgeon prior to commencing anesthesia. The main goals of fluid management are to maintain normovolemia and avoid hypo-osmolarity. In recent years, there has been a move away from liberal fluid management to goal-directed fluid therapy to improve perioperative morbidity and mortality. This is a method of determining the optimal dose of fluid therapy, inotropes, and/or vasopressors by using an algorithm to optimize cardiac output and oxygen delivery**.**

Temperature

In the majority of cases, the patient's core temperature should be monitored to ensure normothermia. Appropriate warming devices such as heated air blankets and fluid warmers are often necessary to ensure normothermia during prolonged procedures. Hypothermia has been investigated as a means of neuroprotection. An updated Cochrane review published in 2015 found no evidence that induced hypothermia was

associated with a significant reduction in mortality or severe neurological disability in patients undergoing brain surgery. This review also concluded that there was no increased risk of harm.

Concerns and Risks

Errors in Patient Identification and Wrong-Site Surgery

A systematic review published in 2015 stated that current estimates for wrong-site surgery are 1 event per 100,000 procedures. In a national survey of practicing neurosurgeons, 25% admitted to having cut skin on the wrong side of the head at least once in their careers, and 32% admitted to having removed lumbar disk material at the wrong level. The American College of Surgeons released a statement on Ensuring Correct Patient, Correct Site, and Correct Procedure Surgery in 2002 with guidelines to eliminate wrong-site surgery. The surgical team should verify the patient identity and procedure to be performed and confirm consent with the patient or their representative; the surgeon should mark the correct site before the patient is given any medications, and all imaging should be in the operating room. There should be a final verification process of correct site with all members of the surgical team during the surgical safety checklist.

Infection

Surgical site infection is a catastrophic complication of neurosurgery. The National Healthcare Safety Network, a national voluntary reporting system, in 2013 reported an overall incidence of 23.1% in surgical site infections. Of these, 2.4% were related to neurological surgery (craniotomy and ventricular shunt). Risk factors for meningitis following craniotomy include leakage of cerebrospinal fluid, concomitant incision infection, male gender, and longer surgical duration. Additional risk factors for infection in spine surgery include age greater than 60 years, smoking, diabetes, previous surgical infection, BMI greater than 25.5, and alcohol abuse.

The Clinical Practice Guidelines for Antimicrobial Prophylaxis in Surgery in 2013 provided a standardized approach to antibiotic use to prevent surgical site infections. This guideline recommends antibiotic prophylaxis for all craniotomies, cerebrospinal fluid shunting procedures, implantation of intrathecal pumps, and spinal procedures with or without instrumentation. The recommended agent for prophylaxis is intravenous cefazolin (2 g, 3 g for patients weighing ≥120 kg). Alternative agents for patients with B-Lactam allergies include clindamycin (600–900 mg) or vancomycin (15 mg/kg). Vancomycin may also be used in patients with known methicillin-resistant Staph. aureus (MRSA). Administration of cefazolin and clindamycin should be within 60 min prior to surgical incision and vancomycin within 120 min because of the required prolonged infusion time. Cefazolin and clindamycin should be re-dosed at 4 and 6 h, respectively, given their short half-lives in patients with normal renal function. Vancomycin has a half-life of 4–8 h and likely does not need to be re-dosed during most surgical procedures. Re-dosing should also be considered in patients if excessive bleeding occurs. Other preventative measures include strict adherence to aseptic technique and maintenance of intraoperative normothermia.

Difficult Airway Management

In 2011 the ASA closed claims analysis stated that difficult intubation remained a concern, representing 5% of claims reported. In the previous 2005 report, 19% of claims were related to patients in the neurosurgical or spine surgical groups. There are published algorithms for management of the anticipated and unanticipated difficult airway.

Emergence from anesthesia is another critical time, especially in patients following neurosurgical or spine procedures where extubation may lead to airway complications and the need for urgent reintubation. Situations include the development of airway compromise with neck hematoma or edema following cervical spinal surgery. Patients who have been in the prone position or park bench for a prolonged period may also develop airway edema and/or macroglossia. Guidelines are also established for extubation. Reintubation may be extremely difficult in these circumstances; thus all patients at risk for airway edema should be carefully evaluated prior to extubation.

Out of the OR Procedures

Increasing numbers of neurosurgical imaging studies and/or interventions are being performed in locations remote from the standard operating room (MRI, CT, angiography, endovascular therapies). Anesthetic care in these remote locations may include monitoring, conscious sedation, general anesthesia, or ventilator and circulatory support to critically ill patients. Providing safe anesthetic care in remote settings can be challenging. Factors that increase risk include unfamiliar environments, lack of anesthesia equipment and support, and lack of consistency in monitoring devices available. The anesthesiologist may have limited access to the patient during the procedure, or the patient may be in a separate room. However, regardless of the setup, the anesthesiologist should be able to see both the patient and the monitor either by direct observation or on a video camera during the procedure. The

equipment, drugs, and resuscitation cart available in these remote locations should be the same as that available in other anesthetizing locations. All sites should be equipped or have access to a difficult airway cart to allow safe and efficient management of the difficult airway. Patients and all personnel involved in the care of patients in remote radiology locations should be advised about and protected from radiation exposure. Anesthesiologists should be aware of the potential safety hazards (electromagnetic, auditory) and required precautions needed specifically in the MRI scanner.

Key Points

- Effective communication between individuals and all disciplines is essential to the safe and efficient function of the operating room team.
- Miscommunication has been implicated in adverse patient events.
- Operative briefings guided by a surgical safety checklist can improve communication and reduce errors in patient identification and wrong-site surgery.
- Patients must be appropriately prepared based on their neurological and medical concerns.
- Psychological preparation of the patients should include a discussion of the requirements of the intraoperative procedure, postoperative implications, and outcome.
- Adequate preparation of all aspects of the operating room is essential to their efficient and safe function including appropriate resuscitative equipment.
- Neurosurgical patients can present unique challenges to airway management during induction and emergence.
- Important aspects of anesthesia management include positioning, hemodynamic goals, fluids, neuroprotection, and the effects of anesthesia on neuromonitoring.
- Surgical site infection is a serious complication of neurosurgery. Risk factors for postoperative infection vary depending upon the specific neurosurgical procedure.
- The indications and administration of presurgery prophylactic antibiotics should be according to established guidelines.
- Neurosurgical and imaging procedures performed remote from the operating room require additional planning and safety precautions.

Suggested Reading

American College of Surgeons [Internet]. Statement on ensuring correct patient, correct site and procedure surgery. [Updated 2002 Dec 1; cited 2015 Dec 15]. Available from https://www.facs.org/about-acs/statements/41-correct-patient-procedure.

American Society of Anesthesiologists Task Force on Intraoperative Awareness. Practice advisory for intraoperative awareness and brain function monitoring – a report by the American Society of Anesthesiologists task force on intraoperative awareness. Anesthesiology. 2006;104(4):847–64.

American Society of Anesthesiologists Task Force on Prevention of Perioperative Peripheral Neuropathies. Practice advisory for the prevention or perioperative peripheral neuropathies – an updated report by the ASA task force on prevention of perioperative peripheral neuropathies. Anesthesiology. 2011;114(4):741–54.

Apfelbaum JL, Connis RT, Nickinovich DG, Pasternak LR, Arens JF, Caplan RA, Committee on Standards and Practice Parameters, American Society of Anesthesiologists Task Force on Preanesthesia Evaluation, et al. Practice advisory for the preanesthesia evaluation – an updated report by the American Society of Anesthesiologists task force on preanesthesia evaluation. Anesthesiology. 2012;116(3):522–38.

Apfelbaum JL, Hagberg CA, Caplan RA, Blitt RC, Connis RT, Nickinovich DG, American Society of Anesthesiologists Task Force on Management of the Difficult Airway, et al. Practice guidelines for the management of the difficult airway – an updated report by the American Society of Anesthesiologists task force on management of the difficult airway. Anesthesiology. 2013;118(2):251–70.

Benes J, Giglio M, Brienza N, Michard F. The effects of goal directed fluid therapy based on dynamic parameters on post-surgical outcome: a meta-analysis of randomized controlled trials. Crit Care. 2014;18(5):584.

Bratzler DW, Dellinger EP, Olsen KM, Perl TM, Auwaerter PG, Boln MK, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm. 2013;70(3):195–283.

Cavallone LF, Vannucci A. Extubation of the difficult airway and extubation failure. Anesth Analg. 2013;116(2):368–83.

Eichorn V, Henzler D, Murphy MF. Standardizing care and monitoring for anesthesia or procedural sedation delivered outside the operating room. Curr Opin Anaesthesiol. 2010;23(4):494–9.

Guercio JR, Nimjee SM, James ML, McDonagh DL. Anesthesia for interventional neuroradiology. Int Anesthesiol Clin. 2015;53(1):87–106.

Hempel S, Maggard-Gibbons M, Nguyen D, Dawes A, Miake-Lye I, Beroes J, et al. Wrong site surgery, retained surgical items and surgical fires – a systematic review of surgical never events. JAMA Surg. 2015;150(8):796–805.

Jhawar BS, Mitsis D, Duggal N. Wrong-sided and wrong-level neurosurgery: a national survey. J Neurosurg Spine. 2007;7(5):467–72.

Martini RP, Larson DM. Clinical evaluation and airway management for adults with cervical spine instability. Anesthesiol Clin. 2015;33(2):315–27.

Merchant R, Chartrand D, Dain S, Dobson G, Kurrek M, Lagace A, et al. Guidelines to the practice of anesthesia- revised edition 2015. Can J Anesth. 2015;62(1):54–67.

Metzner J, Posner KL, Lam MS, Domino KB. Closed claims' analysis. Best Pract Res Clin Anaesthesiol. 2011;25(2):263–76.

Milani W, Antibas P, Prado G. Cooling for cerebral protection during brain surgery (review). Cochrane Database Syst Rev. 2015:1–53. https://www.ncbi.nlm.nih.gov/pubmed/25626888.

Peterson GN, Domino KB, Caplin RA, Posner KL, Lee LA, Cheney FW. Management of the difficult airway: a closed claims analysis. Anesthesiology. 2005;103(1):33–9.

Popat M, Mitchell V, Dravid R, Patel A, Swampillai C, Higgs A, Difficult Airway Society Extubation Guidelines Group. Difficult airway society guidelines for the management of tracheal extubation. Anaesthesia. 2012;67(3):318–40.

Ripolles-Melchor J, Espinosa A, Martinez-Hurtado E, Abad-Gurumeta A, Casans FR, Fernandez- Perez C, et al. Perioperative goal directed hemodynamic therapy in non-cardiac surgery: a systematic review and meta-analysis. J Clin Anaesthiol. 2016;28:105–15.

Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A, et al. Antimicrobial-resistant pathogens associated infections: summary of data reported to the national healthcare safety network at the centers for disease control and prevention, 2009–2010. Infect Control Hosp Epidemiol. 2013;42(1):1–15.

World Health Organization[Internet]. Safe surgery [cited 2016 Jan 18]. Available from http://www.who.int/patientsafety/safesurgery/en/.

Basics of Neurosurgical Techniques and Procedures

21

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Overview

Neurosurgical procedures are a collaborative effort between surgical, anesthesiology, and nursing teams. Approaches to the cranial vault are generally designed to minimize retraction and manipulation of surrounding neural tissue and to provide the shortest distance possible from the surgeon's hands to the surgical target. Cranial procedures are unique in that the approach vector can take on any number of trajectories. The position of the patient's head is determined by the anatomic location of the lesion and the approach and exposure selected by the neurosurgeon. Similarly, approaches to the spine are dependent on the target of interest and are typically posterior, anterior, lateral, or some combination of the three.

Implications for the Neurosurgical Patient

Cranial Surgery

Cranial procedures are often performed with the patient's head in three-point fixation to minimize movement of the operative field during the procedure. Approaches are fashioned depending upon the goal of the operation and the anatomic area of interest. Superficial lesions are most easily operated upon by placing the lesion near the top of the operative field, e.g., frontal lesions are typically positioned supine, occipital lesions prone, and temporal lesions lateral. Surgery of deeper structures such as the cranial nerves and the arteries of the skull base often require retraction of neural structures to adequately visualize and manipulate the surgical target. To minimize neural retraction, many techniques such as CSF diversion, hyperventilation, and/or mannitol administration are frequently utilized. Head of the bed elevation or reverse Trendelenburg positioning is used to produce optimal drainage of blood from the head through veins and venous sinuses. Careful communication must occur between the surgeon and anesthesiologist to balance the desire to have a dry field and the risk of creating a situation which puts the patient at high risk of having a venous air embolus (i.e., surgical site above the level of the heart).

Transsphenoidal resection of sellar region tumors is performed with the patient in a modified beach chair position. Surgeons require access to the nose or mouth, and thoughtful placement of the endotracheal tubing is required, angled to the side opposite the surgeon. The abdomen is often prepared in case a fat graft is needed for closure in instances of CSF leak. Also, hormone-secreting tumors or large tumors compressing the hypothalamic-pituitary neural axis may induce changes in the neuroendocrine baseline or cause a hypopituitarism event that could have implications for cardiovascular and pulmonary function.

Cautery is primarily used to control bleeding in the surgical field by the induction of thermal damage to incompetent blood vessels. The majority of non-neurosurgical procedures rely on monopolar electrocautery, which creates a current between a handheld electrode and an electrode placed on the patient's skin. This typically creates an arc of electricity between the handheld electrode and the tissue in closest proximity. Because this runs a current through the patient's body, neurosurgeons are hesitant to use monopolar electrocautery in an electrically active organ such as the brain, for fear of inducing cortical arrhythmias and/or seizures. Furthermore, the use of monopolar cautery should be used with caution in patients harboring an electrically active device such as a pacemaker or implanted automatic defibrillator. More commonly, bipolar cautery is used for hemostasis in cortical tissue where the current runs between two poles in the forceps-shaped handpiece, obviating the need to run electrical current through the entire body. Other methods of hemostasis typically involve tamponading the bleeding area

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with a biologic agent (such as methoxycellulose) soaked in thrombin. These methods tend not to work as well when the patient is hypertensive.

In patients undergoing cerebrovascular procedures, intraoperative angiograms are occasionally performed to confirm obliteration of the vascular anomaly. These are typically accomplished using a transfemoral approach with a catheter coupled with a fluoroscope. Intracranial Doppler ultrasonography is also used to confirm patency of parent vessels especially after aneurysm surgery. Intraoperative optical angiography is another method, albeit fairly new, that is used to evaluate the circulation in the surgical field. Injection of a fluorescing agent systemically can be visualized through digital infrared processing via the surgical microscope.

Spinal Surgery

The perioperative risk of spinal procedures varies widely and is correlated to the extent of the procedure. Patients with extensive spinal deformity and scoliosis may have decreased range of motion and decreased chest wall compliance, which has implications for intubation and for ventilation. Spinal procedures are performed with the patient in the supine, prone, or lateral positions. Positioning becomes particularly paramount in cases of prior cervical surgery, critical cervical stenosis, and/or instability. The specific intubation technique should be thoroughly discussed preoperatively, as conscious fiber-optic intubation or use of a portable video laryngoscope can be performed to mitigate the chances of cervical spinal injury. Anterior approaches to the thoracic and lumbar spine may involve a thoracotomy and benefit from the anesthesiologist utilizing a double-lumen endotracheal tube. Transoral approaches to the high cervical spine may require keeping the patient intubated postoperatively because of airway edema.

Spinal procedures may be associated with significant blood loss; this is especially true with large multilevel surgeries with pedicle subtraction osteotomies and arthrodesis for spinal deformity. In cases with high expected blood loss, it is common to use intraoperative blood salvage or autologous blood donation and readminister the patient's lost blood. In patients who lack risk factors, such as coronary artery disease or prior thromboembolic phenomena, intraoperative tranexamic acid infusion can be given to decrease expected blood loss. Typically anterior lumbar surgery requires the surgeon to move the iliac blood vessels away from the surgical site. Unfortunately this exposure procedure may result in tearing the blood vessels (most often the iliac vein) and acute massive blood loss, which the anesthesiologist must be prepared to treat through blood and fluid administration, using large bore intravenous access established prior to surgical incision. In addition, positioning for posterior spine surgery attempts to create a balance of having a dry surgical field (operative area above the level of the heart) by optimizing venous drainage from the surgical site while trying to minimize the risk to the patient of venous air embolus.

Electrophysiological Monitoring

Monitoring is done in certain cases where the intended surgical approach puts certain nervous structures at risk. Spinal or cranial nerve monitoring often involves the use of electromyographic needles placed into the various targets of the nerves and requires a working neuromuscular junction. Neuromuscular blockade, therefore, is contraindicated in this regard. Cortical EEG monitoring electrodes are used in somatosensory evoked potentials (SSEPs) and motor evoked potentials (MEPs) monitoring. Various inhalational and intravenous agents such as propofol can drastically affect the EEG. Again, preoperative communication with the surgical and electrophysiological monitoring team is important in identifying these pitfalls.

Stereotactic and Awake Cranial Procedures

Occasionally, patients are kept awake for a portion of or all of a neurosurgical procedure. Procedures such as deep brain stimulation involve the implantation of an electrode in thalamic or subthalamic structures for the treatment of movement disorders. These procedures are often done awake to facilitate the correct placement of these electrodes and to monitor patient progress during the procedure. For these cases, the patient's head is secured in a frame, and for someone to lie with their head secured for an hour or more, especially someone with a movement disorder, this can be difficult. Carefully titrated anesthesia is required to keep the patient comfortable but awake enough so that they can be adequately assessed neurologically. Careful hemodynamic monitoring and control at the time the electrode is placed are necessary as well.

More extensive awake procedures are performed when a lesion, such as a tumor, involves the eloquent cortex of the brain, usually the speech area or the motor cortex. Some centers utilize a fully awake approach for the entire procedure with a scalp block as the only form of anesthesia. Other centers use an anesthetized-awake-sedated technique. In this latter situation, the patient is usually ventilated via an LMA, which is removed after emergence from anesthesia once the brain is exposed. The patient then answers questions or

performs physical tasks, while the surgeons stimulate the cortex to delineate which areas can be safely removed without causing a neurologic deficit. Once the lesion is removed, the patient is sedated for the remainder of surgery.

Shunt and Generator Implantation

These cases are fairly noninvasive neurosurgically but can still be very stimulating for patients. Placement of CSF shunts from the cranium to the peritoneum involves prepping out the patient from the head to abdomen. The large surface exposure is associated with significant convective heat loss for the patient and makes it difficult for the anesthesia team to maintain the patient's body temperature in a normal physiologic range. ECG leads and other monitoring devices must be kept out of the surgical field and are best placed on the back of the patient. Shunt tubing or lead wires are passed between stab incisions to keep the hardware subcutaneous. This portion of the procedure (tunneling in the subcutaneous tissue) can be very stimulating and induce significant hemodynamic changes in the patient.

Concerns and Risks

Placing the patient in "pins" or three-point fixation is quite stimulating, and adequate analgesia should be in place before the patient's cranium is secured by the surgeon. Preemptive strategies that have been employed to prevent hypertension or patient movement during pin placement include intravenous administration of short-acting anesthetics (e.g., propofol bolus), short-acting narcotic (e.g., alfentanil), or local block (either scalp block or local application of anesthetic at pin sites). Occasionally, the pins can cause a skull fracture or rest on the patient's face. This should be avoided. Once the head is secured, the neck is often flexed or extended to provide optimum access to the surgical target. This can cause the endotracheal tube to move proximally or distally, and care should be taken to ensure that the patient remains adequately ventilated after the head is secured. Additionally, severe flexion can cause cerebral venous outflow obstruction, which can be problematic for both the surgeon and the anesthesiologist. Likewise, severe flexion or extension may rarely result in critical impairment of arterial blood flow to the brain or direct cervical neurologic injury with potentially devastating consequences for the patient. Adequate space between the patient's chin and chest should be ensured prior to proceeding with the operation. For prone cranial procedures, the patient's head is typically placed in fixation when they are supine prior to rolling them into the prone position. This roll provides an opportunity for disaster, as carefully placed tubes and lines can be inadvertently pulled during positioning. When the patient is placed in the prone position for cranial procedures, adequate padding of pressure points must also be performed to prevent the formation of pressure sores and nerve injury.

Intraoperative imaging during neurosurgical cases presents additional challenges for the anesthesia team. Special considerations include a need for non-ferromagnetic materials/instruments and a risk of thermal injury to the patient in intraoperative MRI scans, decreased patient accessibility during to the scanning process, and increased duration of the procedure.

In order for the surgeon to expose a large enough working surgical corridor to lesions deep in the brain, brain relaxation is important. This can be achieved with intravascular osmolytes (e.g., mannitol and hypertonic saline) and temporary hyperventilation. The systemic side effects of these two methods must be kept in mind while trying to maintain adequate brain relaxation. CSF drainage catheters, placed either intracranially (external ventricular drain) or intrathecally (lumbar drain), are occasionally used to control intracranial pressures or assist in brain relaxation. Careful communication between anesthesiologist and surgeon regarding the level of placement of these drainage tubes (i.e., "pop-off" level) and how much fluid should be drained is of paramount importance. Excessive drainage can cause subdural hematomas and, in severe cases, herniation syndrome. When brain relaxation does not provide enough visualization, for instance, during surgery of deeper structures at the base of the skull, metal retractor blades are used to gently retract neural tissue. Excessive retraction can cause occult bleeding beneath the retractor or bleed or place tension on cranial nerves that provide autonomic tone to the vascular tree. During intracranial surgery, changes in the patient's vital signs can be very abrupt and should be communicated to the surgeon.

When the surgical field is located on a higher level than the right atrium, the presence of lesions in venous vessels at the surgical site may lead to a venous air embolism and acute hypotension and hypoxia.

Blood pressure management can be critical, especially during cerebrovascular procedures (aneurysms, carotids, and AVMs). During active bleeding, blood pressure should be kept low. When temporary occlusion of arteries is in place to control bleeding, it is helpful to keep blood pressure up to maintain adequate cerebral perfusion via collaterals to the areas of brain at risk for ischemia. Occasionally, during surgery of the brain stem or during surgery where there are rapid changes in intracranial pressure (decompression during trauma surgery or hydrocephalus surgery), changes in blood pressure and heart rate can be noted secondary to traction or disturbance of the baroreceptor areas in the brainstem. These

are often transient in nature but can be severe enough to temporarily require vasoactive pharmacological support. Effective communication of the anesthesiologist with the surgeon can often facilitate surgical amelioration of the inciting factor (e.g., retraction, stimulation, and manipulation) that is causing the hemodynamic instability.

Spinal procedures often have the patient's arms in nonanatomic positions, and care should be taken to ensure that there is not excessive traction on the brachial plexus. In situations where the patient is prone, care should be taken not to have the arms in an extended position. They should be flexed at the shoulder and elbow to prevent nerve and joint injury. Spinal procedures also often involve the use of a fluoroscopic unit (C-arm) to guide hardware placement. When the unit is moved in or out of the surgical field, the technician or surgeon can inadvertently place the unit on the patient's body. In addition, this movement may inadvertently result in premature removal of an intravascular catheter or disconnection of a physiologic monitoring device. Vigilance is key to prevent complications from excessive pressure and traction from the fluoroscopy unit. Significant blood loss is associated with invasive spinal procedures and should be monitored carefully to optimize perioperative management. For posterior spinal operations, retraction of the paraspinal musculature is used to gain adequate exposure to the bony and neural elements of the spine. Prolonged retraction and prone positioning have been known to occasionally result in rhabdomyolysis or postoperative visual loss.

Key Points

- Positioning the patient for either a cranial or spinal operation requires careful communication with the surgical and nursing teams to minimize perioperative morbidity.
- Preoperative planning with the surgical team regarding the planned use of CSF drainage, the use of neuromuscular blockade, or if the patient will remain awake during the procedure is critical.
- Blood pressure management during cerebrovascular procedures is critical during periods of active hemorrhage and temporary ligation.
- Abrupt changes in vitals can occur with rapid changes in intracranial pressure or manipulation of the brain stem and lower cranial nerves.

Suggested Reading

Fletcher S, Lam A. Anesthesia: preoperative evaluation. In: Winn HR, editor. Youmans neurological surgery. 5th ed. Philadelphia: Elsevier; 2004.

Goodkin R, Mesiwala A. Surgical exposure and positioning. In: Winn HR, editor. Youmans neurological surgery. 5th ed. Philadelphia: Elsevier; 2004.

Jenkins AL III, Deutch H, Patel NP, Post KD. Complication avoidance in neurosurgery. In: Winn HR, editor. Youmans neurological surgery. 5th ed. Philadelphia: Elsevier; 2004.

Positioning the Patient for Neurosurgical Operations

22

Katherine O. Heller, Monica S. Vavilala, and Irene Rozet

Pressure-Related Injuries

Positioning should provide optimization of surgical exposure while minimizing positioning-related risks and complications. The most common complications of patient positioning include pressure sores and peripheral nerve damage (brachial, sacral, lumbar plexus, ulnar, radial, sciatic, and common peroneal nerve injuries). Risk factors for pressure-related injuries are listed in the Table 22.1. Most commonly, pressure ulcers occur at the ischium, trochanter, or heel. Care must be taken to appropriately unload or pad pressure points, especially for high-risk patients. Malpositioning can also cause obstruction of arterial blood flow leading to ischemic injury if not recognized, especially in non-supine positions. Intraoperative neurophysiological monitoring, including motor and somatosensory evoked potentials, can be used in spine and neurosurgery to detect mechanical injury due to change in position.

Table 22.1 Risk factors for pressure-related injuries

Surgical factors	Patient factors
Extended duration of surgery	Pre-existing pressure ulcers
Position other than supine	Extremes of age (neonates/elderly)
	Thin body habitus
	Morbid obesity
	Current smoking
	Poor nutritional status
	Pre-existing peripheral neuropathy

Implications for the Neurosurgical Patients

Neurosurgical procedures are often lengthy (longer than 3 h). Therefore, attention must be paid to patient positioning before surgical draping begins and the patient becomes obscured from view. Proper positioning requires an adequate anesthetic depth (or adequate comfort for the patient having an awake procedure) while maintaining ventilation and hemodynamic stability within the desired physiologic range.

Head Positioning

Patient positioning for craniotomies and cervical spine surgeries begins with positioning of the head. The head can be placed in a horseshoe rest, padded with specially made foam headrests, or placed in a pin fixation device. This determination is made based on the position to be used and surgeon preference. Surgical fixation in pins can provide complete immobility and excellent surgical exposure. However, application of a skeletal fixation device has a profound stimulating effect, leading to tachycardia and hypertension if the patient is not adequately anesthetized. This is especially dangerous in the presence of cerebral aneurysms or increased intracranial pressure as it increases the risk of aneurysm rupture or brain herniation upon pin fixation. Deepening the plane of anesthesia, infiltration at the pin site with local anesthetic, and/or a scalp block are necessary before pinning.

Maintaining hemodynamic stability during pinning requires careful hemodynamic monitoring to ensure safe deepening of anesthesia and to prevent hypertensive responses to pinning while preventing hypotension that may compromise cerebral perfusion pressure. If intraoperative invasive blood pressure monitoring is considered, an arterial

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line should be performed prior to pinning. Risks specific to surgical head pins include bleeding from pin sites, air embolism (especially in sitting position), scalp and eye laceration, and cervical spine injury. Care must be taken to avoid all patient movement while in pins. If the surgical procedure is to be done with the patient awake and in a pinned head holder, adequate local anesthetic at the pin sites (skin and periosteum) and placement of a scalp blocks allow for adequate patient comfort.

Risks of unsafe head positioning, regardless of the device used to position, include a decrease in blood flow in vertebral and carotid arteries, increasing risk of brain stem ischemia and quadriplegia. Hyperflexion may reduce the size of the hypopharynx, causing ischemia to the base of the tongue, leading to pharyngeal and tongue edema. The risk of pharyngeal edema is increased by the presence of foreign bodies, such as a transesophageal echo probe or an oral airway. Maintaining 2–3 fingerbreadths thyromental distance is recommended to prevent excess head flexion. The head can usually be safely rotated between 0 and 45° lateral (left to right) along the sagittal access without placing undue traction on nerve or vascular structures. If more than 45° rotation is needed, a supportive chest roll should be placed under the opposite shoulder.

Impairment of cerebral venous outflow can occur for a variety of reasons, including external pressure on the neck from positioning or ETT fixation devices or a head-down position intraoperatively. Impaired venous outflow can cause intraoperative cerebral edema, resulting in poor operative visualization, increased intracranial pressure, increased surgical bleeding, and cerebral hemorrhage or ischemia. At least 15° head-up position is generally optimal for neurosurgery to encourage adequate venous drainage. Neck vein distention, elevated ICP, and elevated jugular bulb pressures can all be signs of inadequate head or neck positioning.

Body Positioning

The most commonly utilized positions in neurosurgery, their risks, and preventive measures for positioning-related complications are described in Tables 22.2, 22.3, 22.4, 22.5, and 22.6.

Ventilation and Oxygenation

Induction of general anesthesia, positive pressure ventilation, muscle relaxant medications, and changes in position can all negatively affect the ventilation and perfusion relationships in the lung. It has been recently shown that both ventilation and perfusion are heterogeneously distributed

Table 22.2 Supine position

Benefits	Risks	Preventative measures
Optimal approach to frontal lobes and anterior spine	Excessive head rotation, flexion, or extension for surgical exposure impairs cerebral blood flow or venous return leading to cerebral ischemia, cerebral edema, or macroglossia	Avoid head rotation more than 45° in relation to body axis. Elevate head by 15–30°. Zero invasive blood pressure transducer at the level of the circle of Willis
Safest position. Provides best access to airway and invasive lines/monitors	Upper airway edema with anterior cervical spine surgery, especially in surgeries >5 h	Avoid excessive neck retraction and monitor the respiratory status of high-risk patients after longer anterior spine surgeries
Minimal risk for venous air embolism (VAE), pneumocephalus, or postoperative vision loss (POVL)		
Minimal risk of upper airway edema		
Minimal risk for genital or breast injuries		

Table 22.3 Lateral position

Benefits	Risks	Preventative measures
Optimal approach to the temporal lobe	Brachial plexus injury and compression of dependent axillary artery	Place axillary roll under the upper chest and away from axilla under dependent side
Good access to the airway	Common peroneal and saphenous nerve injuries	Avoid excessive traction of shoulders
Minimal risk for head position-related injury	May require ET tube disconnection and reorientation of lines/monitors to position	Verify perfusion to dependent arm with arterial line or palpable pulse
Minimal risk for genital and breast injuries	Worsened V/Q matching compared to supine position during mechanical ventilation, overexpansion upper lung	Place pillows between knees and ankles. No tubing or catheters should be allowed under or between the legs
Minimal risk for VAE and pneumocephalus		Careful, coordinated positioning with assistance from OR staff. Special attention to airway and invasive monitors while moving patient
Minimal risk of visual loss		
Less risk for postoperative upper airway edema compared with sitting and prone		

Table 22.4 Prone position

Benefits	Risks	Preventative measures
Optimal posterior approach to spine and posterior fossa	Logistically difficult. Requires ET tube disconnection and reorientation of lines/monitors to position	Leave pulse oximeter and/or arterial line connected during positioning if at all possible
Less risk for VAE compared to sitting position	Poor or no access to airway. Secretions may weaken ETT fixation	Preoxygenate patient before turning prone
Less risk for pneumocephalus and quadriplegia compared to sitting position	Highest risk for postoperative visual loss (POVL)	Carefully secure and check ET tube placement
Less risk for brain ischemia	Increased risk of upper airway and tongue edema and cranial nerve damage	Use frame that avoids abdominal compression (ideally Jackson frame)
Improved V/Q matching and oxygenation vs. supine, especially if the abdomen is free	Risk of brachial plexus injury	Pad and avoid excess pressure on breasts, genitals, ears, nose, and bony prominences
	Increased risk of pressures sores	Ensure that eyes are protected and that there is no ocular pressure, recheck frequently (q30min)
		Avoid excessive head flexion. Maintain at least 2–3 fingerbreadths of thyromental distance. Avoid foreign bodies in the pharynx (TEE probe, oral airway)
		For patients at high risk of POVL, avoid hypotension, anemia, and prolonged head-down positioning

Table 22.5 Sitting position

Benefits	Risks	Preventative measures
Optimal approach to posterior fossa and posterior cervical spine	Risk of VAE and paradoxical air embolism	Use modified sitting (semi-recumbent) position rather than fully upright to minimize hemodynamic consequences
The best surgical exposure and anatomic orientation	Hemodynamic instability due to decreased venous return	Consider precordial Doppler to TEE for monitoring or VAE
Lowers ICP. Good CSF and venous outflow. Minimal bleeding and reduced risk for cranial nerve damage	Edema of upper airway and tongue (macroglossia)	Consider right atrial catheter for aspiration of VAE if necessary
Easy access to airway	Cranial nerve traction and damage due to significant head flexion	Ensure appropriate head position with at least 2–3 fingerbreadths between chin and chest
Low risk for visual loss	Common peroneal and sciatic nerve damage	Prehydrate with crystalloids or colloids to ensure adequate volume status before positioning
Excellent V/Q matching for improved oxygenation and ventilation (vs. supine)	Impairment of brain perfusion	Partially flex knees. Use buttock gel pad to prevent an excessive pressure on the sciatic nerve
	Highest-risk pneumocephalus and tension pneumocephalus	Zero invasive blood pressure transducer at the level of ear canal (the skull base) rather at the level of atrium to reflect cerebral perfusion. Maintain CPP at 60–80 mmHg
	Increase risk paradoxical embolism if PFO present	Discontinue nitrous oxide before the dural closure
		Consider screening for PFO preoperatively
		Avoid hypocarbia unless concerned for critically elevated ICP, as hypocarbia will decrease cerebral blood flow

and matched throughout the lung and not predominantly dependent on gravity. Under anesthesia and mechanical ventilation, the primary diaphragmatic motion shifts from the dependent to nondependent regions. When supine, and especially when lateral, this causes mismatch of ventilation and perfusion, which can contribute to hypoxia. Sitting position increases the risk of complications such as VAE and postural hypotension but provides the best lung compliance and V/Q matching due to downward displacement of the diaphragm, which should optimize oxygenation and ventilation in the absence of hypotension. Prone positioning can improve V/Q matching since dorsal lung zones, where perfusion is increased, become nondependent and better aerated. This has been shown in ICU patients with ARDS and can be extrapolated to positioning in the OR. However, prone position can also decrease lung compliance if the chest wall and abdomen are restricted by positioning devices. Patients with pre-existing lung disease or injury may have worsening hypoxia with prolonged anesthetics or significant fluid shifts, regardless of position.

Table 22.6 Three quarters position

Benefits	Risks	Preventative measures
Necessary for some posterior fossa and parieto-occipital surgeries	Brachial plexus injury due to both compression of brachial plexus on the dependent side and stretching of nondependent shoulder toward the legs for better surgical exposure	Place axillary roll under the upper chest and away from axilla. Avoid an excessive traction of nondependent shoulder
Lower risk of VAE than sitting position	Other risks similar to lateral position	See lateral position notes

ETT endotracheal tube, *TEE* transesophageal echocardiography, *VAE* venous air embolism, *PEEP* positive end-expiratory pressure, *CPP* cerebral perfusion pressure, *POVL* postoperative vision loss

Postoperative Vision Loss

Although the incidence of perioperative visual loss (POVL) has not been reported higher than 0.2%, and is likely much lower on average, POVL represents one of the most devastating complications of modern spine surgery in prone position. POVL can occur from ischemic optic neuropathy, central retinal artery occlusion, or cortical blindness. The predisposing factors include prolonged duration of surgery, significant blood loss, and intraoperative hypotension. Large retrospective reviews show the highest risk after prone spine surgeries and cardiac surgeries. Preventive intraoperative measures include avoiding any external pressure on eyes and rechecking eyes frequently. For high-risk patients and procedures, avoid low arterial blood pressure (goal within 25% of the patient's baseline level), anemia (no lower threshold for blood transfusion is recommended to date), and prolonged head-down position leading to venous congestion. High-risk patients should be identified, and staging of prolonged surgeries should be considered early. This allows the patient to recover 4–7 days between surgeries, avoiding excessive blood loss and hemodynamic instability. Postoperatively, vision should be assessed when the patient is awake. In case of any concern regarding potential POVL, an urgent ophthalmologic consultation should be obtained.

Key Points

- Deepen anesthesia, and use local anesthetic before application of a device for skeletal fixation of the head recommended to prevent hyperdynamic cardiovascular response.
- Avoid hyperflexion of the head to prevent quadriplegia and airway edema. Maintain a minimum of 2–3 fingerbreadths distance between neck and chin. Avoid lateral head rotation more than 45°.
- Head-up position of 15° is optimal for neurosurgical procedures. Neck vein distention, elevation of ICP, and cerebral edema are signs of inappropriate head and neck positioning and an obstruction of the venous outflow from the brain.
- Properly secure the tracheal tube and respiratory circuit in place before positioning, since access to the patient's airway can be difficult due to positioning or draping.
- Postoperative visual loss is a rare but devastating complication of prone positioning. Eyes should be properly protected and checked every 30 min to avoid any external pressure over the eyeballs. Severe anemia and low blood pressure should be avoided.
- Avoid hypotension in sitting position by preventing and rapidly correcting hypovolemia, wrapping the legs with elastic bandages, and slow, incremental adjustment of table position. Consider the semi-recumbent sitting position to avoid severe hemodynamic changes.
- In sitting position, transduce mean arterial pressure (MAP) corrected to the circle of Willis (interauricular plane) to provide a CPP above 60 mmHg.
- Prevent tension pneumocephalus in sitting position by discontinuing nitrous oxide before dural closure. Clinical signs of postoperative tension pneumocephalus include delayed awakening, new neurological deficit, headache, and signs of increased ICP. Consider immediate head CT for differential diagnosis. Twist drill hole and dural puncture for decompression may be needed.
- Use protective padding whenever possible, particularly for upper extremities. Use axillary rolls in lateral position. Ensure that the abdomen is free in prone position.
- If feasible, monitor somatosensory evoked potentials (SSEPs) for early detection of ischemia due to peripheral nerve damage and reposition, if needed.
- Assess and document patient's neurological condition pre- and postoperatively.

Suggested Reading

American Society of Anesthesiologists Task Force on Prevention of Perioperative Peripheral Neuropathies. Practice advisory for the prevention of perioperative peripheral neuropathies: an updated report by the American Society of Anesthesiologists Task Force on prevention of perioperative peripheral neuropathies. Anesthesiology. 2011;114(4):741–54.

Anastasian ZH, Ramnath B, Komotar RJ, Bruce JN, Sisti MB, Gallo EJ, Emerson RG, Heyer EJ. Evoked potential monitoring identifies possible neurological injury during positioning for craniotomy. Anesth Analg. 2009;109(3):817–21.

Cassorla J, Lee JW. Chapter 41: patient positioning and associated risks. In: Miller RD, editor. Miller's anesthesia. 8th ed. Philadelphia: Elsevier/Saunders; 2015. p. 1240–65.

Dilmen OK, Akcil EF, Tureci E, Tunali Y, Bahar M, Tanriverdi T, Aydin S, Yentur E. Neurosurgery in the sitting position: retrospective analysis of 692 adult and pediatric cases. Turk Neurosurg. 2011;21(4):634–40.

Drummond JC, Patel PM, Lemkuil BP. Chapter 70: anesthesia for neurosurgery. In: Miller RD, editor. Miller's anesthesia. 8th ed. Philadelphia: Elsevier/Saunders; 2015. p. 2158–99.

Fathi AR, Eshtehardi P, Meier B. Patent foramen ovale and neurosurgery in sitting position: a systematic review. Br J Anaesth. 2009;102(5):588–96.

Glenny RW. Determinants of regional ventilation and blood flow in the lung. Intensive Care Med. 2009;35(11):1833–42.

Gracia I, Fabregas N. Craniotomy in sitting position: anesthesiology management. Curr Opin Anaesthesiol. 2014;27(5):474–83.

Kitaba A, Martin DP, Gopalakrishnan S, Tobias JD. Perioperative visual loss after nonocular surgery. J Anesth. 2013;27(6):919–26.

Li A, Swinney C, Veeravagu A, Bhatti I, Ratliff J. Postoperative visual loss following lumbar spine surgery: a review of risk factors by diagnosis. World Neurosurg. 2015;84(6):2010–21.

Orliaguet GA, Hanafi M, Meyer PG, et al. Is the sitting or the prone position best for surgery for posterior fossa tumours in children? Paediatr Anaesth. 2001;11:541–7.

St-Arnaud D, Paquin MJ. Safe positioning for neurosurgical patients. AORN J. 2008;87:1156–68.

Winfree CJ, Kline DG. Intraoperative positioning nerve injuries. Surg Neurol. 2005;63(1):5–18.

The Intraoperative Team: Getting the Most Out of Collaborative Care in the Operating Room

23

Debra A. Reeves

Overview

Identifying and overcoming the barriers to collaboration that are inherent in the operating room environment and having a basic understanding of the perioperative nurse's role in caring for the surgical patient are important in preventing and managing complications in the neurological surgery patient.

This chapter, written from the perspective of a neurological surgery circulating nurse, outlines the data that is gathered and analyzed by the nurse to determine the needs of the patient and plan for their care during the procedure. Risks common to various types of neurological surgery procedures and interventions to prevent or manage possible complications will be included. A list of suggestions for overcoming the barriers to effective collaboration will follow in the "risks and concerns" section.

Teamwork and Collaboration

Effective collaboration in the operating room can be defined as optimization of the care of the patient through mutual understanding and respect of the individualized but interdependent roles of each intraoperative team member, as they work together toward a common goal of accomplishing a safe and successful surgical procedure. Intraoperative collaboration is enhanced when team members have at least a basic understanding of each other's roles and responsibilities with associated tasks and priorities.

There are many barriers to effective collaboration in the operating room. It is a dynamic environment that is frequently noisy and sometimes chaotic. Multiple team members are simultaneously carrying out tasks that relate to their own responsibilities within the overall care of the surgical patient. Through the course of the workday, intraoperative team members change during breaks or at shift ends forcing the team to form and reform multiple times. New team members may or may not have similar levels of knowledge and experience but are expected to maintain a high level of functioning while caring for the patient. Each transfer of care between team members carries with it a risk of communication breakdown.

In addition to a difficult physical environment, a surgical schedule runs with an underlying time pressure. The need for decreased costs, increased efficiency, and rapid turnovers for timely accomplishment of procedures can create a hurried atmosphere. Team functioning suffers when team members feel rushed with a resultant increase in risk of error.

Both the scrubbed person and the circulating nurse have well-defined roles during a surgical procedure. The scrubbed person, who could be either a surgical technologist or a registered nurse (RN), focuses primarily on the surgical field. The scrub surgical tech or nurse is responsible for managing the surgical instruments and implants, handing them to the surgeon as they are needed, and assisting with the surgery when necessary, while maintaining the integrity of the sterile field.

The circulating nurse is an RN who has received an average of 6 months of additional training in surgical nursing. During training, the nurse learns basic information about the procedures most common to each surgical specialty, the risks inherent in all procedures such as infection, blood loss, and inability to maintain normothermia, as well as the additional risks caused by the administration of anesthesia, the effects of prolonged immobility on blood flow and skin integrity, and the risks of nerve damage due to positioning of the patient to optimize surgical exposure. The surgical nurse is trained with the holistic view that they function as the patient's primary advocate during a time when they are unable to speak for themselves. The circulating nurse is also responsible for managing the equipment used within the surgical suite and must know how to operate and where to place items such as pneumatic drills, electrocautery units, lasers,

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microscopes, and positioning devices. Nurses who specialize in neurological surgery have received additional training specific to neurological surgery procedures and additional considerations for the patient undergoing neurological surgery.

Implications for the Neurological Surgery Patient

Earlier chapters have discussed preparation for surgery, the basics of surgical techniques, and patient positioning. Specific communication challenges during the perioperative period will be covered in a later chapter.

The following section provides information detailing how the circulating nurse prepares and executes a plan of care for a neurological surgery patient in a sequential format.

- Review the planned procedure:
  - Review scheduling form information, and clarify with surgeon if inconsistencies are found.
  - Determine equipment, instruments, implants, and supplies that will be required.
  - Determine the availability, including ETA if not currently available.
  - Configure the equipment and positioning devices in the room as necessary for operative exposure, equipment function, and sterile field maintenance.
  - Determine the normal risks for the patient due to the type of procedure:
    (a) Hypothermia, DVT, infection: all surgeries
    (b) Skin breakdown: procedure scheduled longer than 4 h
    (c) Massive blood loss; including aneurysm/AVM, intracranial bleed, tumor in cavernous sinus
    (d) Air embolus: sitting craniotomy
- Determine additional risks for the individual patient:
  - Review the patient's H&P, current labs, and allergies.
  - Interview the patient and conduct preoperative assessment including:
    (a) Confirmation that the patient understands what procedure is planned
    (b) Confirmation of allergies and previous surgeries, e.g., joint replacements
    (c) Discussion of other pertinent history, current pain level, and any emotional or spiritual needs
  - Assess for increased risk of skin breakdown using sensory perception, moisture, activity/mobility, nutrition, and friction and shear as well as age criteria (e.g., Braden Scale score).
  - Assess for increased risk of infection including history of MRSA, VRE, trauma, diabetes, and current infection.
  - Assess for increased risk of DVT including positive history and suspended anticoagulant therapy.
  - Assess for increased risk of blood loss including tumor located near major vascular structures, highly vascular tumor, and suboptimal lab values.
- Review patient and procedural data with the anesthesia provider:
  - Need for awake or fiber-optic intubation; unstable C-spine, limited neck mobility.
  - Need for additional invasive lines; arterial line, central line, large bore IV.
  - Discuss any need for deviation from standard preoperative antibiotic.
  - Discuss probability of need for blood products and confirm availability if necessary.
  - Discuss level of readiness and ongoing communication during the procedure.
  - Plan for any known high risks.
- Initiate plan of care from time into the OR through emergence from anesthetic:
  - Accompany the patient to the operating room or receive the patient in the room.
  - Provide warm blanket, apply DVT prevention, and offer emotional support.
  - Assist the anesthesia provider during intubation.
  - Place Foley catheter (if indicated), perform initial count with scrubbed person, and deliver indicated medications to the sterile field.
  - Assist with positioning of the patient for the procedure:
    (a) Cushion pressure points, bony prominences, and vulnerable nerves with gel devices.
    (b) Place support devices such as chest rolls, Mayfield headrest, pillows, overhead arm support boards, etc.
    (c) Place additional devices as needed for patient safety or operative exposure such as warming blanket, safety belt, tape, traction devices, etc.
  - Assist with surgical skin prep and draping of patient for the procedure.
  - Initiate or participate in a pre-procedure pause (or time-out) which includes confirmation of surgical site and procedure description and also involves the surgeon, anesthesia provider, and scrubbed RN or tech. Document according to organization policy.
  - Connect electrical devices, and move equipment into final position at commencement of procedure.
  - Assess room for safe and functional placement of electrical cords, equipment, etc., and adjust as needed.
  - Pre-check blood products with anesthesia provider if there is high probability of need.

  - Call OR charge nurse for assistance if patient experiences airway emergency, code, massive blood loss, or other serious unexpected event.
  - Communicate all necessary information to team members at every patient hand-off during the procedure and when calling report to PACU using a consistent format.

Risks and Concerns

In the absence of effective collaboration, the risk of preventable error during surgery increases. An ineffective team is less likely to identify and collaboratively address unforeseen complications. Historically, the operating room has been a hierarchical and sometimes personality-driven environment. Although current surgical culture has begun to shift away from old attitudes and beliefs, creating high functioning intraoperative teams on a daily basis will continue to be challenging.

Improving the communication among team members is the key to implementing the solutions listed below. Ideally, all intraoperative team members would contribute equally to the effort, but any team member can make a difference. Good communication should be professional, respectful, accurate, comprehensive, timely, and specific without personal emotional content or bias, and always with the goal of exchanging the information needed to provide safe care for the patient.

Some common barriers to collaboration and suggestions for overcoming them:

- The perioperative environment
  - *Noise*: Reduce distracting environmental sounds at key times, and ask for quiet when crucial information is being exchanged.
  - *Chaos*: Coordinate activities with other team members to help avoid distraction when critical tasks are performed.
  - *Time pressure*: Organize tasks, delegate appropriately, and communicate changes in patient condition or procedure plan as they occur. Safety should never be compromised for the sake of time.
- The intraoperative team
  - *Teamwork*: Understand individual roles of surgical team members, resolve interpersonal issues as they arise, and encourage team members to voice questions and concerns.
  - *Team member changes*: Communicate to assess knowledge/experience levels, share relevant information, and encourage questions, comments, and concerns.

Key Points

Intraoperative Team Collaboration

- *Anticipate*: Review the procedure and possible complications specific to the procedure and to the patient.
- *Communicate*: Exchange information with all team members. Confirm any procedural or patient variables.
- *Plan*: Determine the needs for care of the patient, e.g., lines, equipment, instruments, implants, and availability of each. Plan coordination of activities and discuss concerns.
- *Respond*: Take action early when potential problems are identified, and know and utilize resources to avoid complications.
- *Collaborate effectively*: Encourage clear, thorough, respectful, and frequent communication throughout the procedure utilizing communication tools. Ask for debriefing after adverse outcomes or near misses.

Suggested Reading

Amato-Vealey E, Barba M, et al. Hand-off communication: a requisite for perioperative patient safety. AORN J. 2008;88(5):763–70.

Helmreich R, Schaefer HG. Team performance in the operating room in Bogner, MS. Human error in medicine. Hillsdale: Lawrence Erlbaum; 1994. p. 225–53.

Lefevre F, Woolger J. Surgery in the patient with neurologic disease. Med Clin North Am. 2003;87:257–71.

Lingard L, Espin S, et al. Communication failures in the operating room: an observational classification of recurrent types and effects. Qual Saf Health Care. 2004;13:330–4.

Powel SM, Hill RK. My co-pilot is a nurse-using crew resource management in the OR. AORN J. 2006;83(1):178–202.

Next Level Communication

24

Debra A. Reeves and Haley Sands

Overview

The Serious Nature of Communication Failure

According to the Joint Commission, communication failure is the leading root cause of sentinel events reported between 1995 and 2004. In 2013 the *Journal of Patient Safety* concluded that deaths from medical errors occur at the rate of up to 440,000 per year. That would make preventable death from medical errors the third leading cause of death in the United States. Only heart disease and cancer cause more deaths.

Implications for the Neurosurgical Patient

Communication literature suggests that information transfer in healthcare should be both transactional and transformational, providing an accurate exchange of information from person to person and in turn causing an appropriate change or response. Communication failure can be attributed to the omission of information, miscommunication of information, and the misunderstanding of information, on both the part of the giver and receiver. Greenberg et al. showed that while face-to-face or one-on-one verbal communication may seem to be the most reliable, there were patterns of communication breakdown intraoperatively, 92% of which included verbal communication. Additionally, in 57% of cases, information was never transmitted, and in 35% it was transmitted but not accurately received.

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Healthcare providers have access to more information through more sources than at any other time in history. The electronic age has changed both the way information is acquired and displayed but also the way it is communicated. There are multiple routes of communication of information in the modern operating room.

Verbal information can be formal or informal, face-to-face, or over a transmission device. It can involve structure such as a template, checklist, or algorithm. It will be transmitted at certain agreed upon points of care such as pre-procedure pause and also spontaneously during care as circumstances change.

Electronic communication takes many forms such as individual or group emails and electronic chart notes which may or may not include a template. Information may be transmitted by a "Status Board" mounted in a common area. Equipment alarms provide audible alerts of possible malfunctions or significant vital sign changes. The number of devices that healthcare providers interact with has increased also. The wearable device (e.g., Vocera ™) has joined the cell phone, VOIP, and landline in providing instant voice communication. Cell phone text messaging is even more prevalent than text paging in the current healthcare environment. Paging messages can be initiated individually, transmitted to entire groups of providers, or activated automatically when certain events or types of electronic charting occur.

The human factors in communication failure are numerous and complex. Even when communication is transmitted and received, it may not be understood. Healthcare providers communicate with each other in environments that contain constantly varying amounts of ambient noise and disruption. Multiple members of a team may not share the same native language causing potential for miscommunication. Doctors, nurses, and assistive personnel have overlapping but different medical acronyms, slang, and jargon they use to describe common procedures, practices, or medical conditions. Differences in training and experience among healthcare team members may result in a mismatch of communication

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priorities. Even regional variations in language can contribute to miscommunications between healthcare team members.

An organizational structure that supports hierarchy over collaborative teamwork can create a culture where communication flows easily from the top down but not from the bottom up. Healthcare workers who witness a practitioner make a mistake may feel intimidated to speak up about it or fear reprisal if the practitioner is in a position of power or is perceived to be. Healthcare environments that do not support speaking out when errors are observed may inadvertently protect providers who have poor practice or treat others disrespectfully. A practice setting that includes providers who have difficult personalities or dysfunctional behavior creates an environment that inhibits the free flow of information exchange at the expense of patient safety.

Intervention/Prevention

Strategies for improved communication and information transfer can include standardized, closed-loop, concise, and direct communication. Identifying the most appropriate method in a given situation adds an additional layer of complexity to OR and ICU environments. Eliminating any extraneous filler in a dialogue reduces the risk of ambiguity and can help ensure that the intended message is received accurately. One can start by taking care to use simple terms, avoid unneccessary words and keep language as specific as possible.

At critical times when stakes are high, the use of directed communication can help eliminate the risk that an important message is misinterpreted as a request if the urgency of the situation requires immediate action. Speaking in imperative sentences reduces ambiguity, but the overuse of command-style communication may lead to deterioration of the collaborative work environment and should be reserved for true emergencies.

In many cases negative communications carry with them as many risks as lack of communication. In their study, Erez et al. found that a rude comment from a third-party doctor decreased the performance of doctors and nurses by more than 50% during a simulation exercise involving a hypothetical life-or-death situation. Communications in the operating room or the ICU often happen during urgent situations and as a result may be emotionally charged, missing key pieces of information, or otherwise unclear, setting the stage for increased risk of error.

Healthcare organizations have been involved in setting standards and improving the way providers relay information among teams. Verbal orders have been identified as having high potential for error unless confirmed with a "read back" which creates a closed-loop communication. This read back validates that the information transmitted was indeed received accurately. Many electronic health records (EHR) will even prompt the user at the time of entry to confirm that an order was taken verbally with read back.

The use and value of closed-loop communication is not limited to orders but is also an appropriate technique for transferring important or sensitive information such as lab test results, equipment settings, confirming pathology specimen information, and plan of care changes.

With the current shift toward a value-based care model, it becomes more important to increase efficiency and reduce waste, even in communication. This can be done through information standardization which allows for a guaranteed work product that can be re-created and maintained over time. A checklist, for example, can help support a successful completion of tasks or the transfer of a specialized list of information while building a safety structure to prevent essential information from being omitted at critical points of care. Redley et al. found that individual variability in team communication leads to ambiguity regarding plan of care for patients, inconsistent exchange of information, delays in care, and duplication of work.

Time that is saved using communication structures to transmit information in categories common to every patient can be used to focus on information that is unique to a particular patient and vital to providing safe and personalized care. This type of standardization allows all providers to create a consistent communication product and to expect information in a specific manner or location. In order for structured communication tools to be useful in purpose over time, they should be tested periodically and adapted when necessary.

Many programs for communication improvement and standardization available to healthcare organizations have been adapted from other industries. While some (e.g., crew resource management borrowed from the aeronautical industry) combine teamwork and communication training, some emphasize communication alone or may dovetail with other process improvement work such as Toyota Lean Principles which include Kaizen events to drive change or Carnegie's Change Management Principles. Most team and communication training includes structural frameworks that standardize and formalize communication at key points of care such as pre-procedural pauses and hand-off of care. More important for success than the specific framework being used is the organizational commitment to staff training and the individual level of staff engagement in the process.

Summary

The Joint Commission has taken the need for effective communication very seriously in their "Guide to Improving Staff Communication." This manual charges healthcare leaders with recognizing the importance of accurate communication in high-quality patient care, as well as emphasizing their responsibility in managing that information. The Joint Commission Guide highlights the need for constant improvement in the communication of information throughout an

entire organization. As a result, many organizations are actively working toward a stated "culture of safety" through process improvement which emphasizes the important role of clear and accurate communication at all levels.

Effective communication plays a crucial part in safe patient care. It enables an accurate transfer of information, avoids ambiguity, and encourages collaborative care without undermining trust within interdisciplinary relationships. Identifying when to employ one of the above communication strategies can be challenging; however, these basic tools and frameworks can be used to support even the most novice user in order to reduce the risk to patients.

Key Points

- Communication failure is a central factor in medical errors that cause serious injury and death (sentinel events).
- Lack of communication, miscommunication, and rude communication all contribute to communication failure.
- The large volume of patient and procedure information that must be managed daily comes from multiple sources, may be relayed with varying degrees of accuracy, and is transmitted using multiple types of devices. The resulting complexity contributes to communication fatigue and subsequent risk of error.
- A strong personal commitment to improving communication skills as well as full engagement in available organizational training in communication or teamwork can decrease medical errors.

Suggested Reading

Crosby K, Croskerry P. Profiles in patient safety: authority gradients in medical error. Acad Emerg Med. 2004;11:1341–5.

Erez A, et al. The impact of rudeness on medical team performance: a randomized trial. Pediatrics. 2015;136:487–95.

Greenberg C, et al. Patterns of communication breakdowns resulting in injury to surgical patients. J Am Coll Surg. 2007;204:533–40.

Janus J. A new evidence based estimate of patient harms associated with hospital care. Patient Saf. 2013;9:122–8.

Joint Commission on Accreditation of Healthcare Organizations. The joint commission guide to improving staff communication. Oakbrook Terrace: Joint Commission Resources; 2005.

Lencioni PM. The five dysfunctions of a team: a leadership fable, vol. 13: Wiley; 2002.

Manojlovich M, et al. Hiding in plain sight: communication theory in implementation science. Implement Sci. 2015;10(1):58.

O'Daniel M, Rosenstein A. Professional communication and team collaboration. In: Hughes RG, editor. Patient safety and quality: an evidence-based handbook for nurses. Rockville: Agency for Healthcare Research and Quality (US); 2008; Chapter 33.

Patterson K, et al. Crucial conversations: tools for talking when stakes are high. New York: McGraw-Hill; 2002.

Redley B, et al. Interprofessional communication supporting clinical handover in emergency departments: an observation study. Australas Emerg Nurs J. 2017;20(3):122–30.

Stone D, et al. Difficult conversations: how to discuss what matters most. New York: Penguin Books; 2010.

Part IV

Critical Situations During Anesthesia for Brain Surgery in Adults

The "Tight Brain": Cerebral Herniation Syndrome

25

Leslie C. Jameson, Paul D. Mongan, Daniel J. Janik, and Tod B. Sloan

Overview

ICP is the sum of the partial pressures exerted by the intracranial (IC) contents in proportion to their relative normal volume contribution: brain tissue (80%), cerebrospinal fluid (CSF) (8–12%), and venous and arterial blood volume (6–8% and 2–4%, respectively). Normal ICP is less than 15 mmHg with intracranial hypertension (ICH) defined as pressures above 20 mmHg. ICH is categorized as mild (20–29 mmHg), moderate (30–40 mmHg), or severe (>40 mmHg). As in all closed containers, pressure increases as volume expands beyond the ability of other components to contract. Normal physiologic events that briefly increase ICP have little consequence; prolonged pathologic increases can produce brain injury. The severity of the injury depends on rate of ICP increase, duration of increase, and pressure reached. Slow increases in ICP caused by gradual volume increases (e.g., tumor and hydrocephalus) often require little immediate therapeutic action, while rapid increases caused by brain injury and some metabolic derangements (e.g., hepatic coma, hyponatremia, and severe hyperglycemia) require urgent intervention. During craniotomy, treatment is needed to reduce brain swelling to facilitate surgery and occasionally closure of the dura mater. Table 25.1 summarizes common causes of ICP increase.

Table 25.1 Causes of intracranial pressure increase

	Pathologic causes	
Physiologic causes	Acute	Chronic
Increased abdominal/thoracic pressure (Valsalva, cough)	Intraparenchymal hemorrhage (hemorrhagic stroke, aneurysm rupture, postoperative intracranial hemorrhage)	Slow-growing lesion (brain tumor-primary, metastatic, abscess)
Physiologic hypoventilation (sleep, obstructive sleep apnea)	Traumatic hemorrhage (epidural hematoma, acute subdural hematoma)	Disturbance in CSF absorption, production or flow (hydrocephalus, idiopathic intracranial hypertension)
Drug effect (general anesthetics, sedation)	Acute cerebral edema (acute hyponatremia, hepatic coma, Reye's syndrome, cerebral contusion or traumatic brain injury (TBI), severe hypertension)	Chronic subdural hematoma
Increased metabolic demands (seizures, fever)		Congenital anomalies (Arnold-Chiari malformation, stenosis of aqueduct of Sylvii)
Hypervolemia (fluid overload, head down position)		
Hypoperfusion vasodilation (anemia, ischemia, drugs)		

Prevention

ICP management by anesthesiologists and critical care physicians is mitigation of the progression of an existing process; this requires aggressive physiological and pharmacologic therapy until, in many cases, surgical intervention (e.g., tumor excision, shunt placement, and decompressive craniectomy) can occur.

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Crisis Management

Pathophysiology and Clinical Presentation

The most common cause of increased ICP is expansion of the extracellular and intracellular components of the brain parenchyma. Their relative volume is normally maintained by an effective blood–brain barrier (BBB); endothelial tight junctions in blood vessels allow only ions and small molecules (e.g., Na^+, K^+, and glucose) to transport between the extracellular and the intravascular space (Chap. 3). Extracellular edema, usually found along axons, occurs when there is excess fluid permeability and consequently transfer across the BBB. Edema can be caused by increased active fluid leakage (vasogenic edema, angiogenesis factors from brain tumors), passive fluid transfer from reduced osmotic pressure, elevated venous pressure, and elevated CSF pressure. Therapeutic actions that reduce extracellular fluid transfer include increasing serum osmotic pressure, decreasing venous pressure, and reducing CSF pressure. Intracellular edema (particularly in neurons) is usually due to failure of the ion pumps that maintain the cell membrane's integrity leading to swelling and eventually cell death (Chaps. 9 and 18).

The CSF volume is regulated by the balance of active production, passive filtration, and active transport of the noncellular components of blood at the choroid plexus and CSF absorption by the arachnoid villi in dural sinusoids. Obstruction of CSF flow through drainage channels and increases in cerebral venous pressure expand the CSF volume (Chap. 1).

Expansion of intracranial blood volume also increases ICP. Any situation that restricts venous outflow such as head down position, partial obstruction of jugular veins (e.g., excessive neck rotation), and increased central venous pressure (e.g., increased intrathoracic pressure, Valsalva) will increase intracranial venous blood volume and ICP. Arterial volume contributes to elevated ICP when physiologic or drug-induced vasodilation occurs. Increased cerebral metabolic rate (CMR) increases cerebral blood flow and may increase ICP. Direct vasodilators such as nitroprusside or nitroglycerine increase vascular volume and ICP. Pharmacological and physiological changes that reduce arterial volume will lower ICP. These actions are most effective in normal brain since autoregulation in damaged brain is often lost and flow becomes passively associated with cerebral blood pressure.

The clinical presentation of the "tight brain" depends to some degree on the speed of ICP increase. When non-CSF volume expansion is slow, a reduction of 80 cc in flexible intracranial volume (CSF, interstitial fluid, blood) can occur before elevation in ICP begins. With rapid expansion, the ability of the brain to reduce flexible brain volume compartments is reduced, so ICP increases occur more quickly. The relationship between the volume increase and the resulting ICP increase is termed elastance (change in pressure per unit change in volume).

Symptoms of mild ICH are intractable headache that worsens with lying flat, breath holding, or Valsalva (Table 25.2). With moderate ICH, symptoms progress to nausea, vomiting, dizziness, blurred vision, difficulty concentrating, memory lapses, and occasionally abnormal respiratory patterns. The patient may have a characteristic fundoscopic exam or systemic hypertension due to the brain's autoregulatory attempt to maintain cerebral perfusion pressure (CPP) (CPP = mean arterial blood pressure – ICP). Papilledema is a nonspecific sign in all patients but particularly in patients with traumatic brain injury (TBI). Only 3.5% of TBI patients *with* elevated ICP have papilledema. With moderate elevations in ICP, neurologic signs depend on the primary etiology (e.g., hematoma, TBI, subarachnoid hemorrhage (SAH)) and not ICP.

When volume expansion exceeds the brain's ability to compensate, shifting of intracranial tissues into other compartments or herniation will occur. This may force tissue across tentorial structures (falx cerebri, tentorium cerebelli, and foramen magnum) and often results in permanent neurologic disability or death. Symptoms of herniation include obtundation, posturing, third and sixth cranial nerve palsy (third CN, pupil dilation, impaired light reflex; both, disconjugate gaze), Cushing's reflex (severe systemic hypertension, bradycardia, increased ICP), spontaneous hyperventilation, abnormal respiratory pattern (irregular to apnea), and ultimately hypotension then death (Table 25.2). Decerebrate posture (rigid extension of arms, legs, arching of the back and downward pointing toes) can occur with any brainstem injury but is often seen with central transtentorial herniation from high ICP.

Table 25.2 Signs and symptoms of increased ICP

Mild elevation (20–29 mmHg)	Moderate elevation (30–40 mmHg)	Severe elevation (>40 mmHg)
Unrelenting positional headache	Confusion and agitation	Progressive decreased consciousness
Nausea and vomiting	Drowsiness progressing to lethargy	Anisocoria (asymmetric pupils)
Papilledema	Decreased papillary response (constriction, dilation), sluggish	Tonic eye deviation
Blurred vision	Seizures	Seizures
Loss of retinal venous pulsations	Spontaneous hyperventilation	Decerebrate posturing
	Focal motor weakness	Cushing's reflex
		Abnormal respiratory pattern
		Hypotension
		Death

Patient Assessment

While signs and symptoms can be suggestive of increased ICP, a more definitive diagnosis requires screening with computed tomography (CT) and possible placement of an intraventricular catheter for ICP monitoring. Today the speed, resolution, and point-of-care availability of CT have made it the standard imaging technique for suspected neurologic injury (e.g., TBI, basilar skull fracture, intracranial hemorrhage, cerebral edema). CT images can be correlated with ICP elevation. While the presence of normal basal cisterns on CT does not rule out elevated ICP, abnormal basal cisterns are associated with a threefold increased risk of increased ICP; 75% of patients with absent cisterns have an ICP above 30 mmHg. Magnetic resonance imaging (MRI) may be more useful in evaluating selected pathologies (e.g., tumor) but not ICP. Changes seen on MRI or CT are characteristic for elevated ICP and include loss of ventricles, decreased CSF around basal cisterns, midline shift, herniation, edema, and loss of definition of brain structures. Another noninvasive technique for screening is transcranial Doppler (TCD). While it has some operator-related reliability problems, the ICP value predicted by the pulsatile index was within 4 mmHg of the invasive ICP measurement, making it a promising technique. Near-infrared spectroscopy, optic nerve size, and cochlear fluid pressure remain experimental. An intraventricular catheter is the accepted standard and most invasive continuous measure of ICP.

Measurement of ICP is recommended when there is a suspicion of ICH. Table 25.3 combines Glasgow Coma Scale (GCS) (Chap. 10), a directed neurologic exam, patient characteristics, and CT findings to recognize patients where the benefits of ICP monitoring outweigh the significant risks. CT findings alone cannot predict risk for developing ICH. About 60% of TBI patients who have an abnormal CT will have ICH. Only 4% of patients with a normal CT and no risk factors will develop increased ICP; 60% of patients with a *normal* CT *and* two risk factors will develop ICH. Patients who require prolonged general anesthetics or other therapies that prevent adequate neurologic assessments require an ICP monitor. During preoperative assessment, patients who meet the criteria for ICP monitoring should be assumed to have ICH.

Table 25.3 Indications for ICP monitoring

GCS <8 after resuscitation
Abnormal head CT with the evidence of brain edema/mass lesion effect
Rapid neurologic deterioration plus clinical signs of increased ICP
GCS >8 but unable to follow serial neurologic examination due to
Drugs, anesthesia, prolonged non-neurologic surgery
Prolonged ventilation or use of PEEP (e.g., ARDS)
Post-neurosurgery for the removal of intracranial hematoma
Normal CT scan plus 2 of the following
Age older than 40 years
Decerebrate or decorticate posturing
Systolic blood pressure less than 90 mmHg

Invasive ICP monitoring device is placed in the lateral ventricle to achieve the best quality pressure tracing and measure IC elastance by calculating ICP changes with vascular pulsations and draining CSF to reduce ICP. When the lateral ventricle is compressed, CSF drainage becomes difficult, and accurate pressure measurement is lost. Changes in the waveform allow recognition of impending critical ICP elevations (Fig. 25.1). Plateau waves which are sudden and rapid ICP elevation to >40 mmHg for 5–20 min followed by an abrupt ICP decrease are caused by the loss of the brain's ability to autoregulate perfusion. The cascade of events is active vasodilation → increased CBV → ICH → decreased CPP. Finally, active vasoconstriction reverses these events. Plateau waves portend severe refractory ICH. Appearance of B waves, defined as spontaneous slow waves (0.5–2 Hz) with an amplitude of about 20 mmHg, acts as a warning sign of decreased intracranial elastance.

The subdural/epidural "bolt" monitor is a saline-filled hollow screw placed through the skull into the subdural/epidural space. It has less risk of brain injury with placement than the intraventricular catheter but is considered less reliable. It becomes ineffective when occluded by the brain or other material and will not allow CSF removal. When surgery is performed, an intraparenchymal fiberoptic catheter can be placed to monitor ICP when ventriculostomy catheters cannot be inserted. These also cannot be used to drain CSF, and calibration may drift over time.

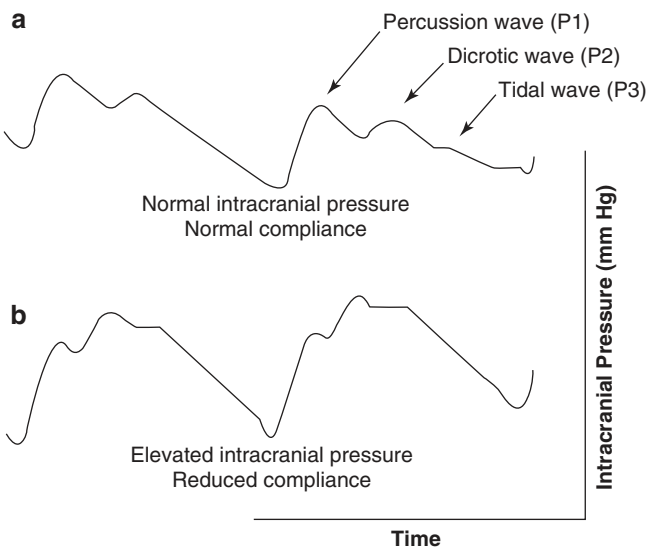

Fig. 25.1 Intracranial pressure waveform in normal (**a**) and abnormal (**b**) pressure volume states. (Modified from Chestnut and Marshal (1991))

Intervention/Treatment

Prevention or treatment of existing ICH or herniation depends on directed management to reduce intracranial volumes. During craniotomy, the management goal is apparent with bulging brain or difficulty accessing the surgical lesion. In the ICU, therapy goals are to maintain ICP <20–25 mmHg while maintaining CPP >60 mmHg. Table 25.4 shows management techniques to reduce specific intracranial component volumes. A chronic mild elevation may require little change in medical management or anesthetic technique during surgery. Acute management of a patient with clinical signs of severe ICH involves the administration of a hyperosmotic solution (mannitol or hypertonic [e.g., 3%] saline), furosemide, intubation, a brief period of hyperventilation, elevation of the head (if blood pressure allows), and sedation if agitated.

Normal responses to physiologic change should be assumed only in normal brain (Chap. 1). Mean arterial blood pressure (BP) should be maintained between 60 and 80 mmHg (or higher if needed to maintain CPP; measured at the acoustic meatus). Hyperventilation, the most rapid method available to reduce intracranial blood volume, acts via vasoconstriction due to the production of a respiratory alkalosis; however, renal compensation and adaptation of the CSF pH correct the alkalosis and eliminate the effectiveness over an 8 h period making it a temporary measure only until other methods to correct the ICP are instituted. Adequate oxygenation must be assured. A CT to guide therapy such as surgical intervention, placement of an intraventricular catheter, excision of a hemorrhagic lesion, or continued medical management is needed. Patients with known space occupying lesions or hemorrhage often proceed immediately to the operating room once a diagnosis is made (Chaps. 9, 27, 30, and 34).

If the patient is to undergo surgery, anesthetic management of the "tight brain" (Table 25.4) requires meticulous continuation of previous medical interventions including:

1. Patient positioning: Maintain head elevation, prevent increases in central venous pressure or jugular venous obstruction.
2. Ventilation: The use of minimum peak airway pressure, avoidance of positive end-expiratory pressure, maintenance of previous $PaCO_2$, avoidance of hypoxemia.
3. Fluids: The use of modest fluid administration of normotonic saline, hyperosmotic solutions.

All of these strategies are important in minimizing further injury. Close attention to ICP or brain swelling can guide therapy. Choosing anesthetic medications that are unlikely to increase in ICP is crucial. Generally it is acceptable to administer volatile anesthetics below 0.75 MAC. Volatile anesthetics increase CBF and ICP. Opioids produce minimal change as long as blood pressure and ventilation are maintained. Intravenous anesthetic sedative agents, with the exception of ketamine, reduce CMR and subsequently arterial volume, thereby reducing ICP. A propofol-based total intravenous anesthetic (TIVA) is often advocated when moderate to severe ICH is present, when herniation is imminent, or where treatment of an intraoperative tight brain is required. A decompressive craniectomy (removal of cranium and possible brain resection) will decompress brain volume. Avoiding hypotension and maintaining BP to support an adequate CPP reduces the risk of hypoperfusion injury to marginally perfused cells.

Table 25.4 The effect of common medical and surgical actions on ICP

Action	Effect on brain	ICP response
Physiologic		
↓ $PaCO_2$ 25–30 mmHg (<8 h)	Arterial vasoconstriction	↓
↓ $PaCO_2$ 25–30 mmHg (>8 h)	None	↔↑
↓ PaO_2 (<50 mmHg)	↑ CBF/volume	↑
↑ BP	Arterial vasoconstriction	↔↓
↓ BP	Arterial vasodilatation	↑
↑ CVP	Venodilatation	↑
Jugular venous obstruction	↑ Venous volume	↑
Head elevation	↓ Venous volume	↓
Agitation/seizures	↑ CMR/arterial volume	↑
Drugs to reduce parenchyma volume		
Mannitol	↓ Interstitial fluid	↓
Hypertonic saline (3%)	↓ Interstitial fluid	↓
Furosemide	↓ CSF production, cellular edema	↓
Dexamethasone – TBI	No effect – TBI	↔
Tumor intraoperative	↓ Interstitial fluid	↓
Drugs used for anesthesia or sedation effects		
Volatile anesthetics (>0.75 MAC)	↑ Arterial/venous volume	↑
Nitrous oxide	↑↔ CMR	↔↑
Intravenous anesthetics		
Propofol	↓ CBF/CMR	↓
Barbiturate	↓ CBF/CMR	↓
Dexmedetomidine	↓ CBF	↓
Ketamine	↑ CBF, ↑ CMR	↑↔
Narcotics	↓ CBF/CMR	↔
Benzodiazepines	↓ CBF	↓↔
Muscle relaxants		
Nondepolarizing	None	↔
Succinylcholine	↑ CVP	↑ (Brief)
Cardiovascular drugs		
Vasodilators	↑ Vascular volume	↑
Vasoconstrictors	↔↓ Vascular volume	↔↓
Surgical interventions		
Intraventricular catheter	Removal of CSF	↓
Remove space occupying lesion (tumor, hematoma)	Removal parenchymal tissue	↓
Decompressive craniectomy	Removal parenchymal tissue	↓

CBF cerebral blood flow, *CMR* cerebral metabolic rate, *BP* mean blood pressure, *CVP* central venous pressure

Key Points

- Normal intracranial components are CSF (10–12%), blood (8–10%), and parenchyma (80%).
- "Tight brain" is an excess intracranial volume causing an increase in ICP.
- The clinical presentation ICH depends on the speed of ICP increase.
- Brain herniation is the shifting of brain tissue across tentorial structures (falx cerebri, tentorium cerebelli, and foramen magnum).
- Increases in cerebral venous and mean intrathoracic pressure increase ICP.
- CT is recommended methodology to assess pathology causing elevated ICP.
- An ICP monitor should be placed in patients with an abnormal CT scan or a normal CT scan and two additional risk factors (over 40 years, posturing, hypotension, or unable to follow a neurologic exam).
- Acute management of ICH includes mannitol/hypertonic saline (3%), furosemide, brief hyperventilation, head elevation, and neutral head position.
- Therapies that increase CMR, jugular venous pressure, vasodilation, and increased airway pressures should be avoided.
- Use of anesthetic drugs which reduce CMR and vasoconstriction are desirable.

Suggested Reading

Artru AA. Cerebrospinal fluid. In: Cottrell J, Smith D, editors. Cottrell and Young's neuroanesthesia. Philadelphia: Mosby; 2010. p. 60–74.

Brain Trauma Foundation, American Association of Neurological Surgeons, et al. Guidelines for the management of severe traumatic brain injury. J Neurotrauma. 2007;24(Suppl 1):S1–106.

Chesnut RM, Petroni G, Rondina C. Intracranial-pressure monitoring in traumatic brain injury. N Engl J Med. 2013;368(18):1751Y1752. https://doi.org/10.1056/NEJMc1301076.

Chestnut RM, Marshal LF. Management of head injury. Treatment of abnormal intracranial pressure. Neurosurg Clin N Am. 1991;2(2):267–84.

Freeman WD. Management of intracranial pressure. Continuum (Minneap Minn). 2015;21(5):1299–323.

Kristiansson H, Nissborg E, Bartek J Jr, Andresen M. Measuring elevated intracranial pressure through noninvasive methods: a review of the literature. J Neurosurg Anesthesiol. 2013;25(4):372–85.

Li M, Chen T, Chen SD, et al. Comparison of equimolar doses of mannitol and hypertonic saline for the treatment of elevated intracranial pressure after traumatic brain injury: a systematic review and meta-analysis. Medicine. 2015;94(17):e736.

Wijayatilake DS, Shepherd SJ, Sherren PB. Updates in the management of intracranial pressure in traumatic brain injury. Curr Opin Anaesthesiol. 2012;25(5):540–7.

Cerebral Ischemia: Options for Perioperative Neuroprotection

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Martin Soehle

Brain or cerebral ischemia is defined as any critical reduction in cerebral blood flow (CBF) that affects the entire brain (global cerebral ischemia) or parts of it (regional or focal cerebral ischemia). As a consequence, the supply of oxygen (and nutrients) to the brain decreases since the arterial supply of oxygen (D_aO_2) is directly related to cerebral blood flow (CBF):

$$D_aO_2\left[\text{ml}\,O_2/\text{min}\right] = C_aO_2\left[\text{ml}\,O_2/\text{ml}\right] \times \text{CBF}\left[\text{ml}/\text{min}\right]$$

where C_aO_2 refers to the content of oxygen in the arterial blood ($C_aO_2 \approx 0.2$ ml O_2/ml blood).

Under resting conditions in an unanesthetized patient, global CBF is approximately 750 ml/min (50 ml/100 g/min) and is unevenly distributed between the gray matter (CBF ≈ 90 ml/100 g/min) and white matter (CBF ≈ 20 ml/100 g/min). The supply of oxygen to the brain ($D_aO_2 \approx 150$ ml O_2/min ≈ 10 ml O_2/100 g/min) exceeds its demand (cerebral metabolic rate of oxygen $CMRO_2 \approx 50$ ml O_2/min ≈ 3.3 ml O_2/100 g/min) by a factor of three under normal conditions. However during brain ischemia, CBF is critically reduced (CBF <250 ml/min ≈ 18 ml/100 g/min) which means that the deterioration of oxygen and glucose supply no longer meets the brain's demand. As a consequence, neuron (and glial cell) function ceases as indicated by an isoelectric electroencephalogram (EEG) (CBF ~16 ml/100 g/min) or lapsed evoked potentials (CBF ~12 ml/100 g/min). A further reduction in CBF (<90 ml/min ≈ 6 ml/100 g/min) will cause irreversible damage resulting in cell necrosis and brain infarction.

Common causes of cerebral ischemia in the context of craniotomy are related to arterial hypotension, occlusion of cerebral vessels – as intended (e.g., during temporary clipping) or not (to control intraoperative bleeding) – or excessive retraction of the brain. Some of those may be affected by the anesthesiologist, whereas others are not. The following text is focused on the former.

Brain Ischemia Due to Arterial Hypotension

Overview

The incidence of intraoperative cerebral ischemic events which are caused by arterial hypotension is unknown. Although short episodes of arterial hypotension occur frequently, it is hypothesized that they seldom lead to cerebral ischemia as long as those events are short and treated immediately.

In the healthy adult brain with its preserved cerebral autoregulation, CBF will not be affected by changes in arterial blood pressure (ABP), at least in the ABP range between 50 and 150 mmHg. However every drop in ABP below the lower autoregulation threshold (mean ABP ~ 50 mmHg) may result in a deterioration of CBF with the risk of cerebral ischemia. It must be noted that the lower threshold is shifted toward higher values in patients with a history of arterial hypertension.

In the diseased brain, cerebral autoregulation is frequently impaired to an extent which is usually unknown in a given patient unless it has been tested by means of transcranial Doppler (TCD) or intracranial pressure-related reactivity (PRx) studies. Moreover, many anesthetics – especially volatile anesthetics – impair autoregulation in a dose-dependent manner.

In clinical practice one should anticipate that every episode of arterial hypotension poses the risk of brain ischemia. Hence any drop in mean ABP below 60 mmHg (or ~70 mmHg in suspected intracranial hypertension) should be recognized and treated immediately. The two main reasons for arterial hypotension are an excessive depth of anesthesia and hypovolemia due to intraoperative blood loss (Table 26.1).

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Table 26.1 Overview of brain ischemia, its etiology, prevention, and management

Extent of cerebral ischemia	Etiology of cerebral ischemia	Prevention of cerebral ischemia	Management of cerebral ischemia
Global	Arterial hypotension due to	Place arterial line for continuous ABP recording	Maintain cerebral autoregulation: avoid more than 1 MAC of volatile anesthetics
	Inadequate anesthetic depth	Use short-acting anesthetics	Decrease anesthetic depth
			Give phenylephrine (50–100 μg boli) meanwhile
	Hypovolemia caused by intraoperative bleeding	Expect sudden and profound blood loss at any time	Apply neither vasopressors nor catecholamines
			Replace volume with crystalloids and/or colloids
			Transfuse packed red blood cells if hemoglobin conc. drops below 6–10 g/dl
Focal/regional	Vessel occlusion	Record EEG to monitor burst suppression or isoelectric EEG	Reduce brain metabolism:
			Increase anesthetic depth (use propofol, thiopental, or volatile anesthetics)
			Induce hypothermia (not recommended)
			Maintain homeostasis (*target*)
			Avoid hypoxia (*paO2 > 70 mmHg*)
			Avoid arterial hypotension (*MABP > 60 mmHg*)
			Avoid hyperglycemia *(glucose < 150 mg/dl)*
			Maintain normocapnia *(35 < p_aCO_2 < 40 mmHg)*

Prevention

- Place an arterial catheter into the radial artery (preferred location; alternatives: brachial, dorsalis pedis, or femoral artery) for continuous ABP monitoring to enable an immediate diagnosis of arterial hypotension.
- Choose anesthetics that allow the anesthesia provider to rapidly adapt the depth of anesthesia to the changing intensity of surgical stimuli, for instance, prefer drugs with short elimination half times. Be prepared for a substantial blood loss by having adequate venous access and readily available fluid and blood for replacement.
- Preserve cerebral autoregulation by avoiding high doses of volatile anesthetics (keep dose <1 MAC)

Crisis Management

Whereas the diagnosis of arterial hypotension is easily obtained based on the actual ABP readings, there is no common agreement below which ABP threshold is to be treated: With respect to the lower limit of cerebral autoregulation (MABP ~50 mmHg) and some safety margin, an ABP threshold for treatment of 60 mmHg seems reasonable. A higher threshold (70–80 mmHg) should be considered in patients with suspected intracranial hypertension or a history of arterial hypertension. Arterial hypotension is treated by removing its cause.

Treatment of Excessive Anesthetic Depth

Depth of anesthesia is usually increased prior to painful stimuli such as endotracheal intubation, placement of the Mayfield head-holder, skin incision, and craniotomy. Arterial hypotension typically occurs thereafter as soon as the stimulus decreases. It is treated by reducing the depth of anesthesia which may take some time depending on the pharmacokinetic and dynamic properties of the anesthetics used. During this period of adjusting anesthetic depth, it is justified to use vasopressors, for example, phenylephrine bolus of 50–100 μg. However the use of vasopressor must not replace the adaptation of the anesthetic depth.

Treatment of Hypovolemia

An average craniotomy is associated with a blood loss of approximately 300–500 ml since skin and subgaleal tissues are well perfused. In adults, this is usually not associated with hypovolemic shock and the blood loss can easily be replaced by fluid therapy. As in other fields of anesthesia, there is no consensus (and no clear evidence) with respect to the type of fluids (crystalloids versus colloids) recommended which is best for volume resuscitation. Profound bleeding may occur without prior warning at any time during craniotomy. In particular, craniotomy in the vicinity of the dural sinus and preparation of cerebral vessels (for instance, during surgery for aneurysms or arteriovenous malformations but as well for tumor resection) are associated with a high risk of sudden and profound bleeding causing arterial hypotension and cerebral ischemia. Ongoing or significant sudden blood loss should not be treated solely by vasopressors or catecholamines which could disguise the extent of hypovolemia and cause lactic acidosis because of diminished splanchnic perfusion. Instead, hypovolemia is treated by volume

replacement. A fast and consistent volume therapy is presumably more important than the type of fluid used for correction of the volume deficit. Eventually, transfusion of packed red blood cells may be indicated to maintain a sufficient oxygen content in the arterial blood in order to assure tissue oxygenation. Depending on patient age and comorbidity, transfusion of packed red blood cells is indicated at hemoglobin concentrations ranging between 6 (young patient without comorbidity) and 10 g/dl (elder patient with coronary heart disease), although there is no agreement within neuroanesthesiologists with respect to transfusion triggers. Fresh-frozen plasma or thrombocyte concentrates should be given whenever coagulation factor activity drops below 50% or thrombocyte count below 50.000/µl, respectively.

Key Points

- Appreciate that every drop in arterial blood pressure might be associated with cerebral ischemia. Therefore, treat arterial hypotension immediately and consistently.
- In adult patients maintain mean ABP of at least 60 mmHg during craniotomy. Higher values (MABP >70 mmHg) should be achieved in patients with intracranial hypertension or a history of arterial hypertension.
- Treat arterial hypotension causally: Decrease depth of anesthesia in case of a diminishing surgical stimulus, and replace volume in case of intraoperative bleeding.
- Vasopressors or catecholamines may be used during the short period of time until depth of anesthesia has been adapted to the actual surgical stimulus or while the initial period of volume resuscitation. However, do not use vasopressors and catecholamines as the sole treatment in case of blood loss since this would disguise the extent of hypovolemia.
- Expect profound bleeding at any time during surgery but especially during craniotomy, preparation of cerebral vessels, and tumor resection.

Brain Ischemia Due to Cerebral Vessel Occlusion

Overview

During surgery, cerebral vessels might be occluded intentionally (e.g., during temporary clipping in aneurysm surgery) to control intraoperative bleeding. Even in the process of otherwise uneventful cerebrovascular reconstruction – such as clipping, coiling, or glueing – perforant arteries or parent vessels might be occluded unintentionally. As a consequence, immediate (focal or regional) ischemia occurs in the brain tissue supplied by the occluded vessel. Since the cause of ischemia (i.e., the vessel occlusion) can neither be affected nor reversed by the anesthesiologist, the therapy aims at making the brain less vulnerable to ischemia and to prevent further (secondary) ischemic events.

Cerebral ischemia leads to an undersupply of the brain with respect to oxygen and nutrients. Theoretically this would be attenuated if the brain's demand could be lowered by means of reducing its metabolism. Mechanisms to diminish brain metabolism include general anesthesia and hypothermia. An alternate experimental approach strives for reducing the brain's susceptibility to ischemia by a mechanism termed "ischemic pre-/postconditioning." This is explained in more detail below.

As already mentioned, a reduction of CBF below the ischemic threshold of 250 ml/min (≈ 18 ml/100 g/min) does not result in an immediate neuronal and glial death. Rather, their function is shut down as can be seen by an isoelectric EEG and lapsed evoked potentials, whereas their structural integrity remains intact. Only if CBF drops further (below 90 ml/min ≈ 6 ml/100 g/min) will neurons and glial cells become necrotic and brain infarction will occur.

Prevention

- Apply *intraoperative neuromonitoring* such as somatosensory-evoked potential monitoring, EEG, jugular bulb oxygen saturation monitoring, near-infrared spectroscopy, or cerebral microdialysis for early detection and monitoring of cerebral ischemia.

Crisis Management

Cerebral ischemia happens unrecognized unless it is detected by neuromonitoring. However it is frequently suspected by the neurosurgeon when occluding a cerebral vessel. Nevertheless ischemia is often not detected until postoperative neurologic examination or imaging reveals signs of cerebral infarction.

The anesthesiologist should consider to reduce brain metabolism in case of suspected or confirmed focal cerebral ischemia, as presented below.

Hypothermia reduces brain metabolism such that every degree Celsius by which body temperature is decreased results in a metabolism reduction of approximately 7%. Hence, hypothermia of 33 °C – as used in the majority of

studies – would diminish brain metabolism by roughly one quarter. However, this effect is much less pronounced (possibly even halved) in both the diseased and the anesthetized brain. Nevertheless, two randomized trials published in 2002 reported that mild hypothermia (32–34 °C) improved favorable neurologic outcome (number needed to treat of 4–13) after an out-of-hospital cardiac arrest as compared to standard treatment. More recently, a large randomized trial showed similar neurologic outcomes in patients treated with targeted temperature at either 33 or 36 °C. As a consequence, guidelines have been modified to target a constant temperature between *32 and 36 °C* for at least 24 h after cardiac arrest. Since fever is associated with poor neurologic outcome, an effective prevention of fever by means of targeted temperature management might be more important than the choice between a target temperature of either 33 or 36 °C. While hypothermia has yielded encouraging effects in *global* cerebral ischemia, reducing brain and body temperature has no or even harmful consequences in *focal* cerebral ischemia: For instance, prophylactic intraoperative mild hypothermia (33 °C) during aneurysm clipping following subarachnoid hemorrhage failed to improve neurologic outcome but was associated with an increased rate of infections according to the IHAST study. Therefore, mild hypothermia is not indicated as a prophylactic measure during aneurysm surgery but may be considered in selected cases as an *ultima ratio* therapy following vessel occlusion. Moderate (30 °C) or deep hypothermia cannot be recommended due to its high complication rate in terms of cardiac arrhythmias, cardiovascular instability, coagulation impairment, and severe infections.

The majority of anesthetics (among others propofol, etomidate, barbiturates, benzodiazepines, and volatile anesthetics) reduce brain metabolism in a dose-dependent manner and to a similar extent as hypothermia: For instance, 1 MAC of isoflurane halves the brain metabolism which is equivalent to hypothermia of 30 °C.

Historically, barbiturates were first observed to suppress the brain's activity as indicated by burst suppression or even an isoelectric EEG. They are without effect in global ischemia, however reduce the neurologic injury in animal models of focal ischemia. Barbiturates were once considered as a gold standard of neuroprotection; however the optimal dosing has never been determined and hence no uniform recommendation exists. A dose of 5 mg thiopental/kg body weight seems to be effective to elicit a burst suppression EEG and to decrease CBF by approximately 45% for a period of approximately 10 min. However, thiopental is associated with cardiovascular depression, profound immunosuppression, and prolonged awakening, especially when given repeatedly in high doses. Hence the neuroprotective effect of thiopental due to the reduction in metabolism may be neutralized by the adverse effect of arterial hypotension. Nowadays, the neuroprotective effect of barbiturates is considered as modest and as overestimated in the past. It is not recommended as a routine measure but may be considered as an ultima ratio option in selected cases.

The ability of propofol to reduce ischemic injury in animal models has been found similar to that achieved with barbiturates but is associated with less cardiovascular depression. An interindividual variable dosage of approximately 15–18 mg/kg body weight/h of propofol is required to achieve an isoelectric EEG. Etomidate reduces cerebral metabolism as well but has been shown to increase infarct volume and to cause adrenal insufficiency. Therefore, etomidate is not recommended to reduce brain injury.

Volatile anesthetics contain neuroprotective properties regardless of the agent used. However, the high concentrations of volatile anesthetics required for an isoelectric EEG will reduce ABP and impede both cerebral autoregulation and metabolic coupling. In contrast, the intravenous anesthetic propofol maintains autoregulation and coupling even at higher doses, which makes it the preferred drug to maximally reduce brain metabolism.

Intraoperative monitoring of EEG is a valuable technique to confirm that the actual chosen dosage of anesthetic is sufficient to suppress the brain's function. Here, therapy should aim for an isoelectric EEG, which is associated with more cerebral protection than burst suppression. For convenience, a bifrontal EEG montage should be used, which might be difficult in some cases of frontal craniotomies. As induction of an isoelectric EEG by anesthetics is associated with more or less pronounced arterial hypotension (depending on the kind of anesthetic chosen), application of vasopressors such as phenylephrine or norepinephrine is usually required to maintain a sufficient cerebral perfusion. To avoid overdosage, the anesthetic dose should be titrated just enough to elicit an isoelectric EEG.

So far, the neuroprotective effect of anesthetics seems to be effective in short and mild to moderate cases of brain ischemia. However anesthetics seem to be ineffective in severe and prolonged ischemia, independent if global or focal in extent. Moreover, their neuroprotective effect seems to be transient and disappears when investigating the long-term outcome. In general, most evidence regarding the neuroprotective effects of anesthetics has been obtained from experimental animal studies, whereas little is known about their neuroprotective effects in humans. Hence, clinical anesthesia should focus on maintaining homeostasis especially with respect to normoxia (p_aO_2 > 70 mmHg), mean ABP

(>60 mmHg), serum *glucose* levels (<150 mg/dl), and normocapnia ($35 < p_aCO_2 < 40$ mmHg) since hypoxia, hypotension, hyperglycemia, and hypo- as well as hypercapnia have been shown to aggravate cerebral ischemia.

Hypocapnia ($p_aCO_2 < 30$ mmHg) as induced by hyperventilation causes vasoconstriction and may reduce CBF below the ischemic threshold. Here, the decrease in CBF is proportional to that in p_aCO_2; hence hyperventilation from a p_aCO_2 of 40 to 30 mmHg lowers CBF by one quarter. On the other hand, hypercapnia ($p_aCO_2 > 40$ mmHg) produces cerebral hyperemia due to vasodilatation, which increases intracranial pressure which in turn reduces CBF.

Induced or permissive arterial hypertension may theoretically increase collateral CBF during temporary vessel occlusion, at least in case of an impaired cerebral autoregulation. However according to the 2012 AHA guidelines for the management of SAH, there is insufficient data on induced hypertension during vessel occlusion to make specific recommendations.

Key Points

- Therapy of focal ischemia caused by vessel occlusion aims at reducing the brain's metabolism and thus making the brain less susceptible to ischemia. This may be achieved by hypothermia and anesthetics.
- Routine application of mild intraoperative hypothermia (~33 °C) does not improve outcome in aneurysm surgery following subarachnoid hemorrhage.
- Induced arterial hypertension may be considered reasonable to augment collateral CBF during temporary vessel occlusion, but there are insufficient data to make specific recommendations.
- The neuroprotective effects of barbiturates have been overestimated in the past. Propofol and volatile anesthetics cause a similar reduction in brain metabolism.
- Anesthetics provide a sustained neuroprotection only under circumstances of mild or modest ischemia however not in severe ischemia.
- Homeostasis should be maintained during the entire course of anesthesia. Especially hypoxia, arterial hypotension, hyperglycemia, and hypo- and hypercapnia have been shown to aggravate cerebral ischemia.

Neuroprotection by Means of Pre- and Postconditioning

A modern yet experimental approach aims at reducing the brain's susceptibility to ischemia by a mechanism termed "cerebral preconditioning." This is based on the observation that a short period of (sublethal) cerebral ischemia results in a decreased vulnerability of the brain to subsequent prolonged (and potentially lethal) ischemia. Moreover, not only previous ischemia, but certain drugs seem to elicit this preconditioning effect. Among these are quite different pharmacological substances such as volatile anesthetics (isoflurane and sevoflurane), antibiotics (erythromycin), hematological factors (erythropoietin), and succinate dehydrogenase inhibitors (3-nitropropionic acid). However, the preconditioning potency, the optimal dosage, and time point of application remain to be determined for these drugs.

After temporary ischemia, cerebral reperfusion takes place which is often characterized by an initial period of hyperemia. Just recently, it has been reported that repetitive interruptions of this reperfusion by short periods of (sublethal) ischemia reduce the injury as caused by the initial prolonged and potentially lethal ischemia. This mechanism has been termed ischemic postconditioning analogous to the previous mentioned preconditioning. Again, postconditioning might be elicited not only by ischemia itself but by pharmacological substances (such as isoflurane) as well. Both pre- and postconditioning offer fascinating perspectives for neuroprotection; however it is unknown so far whether its effects are of clinical relevance and whether they will find their way into clinical medicine.

References

Brain Metabolism

Fitch W. Brain metabolism. In: Cottrell JE, Smith DS, editors. Anesthesia and neurosurgery. 4th ed. St. Louis: Mosby; 2000. p. 1–16.

Hypothermia

Holzer M, Bernard SA, Hachimi-Idrissi S, Roine RO, Sterz F, Müllner M. Hypothermia for neuroprotection after cardiac arrest: systemic review and individual patient data meta-analysis. Crit Care Med. 2005;33:414–8.

Nielsen N, Wetterslev J, Cronberg T et al. for the TTM Trial Investigators. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med. 2013;369:2197–206.
Todd MM, Hindman BJ, Clarke WR, Torner JC. Mild intraoperative hypothermia during surgery for intracranial aneurysm. N Engl J Med. 2005;352:135–45.

Neuroprotection by Anesthetics

Head BP, Patel P. Anesthetics and brain protection. Curr Opin Anaesthesiol. 2007;20:395–9.
Koerner IP, Brambrink AM. Brain protection by anesthetic agents. Curr Opin Anaesthesiol. 2006;19:481–6.

Pre-/Postconditioning

Kitano H, Kirsch JR, Hurn PD, Murphy SJ. Inhalational anesthetics as neuroprotectants or chemical preconditiong agents in ischemic brain. J Cereb Blood Flow Metab. 2007;27:1108–28.
Pignataro G, Meller R, Inoue K, Ordonez AN, Ashley MD, Xiong Z, Simon RP. In vivo and in vitro characterization of a novel neuroprotective strategy for stroke: ischemic postconditioning. J Cereb Blood Flow Metab. 2008;28:232–41.

Massive Hemorrhage During Craniotomy: Emergency Management

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Elizabeth Dryland and Audrée A. Bendo

Overview

The brain is a highly vascular organ, receiving approximately 20% of cardiac output at rest. Thus, rapid exsanguination can result from uncontrolled hemorrhage during a craniotomy. The reported morbidity and mortality from hemorrhage is very high, varying between 5–27% and 0–4%, respectively, in one series, and approximately 8% and 1%, respectively, in another. Therefore, the anesthesiologist must prepare for potential massive intraoperative hemorrhage during craniotomy by anticipating significant blood loss and developing and implementing a massive transfusion protocol. Intraoperative hemorrhage is more likely to occur during surgical procedures that involve the intracranial vasculature, such as clipping of aneurysms and resection of arteriovenous malformations (AVMs).

Aneurysms

The incidence of aneurysm rupture varies with the size and the anatomic location of the aneurysm. In one series, approximately 8% of aneurysm ruptures resulted in frank hemorrhagic shock. In another study, 7% of the ruptures occurred before dissection of the aneurysm, 48% during dissection, and 45% during clip application. Hemorrhage can occur during endovascular or surgical resection procedures and is associated with increased perioperative morbidity and mortality.

Arteriovenous Malformations

AVMs present clinically one-tenth as frequently as aneurysms. Cerebral edema or hemorrhage may occur either during endovascular embolization or surgical resection of AVMs. "Normal perfusion pressure breakthrough" (NPPB) is a theory explaining why intraoperative or postoperative cerebral edema/hemorrhage occurs in AVMs. With the abrupt removal of the shunt (i.e., AVM) from the circulation either by embolization or by surgery, the increase in cerebral blood flow (CBF) into previously hypoperfused areas can lead to cerebral edema and hemorrhage at normal perfusion pressure.

Preparation for/Prevention of Intraoperative Hemorrhage During Craniotomy and Endovascular Procedures

The anesthesiologist must be prepared to manipulate the blood pressure and transfuse blood products emergently during a craniotomy and endovascular procedures. In patients at high risk for hemorrhage, *patient preparation* should include the following:

Insertion of:

- Intra-arterial cannula
- Foley catheter for monitoring of urine output
- Two large bore (16- or 14-gauge) peripheral IVs
- Central venous catheter
- Type and cross (four units of packed red blood cells [PRBC], fresh-frozen plasma, and platelets)

To accurately reflect the cerebral perfusion pressure (CPP = mean arterial pressure (MAP) – intracranial pressure (ICP)), the arterial pressure transducer is placed at mid-head level (usually the level of the external auditory

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meatus) to approximate the MAP at the level of the Circle of Willis.

Intraoperative Monitoring

While assessing for significant blood loss during a craniotomy, it is essential to monitor the surgical field to evaluate for the presence of excessive surgical blood loss. Pay close attention to suction canisters, surgical sponges, and surgical drains.

Standard ASA monitors in conjunction with frequent clinical assessments of the patient allow for monitoring of vital organ perfusion.

Additional monitors to consider are the following:

- Echocardiography
- Cerebral oximetry and near-infrared spectroscopy
- Blood gas and mixed venous oxygen saturation analysis

Intraoperative Management

Several studies suggest that perioperative hypertension (HTN) and coagulopathy (to be discussed under clinical presentation/patient assessment) are factors that predispose craniotomy patients to intracranial bleeding. Intraoperatively, acute hypertensive episodes may occur during:

- Induction
- Epinephrine-containing local anesthetic administration
- Head-pin application
- Periosteal dissection
- Brain manipulation
- Emergence

Therefore, it is important to recognize and vigilantly *prevent* abrupt and major increases in MAP that may cause rupture of a vascular lesion, cerebral vessel or aneurysm, and subsequent hemorrhage (the incidence of aneurysm rupture during induction of anesthesia is reported to be 1–2%). As a general rule, the patient's blood pressure should be maintained within 15–20% of the baseline value, and prophylaxis for the normal hypertensive response to intubation or application of the pin head holder should be instituted before starting either of these procedures.

During the *induction sequence*, minimize the hypertensive response to laryngoscopy and intubation with administration of:

- Lidocaine (1.5 mg/kg iv, 90 s prior to suppress laryngeal reflexes)
- β-Adrenergic antagonists iv (esmolol or labetalol)

Prior to *head-pin holder application*, prevent a hypertensive response by administering:

- Propofol (2–3 mg/kg iv) and/or fentanyl (50–150 mcg iv)/alfentanyl (500–1000 mcg iv)
- A scalp block

To minimize straining or bucking on the endotracheal tube, particularly during movement of the head when the surgical dressing is applied:

- Lidocaine, 1.5 mg/kg iv, is effective, but its duration of action is only about 3–5 min; it can be safely repeated if necessary.

Induced hypotension during *emergence* is recommended to prevent emergence of HTN and elevated ICP. The following intravenous agents are recommended:

- Labetalol, given in 5–10 mg increments.
- Esmolol, given in 0.1–0.5 mg/kg increments, until blood pressure is controlled.
- Hydralazine (2–5 mg iv every 5 min to total of 20 mg in 30 min) and nicardipine (5 mg/h iv, increased by 2.5 mg/h every 15 min to maximum of 15 mg/h) may also be administered, but can rarely cause cerebral vasodilation and increased ICP.

Special Considerations for Endovascular Procedures

Endovascular neurosurgery is a rapidly expanding specialty that involves increasingly complex procedures in a high-risk patient population. Endovascular neurosurgery requires the anesthesiologist to take several considerations into account, many of which revolve around anesthesia being delivered outside the main operating room. Potential obstacles and/or problems relating to administering anesthesia in an interventional neuroradiology suite include:

- Poor access to the patient once the imaging has commenced
- Working in a dark and unfamiliar environment where help is not easily available
- Exposure to ionizing radiation
- Transporting critically ill patients to and from the interventional neuroradiology suite

There are no standardized guidelines currently in practice that dictate whether general anesthesia or monitored anesthesia care should be administered during

endovascular neurosurgery. However, for aneurysm and AVM treatment, general anesthesia is normally preferred due to improved patient safety, lack of motion artifact on imaging, and because of the prolonged duration that these interventions normally necessitate. Regardless of the anesthetic plan selected, using rapid and short-acting anesthetic agents are paramount to facilitate rapid recovery and assessment.

Complications during and after endovascular neurosurgery differ from open surgery, and the anesthesiologist must be vigilant as many problems ensue rapidly and the consequence can be devastating. Adverse events that could occur include the following:

- Injury to intracranial vessels with possible dissection
- Aneurysm perforation leading to intracranial hemorrhage
- Coil displacement into a parent vessel leading to a thromboembolic event
- Contrast nephropathy and contrast allergic reactions
- Hematoma development or hemorrhage at puncture site

Preparation for potential intracranial hemorrhage or aneurysm perforation during endovascular procedures requires pre-procedure planning with interventional neuroradiology personnel. When hemorrhage occurs, blood pressure is temporarily reduced (e.g., esmolol, nicardipine, nitroglycerine), and anticoagulation is reversed (e.g., protamine). Most cases of vascular rupture or perforation are managed in the angiography suite with the interventional neuroradiology team sealing the site endovascularly and aborting the procedure. Additional management as required is implemented, such as, placing a ventriculostomy catheter and sending the patient for emergency computed tomography scan.

Crisis Management

Pathophysiology and Clinical Presentation

Hemorrhage may be multifactorial, and the most common etiologies are:

1. Tissue damage from trauma, aneurysms, or AVM rupture
2. Dilution of coagulation factors/platelets resulting from massive blood and fluid resuscitation
3. Hypothermia
4. Metabolic acidosis
5. Anticoagulation medications
6. Effects of comorbid illness and preexisting hemostatic defects

Tissue Thromboplastin

The injured brain can liberate significant amounts of potent platelet-activating and procoagulant molecules (e.g., tissue thromboplastin or tissue factor) into the system circulation. Thromboplastin complexes with factor VII to initiate thrombin formation, which ultimately leads to the coagulation of blood. Following brain injury, the release of procoagulant molecules into the systemic circulation leads first to increased intravascular coagulation, followed by coagulopathy from consumption due to disseminated intravascular coagulation (DIC). Treatment includes transfusion with platelets, fresh-frozen plasma, and cryoprecipitate since more specific treatment with coagulation factors has not been consistently successful.

Hypothermia

Since the coagulation cascade enzymes are temperature dependent, hypothermia may "slow" enzyme reactions, thus producing coagulopathy. Even a mild level of hypothermia is known to cause hemoconcentration, leukopenia and thrombocytopenia, disordered fibrinolysis, and disruption of platelet function. Hypothermia also adversely affects platelet function by inducing a change in platelet shape and inhibition of aggregation.

Comorbid Illness and Preexisting Hemostatic Defects

Patients with severe liver disease demonstrate multiple coagulation defects since the liver is the sole source of synthesis of all the coagulation factors (except factor VIII and von Willebrand factor). Factor VII levels are most severely affected, and this is manifested as an abnormally high international normalized ratio (INR). Treatment includes:

- Maintenance of platelet count above 50,000
- Administration of antifibrinolytics, such as aminocaproic acid and tranexamic acid, if fibrinolysis is suspected
- Replacement of fibrinogen and clotting factors with either cryoprecipitate, fresh-frozen plasma (FFP), or the off-label use of recombinant activated factor VII (rFVIIa) in select patients

rFVIIa is an effective pro-hemostatic agent for use in patients with congenital or acquired hemophilia. Its efficacy has led to the off-label use of rFVIIa in patients with massive hemorrhage, liver disease, and DIC and patients on anticoagulants. Two studies have shown that rFVIIa has reduced

PRBC transfusion and improved early survival in trauma patients with massive hemorrhage.

Patient Assessment

Diagnostic tests to monitor during hemorrhage include:

- Hemoglobin and hematocrit (changes delayed; normal values during acute hemorrhage can be misleading).
- Platelet count.
- Prothrombin time (PT), INR, activated partial thromboplastin time (aPTT).
- Fibrinogen level.
- Ionized calcium levels (to monitor for hypocalcemia and citrate intoxication).
- Serum osmolality (to monitor effects of mannitol treatment and massive fluid resuscitation).
- Thromboelastogram (TEG), which measures whole-blood thrombus formation and lysis, will provide valuable information on platelet function and the presence of fibrinolysis.
- Patient's core temperature.

Intervention/Treatment

Successful anesthetic management requires effective communication with the surgeon and other members of the perioperative care team. The patient's vital signs, laboratory values (CBC, electrolytes, and coagulation), and operative conditions must be closely monitored. When frank hemorrhage occurs, aggressive fluid resuscitation and blood transfusion must begin immediately. At the same time, the anesthesiologist must be aware of any preexisting condition that may predispose the patient to coagulopathy and uncontrolled bleeding. Further, the anesthesiologist must be aware of the underlying cardiovascular status of the patient, which will help gauge the likely impact of anticipated hemodynamic changes (with hemorrhage and resuscitation) on the balance of myocardial oxygen supply and demand.

Patients on Anticoagulant Medications Requiring Emergent Reversal of Anticoagulation

Patients on anticoagulant medications admitted with an active intracranial hemorrhage present additional challenges for the anesthesiologist. If the patient is emergently taken to the operating room, immediate reversal of anticoagulation is required.

Warfarin

For an INR >2, current recommendations suggest administering a 4-factor prothrombin complex concentrate (4F PCC) rather than fresh-frozen plasma (FFP) for rapid reversal. A disadvantage of PCC is a small prothrombotic risk; however, the faster onset and smaller volume required for administration of the product in comparison to FFP makes it a more favorable option. Overall, PCC has a lower risk of adverse effects when compared to FFP.

Fluid Management

Circulating blood volume should be restored with isotonic crystalloid solutions. The main concern is the development of cerebral edema 24–48 h after resuscitation.

Current intraoperative fluid management recommendations include:

- Maintaining normal serum osmolality
- Avoiding profound reduction in colloid osmotic pressure
- Restoring circulating blood volume with glucose-free crystalloid solutions
- Maintaining normovolemia to preserve CPP

Crystalloids

Isotonic

Blood loss is replaced initially with 3 mL of isotonic crystalloid (e.g., normal saline) for each milliliter of blood loss. Fluids administered to replace blood loss should be near iso-osmolar with respect to plasma (295 mOsm/L). Normal saline (NS) (308 mOsm/L) and lactated Ringer's solution (LR) (273 mOsm/L) are often used. However, lactated Ringer's solution is slightly hypotonic and contains a small amount of Ca^{2+}, which can counteract the citrate anticoagulant in PRBCs. Normal saline in large volumes can cause hyperchloremic metabolic acidosis, which can cause coagulopathy. In the setting of large-volume fluid administration, isotonic solutions of balanced electrolytes, such as Plasmalyte-A and Normosol-R, have the advantage of a pH of 7.4, no Ca^{2+}, and normal osmolarity (295 mOsm/L).

Crystalloid Replacement

- Advantages: Inexpensive, readily available, nonallergenic, noninfectious
- Disadvantages: Lacks oxygen-carrying capacity, lacks coagulation capability, limited intravascular half-life

Hypertonic

Hypertonic saline solutions can be administered for rapid volume resuscitation of hypovolemic trauma victims with brain injury and intracranial HTN. Hypertonic saline helps mitigate the effects of rising intracranial pressure subsequent to initial volume resuscitation. Hypertonic saline will draw fluid into the vascular space from the interstitium. However, be aware that sustained hyperosmolarity (e.g., >320 mOsm/L) caused by any fluid has the potential to result in rebound swelling of the brain if allowed to rapidly autocorrect. Hypertonic saline has also been associated with increased incidence of significant systemic coagulopathy. Another risk is the induction of pontine demyelination (Na increase max. 0.5–1 mmol/L/h). Frequently, hypertonic sodium chloride/acetate solutions are chosen in order to reduce the chloride load and thereby the incidence of hyperchloremic metabolic acidosis.

Colloids

There are few clear indications for the administration of albumin or synthetic colloids. However, colloid infusion is often recommended in neurosurgical patients based on the assumption that increasing colloid osmotic pressure will decrease cerebral edema. If the blood–brain barrier is intact, colloid osmotic pressure exerts little effect. Compared to sodium ions, colloids contribute minimally to osmolality and osmotic pressure. There is new evidence that hypertonic salt solutions combined with colloids may more effectively reduce ICP and restore intravascular volume in neurosurgical patients.

- Dextran and various starch-containing solutions should be avoided because they interfere directly with both platelets and the factor VIII complex and have a small risk of causing an anaphylactoid reaction.
- Several reported instances of bleeding have been attributed to hetastarch administration. However, all of them have involved circumstances in which the manufacturer's recommended limit was exceeded. Therefore, the manufacturer's recommended limit (20 mL/kg/24 h) should be observed, when administered.

To replace fluids, use:

- Isotonic crystalloid solutions (NS, LR, Plasmalyte-A, or Normosol-R)
- Combination of crystalloids and/or colloids

Avoid using:

- Dextran and various starch-containing solutions.
- Dextrose-containing solutions, unless specific indication for its use, e.g., hypoglycemia, can exacerbate ischemic damage and cerebral edema.
- Hypotonic solutions (i.e., 0.45% saline) can result in brain edema.

Blood Products

The major risk of aggressive fluid administration is dilution of circulating blood volume, and this has led to the increased use of blood products. In medically fragile patients (e.g., patients with ischemic cardiomyopathy), aggressive fluid administration may result in cardiovascular impairment (e.g., myocardial ischemia and congestive heart failure).

Whole Blood

The American Association of Blood Banks (AABB) states that the primary indication for whole blood is for patients who are actively bleeding and have sustained a loss of greater than 25% of their total blood volume. Less severe degrees of hemorrhage may be effectively treated with PRBCs. Many blood banks follow the AABB guidelines, and whole blood cannot be obtained in the operating rooms except by special request.

Reinfusion of recovered red blood cells using a cell saver as a blood-sparing intervention in the intraoperative period is encouraged when appropriate.

The most current ASA Practice Guidelines for Blood Component Therapy (American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies 2015) recommend the following:

- The determination of whether hemoglobin concentrations between 6 and 10 g/dl justify or require red blood cell transfusion should be based on the rate and magnitude of active bleeding, intravascular volume status, signs of organ ischemia, and adequacy of cardiac reserve.
- Red blood cells should be administered unit by unit, when possible, with interval reevaluation.
- A massive transfusion protocol (MTP) should be developed and implemented to facilitate the delivery of blood products during massive hemorrhage.

Massive Transfusion Protocol (MTP)

In the event that there is persistent active hemorrhage and the patient remains hemodynamically unstable, MTP should be considered to improve patient outcome, as follows:

- Begin universal blood product infusion rather than crystalloid or colloid solutions to prevent unnecessary hemodilution.
- RBC and plasma should be delivered by a rapid transfuser attached to a blood warmer.
- Note that platelets and cryoprecipitate should *not* be administered through a blood warmer.
- Transfuse PRBCs and plasma in a ratio between 1:1 and 1:2 (plasma to PRBC).
- Transfuse one single-donor apheresis or random donor platelet pool for each six units of RBC.
- Consider the addition of cryoprecipitate only when fibrinogen is less than 80–100 mg/dl in the presence of excessive bleeding or as part of MTP in patient requiring massive transfusion when fibrinogen cannot be measured in a timely fashion.

Packed Red Blood Cells

Advantages

- With an average hematocrit of 60–70%, a unit of PRBCs will restore oxygen-carrying capacity.
- Effectively expands intravascular volume.

Disadvantages

- Risk of transfusion reactions: Thus, cross matching is desirable when time allows (typically about 1 h).
- Type O-negative blood (the "universal donor") can be given to patients of any blood type with little risk of a major reaction. O-negative blood will not sensitize women of childbearing age to the rhesus antigen (if O-positive blood is given in this situation, prophylactic administration of anti-Rh_0 antibody is indicated).
- Risk of transmission of infectious agents.
- Risk of hypothermia: PRBCs are stored at 4 °C and will lower the patient's temperature rapidly (0.25 °C per unit transfused) if not infused through a warming device or mixed with warmed isotonic crystalloid at the time of administration.
- Impair immune function of the recipient.

The following is recommended for administration of PRBCs:

- Premixing with crystalloid will reduce the viscosity of PRBCs and allow more rapid administration.
- Reconstitute PRBCs with a warmed crystalloid or via a warming device.
  - Do not use solutions that contain calcium, as clotting can occur.
  - Lactated Ringer's solution is not recommended for use as a diluent (as lactated Ringer's solution contains calcium).
  - Do not use a diluent that is hypotonic with respect to plasma (if so, the RBCs will swell and eventually lyse).
  - Solutions recommended for dilution of PRBCs are 0.9% saline, Normosol-R with a pH of 7.4, or Plasmalyte-A.
- For PRBC infusions, roughly 1 mL PRBC is used for each 2 mL of blood lost, plus crystalloid. The following equation is used to calculate the necessary volume of PRBCs to be infused:

$$\mathrm{PRBC}_{\mathrm{infused}} = \frac{\left[\left(\mathrm{Hct}_{\mathrm{desired}} \times 55 \times \mathrm{weight}\left(\mathrm{kg}\right)\right) - \left(\mathrm{Hct}_{\mathrm{observed}} \times 55 \times \mathrm{weight}\left(\mathrm{kg}\right)\right)\right]}{0.60}.$$

Plasma

Fresh-frozen plasma contains all the plasma proteins, particularly factors V and VIII, and is an excellent volume expander. Indications for FFP administration according to the most recent ASA Task Force guidelines (American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies 2015) are the following:

- For correction of excessive microvascular bleeding (i.e., coagulopathy) in the presence of an INR greater than 2.0 and in the absence of heparin
- For correction of excessive microvascular bleeding secondary to coagulation factor deficiency in patients transfused with more than one blood volume (approximately 70 ml/kg) and when PT or INR and a PTT cannot be obtained in a timely fashion
- For urgent reversal of warfarin therapy when PCCs are not available
- For correction of known coagulation factor deficiencies for which specific concentrates are unavailable

FFP is not indicated:

- If PT or INR and a PTT are normal
- Solely for augmentation of plasma volume or albumin concentration

The following is recommended for administration of FFP:

- Ten to 15 mL/kg of FFP is administered to achieve a minimum of 30% of plasma factor concentration, except for urgent reversal of warfarin anticoagulation, for which 5–8 mL/kg of FFP usually suffices.
- FFP must be warmed during administration.
- Coagulation parameters (PT, INR, PTT, fibrinogen) should be measured frequently during resuscitation.
- Plasma and PRBCs should be administered prophylactically in a 1:1 ratio to any patient with obvious massive hemorrhage, even before confirmatory laboratory studies are available.
- Plasma requires blood typing but not cross matching; delay in the availability of plasma is caused by the need to thaw frozen units before they can be administered. Prethawed plasma (thawed fresh plasma as opposed to fresh-frozen plasma) can be issued quickly in response to an emergency need.

Platelets

Platelet transfusion may be indicated despite a qualitatively adequate platelet count or in the absence of a platelet count, if there is known or suspected platelet dysfunction (e.g., the presence of potent antiplatelet agents like clopidogel or congenital platelet dysfunction). In craniotomy patients, platelet transfusion is rarely indicated if the platelet count is known to be greater than 100×10^9/l and is usually indicated when the count is less than 50×10^9/l in the presence of excessive bleeding.

Important factors to remember when transfusing platelets:

- Massively hemorrhaging patients may suffer from consumption of coagulation factors.
- Transfused platelets have a short serum half-life (3–4 days).
- Each single unit of platelets may only be expected to increase the count by 10,000–20,000 cells/mm^3.
- Platelets should not be administered through filters, warmers, or rapid infusion devices, since this will cause platelets to adhere to the devices and reduce the number of platelets reaching the patient.

When intraoperative bleeding is still excessive and uncontrollable despite the use of a MTP and blood product replacement, administration of antifibrinolytic agents such as ε-aminocaproic acid or tranexamic acid should be considered. Fibrinolysis should be documented or suspected.

Citrate Intoxication

Citrate is a common anticoagulant added to banked blood to bind free calcium (an essential element in the clotting cascade) in order to prevent clotting. Transfusion of multiple units of banked blood causes a marked reduction in circulating serum calcium, and this can cause "citrate intoxication." Besides a further impairment on the coagulation potential, hypocalcemia in citrate intoxication can have a negative inotropic effect on the heart, causing hypotension despite adequate resuscitation. Thus, ionized calcium should be measured regularly, and calcium should be given in a separate intravenous line from the transfusion line, as needed.

Hemostatic resuscitation does not end when active hemorrhage is controlled. It is important to look beyond normal vital signs as endpoints of resuscitation to more accurate indicators of tissue perfusion, such as arterial pH, base deficit, and lactate level. Massively transfused patients that achieve a normal lactate rapidly after resuscitation have substantially better outcomes.

Key Points

- Rapid exsanguination can result from uncontrolled hemorrhage during a craniotomy.
- The anesthesiologist must be prepared to manipulate the blood pressure and transfuse blood products emergently during a craniotomy.
- It is important to vigilantly prevent abrupt and major increases in MAP that may cause rupture of a vascular lesion and subsequent hemorrhage, especially during induction and emergence.
- Hemorrhage may be multifactorial, and it is important to keep in mind the effect of dilution of coagulation factors/platelets resulting from massive blood and fluid resuscitation.
- The use of rapid and short-acting anesthetic agents is recommended to facilitate rapid recovery and assessment following endovascular neurosurgical interventions.
- Fluids administered to replace blood loss should be near iso-osmolar with respect to plasma (295 mOsm/L).
- To replace fluids, use isotonic crystalloid solutions (NS, Plasmalyte-A, or Normosol-R) or a combination of crystalloids and/or colloids.
- Avoid using dextran and various starch-containing solutions, dextrose-containing solutions, and hypotonic solutions (i.e., 0.45% saline, LRs).
- Transfusion is rarely indicated when the hemoglobin concentration is greater than 10 g/dL and is almost always indicated when it is less than 6 g/dL.

- In the event that there is persistent active hemorrhage and the patient remains hemodynamically unstable, MTP should be considered to improve patient outcome.
- PCCs should be used to reverse warfarin or correct a coagulopathy that arises during massive blood transfusion. FFP should be used as an alternative, if PCC is not available.
- Platelet transfusion should be reserved for clinically coagulopathic patients with a documented low platelet level (<50,000 cells/mm^3) or when there is known to be platelet dysfunction (e.g., from antiplatelet medications).
- Consider the use of antifibrinolytics (i.e., ε-aminocaproic acid, tranexamic acid), if fibrinolysis is documented or suspected and have not yet been administered.
- Hemostatic resuscitation does not end when active hemorrhage is controlled.

Suggested Reading

American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Anesthesiology. 2015;122:241–75.

DeLoughery DG. Coagulation defects in trauma patients: etiology, recognition and therapy. Crit Care Clin. 2004;20:13–24.

Ferrara A, MacArthur J, Wright H, et al. Hypothermia and acidosis worsen coagulopathy in the patient requiring massive transfusion. Am J Surg. 1990;160:515–8.

Patient blood management chapters 61, 62 and 63. In: Miller RD, et al., editors. Miller's anesthesia, 8th ed. Philadelphia: Elsevier; 2015, pp. 1830–67, 1868–1880, 1881–1896.

Rusa R, Zornow MH. Fluid management during craniotomy. In: Cottrell JE, Young W, editors. Cottrell's neuroanesthesia. 5th ed. Philadelphia: Elsevier; 2009. p. 147–60.

Schulenburg E, et al. Anaesthesia for interventional neuroradiology. Curr Opin Anesthesiol. 2011;24:426–32.

Challenges During Anaesthesia for Awake Craniotomy

28

Judith Dinsmore

Overview

Awake craniotomy enables the intraoperative assessment of a patient's neurological status. This allows safer mapping of resection margins in epilepsy surgery, the accurate localization of electrodes for deep brain stimulation and the excision of space occupying lesions in eloquent cortex. Awake craniotomy is becoming more popular as it is associated with a lower requirement for high dependency care, shorter hospital stay and reduced costs. In tumour surgery, awake testing allows maximum resection with minimal post-operative neurological deficit. The anaesthetic techniques for awake craniotomy have evolved along with the surgical indications, but significant challenges remain. The anaesthetic goals are the provision of adequate analgesia and sedation with a safe airway, hemodynamic stability, optimal operating conditions, and an alert, cooperative patient for intraoperative neurological assessment. Various techniques have been described which fall into three main categories:

- Local anaesthesia
- Conscious sedation
- Asleep–awake–asleep (AAA) technique with or without airway instrumentation

Overall, awake craniotomy is safe and well tolerated, but many complications have been described which are summarized in Table 28.1. Several studies have looked at complication rates, but, due to differing case mixes and the variety of anaesthetic techniques used, the incidences vary widely. Catastrophic complications are very rare.

Table 28.1 Complications of awake craniotomy

Complications
Respiratory
Airway obstruction
Respiratory depression
Coughing
Cardiovascular
Hypotension
Hypertension
Neurological
Seizures
Neurological deficit
Brain swelling
Other
Pain
Nausea and vomiting
Local anaesthetic toxicity
Excessive sedation/uncooperative patient
Air embolism

Prevention

The key to success is careful patient selection, an anaesthetic plan tailored to the individual case and meticulous attention to detail. Both the neurosurgeon and the anaesthesiologist should be experienced in awake craniotomy and familiar with the technique chosen. To minimize complications, the following points should be considered:

Communication

- Operative aims and anticipated problems should be discussed between members of the intraoperative team and patient. Pertinent questions to ask include the following: What is the expected duration of the entire procedure, of awake testing, and what is the modality to be tested intraoperatively? Is there raised intracranial pressure (ICP), what is the anticipated blood loss, etc.?

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Patient Selection and Preparation

- Patients must receive a full explanation of what is involved, understand exactly what is expected of them and be able to tolerate lying still for the procedure.
- An uncooperative patient is the only absolute contraindication to this technique.
- Preoperative counselling appears to improve patient satisfaction and reduce pain and anxiety. Psychological profiling may assist in patient selection.
- Relative contraindications include morbid obesity, gastro-oesophageal reflux, a difficult airway or highly vascular tumours. However, with these comorbidities the risk of complications will be increased so the decision for an 'awake craniotomy' should be carefully considered.
- Coexisting medical conditions should be optimized, and routine medications continued including on the day of surgery. Anticonvulsant prophylaxis, dexamethasone and either ranitidine or omeprazole should be prescribed.

Anaesthetic Technique

The technique chosen must be the one considered most appropriate for that particular procedure, the patient's age, existing neurological status and any associated comorbidity. Standard monitoring should be used. Drapes are taped out of the way to allow access to the patient's face and for testing. A warming blanket helps to prevent shivering; padding of pressure areas and a calm relaxed atmosphere in the operating room to minimize patient discomfort and anxiety. Urinary catheterization is required if mannitol is to be given or the duration of surgery prolonged. Antiemetic prophylaxis must be given to all patients, and a loading dose of acetaminophen may provide useful additional analgesia.

Local Anaesthetic

Whatever technique is chosen, effective local anaesthesia is essential. This can be achieved by field infiltration of the incision area and pin sites with long acting agents such as bupivacaine or ropivacaine. Alternatively scalp blocks of individual nerves can be performed. A mixture of two local anaesthetics such as lidocaine and ropivacaine (with epinephrine 1:200,000) will provide both rapid onset and a long duration of action. Local anaesthesia alone removes the risk of excessive sedation or airway compromise. The elderly are often very sensitive to the sedative and respiratory depressant effects of sedative agents. Burr hole procedures or a small craniotomy is often well tolerated under local anaesthetic. However:

- Many patients will not tolerate a long, uncomfortable procedure without sedation.
- Scalp infiltration with large volumes of local anaesthetic or scalp blocks carry the potential risk of local anaesthetic toxicity in patients already prone to seizure.
- Ropivacaine is less cardiotoxic and is advocated by some as the agent of choice.

Sedation

Historically, midazolam, fentanyl and droperidol were most commonly used for sedation and also historically known as 'neurolept analgesia'. Today, propofol is the most popular agent providing controllable sedation, a rapid smooth recovery and, when stopped, minimal interference with electrocorticographic recordings. It is often used as a target-controlled infusion (TCI) in combination with remifentanil. The very short context sensitive half-life of remifentanil ensures reliable elimination whatever the duration of infusion. Remifentanil may also be utilized as a bolus, with a dose range of 0.2–0.5 mcg/kg during periods of stimulation; however bradycardia may result. Dexmedetomidine, an α_2-adrenergic receptor agonist, is also very popular, providing rapidly titratable sedative, analgesic and sympatholytic effects without respiratory depression. It can be used as a sole agent (0.3–0.6 mcg/kg/h), an adjunct (0.01–1.0 mcg/kg/h) or a rescue agent. However:

- Sedation can be notoriously difficult to accurately control.
- In some patients sedation may result in a change in baseline function, compromising mapping and endangering neurological outcome.
- Airway compromise is more common in patients who are obese.
- Neurolept analgesia has a higher incidence of seizures, nausea and vomiting but a lower incidence of respiratory depression when compared with propofol sedation.
- There is a learning curve associated with the use of remifentanil in spontaneously breathing patients. Propofol and remifentanil used for sedation are associated with frequent respiratory complications, but these decrease with experience.
- Sedative synergism has been reported between dexmedetomidine and midazolam.

Asleep–Awake–Asleep

The AAA technique with or without airway intervention is becoming more popular. Hemodynamic and respiratory parameters are easier to both monitor and control providing optimal operative conditions. Typically propofol and remifentanil TCI are titrated against patient response, hemodynamic parameters or bispectral index (BIS) monitoring. The propofol is stopped, and the remifentanil reduced to 0.005–0.01 mcg/kg/min for awake testing. The patient need only be awake for intraoperative testing. Thus, to minimize discomfort the patient is reanaesthetized following tissue resection for wound closure. Alternatively, the patient can remain awake after testing for closure if comfortable. However:

- The AAA technique without airway instrumentation is associated with more respiratory complications: apnoea, arterial desaturation and a higher $PaCO_2$.
- Time to wake up may be prolonged. However, remifentanil significantly reduces propofol requirements, allowing a median wake up time of 9 min.
- Acute emergence delirium may result in patient injury as the patient tries release themselves from the head pins. Thus it is advisable to have the immediate availability of IV medications to administer for rapid reinstitution of general anaesthesia.

Airway Management

There is the risk of hypoventilation or airway obstruction with any sedation technique. Patient positioning may limit access and further contribute to airway compromise.

- There must always be a plan for securing the airway if necessary.
- Airway adjuncts range from a nasopharyngeal airway to an endotracheal tube.
- The laryngeal mask airway is popular for AAA techniques. It is easy to insert and remove, well tolerated at lighter planes of anaesthesia, and it allows ventilation to be controlled, providing optimal operative conditions.
- Based on personal experience, the cuffed oropharyngeal airway (e.g. 'King Airway') may have some utility for ventilatory control for patients in the lateral position.
- Non-invasive positive pressure ventilation (biphasic positive airway pressure and proportional assist ventilation) has been used successfully for awake craniotomy, as has pressure support ventilation for patients with obstructive sleep apnoea.

Crisis Management

The Acutely Restless Patient

The restless patient poses a risk to themselves (especially with head fixation) and operating room staff. An uncooperative patient may also result in failure or inaccuracy of intraoperative testing. Table 28.2 summarizes the possible causes, patient assessment and management.

Nausea and Vomiting

Nausea and vomiting are relatively common but are usually preventable. Table 28.3 summarizes the possible causes, patient assessment and management.

Hypoxia/Airway Obstruction

Hypoxia presents with cyanosis or decreased SaO_2 and may result in bradycardia, hypertension or drowsiness. Both hypoxia and mechanical airway obstruction will increase ICP. Table 28.4 summarizes the possible causes, patient assessment and management.

Table 28.2 The restless or uncooperative patient

Causes
Anxiety
Excessive sedation
Pain/discomfort from positioning
Urinary retention
Hypoxia or hypercapnia
Seizure
Neurological deterioration
Assessment
Is the patient safe?
Is sedation level (BIS?) and analgesia adequate for the stage of procedure?
Check airway
Exclude hypoxia or hypercapnia
Check heart rate and blood pressure
Is there seizure activity or evidence of a new neurological deficit?
Treatment/intervention
Reassure
Give oxygen
Treat remediable causes – pain, adjust head/body position, urinary retention, seizures
Decrease or increase sedation (at what stage is the surgery?)
Dexmedetomidine and remifentanil (bolus) are useful rescue agents

Table 28.3 Nausea and vomiting

Causes
Past history
Lesions in the posterior fossa
Surgical manipulation
Pain
Hypotension
Anaesthetic technique (neurolept is associated with more nausea than propofol)
Raised ICP
Assessment
Check airway
Check pulse and BP
Look for surgical cause such as dural traction
Are there signs of raised ICP?
Has prophylactic anti-emetic been given?
Treatment/intervention
Reassure patient
Stop surgical stimulus
Correct hypotension, e.g. IV fluids or vasopressors
Give adequate analgesia
A combination of anti-emetics of different classes may be needed
Change anaesthetic?

Table 28.4 Hypoxia/airway obstruction

Causes
Reduced oxygen delivery
Respiratory depression (excess sedation or opioids)
Airway obstruction
Aspiration
Laryngospasm
Bronchospasm
Risk factors include obesity, gastro-oesophageal reflux or pre-existing lung disease
Assessment
Check airway, respiratory rate, tidal volume, $EtCO_2$ and FiO_2
Is the patient cyanotic?
Exclude measurement error (oximeter position?)
Look for disconnection of oxygen delivery or breathing system
Listen for air entry, wheeze or crepitus
Assess sedation
Measure arterial blood gas looking for $PaCO_2$ or PaO_2
Treatment/intervention
Give 100%
Relieve airway obstruction (airway, LMA or ET tube as appropriate)
If respiratory depression – reduce/stop sedation or opioids
If laryngospasm – increase the depth of sedation, CPAP, succinylcholine?
Treat aspiration or bronchospasm as appropriate

Seizures

Seizures are a relatively common complication and should be treated promptly. They may present with a sudden loss of consciousness, localized or generalized tonic/clonic activity or development of new neurological deficit. The anaesthetized patient may have unexplained tachycardia, hypertension or a sudden rise in $EtCO_2$. Development of a new neurological deficit may be postictal and should be characterized/observed before surgery continues. Table 28.5 summarizes the possible causes, patient assessment and management.

Table 28.5 Seizures

Causes
Cortical stimulation
Subtherapeutic anticonvulsant levels
Local anaesthetic toxicity
Neurolept sedation is associated with an increased incidence of seizures compared with propofol
Assessment
Check airway, breathing and circulation
If the patient's head is immobilized in pins, ensure safety
Check if the patient has had anticonvulsant prophylaxis
Treatment/intervention
Secure airway and give O_2
Stop cortical stimulation (cold saline to cortex?)
If seizures continue treat – propofol 0.75–1.25 mg/kg, thiopental 1–1.5 mg/kg or low-dose benzodiazepine
For prolonged seizures phenytoin 10–15 mg/kg, levetiracetam 1 g or phenobarbital 200 mg (and repeated to max of 15 mg/kg)

Table 28.6 Hypertension

Causes
Pain
Inadequate sedation
Hypoxemia
Hypercapnia
Raised ICP
Pre-existing hypertension
Urinary retention
Assessment
Establish cause and exclude artefact
Is it associated with painful stimulus?
Are there adequate sedation and analgesia?
What are the heart rate and BP?
Is there hypoxia; what is the SaO_2 or $EtCO_2$?
Is there evidence of raised ICP?
Treatment/intervention
Treat underlying cause
Give analgesia
Increase sedation
Optimize ventilation
Antihypertensives, e.g. labetolol 5–10 mg boluses should then be used as necessary

Hypertension

Hypertension may be a common result of pain, inadequate sedation or other perioperative factors during awake craniotomy. Table 28.6 summarizes the possible causes, patient assessment and management.

Table 28.7 The acutely swollen brain

Causes
Inadequate corticosteroids
Airway obstruction
Hypercapnia
Hypoxia
Hypertension
Raised venous pressure
Assessment
Check airway
Check SaO_2 and $EtCO_2$ (check ABGs)
Assess level of sedation
Is the patient coughing or straining?
Check heart rate and BP
Has patient had corticosteroids?
Venous outflow obstruction
Treatment/intervention
Establish patent airway
Increase FiO_2 and reduce $PaCO_2$ by increasing ventilation
Control BP (see above)
Try head-up tilt 30; consider in-line position; consider removal of jugular venous catheter
Dexamethasone 8–12 mg
Give mannitol 0.25–0.5 g/kg or furosemide 0.25–0.5 mg/kg

Table 28.8 Venous air embolism

Causes
Head-up position
Spontaneous ventilation
Airway obstruction
Assessment
Have a high index of suspicion
$EtCO_2$
Hypoxia
Hypotension
Arrhythmias
Precordial Doppler
Treatment/intervention
Inform surgeon
Flood operative field
Stop N_2O
Lower operative site below level of the heart
Protect airway and FiO_2
Maintain BP with fluids or vasopressors
Other supportive treatment as needed

The Acutely Swollen Brain

Bulging dura on lifting the craniotomy flap is often due to peritumour oedema. Table 28.7 summarizes the possible causes, patient assessment and management.

Venous Air Embolism

There are several reports of venous air embolism (VAE) during awake craniotomy. Patients present with tachypnea, refractory coughing or chest pain or, in the anaesthetized patient, a sudden reduction in $EtCO_2$. Table 28.8 summarizes the possible causes, patient assessment and management.

Key Points

- Awake craniotomy is safe and well tolerated but careful patient selection is vital.
- Use of short-acting, easily titratable agents allows for flexibility of an anaesthetic requiring multiple depths, with multiple levels of stimulation.
- Prepare carefully and do not rush.
- Do not underestimate the importance of the doctor–patient relationship.
- Assess the patient yourself; check history, allergies and airway.
- The prevention of complications is easier than their treatment.
- Meticulous attention to detail and good communication are the keys to success.
- Always have a back-up plan.
- Know your limits and do not be afraid to ask for help.

Suggested Reading

Dinsmore J. Anaesthesia for elective neurosurgery. Br J Anaesth. 2007;99:68–74.

Frost EA, Booij LH. Anesthesia in the patient for awake craniotomy. Curr Opin Anaesthesiol. 2007;20:331–5.

Keifer JC, et al. A retrospective analysis of a remifentanil/propofol general anesthetic for craniotomy before awake functional brain mapping. Anesth Analg. 2005;101:502–8.

Potters JW, Klimek M. Awake craniotomy: improving the patient's experience. Curr Opin Anaesthesiol. 2015;28:511–6.

Serletis D, Bernstein M. Prospective study of awake craniotomy used routinely and nonselectively for supratentorial tumors. J Neurosurg. 2007;107:1–6.

Skucas AP, Artru AA. Anesthetic complications of awake craniotomies for epilepsy surgery. Anesth Analg. 2006;102:882–7.

Perioperative Challenges During Stereotactic Neurosurgery and Deep Brain Stimulator Placement

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Mitchell Y. Lee and Marc J. Bloom

Overview

Stereotactic surgery is based on three-dimensional coordinates, which accurately localize the area of interest. With the advancement of radiology, essentially any specific region within an organ can be localized with stereotactic equipment. In neurosurgery, stereotactic technique is especially beneficial since the localization allows for conduct of minimally invasive surgery, thereby preserving other important structures in the brain.

Stereotactic surgery can be performed with or without a head frame. Frameless systems such as Brain Lab or Cygnus PFS are often used as a navigation aid during a standard craniotomy for the neurosurgeons. A frame-based system allows the neurosurgeon not only to establish the frame of the reference but also to mount a guiding device to minimize the margin of error when approaching a deep target within the brain. The use of the frameless system affects anesthesiologists minimally; therefore, the discussion will focus on *frame-based systems*.

The head frame presents several issues that need to be considered by the anesthesiologist preoperatively. During the patient interview, the anesthesiologist should evaluate whether the patient can tolerate local anesthesia and the prolonged time in the head frame. Once the head frame is applied, the patient is transferred to and from the radiology suite for the imaging studies, which may take several hours. Patients often complain of pain at the pin sites, neck stiffness, claustrophobia, and headache. Since the patient may be transferred from one area to another area by a nonclinical transport aid, it is critical that the patient has completely emerged from any sedation or analgesic medications that were administered during the imaging period.

Patients with airway difficulty or history of obstructive sleep apnea should be accompanied by an individual with appropriate clinical training (e.g., nurse or physician). The airway must be considered not only during the time of the head frame placement but also when the patient presents for the actual stereotactic procedure. In the worst case scenario, the difficult airway patient should be considered for general anesthesia for the entire event from the placement of the head frame to imaging and surgery. Every part involved should be organized so that the patient is exposed to the minimal amount of anesthetic medications.

Deep brain stimulation (DBS) is performed for the patients with movement disorders such as Parkinson's disease or essential tremor. Although stereotactic coordinates allow the neurosurgeon to reach the exact target with great accuracy, the chosen target may or may not be the optimal location for stimulation to alleviate clinical symptoms. Therefore, once the target is reached, trial stimulation allows the surgeon to confirm appropriate probe location. To assess the optimal area for the placement of the stimulating probe, the patient is instructed to withhold any medication that controls the symptoms. The importance of not taking the medication (e.g., antiparkinson medication) must be emphasized during the preoperative visit. Since the anesthesiologist instructs the patient which medications to take for the day of the surgery, the half-life and the timing of the individual medication also must be considered since some Parkinson's medications may take more than 24 h to clear. Careful history taking will also allow the anesthesiologist to understand the timing of symptom deterioration with dose-holding based on the patient's past experience with forgetting to take their therapeutic medication(s). The symptomatic patients are often anxious and uncomfortable; tremors may not only cause discomfort but also may be severe enough to disturb

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the operation. These patients require extensive reassurance and presurgical preparation.

Prevention

Airway

If general anesthesia is to be induced, the head frame is a major obstacle for airway management. Once the head frame is placed, even mask ventilation becomes difficult. Most of the head frames have a removable front section. However, the opening is not often large enough to accommodate an adult-sized mask. The space between the front of the face and the head frame can be adjusted at the time of the placement. If the space is too narrow, the mask may not fit underneath the frame, and a smaller mask or deflated mask can be used. A quick reminder by any member of the operative team at the time of the frame placement (preprocedural pause) will save a lot of trouble later. Allen wrench or other equipment for the removal of the frame must be available at all times.

Proper positioning with a shoulder roll, a wedge, and a head support will result in the patient being fixed in a sniffing position but may not give an adequate space to manipulate a standard laryngoscope during the time of anesthetic induction and tracheal intubation. Fiber-optic bronchoscope, glide scope, video laryngoscope, and intubating laryngeal mask airway (LMA) (or standard LMA and hollow stylette, e.g., Aintree) have all been used to intubate the trachea in patients fixed in a stereotactic head-holding device. The fiber-optic bronchoscope is one of the most effective tools in advanced airway management. However, effective use of this tool requires advanced technical ability, which may take years to achieve an appropriate level of competence for effective airway management in patients who have their head fixed in a stereotactic holding device. In addition, the fiber-optic bronchoscope is expensive to purchase and has a high cost for maintenance, which often limits its usage. The GlideScope is a lighted fiber-optic camera on a strongly curved laryngoscope blade that projects an image to attached video screen. Visualization of the vocal cords is simple, but inexperienced users often find it very difficult to place the endotracheal tube through the cords because of limited mouth opening and the acute turn that the tube must take between the lips and vocal cords. The intubating LMA has a large enough lumen to accept a standard wire-reinforced endotracheal tube and a preformed curve that directs the tube through the vocal cords. Unfortunately, it is difficult to establish reproducible competency with the intubating LMA and has a higher failure rate than a fiber-optic bronchoscope. It is also possible to intubate the trachea through a classic LMA, using a hollow stylette (e.g., Aintree) loaded on to a fiber-optic bronchoscope. Once the stylette is positioned in the trachea, the bronchoscope and LMA are removed, and an endotracheal tube (e.g., Parker endotracheal tube) is advanced into the trachea over the stylette, which is then also removed.

Once the head frame is attached to the OR table, it becomes impossible to manipulate the head. Do not transfer the patient to the operating table until airway management is complete. As for prone or lateral position, the endotracheal tube must be taped securely. A circumferential taping, however, should be avoided to ensure adequate venous drainage from the head and face, as facial swelling could prevent an ability to safely extubate the trachea at the end of surgery. Other airway complications include apnea, airway obstruction, endotracheal tube malposition and obstruction, and accidental extubation.

Positioning

For both stereotactic surgery and deep brain surgery, sitting position or reverse-Trendelenburg position with the neck flexion is often required. Although the procedure requires a smaller craniotomy or a Burr hole, venous air embolism is a known risk. Early detection and prevention of further venous air embolism are the best course of action. Precordial Doppler may be used for the stereotactic surgery, but for the DBS procedure, the Doppler may interfere with the neurophysiology monitoring. If this is the case, precordial Doppler use can be limited to the initial opening and the exposure of the brain. For an awake or sedated patient, air embolism may present as coughing, chest discomfort, or sudden sense of anxiety. For such minimally invasive surgery, central venous catheter is not usually indicated. If venous air embolism was to occur, the treatment options are Trendelenburg position, flooding of the surgical field, and packing the area with Gelfoam or bone wax.

For DBS placement procedures, the patients are often kept awake or minimally sedated. Sedated patient should be positioned so that there is an adequate space for breathing and ventilation. The positioning should allow the patients to be as comfortable as possible, and lumbar support, arm rests, leg support, and possible Foley catheter should be considered. At some institutions, the services of a professional massage therapist have been utilized during the procedure to alleviate the discomfort for staying in one posture for a prolonged time.

Crisis Management

Seizures

Stereotactic surgery: If seizure activity is suspected, intubated patients should be treated with induction agents such

as propofol or barbiturates (e.g., thiopental). Other treatments include benzodiazepine or cool saline irrigation to brain.

DBS in awake patients: If a seizure occurs in the awake or sedated patient, clinical judgment will be required to determine whether the seizure will be of short duration and simply observed or prolonged and require administration of a short-acting benzodiazepine and potentially airway management.

The alpha-2 receptor agonist, dexmedetomidine, may be proconvulsant, especially if given as an intravenous bolus and inhalational gas is used. However, dexmedetomidine has been used for patients with a seizure history without problems at the normal clinical dosage. No real evidence exists to establish if intravenous dexmedetomidine is protective for seizures.

Hemorrhage

Due to the small size of the opening, any bleeding can be dangerous. Bleeding may result in hematoma formation deep at the target site, anywhere along the path of the probe transit through brain parenchyma or at the brain surface (e.g., subdural near the site of the craniectomy). Most often hematoma is diagnosed from postprocedure neuroradiology studies and has no clinical importance. Rarely, the patient may present with acute neurologic deterioration from procedure-related cerebral hemorrhage. In these cases, immediate support with airway management, blood pressure control, and position change must be achieved. If significant subarachnoid blood accumulates, (rare) postoperative vasospasm should be considered and treated as indicated.

Nausea and Vomiting

Prevention of nausea and vomiting is key. Nausea and vomiting during the procedure may make it impossible for the neurosurgeon to appropriately position the brain probe and is very unpleasant for the patient. In addition, with the patient's head fixed in the stereotactic holder, it may be impossible to prevent aspiration of regurgitated material. It is, therefore, critical that strict NPO guidelines be followed for these patients. In choosing pharmacologic agents to prevent nausea and vomiting during the procedure, care must be taken to avoid administration of medication that interacts negatively with antiparkinson therapy. For example, metoclopramide (Reglan) may exacerbate Parkinson symptoms due to its effect on central dopaminergic receptors. Other medications such as phenothiazines (e.g., Compazine [prochlorperazine]) and butyrophenones (droperidol) also are included in this group. Ondansetron (Zofran) and dexamethasone combination can be very effective with minimal risk of complication. Newer agents such as aprepitant, an NK1 antagonist, may be prescribed prior to surgery as a preventative measure.

Cardiovascular

The Parkinson patients who take bromocriptine or pergolide may experience severe and precipitous hypotension during the induction of general anesthesia (central dopamine receptor stimulation and peripheral vasodilatation), particularly in the presence of other antihypertensives, as, for instance, angiotensin-converting enzyme (ACE) inhibitors. Careful review of the medication is a must where this group of patients is concerned. Severe bradycardia and cardiac arrhythmia have been reported during DBS surgery. Therefore, adequate venous access must be assured to allow rapid intravenous administration of cholinergic antagonists (e.g., atropine) and vasoactive drugs (e.g., epinephrine and ephedrine). Intraoperative arterial line placement may not be necessary for many of the procedures, but access to emergent arterial line should be ensured.

Other Complications

Stereotactic surgery is based on establishing the frame of reference. If any objects or maneuvers interfere with the reference points, stereotactic surgery will fail. Operating room tables or the frame bracket cannot be moved or disturbed. The "Cygnus" system depends on X-ray detectable fiducial markers and they may not be moved. Since the fiducials are placed on the skin, any changes to the surface anatomy may affect the reference point. The "Brain Lab" system incorporates facial features as well as fiducial markers. Tape on the eyes, local anesthetic for scalp block, or processed EEG monitor sensors such as BIS strip may interfere with the setup of the reference point. Effective communication between anesthesiologist and surgeons as well as OR technicians is a must to prevent inadvertent disruption of stereotactic reference points.

During the DBS procedure, even the slightest electrical noise may interfere with the neurophysiology monitor. Common sources of electrical noise in the operating room that interfere with neurophysiologic monitoring include cellular phone use, florescent lighting, or any instrument or device (e.g., convective warmers) connected to an electrical outlet. Battery-operated monitors and infusion pumps should be considered for use during cases requiring neurophysiologic monitoring to minimize the risk of noise from AC power sources affecting the monitoring.

Key Points

- Minimally invasive procedures such as stereotactic surgery and DBS procedures can present significant challenges to the anesthesiologists.
- Understanding the patient population, different types of surgical procedures, the preoperative preparation, and the complications is essential.
- Airway management can be difficult in patients with head frames and requires careful planning and expertise.
- Functional brain surgery frequently requires an awake procedure, which requires close cooperation between patient, anesthesiologist, and surgeon and poses significant risks.
- Complications include seizures, cerebral hemorrhage, intraoperative nausea, and vomiting followed by tracheal aspiration and sudden cardiovascular deterioration.

Suggested Reading

Dinsmore J. Anaesthesia for elective neurosurgery. Br J Anaesth. 2007;99(1):68–74.

Fabregas N, Craen RA. Anaesthesia for minimally invasive neurosurgery. Best Pract Res Clin Anaesthesiol. 2002;16(1):81–93.

Nichoson G, Pereira AC, Hall GM. Parkinson's disease and anaesthesia. Br J Anaesth. 2002;89:904–16.

Oda YMP, et al. The effect of dexmedetomidine on electrocorticography in patients with temporal lobe epilepsy under sevoflurane anesthesia. Anesth Analg. 2007;105:1272–7.

Spiekermann BF, et al. Airway management in neuroanaesthesia. Can J Anaesth. 1996;43(8):820–34.

Venkatraghavan L, et al. Anesthesia for functional neurosurgery. J Neurosurg Anesthesiol. 2006;18:64–7.

Perioperative Challenges During Posterior Fossa Surgery

30

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Overview

The posterior fossa contains vital brainstem centers for respiration, the cardiovascular system and consciousness, as well the cranial nerves and their nuclei. This high concentration of delicate structures, added to the poor accessibility, makes posterior cranial fossa surgery a major challenge for the neurosurgeon. When such surgery is performed in the sitting position, additional anesthesiological risks ensue, notably venous air embolism (VAE), pneumocephalus, and mid-cervical myelopathy. This chapter is based on the authors' personal experience with more than 4500 posterior fossa procedures performed in the sitting or semi-sitting position.

A wide spectrum of lesions may require surgical exploration of the posterior cranial fossa, e.g., tumors (acoustic neuromas, meningiomas, or metastases), aneurysms or AV malformations, traumatic contusions or hemorrhages, as well as developmental anomalies (Chiari malformation I and II).

Posterior fossa surgery can be performed in different positions to facilitate access to the cerebellum, cerebellopontine angle, or brainstem. These include the sitting, prone (midline suboccipital), or modified lateral position (park bench). There are no valid outcome data and prospective studies to support superiority of one approach over the other. The choice depends on the clinical experience and preference of the local practitioners.

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Clinical Characteristics of Mass Lesions and Neurosurgical Procedures in the Posterior Fossa

- Even small space-occupying lesions (e.g., hematoma/edema) can prove rapidly fatal due to the paucity of space. The resulting compression of the brainstem leads to rapid catastrophic neurological compromise (see Fig. 30.1).

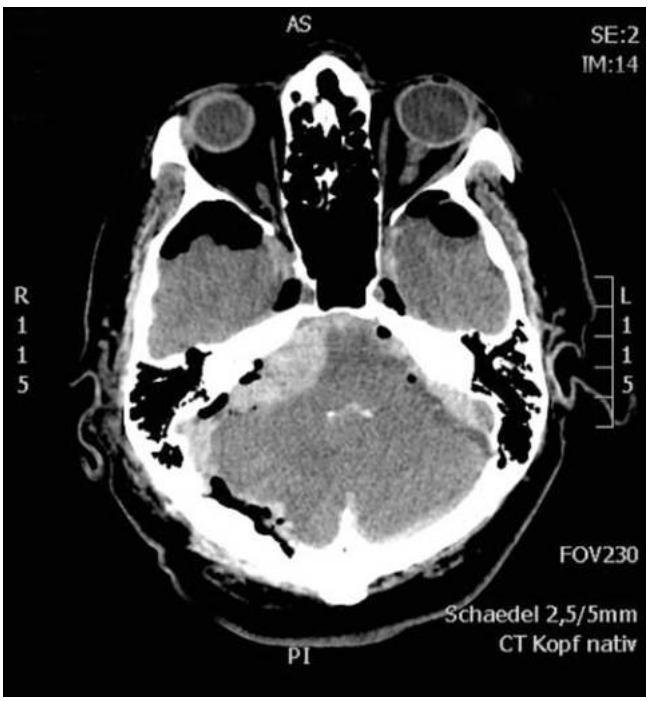

Fig. 30.1 Postoperative CT scan showing a hematoma with resulting shift of the brainstem after an acoustic neurinoma resection

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- The immediate proximity of surgical field to the brainstem and the cranial nerves IX, X, and XII can cause intraoperative hemodynamic instability (e.g., hyper-/hypotension, arrhythmia), reflexes (e.g., coughing, deep inspiration), and postoperative cranial nerve dysfunction (e.g., dysphagia).
- Positioning (e.g., sitting, prone, or park bench position) can lead to special complications, most notably air embolism, hypotension, or obstruction of jugular venous outflow. Craniotomy in the posterior fossa, especially in the sitting position, causes a set of unique and potential hazardous problems.

Preoperative
- Deterioration of the neurological status and cranial nerve dysfunction
- Obstructive hydrocephalus

Intraoperative
- Complications due to intraoperative positioning
  - VAE and paradoxical air embolism (PAE)
  - Peripheral nerve injuries
  - Hemodynamic instability
  - Jugular venous outflow obstruction
  - Mid-cervical quadriplegia
- Brainstem injury or surgical manipulation
- Impairment of ventilation and airway

Postoperative
- Compression or herniation of the brainstem or midbrain structures by hematoma or edema
- Cranial nerve injury
- Brainstem injury
- Pneumocephalus and tension pneumocephalus
- Swelling of the upper airway (e.g., tongue, due to venous obstruction, particularly when an oral airway was in use during surgery)

The incidence of complications in relation to the position in posterior fossa surgery is shown in Table 30.1.

Table 30.1 Incidence of clinically significant complications in the sitting position vs. horizontal position (0, +, ++, +++ indicate probability)

Venous air embolism[a]	+++ vs. + – ++
Paradoxical air embolism[a]	Rare[b]
Arterial hypotension	++ vs. + – ++
Pneumocephalus	+++ vs. +
Mid-cervical quadriplegia	Rare[b]

[a]Incidence varies according to the method of detection
[b]Exact incidence unknown

Prevention

The first step to prevent complications in the management of posterior fossa surgery is adherence to good clinical practice: careful and accurate preoperative evaluation, meticulous maintenance of perioperative homoeostasis, and improvement of surgical conditions.

Secondly, perioperative management aims at *prevention* of specific crises as outlined in Table 30.2.

Crisis Management

Anesthesia and critical care for posterior fossa surgery require a detailed understanding of anatomy, physiology, and pathophysiology.

The cornerstone for patient safety and crisis management includes detailed preoperative assessment, strict prevention of complications, and excellent team-coordinated work, based on anesthesia and neurosurgical protocols.

Preoperative Crisis Management

Preoperative Assessment

Obstructive hydrocephalus is evident on preoperative CT or MRT scans and should be treated pre- or intraoperatively. Any preoperative medication in patients with posterior fossa lesions must be individualized, taking into account physical status and ICP.

Preoperative Crisis: Pathophysiology, Clinical Presentation, and Intervention

- *Deterioration of the neurological status preoperatively* and/or cranial nerve dysfunction:
  - *Pathophysiology*: patients with posterior fossa lesions are more sensitive to sedatives and analgesics, in particular with increasing mass effect of the lesions.
  - *Symptoms*: altered state of consciousness and difficulties to maintain a patent airway.
- *Obstructive hydrocephalus*:
  - *Pathophysiology*: infratentorial masses can obstruct the outflow of CSF and markedly increase ICP.
  - *Symptoms*: continued impairment of neurological function.
  - *Intervention:*
    - Perform ventriculostomy or external ventricular drainage.

Table 30.2 Guide to prevention

Crisis	Methods to prevent the crisis
Preoperative	
Deterioration of the neurological status/ cranial nerve dysfunction	Examination of the cranial nerves IX, X, and XII
	Administration of sedatives and opioid analgesics is adapted to patient physical status, evidence of increased intracranial pressure (ICP), and level of patient anxiety
	Use these agents with caution in patients with any posterior fossa lesion
Obstructive hydrocephalus	Perform ventriculostomy or external ventricular drainage
	Be aware of excessive drainage resulting in upward cerebellar herniation. Always check positioning of the drip chamber in relation to the external auditory meatus
Intraoperative	
Venous air embolism (VAE)	Use sensitive monitors to detect air entrainment (<0.25 ml): Precordial Doppler or transesophageal echocardiography (TEE)
	Central venous line placed in the right atrium at its junction with the superior vena cava (correct catheter position confirmed by intravascular ECG or TEE)
	Surgeon should accept a gradient as small as possible between the heart and site of surgery
	Careful surgical technique (e.g., apply bone wax)
	Temporary compression of the jugular veins to identify sources of venous bleeding
	Avoid nitrous oxide
	Avoid hypovolemia
	Avoid hyperventilation
Paradoxical air embolism (PAE)	Examine for patent foramen ovale by TEE or transcranial Doppler (TCD)
	Critical risk-benefit assessment is obligatory when adopting the sitting position in patients with known patent foramen ovale or pulmonary AV fistula
	Avoid high PEEP (>10 cm H_2O)
	Avoid hypervolemia
Damage due to positioning	Meticulous attention to positioning; neurophysiological monitoring (SSEP, MEP, BAEP, EEG, EMG, etc.) helps to avoid injuries
General aspects	Avoid excessive neck rotation and flexion (minimum 5 cm space between the chin and sternum)
	Exclude severe degenerative diseases of the cervical spine (X-ray, CT, functional test)
Peripheral nerve injuries	Care must be taken to pad all pressure points (elbow, fibula, heels, etc.) and to avoid stretching or compression of the brachial plexus and peripheral nerves
Mid-cervical quadriplegia	Avoid excessive neck rotation and flexion (see general aspects above)
Jugular venous outflow obstruction and swelling of the upper airway	Avoid excessive flexion of the neck to allow adequate venous drainage (see general aspects above)
Hemodynamic alteration and instability	Maintain normovolemia, use vasopressors to avoid hypotension caused by positioning, and ensure cerebral perfusion
	Ensure abdominal and femoral venous return
	Pressure transducer should be positioned and zeroed at the level of the base of the skull (tragus) to correctly estimate CPP
Brainstem/cranial nerve injury	Use SSEP/MEP (cortical integrity), BAEP (N. VIII) and/or EMG (N. VII; in incomplete neuromuscular blockade)
	Alert the surgeon immediately in case of autonomic disturbance
Impairment of ventilation	Secure airway (e.g., proper fixation of the armored endotracheal tube), and ensure access to the airway
	Allow adequate diaphragmatic excursion
Postoperative	
Deterioration of neurological status	Monitor all patients in an intensive care setting
	Normotension. Treat arterial hypertension quickly
	Be aware that patients with posterior fossa lesions are more sensitive to sedatives and analgetics after emergence from anesthesia
	Be aware that even a small degree of edema or bleeding in the posterior fossa can lead to catastrophic neurological compromise
	Leave the patient intubated if postoperative deterioration or damage to cranial nerves (IX, X, XII) is anticipated
Pneumocephalus	Avoid nitrous oxide
	Be aware, especially in the sitting position
Swelling of the upper airway (e.g., tongue)	Avoid excessive flexion of the neck and allow venous drainage
	Consider glossal edema before extubation, delay extubation to allow the edema to resolve

Intraoperative Crisis Management

Intraoperative Assessment

Routine monitoring includes electrocardiography, pulse oximetry, capnography, temperature, urinary output, and relaxometry. Strictly recommended in posterior fossa surgery are an intra-arterial line (beat-by-beat measurement of systemic blood pressure to estimate cerebral perfusion pressure and assessment of $paCO_2$) and a central venous line (e.g., application of catecholamines, aspiration of air). Supplementary monitoring is directed toward the detection and treatment of VAE when the risk of VAE is high: precordial Doppler, TEE, and the use of central venous line as a right atrial catheter.

Intraoperative Crisis: Pathophysiology, Clinical Presentation, and Intervention

- *Venous air embolism*:
  - *Pathophysiology*: Pressure in a noncollapsible vein (e.g., dural sinus or diploic vein) becomes subatmospheric when the head is elevated above the heart. The pathophysiological consequences depend on the volume and rate of air entry, pulmonary clearance, as well as on cardiac function; cardiac output decreases in response to the increased right ventricular afterload which can result in *acute right heart failure* and/or reduced left ventricular filling.
  - *Symptoms*: Bubbles observed through transesophageal echocardiography (TEE) (see Fig. 30.2), roaring sounds of the precordial Doppler (PCD) signal, decrease of end-tidal CO_2 reflecting increased pulmonary dead space, decrease of arterial oxygen saturation, arterial hypotension, low output, and cardiac arrest. Some authors have argued against the use of TEE for monitoring, as it may alert the anesthesiologist to small amounts of air, which will never have hemodynamic consequences.
  - *Prevention:* See Table 30.2.
  - *Intervention:* See Table 30.3.

- *Paradoxical air embolism*:
  - *Pathophysiology*: see VAE, presence of a patent foramen ovale, or pulmonary shunts/AV fistula; air can traverse to the arterial circulation.
  - *Symptoms*: stroke and/or coronary occlusion (may be apparent postoperatively).
  - *Intervention:* See Tables 30.2 and 30.3.

- *Hemodynamic instability*:
  - *Pathophysiology*: venous pooling as a result of intraoperative patient positioning, influenced by intravascular volume status, BMI, depressant effects of anesthetic agents, etc.
  - *Symptoms*: arterial hypotension
  - *Differential diagnosis*: brainstem injury/manipulation
  - *Intervention:*
    - Communicate with the surgeon (e.g., to interrupt manipulation).
    - Administer vasopressors to treat hypotension, and expand intravascular volume in case of hypovolemia.
- *Brainstem injury*/manipulation:
  - *Pathophysiology*: direct surgical manipulation, traction, or ischemia of the brainstem centers, as well as cranial nerves or their nuclei; damage to respiratory centers is almost always associated with hemodynamic instability.

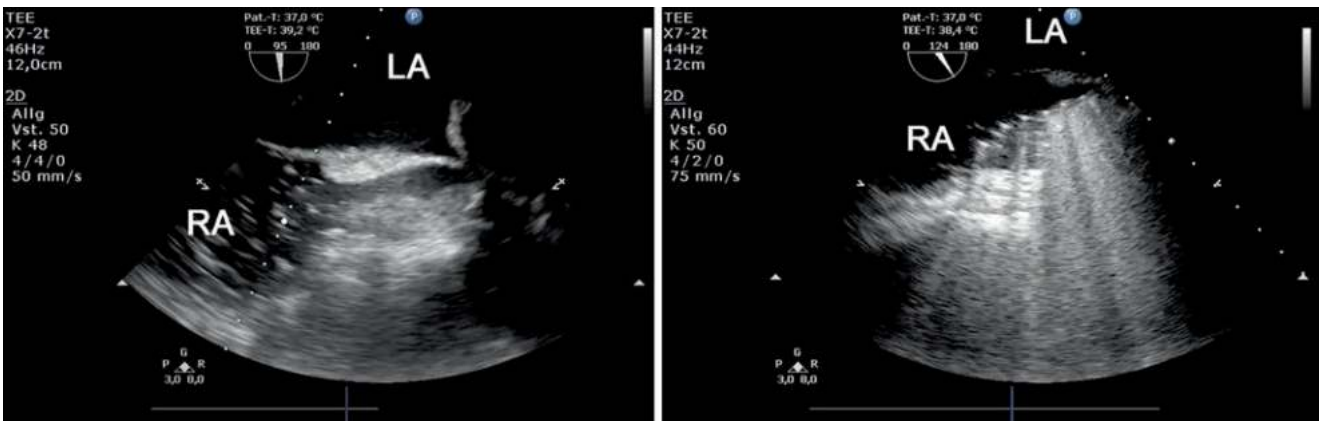

Fig. 30.2 Visualization of intracardiac air by transesophageal echocardiography. Bicaval view of the heart at the midesophageal level of the left (LA) and right atrium (RA). Microbubbles represented by high-intensity echoes in the RA in case of venous air embolism with only characteristic change in the Doppler tone (left frame) and in one case of severe venous air embolism with drop of $etCO_2$ (right frame)

Table 30.3 Treatment of venous air embolism

Step 1: Detection of venous air embolism
Inform the neurosurgeon immediately about air entrainment
Temporary bilateral jugular vein compression (in communication with the neurosurgeon, to identify the source of air embolus)
Surgical field can be flooded with saline or packed; bone wax may be applied to the skull edges
Request assistance
Ventilate the patient with 100% oxygen, discontinue N_2O – if applicable
Step 2: Persistence of venous air embolism
Lower patient's head if possible
Aspirate air from the right atrium through central venous line
Regularly reevaluate the patient status (hemodynamic, blood gas analysis)
Consider bilateral jugular vein compression in communication with the neurosurgeon
Management of acute right heart failure and/or reduced left ventricular filling
Treat hypotension with vasopressors to secure sufficient coronary perfusion
Consider TEE findings (e.g., volume status, right ventricular dysfunction)
Apply PEEP cautiously (>8–10 cm H_2O); excessively high PEEP levels may promote paradoxical air embolism
Carefully treat hypovolemia; avoid hypervolemia
Step 3: Severe venous air embolism
Persistent circulatory instability should prompt the surgeon to terminate surgery rapidly
Circulatory arrest requires return to the supine position to apply ACLS algorithms
Continue postoperative ventilation; check for signs of pulmonary edema

Fig. 30.3 Electrocardiography, invasive arterial blood pressure and pulse oximetry monitoring showing asystole episode due to surgical retraction near the cerebellopontine angle

- *Symptoms*: hyper-/hypotension, arrhythmia (tachy-/bradycardia); sudden shifts of autonomic discharge (unpredictable alternation between bradycardia/asystole and tachycardia/hypertension) (see Fig. 30.3).
- *Intervention:*
  - Inform the surgeon, who should interrupt manipulation, which will alleviate the disturbance/problem immediately in most cases.
  - When the hemodynamic situation has stabilized, prophylactic measures should be considered (e.g., glycopyrrolate, ephedrine, or atropine in bradycardia or β-adrenergic blockade, if sympathetic reflexes are involved).

Postoperative Crisis Management

Postoperative Assessment

All patients should be cared for in an intensive care setting to maintain or reestablish systemic and brain homeostasis. The aim is close clinical monitoring and assessment of the neurological status. Life-threatening deterioration due to hematoma occurs mostly within 6 h after surgery.

Three typical scenarios occur in the management of patients undergoing posterior fossa surgery: (1) *early emergence and tracheal extubation*, (2) *postoperative neurological status is worse than preoperative*, and (3) *anticipation of cranial nerve dysfunction* (see Table 30.4).

Postoperative Crisis: Pathophysiology, Clinical Presentation, and Intervention

- *Brainstem compression*:
  - *Pathophysiology*: even a small amount of mass (e.g., hematoma/edema) can prove rapidly fatal due to the paucity of space and the immediate compression of the brainstem or herniation (downward through the foramen magnum or upward – transtentorial herniation) (see Fig. 30.1).
  - *Symptoms*: delayed awakening and continued impairment of neurological function and respiratory and cardiovascular derangement (including apnea or abnormal breathing pattern, persistent hypertension, etc.).
  - *Intervention:* see Table 30.4 (scenario 2).
- *Cranial nerve dysfunction*:
  - *Pathophysiology*: direct surgical trauma, traction, manipulation, or ischemia causes temporary or permanent dysfunction (particularly cranial nerves IX, X, and XII).
  - *Symptoms*: difficulties to swallow or to maintain a patent and protected airway (dysphagia, aspiration, stridor, respiratory distress).
  - *Intervention:* see Table 30.4 (scenario 3).
- *Brainstem injury*:
  - *Pathophysiology*: see above (intraoperative crisis).
  - *Symptoms*: abnormal breathing pattern or inability to maintain a patent airway after tracheal extubation.
  - *Intervention:* see Table 30.4 (scenario 2).

Table 30.4 Postoperative assessment

Scenario 1: Early emergence and extubation
The aim of emergence is early awakening to allow assessment of the neurological status
Preconditions for tracheal extubation are normal systemic and brain homeostasis
Normothermia
Normocapnia
Normotension
Normovolemia
A level of consciousness that allows management of secretions
Absence of airway edema
Return of protective airway reflexes
Scenario 2: Postoperative neurologic status is worse than preoperative
Emergency evaluation and treatment is indicated. Time to diagnosis is a critical determinant of outcome
Approach to the scenario
Maintenance of adequate ventilation and oxygenation (reintubate if necessary)
Quickly obtain imaging studies (CT) to rule out structural causes of intracranial hypertension, including hematoma, edema, tension pneumocephalus, and hydrocephalus
Important differential diagnoses to be ruled out
Metabolic derangement (e.g., hypoglycemia, hyponatremia)
Pharmacological/persistent anesthetic effect (caused by anesthetic agents, muscle relaxants; central anticholinergic syndrome)
Seizure (e.g., nonconvulsive)
Paradoxical air embolism (consider MRI)
Mid-cervical quadriplegia (consider MRI)
Scenario 3: Anticipation of caudal cranial nerve dysfunction
Certain scenarios (e.g., prolonged surgery, close proximity to the brainstem) carry a high likelihood of postoperative worsening of the neurological status, secondary to cerebral edema or pneumocephalus. In these cases, prolonged intubation and ventilation may be necessary until neurological function will allow extubation
Approach to the scenario
Return of protective airway reflexes (including swallowing, sticking out the tongue) is essential
Extubation under fiber-optic visualization, withdrawal of the endotracheal tube to hypopharynx
Fiber-optic assessment of laryngeal function and ability to swallow

- *Pneumocephalus/tension pneumocephalus*:
  - *Pathophysiology*: air is retained in the cranial cavity after all craniotomies, located over the cerebral convexities, in the ventricles and/or posterior fossa; air is usually resorbed with symptomatic improvement within 1–3 days (*pneumocephalus*) (see Fig. 30.4). Intracranial gas expansion may result in elevated intracranial pressure and mass effect (*tension pneumocephalus*; mechanisms include the presence of N_2O which diffuses into preexisting air-filled spaces ["valve effect"] and rewarming of the patient).
  - *Symptoms*: delayed awakening and continued impairment of neurological function (confusion, lethargy, reduced consciousness/coma, nausea and vomiting, seizures).
  - *Intervention:* see Table 30.4 (scenario 2).
  - *Treatment of tension pneumocephalus*:
    - Ventilation with 100% O_2
    - Burr hole to release trapped air under local or general anesthesia
    - Rapid improvement occurs with the release of gas under pressure
- *Upper airway edema*:
  - *Pathophysiology*: edema of the mucosa due to venous and lymphatic obstruction.
  - *Symptoms*: tongue and soft tissue edema with inability to maintain airway patency (cardinal symptom: inspiratory stridor).
  - *Intervention:*
    - Critical assessment of the airway (direct or indirect visualization through (video-) laryngoscopy, fiber optics)
- *Mid-cervical quadriplegia*:
  - *Pathophysiology*: myelopathy presumably due to excessive flexion with compression of the anterior spinal artery; preexisting degenerative disease of the cervical spine is considered a risk factor.
  - *Symptoms*: quadriplegia.
  - *Intervention:* see Table 30.4 (scenario 2).

Key Points

- Even a small amount of mass (e.g., hematoma/edema) in the posterior fossa can cause severe neurologic compromise due to the paucity of space and the immediate compression of the brainstem. Patient positions that permit surgical access to the posterior fossa are associated with unique difficulties, notably due to the risk of VAE, jugular venous outflow obstruction, and pneumocephalus.
- Intracranial hypertension may develop secondary to increased abdominal pressure, venous congestion, or outflow obstruction (excessive flexion/rotation of the neck) and arterial hypotension; preventive measures need to be applied to minimize these effects.
- All patients have to be monitored in an intensive care setting to maintain or establish systemic and brain hemostasis. Life-threatening deterioration due to hematoma occurs most within 6 h after surgery.
- The cornerstone of patient safety and crisis management during posterior fossa surgery is detailed preoperative assessment, strict prevention of complications, and excellent team-coordinated work, based on standardized anesthesia and neurosurgical protocols.

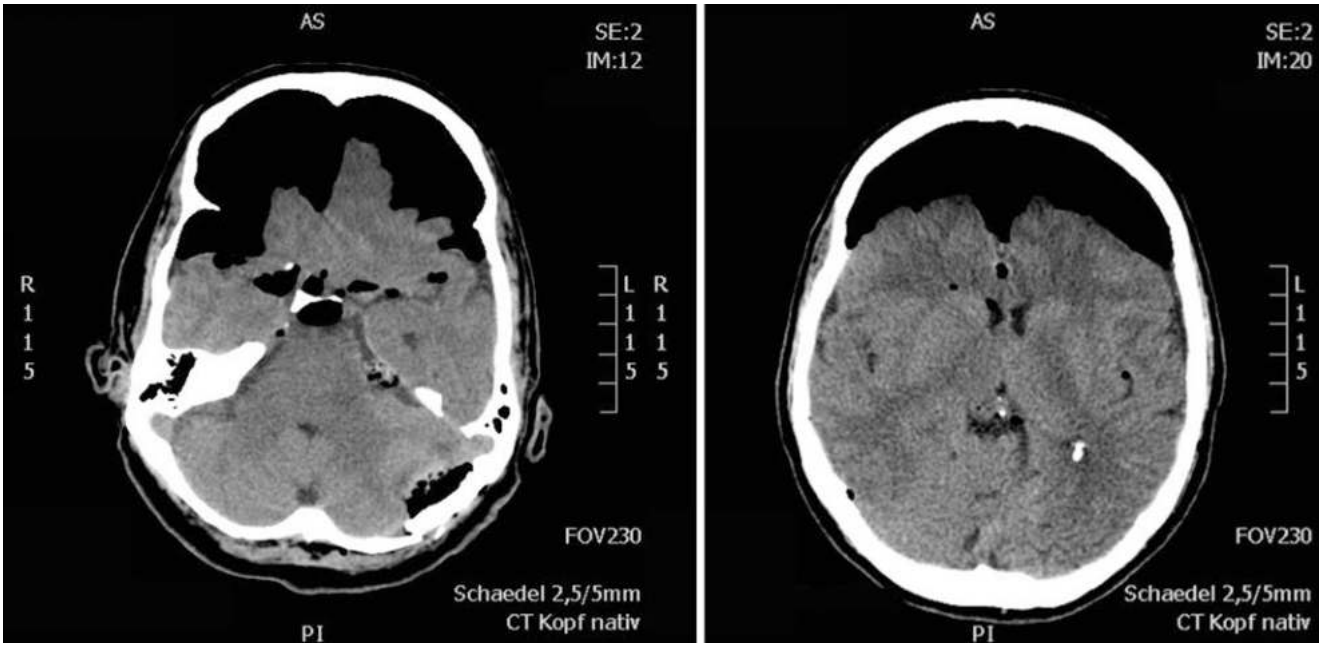

Fig. 30.4 Postoperative CT scan demonstrating a large pneumocephalus following acoustic neurinoma resection

Suggested Reading

Black S, Ockert DB, Oliver WC Jr, Cucchiara RF. Outcome following posterior fossa craniectomy in patients in the sitting or horizontal positions. Anesthesiology. 1988;69:49–56.

Fàbregas N, Bruder N. Recovery and neurological evaluation. Best Pract Res Clin Anaesthesiol. 2007;21:431–47.

Feigl GC, Decker K, Wurms M, Krischek B, Ritz R, Unertl K, Tatagiba M. Neurosurgical procedures in the semisitting position: evaluation of the risk of paradoxical venous air embolism in patients with a patent foramen ovale. World Neurosurg. 2014;81(1):159–64.

Gracia I, Fàbregas N. Craniotomy in sitting position. Curr Opin Anaesthesiol. 2014;27(5):474–83.

Schott M, Thuermer G, Jantzen JP. VAE associated with neurosurgery in the semi-sitting position does not affect outcome. Retrospective analysis of 793 cases. J Neurosurg Anesthesiol. 2013;25:459.

Smith DS. Anesthetic management for posterior fossa surgery. In: Cottrell J, Young WL, editors. Cotrell and young's neuroanesthesia. 5th ed. Philadelphia: Mosby; 2010. p. 203–17.

von Gösseln HH, Samii M, Suhr D, Bini W. The lounging position for posterior fossa surgery: anesthesiological considerations regarding air embolism. Childs Nerv Syst. 1991;7:368–74.

31 Perioperative Challenges During Surgical Evacuation of Subdural and Epidural Hematomas

Walter M. van den Bergh, Anthony R. Absalom, and Olaf L. Cremer

Overview

Following head injury, blood may accumulate between the inner surface of the skull and the dura mater (epidural hematoma, EDH – Fig. 31.1), between the dura and the arachnoid mater (subdural hematoma, SDH – Fig. 31.2), in the subarachnoidal space, or within the brain parenchyma itself (hemorrhagic contusions and intracerebral hematomas). Although the findings in individual patients can vary significantly, some characteristics that are considered "typical" for the presentation of patients with acute EDH, acute SDH, and chronic SDH are summarized in Table 31.1. Details of the presentation and management of patients with traumatic subarachnoidal or intraparenchymal hemorrhage are covered elsewhere in this book.

While some intracranial hematomas (e.g., those with a maximum diameter <10 mm and not causing a change in consciousness) can be managed conservatively by careful monitoring, many intracranial hematomas will compress the underlying brain, causing volume shifts and clinical deterioration, and thus require urgent surgical decompression. The prognosis in such patients depends critically on the extent of primary neurological damage and the timing of surgery. It is also influenced by the occurrence of secondary neurological injury during the ensuing hours and days and the severity of injuries to other organs.

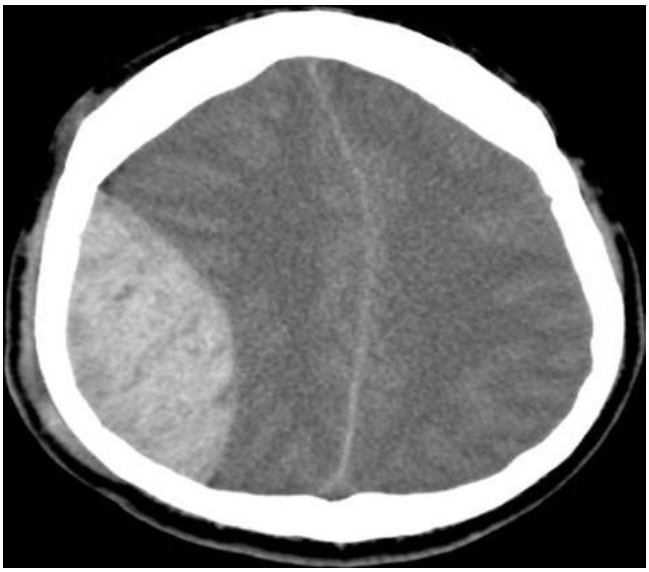

Fig. 31.1 Epidermal hematoma

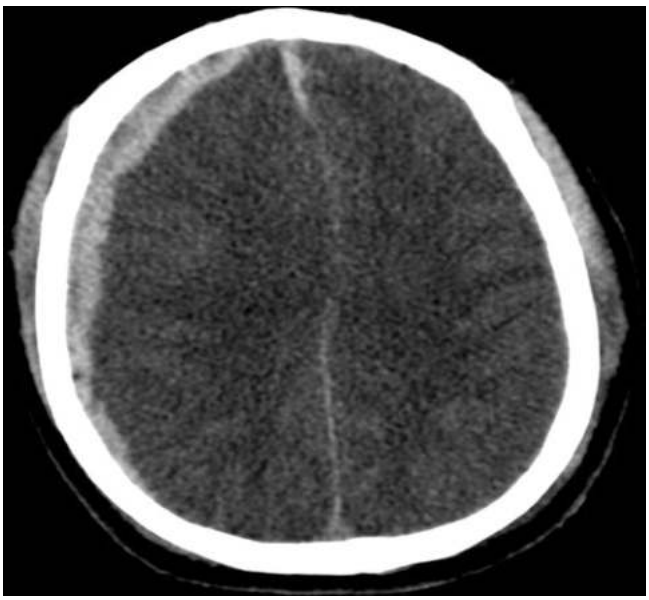

Fig. 31.2 Subdural hematoma

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Risks

The injured brain is extremely vulnerable to systemic insults that contribute to secondary injury, such as arterial hypotension, hypoxemia, hypercapnia and hypocapnia, hyperglycemia, coagulopathy, and pyrexia. Perioperative management should, therefore, be primarily directed toward timely surgical management and avoidance or reversal of secondary derangements that are associated with poor neurological outcome. Among these, the common problems that may occur prior to or during evacuation of acute SDH and EDH include:

- Raised intracranial pressure and brain swelling
- New or recurrent bleeding
- Neurogenic pulmonary edema (NPE)
- Perioperative seizure
- Sudden arterial hypotension upon opening of the dura

The perioperative management of a *chronic* SDH is less complicated, and satisfactory outcomes are usually easier to achieve than with acute intracranial bleeding. This topic will not be further discussed in this chapter.

Raised Intracranial Pressure and Brain Swelling

Prevention

Early assessment, intubation, and resuscitation of patients with severe traumatic brain injury should be performed according to generally accepted trauma life support principles. If clinical signs of intracranial hypertension are present or if the head CT scan shows evidence of mass lesions with midline shift or obliteration of the basal cisterns, urgent craniotomy may be indicated.

During induction of anesthesia and endotracheal intubation, care must be taken to maintain adequate cerebral perfusion while preventing inadvertent increases in ICP. The following considerations apply:

- Take precautions against the risk of aspiration – perform a rapid sequence induction (RSI). In modern practice a modified RSI technique is commonly performed and may be associated with better outcomes than a traditional RSI.
- Careful choice of hypnotic. Each induction agent has advantages and disadvantages, and no single drug is clearly contraindicated. Use a familiar agent (experience

Table 31.1 Etiology, typical findings, and mortality of epidural and subdural hematomas

Type	Etiology	Associations	Presentation patterns	Neurologic findings	Mortality
Epidural, acute	Middle meningeal artery rupture	Young age	18%: brief loss of consciousness with lucid interval followed by sudden deterioration (minutes to hours)	84%: lethargy, headaches, nausea	20–60%
		High-velocity trauma		50%: ipsilateral mydriasis	
	Venous bleeding from fractured cranial bone	85%: cranial bone fracture		62%: contralateral hemiparesis	
			35%: immediate loss of consciousness with rapid, progressive deterioration	Coma	
Subdural, acute	Shearing of bridging veins	All ages	Immediate loss of consciousness	Focal deficits (associated with brain contusions)	50%
		High-speed rotational or linear acceleration–deceleration injury	Subacute loss of consciousness (within minutes to hours)	Cardiorespiratory instability (associated with brain stem lesions)	
		Underlying brain contusion and/or brain stem injury	Cerebral contusion produces focal symptoms		
			Brainstem damage (60%) resulting in respiratory disorders and pulse and systemic blood pressure fluctuations	Acute psychosis or disorientation	
				Seizures	
			Acute psychotic manifestations and disorientation for varying periods of time	Coma	
			Convulsive seizures (25%) (late complications)		
Subdural, chronic	50%: spontaneous or only minimal trauma	Elderly and alcoholics with brain atrophy	Insidious onset of symptoms (days to weeks)	Altered mental status	<20%
		Anticoagulant use		Headache	
				Focal deficits	
				Reduced level of consciousness	

with thiopental is dwindling). In hemodynamically unstable patients, etomidate 0.1–0.2 mg/kg may be preferable.
- Consider administration of an analgesic (such as fentanyl 1.5 mcg/kg) as part of a modified RSI. Without an analgesic a larger dose of hypnotic is needed to attenuate the stress response to intubation, but this can be accompanied by subsequent hypotension after intubation. A modest dose of an analgesic can help optimize hemodynamic stability by reducing the hypnotic dose requirement while still attenuating the stress response during laryngoscopy and intubation.
- For rapid sequence induction, succinylcholine (1.5 mg/kg) has traditionally been the drug of choice, but this has been associated with transient increases in ICP and serum potassium. Rocuronium (1.0–1.2 mg/kg) is a suitable alternative.
- Lidocaine spray applied to the vocal cords may help avoid coughing during and after intubation.

During maintenance of anesthesia (as well as during continued sedation in the emergency room or intensive care unit), the anesthesiologist must aim to attenuate rises in intracranial pressure and minimize ischemic–hypoxic brain injury. The following considerations apply:

- Maintain adequate depth of anesthesia. Propofol is usually the agent of choice. If volatile agents are used, bear in mind that doses above 1 MAC can increase intracranial pressure by causing cerebral vasodilation.
- Administer adequate analgesia. If early extubation is likely, consider the use of remifentanil. If not, and particularly if there are concomitant injuries, then longer-acting analgesics may be used.
- Maintain adequate cerebral perfusion pressure (CPP): since ischemia due to low CBF occurs predominantly in the first hours after injury, it may be sensible to aim for a CPP 60–70 mmHg during this phase, whereas a CPP target >50 mmHg seems acceptable on ensuing days if cerebral hyperemia prevails. Avoid systolic blood pressure <90 mmHg at all times.
- If spontaneous arterial hypertension ensues despite adequate levels of anesthesia and analgesia, this may represent sympathetic activation in a setting of raised ICP. It is thus advisable to accept hypertension within reasonable limits (e.g., allow MAP increase up to 130 mmHg) until surgical decompression has been obtained.
- Maintain strict normocarbia. If metabolic acidosis is present, adjust ventilator settings to preserve normal pH.
- Maintain normothermia. Aggressively treat pyrexia >37.5–38.0 °C at all times, since it can worsen neurological injury.
- Maintain normoxia. Avoid SaO_2 <90% at all times.
- Maintain head-up position (30°) unless hemodynamic instability is present.
- Prevent jugular venous outflow obstruction (neutral head position, avoid neck compression).
- Do not administer hypotonic fluid solutions (preferably use 0.9% or hypertonic saline for IV fluid resuscitation).
- Avoid coughing and bucking by a combination of adequate anesthesia and analgesia (opioids have antitussive effects), muscle relaxation, and avoidance of unnecessary endotracheal suctioning.
- Avoid shivering (avoid hypothermia, if necessary administer muscle relaxants).

Crisis Management

Cerebral swelling and edema following brain injury may result from intracellular fluid accumulation (cytotoxic edema), fluid extravasation (vasogenic edema), hyperemia/vascular engorgement (vasodilatation), or, rarely in the context of EDH and SDH, an obstruction of cerebrospinal fluid outflow. Thus, the underlying causes of swelling of brain tissues are cellular energy failure, inflammation, and blood–brain barrier disruption. After evacuation of a SDH, profound edema of the ipsilateral hemisphere may occur because a sudden reduction in ICP can cause an associated abrupt increase in the transmural capillary pressure gradient, which promotes the development of hydrostatic edema.

Table 31.2 lists various recommendations for crisis management of intracranial hypertension. Hyperventilation should only be used as a temporary measure in the case of impending herniation, as hypocapnia-/alkalosis-induced vasoconstriction may aggravate cerebral ischemia. Furthermore, ICP-lowering effects during sustained hypocapnia are only transient (lasting 4–12 h), as compensatory reductions in cerebral extracellular bicarbonate levels will restore pH over time. The success of hyperosmolar therapy (e.g., mannitol) depends on preserved blood–brain barrier function. If the latter is seriously compromised (e.g., in areas of contusion or hemorrhage), osmotic agents may enter the interstitial space, where they can produce reverse osmotic shifts and cause "rebound" intracranial hypertension. Mannitol has traditionally been administered as repeated 0.25–1 g/kg bolus infusions. In critical cases, it can be combined with a loop diuretic, but care must be taken to maintain normovolemia. Hypertonic saline is an alternative osmotic agent that is also useful for early fluid resuscitation in hypovolemic trauma patients and may be particularly effective in cases of refractory intracranial hypertension. It is important to stress that steroids are not recommended for the treatment of posttraumatic cerebral edema and may be associated with increased mortality.

Although drugs may cloud recovery and impair reflexes, it is crucial that an absent pupillary light reflex should never be attributed to drugs alone but should always instigate further examination.

Table 31.2 Management of raised intracranial pressure and brain swelling

Clinical findings	Patient assessment	Intervention/treatment
Decreased level of consciousness	Standard hemodynamic and respiratory monitoring	Increase depth of anesthesia (consider additional bolus administration of propofol or barbiturate)
Pupillary asymmetry	Intra-arterial pressure monitoring	
Focal or lateralizing neurological signs	Consider need for central venous access and CVP monitoring	Vasopressors and fluid loading to maintain adequate CPP
Hemodynamic instability	Order laboratory studies	
	Arterial blood gas analysis	
Hypertension–bradycardia	Sodium or osmolality	Hypertonic solutions
	Coagulation studies	Saline 2.9–7.5% as a 150–300 cc bolus
	If available use ICP monitoring with intraparenchymal probe or ventriculostomy to allow venting of CSF	Mannitol 20% 0.25–1 g/kg bolus infusion
		Maintain serum osmolality <320 mOsm/L
		Hyperventilation
		Target pH ~7.50
		Hyperventilation is only temporarily effective and may worsen cerebral ischemia
		If jugular venous oximetry is available maintain $SjvO_2$ >55%

Uncontrolled or Recurrent Bleeding

A postoperative hematoma is present in approximately 50% of patients who show clinical deterioration *within 6 h* of craniotomy. However, please note that up to 20% of postoperative hematomas may develop more than 1 day after the procedure, especially in the cases following emergency surgery.

Risk factors for recurrent bleeding include:

- Intraoperative or immediate postoperative hypertension (within 12 h)
- Intraoperative blood loss > 500 mL
- Age > 70 years
- Hypoxia and hypercapnia
- Coughing
- Increased prothrombin time, low-fibrinogen level, low-platelet count

Prevention

One of the most effective ways to reduce the risk of perioperative bleeding complications is by strict blood pressure management. Patients with hypertension are 3.6 times more likely to develop recurrent than matched controls. Moreover, the risk of postoperative intracranial hemorrhage is strongly associated with patients being normotensive intraoperatively but hypertensive postoperatively. In the postoperative period, systolic blood pressure is, therefore, commonly managed in the range of 120–150 mmHg. Short-acting intravenous antihypertensive drugs are generally preferable (e.g., labetalol, a mixed α- and β-antagonist, or urapidil, a selective α1-antagonist that does not cause reflex tachycardia). Other measures to reduce the risk of bleeding include:

- Avoid jugular venous obstruction.
- Maintain head-up position (e.g., 30°).
- Prevent hypothermia (keep temp >35 °C).
- Order coagulation studies and maintain:
  - Hb >6 mmol/L or >7 g/dL
  - (Activated) prothrombin time <1.5 × reference
  - Platelets > 50×10^9/L
  - Fibrinogen > 0.8 g/L or >150 mg/dL
  - Ionized Ca^{++} > 1.0 mmol/L
- Antagonize anticoagulants as appropriate.
- Minimize stress during recovery from anesthesia:
  - Maintain body temperature > 36.5 °C to prevent shivering.
  - Prevent and manage pain.

Crisis Management

Treat hypertension aggressively in all cases of intraoperative or immediate postoperative bleeding, but do not over-treat: maintain a minimally acceptable CPP of 50–70 mmHg in the face of elevated ICP (invasive arterial BP measurements are recommended) (Table 31.3). Labetalol is most widely used, but urapidil is also gaining popularity. A continuous infusion of the calcium channel blocker nicardipine may be useful for rapid titration.

Neurogenic Pulmonary Edema

Prevention

In patients with acute traumatic brain management of uncontrolled or recurrent bleeding injury, impaired pulmonary function due to neurogenic pulmonary edema (NPE) is a common complication (>50% of patients will develop NPE to some extent). The mechanisms leading to NPE are poorly

understood but are probably related to a massive sympathetic adrenergic discharge at the time of injury, which results in increased pulmonary microvascular hydrostatic pressures and increased capillary permeability. Alpha-adrenergic blockade (e.g., with phentolamine) prevents the formation of NPE in an experimental setting, but no specific measures are known to be beneficial in the clinical situation.

Crisis Management

Treatment must be focused on the underlying disorder. As NPE resolves within 48–72 h in the majority of affected patients, management can be supportive. Mechanical ventilation is necessary in the majority of patients to assure adequate oxygenation and ventilation. To prevent iatrogenic lung injury, a ventilation strategy is used, involving tidal volumes between 5 and 8 mL/kg (ideal body weight) to avoid excessively high inflation pressures and positive end-expiratory pressure (PEEP) to prevent atelectasis. High levels of PEEP may be required to treat severe hypoxemia. Caution is advised, however, since high levels of PEEP can compromise cerebral venous return and increase intracranial hypertension. For the same reasons, the peak inspiratory (plateau) pressure should be kept below 30–35 cm water, and normocapnia should be maintained to avoid further increases in intracranial pressure. Several pharmacological agents such as alpha-adrenergic antagonists, beta-adrenergic blockers, and chlorpromazine are advocated by some authors, but assessment of their effectiveness is difficult because NPE is usually a self-limiting condition that recovers spontaneously (Table 31.4).

Table 31.3 Management of uncontrolled or recurrent bleeding

Clinical findings	Patient assessment	Intervention/treatment
60%: decreased level of consciousness	Order coagulation studies:	Treat arterial hypertension
		Maintain temp >35 °C
90%: elevated ICP (when monitored)	Prothrombin time	Give packed red cells
		Give plasma
Focal findings	Platelets	Give platelets
	Hb	Maintain ionized calcium >1.0 mmol/L
	Fibrinogen	Consider prothrombin complex concentrate (PPSB)
	Ca^{2+}	
		Consider desmopressin (DDAVP) 0.3 μg/kg
		Consider coagulation factor concentrates
		Consider use of controlled hypotension

Seizures

Prevention

In the absence of anti-epileptic prophylaxis, the incidence of early posttraumatic seizures varies between 4% and 25%. The presence of either an acute EDH or SDH is a risk factor for developing posttraumatic seizures. Anticonvulsant drug therapy may be used to decrease the incidence of posttraumatic seizures (within 7 days of injury). However, the occurrence of early posttraumatic seizures by itself is not associated with worsened outcomes, and anticonvulsants have been associated with adverse effects. Most clinicians administer a loading dose of phenytoin, valproic acid, or levetiracetam (over 20–30 min) followed by a daily maintenance dose only if seizures have been witnessed or are suspected to have occurred after injury. If no further seizures occur, taper and discontinue the anticonvulsant after 1 week.

Crisis Management

Airway management is critical to avoid exacerbating status epilepticus through hypoxia. If endotracheal intubation under neuromuscular blockade is necessary, use a non-depolarizing agent such as rocuronium (1.0–1.2 mg/kg for rapid sequence induction). Bear in mind that as muscle relaxation will obscure the motor signs of seizure activity, EEG monitoring may be needed to confirm effective seizure control. Give a benzodiazepine such as lorazepam 0.2 mg/kg, and repeat every 5 min as necessary. Consider an intravenous loading dose of an anticonvulsant (such as phenytoin 15–20 mg/kg or levetiracetam 1000 mg) at the same time. If status epilepticus persists, give midazolam with a loading dose of 0.2 mg/kg followed by an infusion of 0.2–2.0 mg/

Table 31.4 Management of neurogenic pulmonary edema

Clinical findings	Patient assessment	Intervention/treatment
Onset within minutes to hours following trauma	Order laboratory studies (including arterial blood gas analysis)	Maintain adequate level of sedation
		Treat intracranial hypertension
Sudden onset of dyspnea		Start mechanical ventilation using adequate PEEP to keep the lung open
	Order chest X-ray	Consider ventilation with TV less than 6 mL/kg of predicted body weight might
Mild hemoptysis	Assess need for mechanical ventilation	
Protein-rich pulmonary edema		Consider head of bed elevation
		Consider use of diuretics (treat hypervolemia)
		Consider the use of intravenous alpha-/beta-adrenergic receptor antagonists (phentolamine, labetalol, esmolol)

Table 31.5 Management of seizures

Clinical findings	Patient assessment	Intervention/treatment
Tonic–clonic convulsions	Check airway, breathing, and circulation	Secure airway (if applicable)
Loss of consciousness (no convulsions may be apparent)		Increase FiO_2
	If the patient's head is immobilized in pins, ensure safety	Give lorazepam 0.2 mg/kg IV, (repeat as necessary)
		Give phenytoin 20 mg/kg loading dose IV
		Consider additional agents as required (propofol, barbiturates)

kg/h, or administer propofol 2–3 mg/kg as a bolus followed by 1–15 mg/kg/h to achieve seizure control. Should the seizures not be controlled with propofol, administer pentobarbital 20 mg/kg at 0.2–0.4 mg/kg/min as tolerated, followed by an infusion of 0.25–2.0 mg/kg/h as determined by EEG monitoring. The administration of volatile anesthetics can be considered as a last resort to control intractable seizure activity in emergency situations (Table 31.5).

Sudden Arterial Hypotension Upon Opening of the Dura

Prevention

During all neurosurgical procedures, the anesthetist should aim for normovolemia and maintenance of adequate cerebral perfusion. Prior to dural opening, hypovolemia may be masked by the physiological (sympathetic) responses to intracranial hypertension. Dural opening can cause an abrupt decline in ICP and cause sudden arterial hypotension. The following considerations apply:

- Always ensure large bore venous access.
- Frequently check the operative status; communicate with the surgeons. Ideally the surgeon should warn the anesthesiologist when dural opening is imminent.
- Consider fluid loading before decompression occurs.
- Have vasopressors on standby.

Crisis Management

Hypotonic fluid administration should be avoided, although modest volumes (1–3 L) of lactated Ringer's are acceptable. When larger volumes are needed, a combination of isotonic crystalloids (e.g., 0.9% saline) and blood products (if indicated) is preferred. Hypertonic saline is useful when there is both arterial hypotension and intracranial hypertension. Circulatory support should be provided to maintain

Table 31.6 Management of arterial hypotension during opening of the dura

Clinical findings	Patient assessment	Intervention/treatment
Sudden arterial hypotension	Consider volume status	Give fluids
Sudden tachycardia	Order laboratory studies	Consider vasopressors
Decrease of end-tidal CO_2	Hb/Ht	Avoid excessive depth of anesthesia
	Sodium or osmolality	

CBF. Bear in mind that agents that are pure vasoconstrictors may decrease cardiac output and that recent evidence suggests that this can have detrimental effects on cerebral blood flow and oxygenation. For this reason noradrenaline (which has also some beta-adrenoreceptor activity) may have advantages over pure α-agonists such as phenylephrine. Patients with poor myocardial reserve are likely to also require an agent with inotropic properties, such as dopamine, dobutamine, or (nor)epinephrine (Table 31.6).

Key Points

- The prevention of complications is easier than their treatment.
- Maintain good communication between all team members.
- Maintain blood pressure, temperature, coagulation status, electrolytes, and arterial blood gases within their normal ranges.
- Maintain CPP between 50 and 70 mmHg if ICP monitoring is available; avoid systolic blood pressure <90 mmHg at all times.

Suggested Reading

Brain Trauma Foundation, American Association of Neurological Surgeons, Congress of Neurological Surgeons. Guidelines for the management of severe traumatic brain injury. J Neurotrauma. 2007;24(Suppl 1):S1–106.

Maas AI, Stocchetti N, Bullock R. Moderate and severe traumatic brain injury in adults. Lancet Neurol. 2008;7(8):728–41.

Meng L, Hou W, Chui J, Han R, Gelb AW. Cardiac output and cerebral blood flow: the integrated regulation of brain perfusion in adult humans. Anesthesiology. 2015;123(5):1198–208.

Perry JJ, Lee JS, Sillberg VAH, Wells GA. Rocuronium versus succinylcholine for rapid sequence induction intubation. Cochrane Database Syst Rev. 2008;(2):CD002788. https://doi.org/10.1002/14651858.CD002788.pub2.

Perioperative Challenges During Cerebrovascular Surgery

32

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Overview

The challenges of perioperative management of cerebrovascular cases arise from the unique anesthetic and critical care requirements as well as the complex pathophysiology of the cerebrovascular system. We focus on the most common and challenging cases, which include aneurysm repair, arteriovenous malformation (AVM) resection, and cerebrovascular bypass surgery.

- Aneurysm repair:
  - Surgical procedure: clip placed across neck of aneurysm to exclude aneurysm from blood flow, thereby preventing rupture
  - Indications:
    (a) Any ruptured aneurysm
    (b) Symptoms from mass effect
    (c) Elective surgery for unruptured aneurysms:
      - Incidental aneurysms >6 mm in the anterior circulation (except posterior communicating artery: PCOM)
      - Any size of aneurysm of the PCOM or posterior circulation
      - Any aneurysm in a patient with a history of ruptured aneurysm or a strong family history of subarachnoid hemorrhage (SAH)
- AVM resection:
  - Surgical procedure: clips placed across feeding vessels and AVM nidus excised
  - Indications:
    (a) AVMs are generally resected if risk of surgery is acceptable, based on the quality of the individual surgeon, location of the AVM, and the pattern of arterial feeders and venous drainage.
    (b) Prior symptomatic bleeding in past (annual risk of bleeding is substantially increased).
- Cerebral bypass surgery:
  - Extracranial-intracranial (EC-IC) bypass surgery:
    (a) Surgical procedures:
      - Donor vessels: superficial temporal (STA), occipital (OA), or proximal external carotid (ECA) arteries
      - Recipient vessels: middle cerebral (MCA), anterior cerebral (ACA), posterior cerebral (PCA), superior cerebellar (SCA), posterior inferior cerebellar (PICA) arteries
      - Anastomosis:
        1. Direct: donor ECA vessel sewn directly to branch intracranial vessel
        2. Indirect:
           - Donor ECA vessel sewn to pial surface
           - Over time, collateral circulation forms, connecting ECA vessel to intracranial circulation

    (b) Indications:
      - High-grade stenosis or occlusion of the internal carotid artery (ICA), MCA, PCA, or basilar artery in patients with demonstrated inadequate cerebral reserve (hemodynamic stroke, diamox CT or MR perfusion studies, PET)
      - Moyamoya disease
  - Adjunct to aneurysm repair or skull base tumor resection:
    (a) Surgical procedures:
      - EC-IC bypass, as above.

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- Direct bypass from one major intracranial vessel to another; choice of graft depends on flow characteristics.
  1. Low flow: generally use STA, OA, or ECA (used for M3-branches of MCA)
  2. Intermediate flow: radial artery or saphenous (used for P2 or M2-branches of MCA)
  3. High flow: large caliber saphenous vein graft (used for M1/M2 branches of MCA or for ICA bypass)

(b) Indications:
- Preservation of blood flow via the bypass when aneurysm clipping requires sacrifice of a critical portion of a cerebral blood vessel.
- Tumors encasing or invading major arteries at the skull base; bypass allows adequate distal cerebral blood flow (CBF).

– Transposition of vertebral artery: used for patients with symptomatic vertebral artery stenosis at origin

Prevention of Complications

The most feared perioperative complications are as follows:

- Intracranial hemorrhage from an unsecured vascular malformation (cerebral aneurysm or AVM) prior to definitive surgical treatment.
- Ischemic stroke from inappropriate cerebral perfusion during surgery, a complication that cannot be reliably detected because the patient is under anesthesia and the neurologic exam is unavailable.
- Complications from increased or rapidly decreased ICP.
- Retraction injury (particularly in skull base surgeries), which may result in cerebral edema, ischemia, or hemorrhage; this type of injury may be mitigated by interventions to "relax" the brain tissue, by reducing total brain tissue or CSF volume.

Based on these major complications, the basic goals for the prevention of perioperative complications during cerebrovascular surgery are as follows:

- Prevent aneurysm/AVM rupture
- Maintain cerebral perfusion pressure (CPP) and CBF
- Control ICP and decrease brain tissue volume ("brain relaxation") to improve surgical approach/visualization

It is important to keep in mind that CBF and ICP are affected by cerebral autoregulation, partial pressure of carbon dioxide ($PaCO_2$), partial pressure of arterial oxygen (PaO_2), cerebral metabolic rate ($CMRO_2$), and anesthetic agents.

General considerations for prevention:

- Controlled induction and maintenance of anesthesia
  - Adequate doses of opioids to prevent hemodynamic response to laryngoscopy and endotracheal tube placement (e.g., 3–7 mcg/kg of fentanyl); lidocaine IV can also be used as an adjunct.
  - Use esmolol during induction to prevent blood pressure spikes.
  - Additional doses of opioids or hypnotic drugs to deepen anesthesia during placement of head pins.
  - When practical, avoid succinylcholine in patients with high ICP.
- Choice of anesthetic agents:
  - Many anesthesiologists currently advocate for a combination of IV hypnotics and volatile anesthetics in order to control unwanted side effects and benefit from certain pharmacodynamic characteristics; others advocate for total IV anesthesia using propofol.
  - In patients with known or suspected elevated ICP, volatile anesthetics should be limited or avoided entirely in favor of short-acting intravenous medications, typically propofol in combination with short-acting opioids. Alternatively, the use of propofol with sub-MAC doses of desflurane has been shown to improve brain tissue oxygenation while maintaining low ICP.
  - Volatile anesthetic agents disrupt cerebral autoregulation, reduce $CMRO_2$, are potent vasodilators, and increase ICP. Sevoflurane better preserves cerebral autoregulation and has the least effect on CBF and ICP; high doses of sevoflurane or isoflurane will lower the seizure threshold.
  - Propofol and thiopental reduce CBF, suppress $CMRO_2$, and reduce ICP. Benzodiazepines and opioid medications have the same effect but to a lesser degree.
  - While etomidate also reduces CBF and reduces $CMRO_2$, it is associated with exacerbation of cerebral ischemia and should be avoided.
  - Nitrous oxide increases CBF and $CMRO_2$ and may exacerbate pneumocephalus. It should be avoided.
  - Ketamine increases $CMRO_2$ and CBF and has traditionally been avoided in cerebrovascular surgery.
- Ventilation:
  - $EtCO_2$ monitoring should always be performed and used to manage the pCO_2 levels throughout surgery.
  - Check ABG regularly during surgery to correlate $EtCO_2$ with pCO_2.
  - Mild hyperventilation (pCO_2 30–35 mmHg) is indicated in patients with suspected or known increased ICP for "brain relaxation" (1–3) to counteract cerebrovascular vasodilation caused by volatile anesthetics.

  - There is a linear correlation between CBF and $PaCO_2$ for $PaCO_2$ values between 20 and 80 mm Hg; a 1 mmHg change in $PaCO_2$ results in a 3–4% change in CBF.
  - Excessive ($PaCO_2$ <30 mmHg) and prolonged hyperventilation may result in cerebral ischemia.
- Enhanced surgical access:
  - Mannitol 50–75 g (0.5–1 g/kg) or 3% hypertonic saline 250 ml given prior to surgical incision for "brain relaxation"; particularly during opening of the dura, careful titration of osmotherapy and its effects on blood pressure (mannitol may decrease blood pressure; hypertonic saline may increase it) is necessary in patients with unsecured cerebral malformations in order to maintain a stable aneurysmal transmural pressure gradient and prevent rupture.
  - Use of CSF diversion via ventriculostomy, lumbar drain, or direct CSF drainage via craniotomy.
- Positioning:
  - If possible, keep head at least 20 cm above heart to prevent decreased venous outflow from the brain and elevated ICP.
- Bleeding:
  - Although rare, massive and rapid blood loss can occur during surgical manipulation of cerebral blood vessels.
  - It is, therefore, essential to have adequate vascular access and blood products available.
- Monitoring:
  - Cerebrovascular surgeries should be monitored using ASA standard monitoring plus invasive arterial blood pressure (placed prior to induction, if not too stimulating for the patient) and urine output measurement.
  - Central venous access should be considered for cerebral venous pressure (CVP) monitoring, for hemodynamic management, and for fluid resuscitation, particularly in patients who are at high risk of vasospasm requiring subsequent hypertensive therapy. Although subclavian access is associated with higher frequency of pneumothorax, it may be preferable in patients with high intracranial pressure to maintain optimal cerebral venous return and may be associated with lower frequency of catheter-associated bloodstream infections.
  - In patients with ruptured aneurysms or AVM, ICP monitoring with an external ventricular drain allows for both ICP measurement and CSF removal. It is very important to ensure that ICP monitors are closed prior to position changes and subsequently leveled with respect to the patient's tragus in order to prevent over- or underdrainage of CSF.
  - Electrophysiological intraoperative monitoring:
    (a) Somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), brainstem auditory evoked potentials (BAEPs), and electroencephalography (EEG) are the most commonly used modalities.
    (b) May allow for early detection of ischemia.
    (c) Anesthetic used should be tailored to allow for intraoperative monitoring:
      - The use of >1 MAC of volatile anesthetic agents drastically decreases SSEPs, MEPs, and BAEPs. While at lower concentrations (<0.5 MAC) the effect should be minor, these agents may still interfere with readings, especially in patients with neurologic deficits.
      - Propofol and opioids have minimal effects on evoked potentials at typical doses. However, high doses and bolus administration of propofol do suppress MEPs and SSEPs.
      - Therefore, when monitoring is required, the use of propofol/ opioid infusions with or without a small dose of volatile anesthetic is preferred.
      - EEG monitoring does not limit the anesthetic choice.
- Fluid management:
  - Isotonic or hypertonic fluids as needed; consider high fluid and electrolyte loss secondary to osmotherapy.
  - Little evidence exists to support the use of solution containing albumin or synthetic starches, and they have been shown to be harmful in patients with traumatic brain injury.
  - As a rule, replace urine output due to osmotic diuresis with at least 0.5:1 by volume. Volume resuscitation does not have negative effects on cerebral edema as long as plasma osmolarity is preserved.
  - Dextrose-containing fluids are contraindicated for fluid management as hyperglycemia may be detrimental in the setting of brain injury.
  - Hypotonic fluids should be avoided due to the risk of exacerbating cerebral edema.
- Hemodynamic management:
  - The goal is arterial normotension (ensuring CPP >50–70 mmHg) prior to securing the aneurysm or AVM.
  - After the aneurysm or AVM is secured, the blood pressure goals are specific for each scenario and described below.
- Temperature management:
  - The IHAST randomized controlled study demonstrated no benefit of hypothermia in patients undergoing cerebral artery aneurysm surgery.
  - Likewise, hyperthermia is associated with poor outcome; hence, normothermia is usually targeted.
  - Prior to awakening, patients should be normothermic to avoid postanesthesia shivering.

- Controlled emergence:
  - Blood pressure often increases during emergence and should be controlled to baseline values.
  - Rapid emergence allows immediate neurological examination. Therefore, agents such as propofol, thiopental, and volatile anesthetics, in combination with analgesics such as remifentanil or fentanyl, which offer the potential for rapid emergence, are preferred.

In addition, specific considerations relate to particular surgical procedures:

- During repair of cerebral aneurysms:
  - Maintenance of stable transmural pressure gradient (TMPG):
    (a) TMPG = pressure within blood vessels-pressure outside = MAP-ICP.
    (b) Higher TMPG increases risk of rupture.
    (c) Therefore, marked decreases in ICP, particularly in the context of elevated arterial blood pressure, may increase the risk of rebleeding.
  - Fluid management:
    (a) Only isotonic or hypertonic fluids should be administered.
    (b) Prior to clipping, replace overnight fluid losses and maintain rate to account for hourly losses and diuresis from mannitol.
    (c) After clipping, replace intraoperative fluid loss and bolus additional fluids for goal euvolemic to mildly hypervolemic state in order to improve cerebral perfusion distal to aneurysm clipping.
  - Blood pressure management:
    (a) Hypertensive episodes may result in aneurysm rebleeding, and hypotension may result in cerebral ischemia secondary to hypoperfusion.
    (b) Prior to aneurysm clipping, maintain blood pressure in a low normal range unless significant vasospasm is present, in which case higher blood pressure goals are desirable.
    (c) After clipping, target blood pressure may be liberalized to a level slightly above baseline (improved collateral perfusion).
    (d) Propofol may result in hypotension that should be avoided or promptly corrected with the use of pressors.
  - Interventions during "temporary clipping":
    (a) Vascular clips are applied temporarily to parent artery in order to improve surgical visualization for application of permanent clip to aneurysm.
    (b) No intervention necessary if temporary clip is applied for less than 2 min.
    (c) If clip is applied for 2 min:
      - Increase FiO_2 to 100%.
      - Increase inspired concentration of desflurane (consider phenylephrine to maintain blood pressure at or above baseline level). An immediate bolus dose of barbiturates or propofol may be used instead, although convincing support from clinical studies is lacking.
    (d) If clip is applied for >10–15 min:
      - Consider slightly augmenting blood pressure to preserve perfusion via collaterals.
      - Discuss with surgical team the necessity for administration of anesthetic agents (e.g., desflurane) to induce burst suppression on EEG. In this situation, many anesthesiologists provide IV barbiturates, e.g., thiopental, or IV propofol, but the evidence from clinical studies is highly controversial regarding this practice. Recent clinical studies suggest that the combination of desflurane and propofol results in better brain tissue oxygenation than propofol alone.
      - Ischemic stunning may require postoperative management in the ICU, including continued mechanical ventilation and adequate sedation.
  - Criteria for extubation in OR:
    (a) Good preoperative level of consciousness (without sedation)
    (b) Mild brain swelling during surgery
    (c) Short period of temporary clipping
    (d) Adequate strength, demonstrated by sustained head lift, strong hand grasp, or leg lift
    (e) Awake and able to accurately follow commands
    (f) Evidence of leak at 20 cm of water pressure (or less), with the endotracheal tube cuff deflated
- During AVM resection:
  - Postoperative blood pressure management:
    (a) Elevations in blood pressure postoperatively are associated with increased bleeding from the AVM resection cavity and may exacerbate normal perfusion pressure breakthrough (edema or hemorrhage resulting from increased perfusion following removal of the AVM; discussed further below).
    (b) Aggressive postoperative blood pressure control has been shown to substantially decrease postoperative hematoma formation as well as the risk of brain edema formation.
    (c) The most vulnerable period for hematoma formation is probably during emergence from anesthesia; the risk of brain edema formation remains elevated for at least 48 h after surgery.
- Cerebral bypass procedures:
  - Patient population with inadequate cerebral blood flow and preexisting cerebral infarcts:

(a) Most likely periods of hypotension (relative or absolute) will occur during induction of anesthesia and during temporary clipping of recipient vessel. The use of pressors is recommended to avoid hypotensive events.
(b) During these time periods, arterial hypotension – even over short periods – is likely to result in watershed ischemia and subsequent cerebral infarction.

– The goal is to minimize inadequate flow in the areas of tissue at risk:
(a) During temporary clipping, either maintain or slightly augment blood pressure (up to about 20% of baseline).
(b) During ischemic time (while the artery to be bypassed is clamped and graft not yet completed), blood pressure may be augmented to 20% above baseline, and burst suppression EEG may be considered.
(c) After graft placement, blood pressure targets in the first 2–3 days should be low to normal. This will prevent graft leakage and excessive cerebral perfusion but preserve graft patency; reasonable goals are systolic blood pressure (SBP) 100–120 in normotensive individuals; SBP 120–140 (with a history of hypertension).
(d) Antiplatelet agents and intraoperative heparin are often used to preserve graft patency. For elective procedures, a common regimen is oral aspirin 325 mg per day.
(e) For emergency procedures, aspirin may be loaded as either 325 mg po (or via NGT) or 650 mg rectally.

- Interventional neuroradiology procedures.
  – Specific challenges:
  (a) Usually separate from the main OR site, resulting in difficulty accessing additional equipment and personnel.
  (b) Minimize the use of long-acting anesthetics and opioids given the generally shorter duration of most endovascular procedures and the importance of early post-procedure assessment.
  – The choice between general anesthesia and monitored sedation is dependent on the patient's clinical status, the need for limited motion during interventions, the complexity and duration of the procedure, as well as patient preference and ability to cooperate during the procedure.
  – Most endovascular diagnostic tests, as well as interventions for extracranial pathology, such as carotid or vertebral artery stents, generally do not require general anesthesia. However, interventions for intracranial pathology, including aneurysm, AVM and dAVF embolization, as well as intracranial stents, require the patient to be completely immobilized, and paralytic in addition to general anesthesia is preferred.
  – For patients undergoing MAC, small intermittent intravenous boluses of midazolam (1–2 mg) and fentanyl (25–50 μg) in combination with local anesthetic are sufficient in most cases.
  – Invasive hemodynamic monitoring is sometimes required for INR procedures:
  (a) Hemodynamic management of patients with intracranial vascular lesions, hemorrhage, or stroke.
  (b) During treatment of cerebral vasospasm, balloon angioplasty may cause hypertensive episodes, while intra-arterial injection of vasodilators may lead to hypotension.
  (c) After placement of carotid or other intravascular stents, blood pressure must be strictly controlled to avoid hypertension and intracranial hemorrhage. Blood pressure parameters are dependent on the patient's pre-procedural baseline but are commonly <120 or <140 mmHg.
  – The administration of anticoagulation during the procedure must be clearly communicated and recorded.
  – Electrophysiological intraprocedural monitoring may be used for certain endovascular procedures such as aneurysm embolization:
  (a) Somatosensory evoked potentials (SSEPs), motor evoked potentials (MEPs), brainstem auditory evoked potentials (BAEPs), and electroencephalography (EEG) are the most commonly used modalities.
  (b) May allow for early detection of ischemia.
  (c) Anesthetic used should be tailored to allow for intraprocedural monitoring in a similar manner to cerebrovascular OR cases.

Crisis Management

During cerebrovascular surgery, certain complications may rapidly result in a life-threatening crisis, which require immediate intervention. The most critical are (1) acute rise in ICP and impending brain herniation; (2) CSF overdrainage; (3) seizures; (4) intracranial hemorrhage; and (5) stroke.

- Elevated ICP compromises CBF and increases the risk of intraoperative brain swelling after durotomy.
  – Elevate head of bed.
  – Check for venous outflow obstruction at the internal jugular vein (e.g., tape around neck for securing an endotracheal tube, head turning).
  – Drain additional CSF if drain in place.
  – Mild hyperventilation (arterial pCO_2 30–35).

  - Avoid hypoxemia (PaO_2 <50 mmHg drastically increases CBF and ICP).
  - Administer osmolar therapy (mannitol 0.5–2 g/kg, hypertonic saline 3% 250 ml, or hypertonic saline 23.4% 30 ml). Furosemide is often used in combination with mannitol.
  - Switch from volatile agents to total intravenous anesthesia (e.g., propofol + fentanyl) at high doses.
  - Consider thiopental bolus 1 g ± infusion 4–5 mg/kg/h (or adequate doses of propofol) to reach burst suppression EEG.
- CSF overdrainage in patients with external ventricular drain (EVD) or lumbar drain.
  - Overdrainage of CSF can lead to downward herniation.
  - If suspected, immediately clamp EVD or lumbar drain.
  - Consult with neurosurgeon regarding need for intrathecal instillation of saline.
- Seizure.
  - Perioperative seizure may occur with any type of intracranial surgery.
  - If prolonged seizures are suspected at any time during the perioperative period, treat with lorazepam 0.05–0.1 mg/kg, and load with a longer-acting medication (fosphenytoin (20 PE/kg), levetiracetam (1000–1500 mg), or valproate (20 mg/kg)).
  - If seizures continue despite the above measures, patient should be immediately intubated and begun on high-dose propofol or midazolam infusion; seizures during surgery are extremely rare and require deepening of anesthesia. In the anesthetized and paralyzed patient, seizures should be considered if the patient demonstrates significant hypertension that cannot be attributed to surgical stimulation.
  - Subclinical seizures and nonconvulsive status are an important differential diagnosis when the patient fails to wake up after brain surgery.

Some high-risk complications are specific for particular types of cerebrovascular surgeries and require specific interventions.

In patients undergoing aneurysm repair:

- Intraoperative or intraprocedural aneurysm rupture:
  (a) Risk:
    - About half of the aneurysms tear or rupture while the clip is placed; this usually does not result in substantial blood loss.
    - The risk of perioperative rupture without immediate access to the aneurysm by the surgeon (i.e., during induction or during preparation) is about 11% in patients with previously ruptured aneurysms (i.e., status post SAH) and 1% in elective cases (previously unruptured aneurysm).
    - In 8% of cases in which intraoperative rupture occurs without immediate access to the source of bleeding, hemorrhagic shock results (<1% of total surgeries).
    - The risk of intraprocedural rupture during coil embolization of intracranial aneurysms is 1–5% and is higher in ruptured aneurysms than in elective cases.
  (b) Intervention: aggressive transfusion of blood products and reversal of anticoagulation:
    - Patients should have at least two large-bore intravenous lines and an a-line to allow for efficient resuscitation.
    - For interventional procedures, 50 mg protamine sulfate should be administered I.V. after discussion with the interventional team.
  (c) Blood pressure goals during intraoperative rupture are controversial, and communication with surgeons is essential:
    - If control of bleeding cannot be immediately accomplished, permissive arterial hypotension (MAP 40–60) may facilitate hemostasis (frequently clipping of aneurysm or temporary clipping of the parent artery is delayed in this situation secondary to poor visualization or completion of coil embolization).
    - Even if arterial hypotension is the goal, fluid resuscitation should target euvolemia.
    - Once temporary or definitive clips are applied or coil embolization is completed:
      1. Consider thiopental and hypothermia to decrease metabolic demand.
      2. Consider blood pressure augmentation MAP 70–90 for increased collateral circulation.
      3. An emergent EVD may be needed in this situation, if no drain has been previously placed.
    - In patients with significant vasospasm or elevations in intracranial pressure, blood pressure should be preserved at preoperative baseline.
- Neurogenic pulmonary edema:
  (a) Occurs in about 5% of patients with SAH, generally in the first 48 h.
  (b) Treat with supportive care and modified lung-protective ventilation (low tidal volume, high PEEP with attention to possible effects on ICP, avoid hypercapnia to allow adequate ICP control).
- Cardiac dysfunction:
  (a) Cardiac arrhythmias are extremely common in SAH and include signs of myocardial ischemia (ranging from nonspecific T-wave abnormalities to diffuse ST segment elevations or depressions) as well as brady- or tachyarrhythmias.
  (b) Neurocardiogenic stress cardiomyopathy occurs in up to 30% of patients; in most cases pressors with inotropic effects are preferred, e.g., norepinephrine.

(c) Pharmacologically induced arterial hypotension: Nimodipine is a peripheral calcium channel blocker that is administered for 21 days. This oral agent may decrease the risk of vasospasm after SAH and may have neuroprotective attributes.
(d) Perioperatively, if nimodipine results in a significant decrease in blood pressure, it should be held temporarily.

In patients undergoing AVM repair:

– Intraoperative rupture:
  (a) Massive hemorrhage is possible; respond with aggressive transfusion of blood products to maintain a hemoglobin level of 8–10 g/dl.
– Postoperative hemorrhage:
  (a) Goal low normal blood pressures.
  (b) If significant mass effect, consider osmotherapy (hypertonic saline or mannitol), hyperventilation (pCO_2 30–35), and emergent return to the operating room.
– Perioperative brain ischemia:
  (a) Cerebral steal: cerebral ischemia resulting from shunting of blood through AVM and away from adjacent normal tissue may cause symptomatic ischemia. If some arterial feeders are occluded and others are not, this will change blood flow characteristics through AVM and increase perfusion in adjacent areas of the brain which have been chronically adapted to lower perfusion pressures, resulting in postoperative "normal perfusion pressure breakthrough":
    • Postoperative cerebral edema (or, in severe cases, intraparenchymal hemorrhage) attributed to cerebral hyperemia from exposure of areas of the cerebral vasculature with relative hypotension preoperatively (due to shunting from AVM) to increased perfusion pressures postoperatively (once the shunt is eliminated).
    • Occurs in <5% of cases.
– Endovascular considerations:
  (a) Most often, complete AVM embolization is not the goal of endovascular procedures for AVM treatment.
  (b) In a minority of cases, endovascular embolization with curative intent may be attempted, in which case the perioperative considerations outlined above apply.

Cerebral bypass:

– Intraoperative graft thrombosis:
  (a) Rare; detected by surgeon under direct visualization.
  (b) Check activated clotting time (ACT) if available, heparanize patient, and check coagulation parameters afterward.
  (c) Surgeon will place temporary clips and reexplore grafts.
– Postoperative graft thrombosis:
  (a) More common than intraoperative thrombosis.
  (b) May be treated with blood pressure augmentation or, rarely, with endovascular thrombectomy/thrombolysis.

Key Points

- Intracranial hemorrhage is the most feared complication.
  – Prepare for hemodynamic compromise with adequate monitoring and availability of blood products.
  – Postoperative hemorrhage generally requires immediate reoperation or, in the case of interventional neuroradiological procedures, immediate operative intervention.
- Tight control of intra- and perioperative blood pressure is essential.
  – Lower blood pressures and avoidance of blood pressure spikes are usually desirable when bleeding complications are a concern.
  – Higher blood pressures and avoidance of hypotension are critical when cerebral ischemia is a concern.
  – Anticipate, to prevent blood pressure spike during endotracheal intubation, placement of head pins, and surgical incision.
  – Anticipate hypotension after induction of anesthesia and sudden absence of surgical stimulation.
- Consider anesthetic strategies with limited use of highly soluble volatile anesthetics rapid emergence.
- Establish continuous communication with surgical team, particularly during acute crisis.

Suggested Reading

Bendo AA. Intracranial vascular surgery. Anesthesiol Clin N Am. 2002;20:377–88.
Dagal A, Lam AM. Cerebral autoregulation and anesthesia. Curr Opin Anaesthesiol. 2009;22:547–52.
Hashimoto T, Young WL. Anesthesia-related considerations for cerebral arteriovenous malformations. Neurosurg Focus. 2001;11:e5.

Hindman BJ, Bayman EO, Pfisterer WK, Torner JC, Todd MM, IHAST Investigators. No association between intraoperative hypothermia or supplemental protective drug and neurologic outcomes in patients undergoing temporary clipping during cerebral aneurysm surgery: findings from the Intraoperative Hypothermia for Aneurysm Surgery Trial. Anesthesiology. 2010;112(1):86–101.

Jellish WS. Anesthetic issues and perioperative blood pressure management in patients who have cerebrovascular diseases undergoing surgical procedures. Neurol Clin. 2006;24:647–59, viii.

Randell T, Niskanen M. Management of physiological variables in neuroanaesthesia: maintaining homeostasis during intracranial surgery. Curr Opin Anaesthesiol. 2006;19:492–7.

Randell T, Niemela M, Kytta J, Tanskanen P, Maattanen M, Karatas A, et al. Principles of neuroanesthesia in aneurysmal subarachnoid hemorrhage: the Helsinki experience. Surg Neurol. 2006;66:382–8. Discussion 388.

Sekhar LN, Natarajan SK, Ellenbogen RG, Ghodke B. Cerebral revascularization for ischemia, aneurysms, and cranial base tumors. Neurosurgery. 2008;62:1373–408. Discussion 1408–10.

Perioperative Challenges During Pituitary Surgery

33

Shuji Dohi

Risk and Incidence

Pituitary tumors account for approximately 18% of all primary brain tumors. Of these, approximately two-thirds of pituitary tumors have a final diagnosis of adenoma. The three most common disorders of pituitary hyperfunction are those related to excesses of prolactin (amenorrhea, galactorrhea, and infertility), adrenocorticotropic hormone (ACTH) (Cushing's disease), or growth hormone (GH) (acromegaly) (Table 33.1).

Risks for anesthesia and surgery are related to surgical approach, as well as to individual manifestations of patients' disorder as shown in Table 33.2. A transcranial approach with suprasellar invasion may cause cerebral spinal fluid (CSF) leakage and visual loss. Transsphenoidal and transnasal approach may cause numbness of upper lip and teeth, nasal CSF leakage, and venous air embolism. Neurogenic diabetes insipidus (DI) could occur with any approach.

In acromegalic patients, difficulty of airway management occurs approximately three times more often than the other pituitary disorders (9.1% vs. 2.6%). Patients with Cushing's disease and those with a prolactinoma are no more difficult to intubate than patients with nonfunctioning tumors.

Neurogenic DI occurs in approximately 20% of patients undergoing transsphenoidal resection of a pituitary adenoma in the immediate postoperative period. In addition, surgery in the sella turcica may also cause hypofunction of the hypothalamic-pituitary axis, vision disturbance, bleeding, and local edema. Though rare, air embolism could occur during surgery in patients in semi-Fowler (being head with 20–30 cm higher than the lower part of the body) or lounging position (position in a chair with head bend back on a sofa).

Table 33.1 Incidence of tumors in the pituitary region

Type of tumor	Incidence/percent
Pituitary tumors (adenoma)	10% of all autopsies
	10–15% of all brain tumors
	Majority of suprasellar tumors
Nonfunctional pituitary tumor	~30%
Functional pituitary tumor	~70%
Prolactin-producing tumor	43%
Growth hormone-producing tumor	17%
ACTH-producing tumor	7%
Thyroid-producing tumor	3%
LH-, FSH-producing tumor	Rare
Craniopharyngiomas	0.5–1:100,000/year
	1–3% of all brain tumors
	13% of all suprasellar tumors

Table 33.2 Complications associated with pituitary surgery

Surgical approach	Complications
Transcranial	DI, CSF leakage, ischemia in forebrain, air embolism
Transsphenoidal	DI, numbness of upper lip and teeth, visual loss, nasal CSF leakage, meningitis
Transnasal (endoscopic; "minimally invasive")	DI, skin lesion due to endoscopy, venous air embolism

DI Diabetes insipidus

Preoperative Problems

Anticipated problems following pituitary surgery are dependent upon pathophysiological changes associated with tumor-induced altered endocrine function in combination with endocrine changes associated with general surgical stress. Hypothalamic stress results in two categories of responses: rapid effects mediated through the sympathetic nervous system and adrenal medulla and neuroendocrine responses mediated through the pituitary gland and adrenal

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cortex. Such main disorders challenging transsphenoidal surgery include acromegaly and Cushing's disease.

Although neither nonfunctional nor functional adenomas usually cause ICP to increase, the tumor growth in the restricted space of the sella turcica may represent clinical signs such as visual disturbance, as it impinges on the optic chiasm.

Acromegaly is a rare syndrome that typically manifests in the second or third decade of life in response to excess secretion of adenohypophyseal GH and is characterized by enlargement of the bone, connective tissue, and viscera. Physical signs are most remarkable in the hands, feet, face, mandible, and head. Increase in subcutaneous connective tissue thickens the lips, skin folds, and tongue and often causes glossoptosis. As a result, the large tongue and hypertrophied tissues in and around the upper airway reduce the airway space and predispose patients to airway obstruction. Thus, tracheal intubation is three times more difficult in patients with acromegaly.

Cushing's disease diagnosed before age 40 is typically associated with a hormone-producing pituitary adenoma. In contrast, when diagnosed in patients in their 60s or older, the most likely cause is an adrenal carcinoma. Associated problems include mild diabetes, hypertension, degenerative vascular disease, and heart disease, particularly in patients with hyperadrenocorticism. In Cushing's disease, hypokalemia, hypernatremia, increased intravascular fluid volume, and skeletal muscle weakness are commonly present. Prevention of long-term consequences involves early diagnosis and removal of the tumor, while treating secondary events (e.g., hypertension).

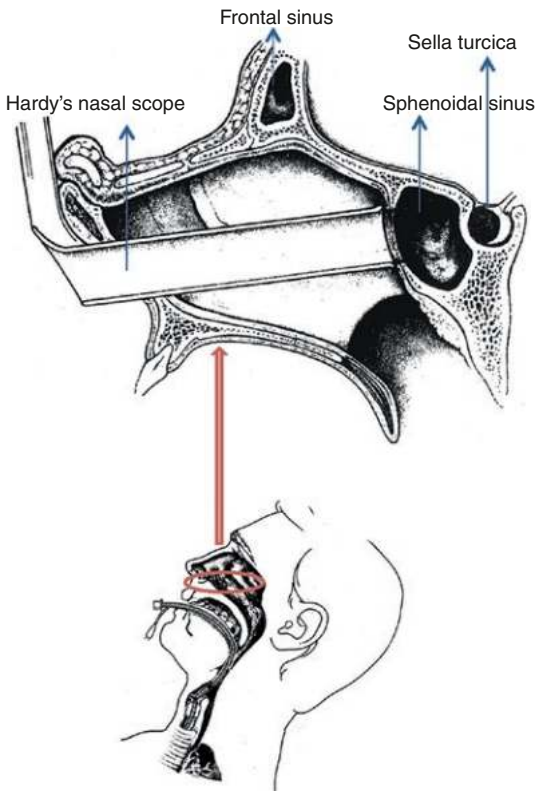

Fig. 33.1 A Hardy scope was used to obtain a direct view of the base of the skull, from the nostril, and then endoscopic transnasal and transsphenoidal microsurgery is performed

During Anesthesia and Surgery

All patients undergoing pituitary surgery should be monitored using ASA standard monitoring plus invasive arterial pressure line, $ETCO_2$ and urine output. In patients with acromegaly, the anesthesiologist must anticipate difficulty with airway management due to a large tongue, abundant soft tissue folds, and enlarged facial structures. As induction of general anesthesia in these patients carries a higher risk (cannot ventilate/cannot intubate scenario after induction), it is most conservative to intubate the trachea with the patient awake and breathing spontaneously, most commonly with a fiberoptic approach and local anesthesia.

For all pituitary surgery, it is safest to maintain general anesthesia including muscle paralysis once the trachea is intubated. This helps to prevent injury from patient movement while in headpins (e.g., Mayfield head holder) and during surgery through the rigid Hardy nasal scope. It is important to remember to consider reducing the initial dose of muscle relaxant and compulsively dose these drugs based on train-of-four testing, in view of skeletal muscle weakness in Cushing patients (Fig. 33.1).

Emergence from Anesthesia and Postoperative Period

Tissue edema caused by surgical trauma may further decrease the oropharyngeal space and contribute to the upper airway obstruction after airway extubation. Prior to extubation, the clinician should at minimum confirm that there is a leak around the endotracheal tube, at a pressure below 20 cm H_2O, after the cuff is deflated. Some experts also advocate that an extubation catheter should be placed in the trachea prior to extubation in order to facilitate rapid reintubation in the event that extubation results in acute airway obstruction. Similarly, other experts advocate that extubation should be done in these high-risk patients over an intubating bronchoscope. Last, it is always prudent to make sure that extubation of high-risk patients is done at a time when an experienced surgeon would be available to establish a surgical airway of extubation and initial noninvasive techniques for reintubation fail. Thus, it is important to at least communicate plans for extubation of high-risk patients with the neurosurgeon. It is

optimal to have that surgeon at the patient's bedside during the extubation.

Neurogenic diabetes insipidus (DI) can occur in patients undergoing transsphenoidal resection of pituitary adenomas in the immediate postoperative period. Often this results from surgical trauma to the posterior pituitary where antidiuretic hormone (ADH) secretions originate. Treatment is demanding because DI typically occurs in two phases in the first 24–48 h postoperatively: high urine output followed by reduced urine output and then the chronic degree of DI is established, without apparent correlation to the initial degree of increased or reduced urine output.

Prevention

The basic principles of pituitary surgery remain unchanged with the other neurosurgical patients. They include the provision of optimal operative conditions, maintenance of cerebral perfusion pressure and cerebral oxygenation during anesthesia, and speedy recovery from anesthesia. Anesthesiologists should maintain optimal physiologic condition of the airway, respiratory and cardiovascular systems, fluid and plasma electrolytes, and metabolic conditions.

As mentioned above, airway management may be challenging in patients with acromegaly, and fiber-optic intubation of the awake and spontaneously breathing patient is likely the safest approach. In all cases, the patients should be monitored with ECG, noninvasive BP, pulse oximetry, and ETCO2. More invasive monitoring (e.g., invasive arterial pressure monitoring) should be considered in patients with significant comorbidities (e.g., ischemic heart disease).

Crisis Management (Clinical Presentation)

Complications with Airway Management and Ventilation

Patients who, by physical examination or history, appear to be difficult to intubate or mask ventilate should always be managed conservatively in the awake state. In others, prior to inducing anesthesia, it is important to have the patient in an ideal sniffing position. It is also critical to have easy access to airway adjuncts in the event of an emergency situation, including oral and nasal airways, an LMA (or other supraglottic device), and flexible fiber-optic endoscopy equipment and supplies necessary for establishing an emergency surgical airway. Failure of mask ventilation and tracheal intubation in the anesthetized state should invoke use of the ASA difficult airway algorithm.

For induction of anesthesia, it is safer to induce anesthesia with agents that have a short half-life or are easily reversed in the event difficulties with tracheal intubation. Mask ventilation may be facilitated with the use of an oral airway. Whenever possible, neuromuscular blocking agents should be withheld until the clinician confirms their ability to mask ventilate the patient. Some centers recommend the placement of a sponge in the pharynx during surgery to prevent blood from entering the airway during transnasal or transsphenoidal approach.

Despite attempts to suction the airway and pharynx prior to extubation, there is often blood draining from the surgical site into the mouth. Emergence and extubation are facilitated with the patient in a head-up position and awake. It is critical to assure that the patient will be awake and strong enough after extubation to manage secretions and blood from the surgical site. The increased volume of secretions in the airway of these patients may predispose them to laryngospasm.

Cardiovascular Complications/Venous Air Embolism

Transnasal transsphenoidal resection of pituitary tumors involves wide fluctuation in hemadynamics and causes hypertension and tachycardia due to noxious stimuli during various stages of surgery. Hypertension is anticipated during placement of the patient in the Mayfield head holder (particularly when the periosteal pins are placed) and when the surgeon is administering the topical/local anesthetic in the nostrils or the others. Typically, surgeons use epinephrine (1:200,000) with cocaine on cotton to cause local anesthesia and vasoconstriction. The degree of hypertension can be minimized by closely monitoring patients so that treatment can be provided in a timely fashion. Invasive arterial pressure monitoring is indicated in patients with cardiovascular comorbidities in whom transient significant hypertension is likely to cause significant myocardial ischemia. Next, it is important to preemptively deepen the level of anesthesia with short-acting anesthetic agents (e.g., alfentanil, propofol) or directly cardiovascular acting agents (e.g., esmolol, nitroglycerin, nitroprusside) in order to mitigate the degree of hypertension. The administration of α-2 adrenergic receptor agonist, oral clonidine premedication, or intraoperative dexmedetomidine infusion is often effective in preventing extreme hemodynamic instability and thereby may decrease anesthetic requirements in patients undergoing the pituitary tumors resection.

Severe hypotension may rarely occur as the result of a sudden pronounced blood loss due to accidental surgical injury of the cavernous sinus or carotid artery, both of which are immediately lateral to the area of surgery. Invasion of either of these structures by the surgeon may require institution of a massive transfusion protocol in order to save the patient's life. In contrast, severe hypotension may also occur

secondary to venous air embolus. Whereas surgical invasion of the cavernous sinus or carotid artery are associated with apparent significant hemorrhage, venous air embolus is associated with a dry surgical field. If a venous air embolus is suspected, the anesthesiologist must communicate their concern with the surgeon, ask the surgeon to flood the surgical field, and support the blood pressure pharmacologically.

Endocrine Failure

Pituitary surgery may result in significant hormonal deficiency requiring acute and/or chronic therapy. Deficiency in production of ACTH will result in reduced production of cortisol from the adrenal glands. Cortisol is necessary for maintaining vascular tone and affects bone density, growth, kidney function, the immune system, and behavior and cognition. Secondary adrenal insufficiency from inadequate ACTH production can be life-threatening if untreated because of significant electrolyte (particularly sodium and potassium) abnormalities and hypotension. The treatment of choice is hydrocortisone; first, intravenously and then by oral administration. In the acute postoperative period, the patient should receive at least 100 mg/day in order to help address the stress of surgery. Ultimately, most adults take a dose of hydrocortisone of 20–25 mg/day, with most given in the morning to mimic the normal physiology of cortisol release.

Diabetes insipidus (DI) is characterized by decreased release of ADH (ADH, vasopressin) from the posterior pituitary gland, which results in reduced water retention by the kidneys and in urine output that is in excess of the fluid intake of the patient. ADH deficiency leads to DI which is characterized by excessive urination and thirst. DI is occasionally already present preoperatively secondary to mass effect of the pituitary tumor but more frequently is caused by invasively growing tumors that directly damage the hypothalamus or as a consequence of pituitary surgery itself. Diagnostic components of DI are provided in Table 33.3. Patients often present with three phases of DI in the immediately postoperative period. Initially urine output is very high, and treatment includes fluid (carefully following serum electrolyte concentrations) and intravenous infusion of ADH. This is often followed by a period of marked reduction in urine output, and ADH infusion should be stopped. Ultimately, the patient will reach their state of chronic ADH reduction. In this final phase, the patient should be treated with once or twice a day dosing of desmopressin acetate (ddAVP: synthetic analogue of the natural pituitary hormone 8-arginine vasopressin (ADH)) which can be administered orally or via nasal spray preparation. Dose of ddAVP should be determined after careful assessment of the patient's fluid status and serum electrolyte (particularly sodium) concentration measurements.

Table 33.3 Diagnosis of diabetes insipidus

Urine	
Specific gravity	<1.005
Output	>250 mL/h
Osmolarity	<200 mOsm/kg
Serum	
Osmolarity	>300 mOsm/kg
Sodium concentration	>150 mg/L

After the acute postoperative period, clinicians must also carefully assess the need for replacement of other pituitary hormones including thyroid-stimulating hormone (TSH), GH, follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and oxytocin. It is rare to need to replace any of these hormones in the acute postoperative period. However, left untreated, chronic reduction in TSH may result in significantly reduced metabolism and cause hypothermia, coma, and death.

Complications Secondary to Structural Disruption

Hematoma Formation/Visual Deficit

In the immediate postoperative period (until the time of hospital discharge), it is important to monitor for the effects of surgery on anatomic structures in the area of surgery. Disruption to the optic chiasm may be diagnosed by loss of peripheral visual fields immediately after emergence from anesthesia. In this situation, radiologic evaluation is necessary to determine if this deficit is due to formation of a hematoma that may require immediate surgical evacuation. More delayed loss of visual fields may occur as a result of edema and require only supportive care.

It is also important to carefully inspect the nasal cavity and lips for evidence of excessive surgical injury. Injury from the exposure may rarely require plastic surgery intervention.

CSF Leak

Although the pituitary gland is outside of the CSF space, it is in close proximity, and surgical intervention may result in dural leak. If a dural injury is observed at the time of surgery (up to 30% of patients), it is common for the surgeon to place a fat graft in the surgical site to promote healing of the disruption. Postoperative CSF leak is diagnosed in up to 6% of patients after evaluation for postoperative rhinorrhea. Since CSF contains glucose but mucus does not, nasal or ear leakage should be tested for glucose. A laboratory glucose value >30 mg/mL identifies CSF. Risk of persistent CSF leak

includes meningitis, tension pneumocephalus, and secondary neurologic injury. Treatment includes reoperation to try to seal the leak (fat graft), often in conjunction with the placement of a lumbar subarachnoid drain that allows to reduce the pressure on the surgical tear and promote normal healing/scarring.

Key Points

- Airway management is likely to be difficult in patients with excess production of GH. A conservative, awake approach to airway management in those patients is recommended.
- Significant hypertension is anticipated during placement of the Mayfield head holder and during topicalization of the nasal mucosa with epinephrine and cocaine, which should be treated immediately.
- Intraoperative treatment with hydrocortisone will prevent the postoperative physiologic consequences of low ACTH levels in the immediate postoperative period. Before extubation, confirm no material or blood clots on the base of the patient's pharynx, in addition to confirm no airway obstruction due to edema.
- Treatment of DI in the postoperative period must take into consideration the three phases of this disease in patients immediately following pituitary surgery.
- Postoperative diagnosis of either visual field abnormality or CSF leak requires immediate evaluation and treatment.

Suggested Reading

Ali Z, Prabhakar H, Bithal PK, Dash HH. Bispectral index-guided administration of anesthesia for transsphenoidal resection of pituitary tumors: a comparison of 3 anesthetic techniques. J Neurosurg Anesthesiol. 2009;21:10–5.

Ammirati M, Wei L, Ciric I. Short-term outcome of endoscopic versus microscopic pituitary adenoma surgery: a systematic review and meta-analysis. J Neurol Neurosurg Psychiatry. 2013;84:843–9.

Atkinson JL, Young WF Jr, Meyer FB, Davis DH, Nippoldt TB, Erickson D, et al. Sublabial transseptal vs transnasal combined endoscopic microsurgery in patients with Cushing disease and MRI-depicted microadenomas. Mayo Clin Proc. 2008;83:550–3.

Burkhardt T, Rotermund R, Schmidt NO, Kiefmann R, Flitsch J. Dexamethasone PONV prophylaxis alters the hypothalamic-pituitary-adrenal axis after transsphenoidal pituitary surgery. J Neurosurg Anesthesiol. 2014;26:216–9.

Dinsmore J. Anaesthesia for elective neurosurgery. Br J Anaesth. 2007;99:68–74.

Dunn LK, Nemergut EC. Anesthesia for transsphenoidal pituitary surgery. Curr Opin Anaesthesiol. 2013;26:549–54.

Gondim JA, Almeida JP, de Albuquerque LA, Gomes E, Schops M, Mota JI. Endoscopic endonasal transsphenoidal surgery in elderly patients with pituitary adenomas. J Neurosurg. 2015;123:31–8.

Nemergut EC, Zuo Z. Airway management in patients with pituitary disease: a review of 746 patients. J Neurosurg Anesthesiol. 2006;18:73–7.

Ovassapian A, Doka JC, Romsa DE. Acromegaly-uses of fiberoptic laryngoscopy to avoid tracheostomy. Anesthesiology. 1981;54:429–30.

Schmitt H, Buchfelder M, Radespiel-Tröger M, Fahlbusch R. Difficult intubation in acromegalic patients: incidence and predictability. Anesthesiology. 2000;93:110–4.

The Committee of Brain Tumor Registry of Japan. Report of brain tumor registry of Japan (1969–1993) 10th edition. Neurol Med Chir. 2000;40:1–102.

Perioperative Challenges During Craniotomy for Space-Occupying Brain Lesions

34

Chanannait Paisansathan and Verna L. Baughman

Overview

Primary malignant and benign brain tumors account for 85–95% of all central nervous system tumors. In 2016 an estimated 23,770 Americans will be diagnosed with brain tumors, which will result in 16,050 deaths. The majority of these brain tumors are located within the supratentorial compartment. The most commonly reported histology is anaplastic astrocytoma and glioblastoma (38%), followed by meningiomas and other mesenchymal tumors (27%). Surgery remains the mainstay of treatment. Patients present to the operating room for surgical diagnosis (biopsy) and for curative resection or debunking. The goal is complete resection, which can be difficult based on histopathology, location, vascularity, and adjacent structures. Chemotherapy and radiation are used as adjunct therapies, depending on the type of tumor and location. Nonprimary brain masses include metastatic lesions and brain abscess. Resection of metastatic tumors is performed to improve the patient's quality of live. This chapter focuses on the complications associated with craniotomy for space-occupying lesions during preoperative, intraoperative, and postoperative periods.

Preoperative Complications

Space-occupying lesions (brain tumors and abscess) can cause symptoms related to mass effect, parenchymal infiltration, and tissue destruction. Disruption of the blood-brain barrier results in leakage of plasma across the vessel wall and causes brain edema surrounding the tumor ("vasogenic brain edema"). The clinical signs depend on the location of the tumor and the extent of edema. It is not uncommon that the peritumor edema effect can exceed the mass effect induced by the tumor itself. Peritumor edema can decrease cerebral blood flow in the surrounding neurons, putting them at risk for ischemia. Headache is the most common presenting symptom. Nausea, vomiting, focal neurological deficits, and a change in mental status may occur. Seizures happen in 15–95% of patients depending on the type of tumor. Cerebral blood flow autoregulation is usually impaired in the tumor bed, so hypertension can lead to worsening of brain edema and cause bleeding. An acute rise in intracranial pressure (ICP) can exceed brain compensatory mechanism and produce fatal brain herniation.

Premedication

Patients with no evidence of significant increase in ICP will benefit from an anxiolytic and/or a small dose of narcotics prior to surgery to treat anxiety. Stress can aggravate vasogenic edema and ICP due to an increase in cerebral metabolism and blood flow. However, careful titration is required to avoid hypoventilation, which leads to hypercapnia and hypoxia. To facilitate anxiolysis, it is best to use drugs that have specific antagonists (e.g., benzodiazepines and opiates), as patients with brain tumors may have an exaggerated sedative effect from even small doses of these agents.

Intraoperative Complications

Complication during Induction and Maintenence of Anesthesia

Anesthetic management goals are: (1) avoid a secondary brain insult during surgery, (2) optimize operating conditions, (3) permit brain function monitoring, and (4) promote rapid emergence from anesthesia for neurological assessment.

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Independent risk factors for brain swelling during craniotomy are ICP >13 mmHg, degree of midline shift, and tumor histology. The drugs used for induction and maintenance of anesthesia have not been identified as independent risk factors, although there is some suggestion that propofol produces more favorable characteristics in cerebral hemodynamics [ICP, cerebral perfusion pressure (CPP), and arteriovenous oxygen difference ($AVDO_2$)] compared with inhalational anesthesia during normocapnia to mild hypocapnia ($PaCO_2$ 30–40 mmHg). Both inhalational anesthetics (except N_20) and intravenous anesthetics (except ketamine) decrease cerebral metabolism. Propofol produces cerebral vasoconstriction, which is coupled to the decrease in cerebral metabolism, while inhalational anesthetics and N_2O cause vasodilation which can be blunted with hyperventilation. Total intravenous anesthesia (TIVA) may be necessary to permit transcranial motor-evoked potential (TcMEP) monitoring.

Brief hyperventilation ($PaCO_2$ 25–30 mmHg) is useful to improve surgical working condition by decreasing brain bulk; however, this may be accompanied by a risk of cerebral hypoperfusion. Mannitol and hypertonic saline in equiosmolar concentrations can achieve similar brain relaxation. However, they produce opposite electrolyte imbalances. Mannitol (0.25–1 g/kg) can cause acute hyponatremia and increase serum potassium due to an intracellular to extracellular shift. Conversely, hypertonic saline (3–23.4%) can increase blood sodium with acute but transient hypokalemia. Theoretically, both agents can initially increase intravascular volume and cause heart failure or pulmonary edema in patients with poor cardiovascular reserve. Serum osmolality should not exceed 320 mOsm/l. Mannitol 1–2 g/kg has been shown to increase serum osmolality by approximately 18 mOsm/L and decrease brain water by 90 ml for several hours. The need for osmotic diuresis should be discussed with the neurosurgeon when the lesion is small and/or a neuro-navigating system is used.

Location of the tumor is the primary determinant for the use of neurophysiologic monitoring. The common techniques employed with supratentorial lesions are electroencephalogram (EEG), somatosensory-evoked potentials (SSEP), electromyography (EMG), and transcranial motor-evoked potentials (TcMEP). Communication between anesthesiologist, neurophysiologist, and neurosurgeon is essential for successful monitoring to prevent neurological injury during resection. The anesthetic technique and use of muscle paralysis must be planned with these monitoring techniques in mind. Anticonvulsant administration for several days can produce resistance to neuromuscular-blocking drugs. Dosing muscle relaxant drugs based on a nerve stimulator placed on a paretic limb will result in a significant over dosage.

Fast recovery from anesthesia is desirable in neurosurgical patients to diagnose surgical complications such as bleeding, brain swelling, and cerebral ischemia. Ideally, patients should be extubated within 15 min after surgery. There is no clear advantage of IV agents (propofol, narcotics) over inhalation agents (isoflurane, sevoflurane, desflurane). Hypertension often occurs during emergence and may predispose to cerebral edema and/or intracranial bleeding. Coughing and straining on the endotracheal tube must be minimized. Intravenous lidocaine and nonanesthetic agents (β blockers, α–β blockers, calcium channel blockers, and nitroprusside) are used successfully to blunt the hemodynamic response during emergence and endotracheal extubation.

Postoperative Complications

Worrisome complications at the end of surgery are delayed emergence (failure to awaken), new neurologic deficit, and decrease in level of consciousness. Patients should be able to perform simple neurological functions such as motor movement, eye opening on command, and recovery of airway reflex within 10–15 min after termination of the anesthesia. If not, patients should remain intubated, and one needs to search for the cause such as residual anesthesia, brain edema, intracerebral hematoma, deep vein thrombosis, cerebral ischemia, tension pneumocephalus, seizure, and metabolic or electrolyte disturbances. A neurologic examination including pupil size should be performed. Bilateral miotic pupils can result from brainstem compression or narcotic effect. The administration of naloxone can be considered; however, rapid narcotic reversal is not without risks including cardiac arrhythmias, myocardial infarction, and pulmonary edema. If the patient regains consciousness after naloxone titration, a potential for re-narcotization exists. In patients who do not emerge from anesthesia as expected, obtaining an urgent CT scan is helpful for diagnosing intracranial events (hematoma, pneumocephalus, progressive cerebral edema).

Other complications which can occur in the postoperative period include inadequate pain control, nausea/vomiting, seizure, wound infection, and pseudoankylosis of the mandible after supratentorial craniotomy. Post-craniotomy headache (PCH) starts within 7 days after surgery. If the pain lasts longer than 3 months, it is considered persistent. The headache is reported to be “tension-type pattern” and can affect social activity and mood. The incidence is more prevalent in craniectomy than craniotomy and cranioplasty. Currently there is no evidence of effective prophylactic medication/strategy for PCH.

Prevention

Preoperative Complications Prevention

Patients with evidence of vasogenic edema associated with tumors should receive steroid treatment which reduces peri-

Table 34.1 Preoperative prevention

Preoperative complication	Prevention
Brain edema	Dexamethasone 4 mg q 6 h
Seizure	Phenytoin
	Loading dose 15–20 mg/kg
	Maintenance 100 mg TID
	Levetiracetam
	Loading dose 1 g
	Maintenance 500 mg BID
Increased ICP	Avoid hypoventilation
	Avoid large dose narcotics or benzodiazepines
Gastrointestinal effects	H_2 blocker, metoclopramide

tumor edema and symptoms. An intravenous dexamethasone dose of 4–10 mg, followed by 4 mg every 6 h, is suitable initial treatment. It can take 24–72 h before the full effect of corticosteroid therapy is achieved. Electrolytes and glucose levels should be monitored.

The use of anticonvulsants is important for tumor patients who present with seizures. The phenytoin blood level should be determined before the craniotomy, if possible, so that an additional dose can be administered if the level is subtherapeutic (phenytoin goal: total = 10–20 mcg/ml, free = 1–2 mcg/ml). However, for newly diagnosed brain tumor patients presenting without seizures, the Quality Standards Subcommittee of the American Academy of Neurology (2000) concluded that no benefit could be established for routine prophylactic use of antiepileptic drugs. They felt that the efficacy of corticosteroid therapy is less and the stimulation of the cytochrome P450 enzyme system accelerates drug metabolism which can produce inadequate chemotherapy blood levels. If elected to start antiseizure prophylaxis for patients with supratentorial brain tumors, the newer generation levetiracetam can be considered. Patient complaints of headache should be treated with caution. A large narcotic or benzodiazepine dose might lead to respiratory depression, hypercarbia, and an increase in ICP. The initiation of H_2 blocker and/or metoclopramide can be considered in the preoperative period because increased ICP can decrease gastric emptying and steroid treatment can increase gastric acid secretion (Table 34.1).

Intraoperative Complications Prevention

Massive intraoperative blood loss from tumor resection along with the combination of osmotic diuresis can result in hypovolemia and hypotension. Adequate IV access is essential (two large-bore catheters). Consider CVP placement when the tumor is located near a sinus due to the risk of venous air embolism, for procedures scheduled for longer than 6 h, and for vasoactive drug infusions. Invasive arterial blood pressure monitoring is recommended for CPP monitoring and analysis of blood gases, electrolytes, and glucose. Arterial transducer height should be at the level of the Circle of Willis. CPP should be kept >60 mmHg to prevent cerebral ischemia from brain retraction during surgery.

Brain edema and swelling is not desirable. Mannitol is administered at skin incision since it has a 15–30 min delay in effect. A rebound increase in ICP can occur after 24–48 h of administration. Impeding cerebral venous drainage can occur after positioning for craniotomy. The head should be elevated about 30° in the patient with a poorly compliant brain. Inadequate ventilation can lead to hypoxia and hypercarbia, which increase cerebral blood flow and ICP. Any factors that contribute to increased cerebral metabolism such as seizure and pain will couple with cerebral blood flow and result in a "tight" brain.

Antiseizure prophylaxis for tumor surgery is used to decrease the potential for intraoperative and postoperative seizures. Craniotomy, evoked potential monitoring (especially TcMEP), remifentanil, and hyperventilation can all lower the seizure threshold. Phenytoin has long been used as antiseizure prophylaxis, but it can cause hypotension, arrhythmias, and mental status depression, especially with rapid intravenous administration (>50 mg/min). The prodrug fosphenytoin has a better safety profile. It is dosed using PEU (phenytoin equivalent units) rather than milligrams. This makes it easier for the clinician, as 1 PEU = 1 mg phenytoin. Recently levetiracetam (Keppra®) has been used for seizure prophylaxis. It is easier to use, with fewer hemodynamic side effects and blood levels do not need to be measured. However, it has recently been suggested that levetiracetam may not be as effective in blocking intraoperative seizure activity. Future studies are needed to confirm or refute this concern.

Electrolyte imbalance and hyperglycemia from steroid administration and surgical stress can occur. Hyperglycemia has been reported to increase morbidity and mortality in critically ill patients and worsen neurological outcome. A single dose of 10 mg dexamethasone given intraoperatively can increase blood glucose in diabetic and nondiabetic patients alike. Dextrose containing IV fluids should be avoided. Of note: several vasoactive and antibiotic infusions may contain dextrose. Hyperglycemia should be monitored and treated; however, hypoglycemia is also dangerous in the neurosurgical population (Table 34.2).

Postoperative Complication Prevention

Brain edema after craniotomy can result in herniation and death. Contributing factors include excessive brain retraction and subtotal resection of malignant tumors, especially glio-

Table 34.2 Intraoperative prevention

Complication	Prevention
Intraoperative hemorrhage	Adequate IV access: two large-bore catheters
	CVP is optional
	Arterial line recommended
Intraoperative hypotension	Check volume status
	Blood loss
	Excessive diuresis
	Monitor for air embolus
	Precordial Doppler
	Transesophageal echocardiogram (TEE)
	Et CO_2
	Check for cardiovascular compromise
	Severe bradycardia or arrhythmia
	Myocardial ischemia
Increase brain edema and swelling (tight brain)	Check patient position – avoid extreme neck flexion
	Evaluate for seizure activity
	Deepen anesthesia
	Treat hypoxia
	Treat hypercarbia
Electrolyte imbalance (Na^+, K^+, and glucose)	Monitor electrolytes every 1–2 h
	Monitor glucose hourly if on insulin infusion
	Check serum osmolality if using large dose of mannitol/hypertonic saline or diabetes insipidus suspected

Table 34.3 Postoperative prevention

Complication	Prevention
Brain edema	Avoid excessive brain retraction
	Avoid excessive IV fluid
Postoperative hematoma	Smooth emergence (avoid hypertension, coughing, straining)
	Avoid excessive brain shift
Venous thrombosis, arterial injury	Proper surgical technique
Inadequate pain control	Local anesthetic scalp infiltration, nerve blocks, analgesics
Nausea and vomiting	PONV prophylaxis (i.e., ondansetron, metoclopramide)
	Consider adding propofol infusion as part of anesthetic regimen
Postoperative wound infection	Prophylaxis antibiotic (i.e., cefazolin)
Ankylosis of the mandible	Limited jaw opening posttemporal craniotomy, resolves after 3–4 weeks

blastoma. Proper surgical technique to identify venous and arterial structures will minimize complications associated with major vein thrombosis and arterial injury. Smooth emergence from anesthetic is crucial to prevent the disruption of hemostasis at the tumor bed. The patient should be pretreated with antihypertensive drugs to counteract the increase in sympathetic tone during emergence from anesthesia. Debate exists concerning the relative merits of beta blockade versus vasodilation. Postoperative pain should be treated with caution and postoperative nausea, and vomiting prophylaxis is recommended for neurosurgical patients (Table 34.3).

Crisis Management

Preoperative Crisis Management

Brain Herniation (Transfalx, Transtentorium, Transmagnum, Transdural)

Supratentorial brain tumors are often slow growing with the increase in volume compensated by a parallel volume reduction in the blood and CSF compartments (because brain is incompressible). A change in any one of the intracranial compartments, such as hemorrhage into the tumor or an increase in cerebral blood flow (from hypoxia, hypercarbia or seizure), will lead to an exhaustion of compensatory mechanisms and an acute rise in ICP with potential for brain herniation. Patients present with signs and symptoms such as mental status depression, decrease in Glasgow Coma Score, Cushing triad (hypertension, reflex bradycardia, and abnormal respiratory pattern), new focal neurological deficit, and fixed/dilated pupils, all of which need immediate intervention to prevent further brain injury or fatal brain herniation (Table 34.4).

Intraoperative Crisis Management

Blood and volume resuscitation should be readily available in the event of bleeding and hypotension. If there is brain swelling, hyperventilate, elevate the head, and administer diuretic, narcotic, and a bolus of thiopental or propofol. Closely monitor electrolytes and glucose intraoperatively. Intraoperative seizure activity is typically associated with acute brain swelling due to the hypermetabolic state and increased CBF. Monitor for signs of venous air embolism. If intraoperative seizures occur, additional antiseizure drug administration, deepening the level of anesthesia, and decreasing hyperventilation should be considered (Table 34.5).

Postoperative Crisis Management

Twenty percent of postoperative brain tumor patients develop elevated ICP (50% due to bleeding, 50% due to cerebral edema). Risk factors include surgery for glioblastoma, repeat surgery, and surgery lasting more than 6 h. Postoperative hematoma after supratentorial craniotomy can occur due to incomplete tumor bed hemostasis or with remaining vascular tumor. Remote bleeding such as subdural and/or epidural hematoma and cerebellar hemorrhage has been reported. Major venous thrombosis can produce a delayed hemor-

Table 34.4 Preoperative crisis management

Acute brain herniation treatment in the preoperative period	
Airway	Intubate
	Hyperventilate (acute effect last 6–8 h)
	$PaCO_2$ between 28 and 32 mmHg
	PaO_2 >100 mmHg
	Avoid PEEP
Position	Neutral head position
	Elevate head 15–30°
Hemodynamics	Optimize cerebral perfusion pressure (CPP = MAP-ICP)
	↑MAP to 90–100 mmHg if no cerebral hemorrhage
Brain extracellular volume reduction	Diuretics
	Mannitol
	Hypertonic saline
	Furosemide
	Steroids to decrease peritumor edema
	Extraventricular drain (EVD) placement

Table 34.5 Intraoperative crisis management

Complication	Crisis management
Intraoperative hemorrhage	Blood products available, consider giving clotting factors early if disseminated intravascular coagulopathy is suspected
Intraoperative hypotension	Blood replacement
	Fluid bolus (250–500 cc) isotonic saline or albumin
	Vasoactive drugs
	Keep CPP >60 mmHg
	Watch for overhydration due to a risk for cerebral edema
Venous air embolism	Notify surgeon/flood surgical field
	Aspirate air from CVP
	Hemodynamic support – vasoactive drugs (phenylephrine, dopamine, norepinephrine, epinephrine)
	Cardiac resuscitation
Cardiovascular compromise (severe bradycardia, arrhythmia)	Alert surgeon
	Treat bradycardia with atropine or epinephrine
	Treat ↑ICP if it is causing cardiovascular compromise
Increase brain edema and swelling (tight brain)	Elevate head 15–30°
	Anticonvulsant therapy
	Bolus thiopental or propofol
	Consider switching to intravenous anesthesia
	↑FiO_2, decrease/avoid PEEP, hyperventilate
	Mannitol, furosemide, hypertonic saline
Electrolyte imbalance (Na^+, K^+, and glucose)	Consider DDAVP if DI is suspected
Seizures	Replace K^+ if <3.0 mEq/l
	Treat glucose with insulin if >180 mg/dl
	Dose/redose antiseizure medication
	Increase depth of anesthesia
	Decrease hyperventilation

Table 34.6 Postoperative crisis management

Complication	Crisis management
Brain edema	Proper head position
	Hyperventilation
	Steroid, diuretics
Postoperative hematoma	Treat hypertension (β blocker, vasodilator)
	Prevent coughing, straining (i.e., narcotics, lidocaine 1–1.5 mg/kg)
	Administer neuromuscular reversal agent after removal of head pins
	Avoid excessive brain shift
	Gradually normalize $PaCO_2$
	Gently rehydrate to facilitate brain expansion
Major vein thrombosis and arterial injury	Mannitol (10–20 cc/h of 20% solution) and rehydration may improve the rheologic profile sufficiently to prevent complete venous occlusion
Inadequate pain control	Titration of long-acting opiates, scalp nerve blocks
Nausea and vomiting	Dexamethasone 4 mg
	5 HT3 antagonist, NK1 antagonist
Postoperative wound infection	Antibiotics should be administered within 1 h prior to skin incision (2 h for vancomycin)
Ankylosis of the mandible	Consider fiber-optic intubation
"Slow awakening"	DDx: seizure, hypoxia, hypercarbia, hypoglycemia, hypothermia, residual anesthesia (inhalational agents, narcotics, muscle relaxants), hematoma, edema, vascular thrombosis, and pneumocephalus

rhagic stroke. Arterial injury, on the contrary, produces an immediate neurological deficit. Seizures occur in 15–35% of postoperative tumor patients without intraoperative antiseizure therapy, which is reduced by approximately 50% with treatment. Pneumocephalus is common: up to 66% of patients have significant intracranial air 2 days after surgery, and 12% of patients have moderate to large pneumocephalus up to 2 weeks following craniotomy. Thus, administering nitrous oxide to a patient with a recent craniotomy (within 3 weeks) is not recommended. Tension pneumocephalus is rare in non-sitting craniotomy (Table 34.6).

Key Points

- Thorough evaluation for severity of increased ICP, neurological function, and location of a space-occupying lesion, along with patient's medical condition, is essential for minimizing neurological injury during surgery.
- The anesthetic goals for craniotomy in patients with space-occupying lesions are for smooth induction, maintenance of adequate CPP, maximization of surgical exposure, maintenance of normal neurophysiological functions, and homeostasis (water, electrolyte, and glucose) followed by rapid emergence with controlled hemodynamic and minimized coughing and straining during tracheal extubation.

Suggested Reading

Berger MS, Hadjipanayis CG. Surgery of intrinsic cerebral tumors. Neurosurgery. 2007;61(SHC Suppl 1):SHC 279–305.

Board, P.D.Q.A.T.E. Adult central nervous system tumors treatment (PDQR): health professional version. In: PDQ cancer information summaries. Bethesda: National Cancer Institute (US); 2002–2015. Published online January 2016.

Burnstein R, Banerjee A. Anesthesia for supratentorial surgery. In: Gupta AK, Gelb AW, editors. Essentials of neuroanesthesia and neurointensive care. Philadelphia: Saunders Elsevier; 2008. p. 106–10.

Glantz MJ, et al. Practice parameter: anticonvulsant prophylaxis in patients with newly diagnosed brain tumors. Report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology. 2000;54(10):1885–93.

Pasternak JJ, Lanier WL. Neuroanesthesiology update -2014. J Neurosurg Anesthesiol. 2015;27(2):87–122.

Weston J, Greenhalgh J, Marson AG. Antiepileptic drugs as prophylaxis for post-craniotomy seizures. Cochrane Database Syst Rev. 2015;3:Cd007286.

Part V

Critical Situations During Anesthesia for Spinal Surgery in Adults

Perioperative Challenges in Patients with Unstable Spine

35

Carl Helge Nielsen

Overview

Blunt trauma from high-speed motor vehicle accidents, falls from excessive heights, dives into shallow water, and penetrating trauma from gunshot wounds cause the majority of spine lesions; most of these do not involve permanent injury. Spinal cord injury occurs in 12,000–15,000 people per year in the USA; about 10% of these injuries cause permanent damage. Most spinal cord injuries occur in young men between the age of 15 and 25 years. About 5% occur in children.

Nearly 10% of patients with spinal cord injury have a second nonadjacent fracture elsewhere in the spine. Approximately 55% of spine injuries occur in the cervical spine; the remaining 45% are evenly distributed between the thoracic, thoracolumbar, and the lumbosacral regions. Instability of the spine is defined as the loss of the ability of the spine to tolerate physiologic loading without incurring neurologic deficit, pain, or progressive structural deficit. Patients with a suspected spine injury need to be immobilized, and their injuries, including life-threatening lesions, are attended to while movement of the spinal column is kept at a minimum. The immobilization is maintained until a spine injury is excluded.

Prevention

Plans to reduce both the number and the severity of unstable spine injuries are of paramount importance, albeit outside the scope of this text. The primary goal of resuscitation is to protect the spinal cord by reducing additional and secondary injuries. Thus, basic resuscitation and spine stabilization at all times are crucial. This requires that the anesthesiologist have intimate knowledge about the pathophysiology and the risks and benefits of multiple alternative approaches to both acute trauma care and anesthesia techniques. Spinal immobilization is a priority in multiple trauma; "spinal clearance" is not.

Specific pharmacologic management of patients with acute spinal cord injury in the USA focuses on the benefits of initiation of very high-dose steroid therapy within 8 h after the injury. Improved degree and rate of neurologic recovery has been shown by using 30 mg/kg bolus of methylprednisolone over 15 min followed by an infusion of 5.4 mg/kg/h for 23 h. The National Acute Spinal Cord Injury Study (NASCIS) in 1990 showed that high-dose methylprednisolone (30 mg/kg) given within 8 h of ASCI improved neurological function. However, some patients showed no improvement, and no patient recovered neurological function completely. This study has resulted in the widespread clinical use of high-dose steroids in ASCI, although controversy persists.

Crisis Management

Pathophysiology and Clinical Presentation

Symptoms from an unstable spine are in a wide range from mild local site pain to quadriplegia and death. They depend both on the severity of the injury and the level of involvement. Instability above the first thoracic spinal segment may show features of upper limb involvement. Above the fourth cervical vertebra, instability may lead to respiratory compromise. Involvement of the conus presents predominantly with bowel and bladder involvement. Patients may additionally present with varying degrees of autonomic dysfunction.

Both experimental and clinical observations of spinal cord injuries have demonstrated a spectrum of pathology that evolves over the days following the injury; this has led to the concept that the injury process is a result of both primary and secondary insults.

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Primary mechanism of cord injury can be due to four kinds of mechanical forces:

- Impact with persisting compression: e.g., fractures, dislocations, and disc herniations
- Impact with no persisting compression: e.g., hyperextension injuries
- Distraction: e.g., hyperflexion injuries
- Laceration/transection: penetrating injuries, fracture dislocation

Secondary injury mechanisms that may be involved are:

- Systemic shock: profound hypotension and bradycardia (often lasting for days) follows cord injury and may further compromise an already damaged cord.
- Local microcirculatory damage may occur due to mechanical disruption of capillaries, hemorrhage, thrombosis, and loss of autoregulation.
- Biochemical damage may occur due to excitotoxin release (glutamate), free radical production, arachidonic acid release, lipid peroxidation, eicosanoid production, cytokines, and electrolyte shifts.

All these factors (along with edema) lead to loss of energy-producing ability with consequent loss of impulse transmission, cell swelling, membrane lysis, and cell death.

Patient Assessment

Instability must be assumed (and the spine stabilized) in any patient with:

- Complaints of a sense of instability (patient holds his head in the hands)
- Vertebral column pain
- Tenderness over the midline or the spinous processes
- Neurologic deficit
- Altered mental status
- Any suspected spine injury notwithstanding lack of proof

The initial assessment of patients presenting with trauma is called the primary survey. During this assessment, life-threatening injuries are identified, and, simultaneously, resuscitation is begun. A simple mnemonic, "ABCDE," is used as a memory aid as to the order in which problems should be addressed.

1. Airway maintenance with cervical spine protection
2. Breathing and ventilation
3. Circulation with hemorrhage control
4. Disability (neurologic evaluation)
5. Exposure and environment

When the primary survey is completed, resuscitation efforts are well established, and the vital signs are normalizing, the secondary survey can begin.

The secondary survey is a head-to-toe evaluation of the trauma patient, including a complete history and physical examination, including the reassessment of all vital signs. Each region of the body must be fully examined. X-rays indicated by examination are obtained.

If at any time during the secondary survey the patient deteriorates, another primary survey is carried out, as a potential life threat may be present.

Spinal shock is the term for all the phenomena surrounding physiologic or anatomic transection of the spinal cord that results in temporary loss or depression of all or most spinal reflex activity below the level of the injury. Ditunno et al. proposed a four-phase model for spinal shock (Table 35.1).

Two additional considerations are particularly important to the anesthesiologist in the chronic phase: supersensitivity of cholinergic receptors and autonomic hyperreflexia.

In response to denervation, cholinergic receptors proliferate beyond the end plates of voluntary muscle fibers, eventually to invest the entire cell membrane. The muscle becomes "supersensitive" and contracts maximally in response to a concentration of acetylcholine of only 25% that is needed to initiate contraction in normal muscle. Potassium ion is released suddenly along the entire length of the fiber rather than gradually as the action potential propagates. This produces a rapid rise in serum potassium levels. Succinylcholine induces an identical response and may be associated with a serum potassium increase of 4–10 meq/L. Although succinylcholine is safe during the first day of paraplegia, it should be avoided completely after the third day.

The chronic phase in which spinal reflexes reappear is characterized by autonomic hyperreflexia in a high proportion of patients. Cutaneous, proprioceptive, and visceral stimuli, such as urinary bladder distention, may cause violent muscle spasm and autonomic disturbances. The

Table 35.1 Phases of spinal shock

Phase	Time	Physical exam finding	Underlying physiological event
1	0–1 day	Areflexia/ hyporeflexia	Loss of descending facilitation
2	1–3 days	Initial reflex return	Denervation supersensitivity
3	1–4 weeks	Hyperreflexia (initial)	Axon-supported synapse growth
4	1–12 months	Hyperreflexia, spasticity	Soma-supported synapse growth

symptoms of autonomic hyperreflexia are facial tingling, nasal obstruction, severe headache, shortness of breath, nausea, and blurred vision. The signs are hypertension, bradycardia, dysrhythmias, sweating, cutaneous vasodilatation above and pallor below the level of the spinal injury, and occasionally loss of consciousness and seizures. The precipitous blood pressure increase may lead to retinal, cerebral, or subarachnoid hemorrhage, increased myocardial work, and pulmonary edema. Patients with chronic spinal cord lesions above T-6 are particularly at risk for this response: 85% will display autonomic hyperreflexia at some time during the course of daily living. Of course, surgery is a potent stimulus to autonomic response even in patients who give no history of the problem.

Intervention Treatment

The recommendations from Advanced Trauma Life Support are used: aggressive resuscitation and management of life-threatening injuries, as they are identified, is essential to maximize patient survival.

Assume a cervical spine injury in any patient with multisystem trauma, especially when there is associated altered level of consciousness or a blunt injury above the clavicle. Measures to establish and/or maintain a patent airway must be instituted with cervical spine protection. New neurologic deficits occur 7.5 times more frequently with an unrecognized injury, and up to 10% of patients with a cervical spine injury will suffer a new neurologic deficit if not immobilized.

Prehospital care personnel usually have immobilized the patient before transport to the hospital. The patient with an injured spine must be fitted with a semirigid cervical collar, placed on a spine board, foam bolsters positioned at each side of the head, and straps used to maintain the neutral position.

Supplemental oxygen is provided. Airway patency may be achieved with simple maneuvers; basic chin lift and jaw thrust maneuvers are applied, while force is limited to prevent movement of the immobilized cervical spine. Airway compromise or altered mental status with a Glasgow Coma Scale score 8 or less require endotracheal intubation. There are no clear guidelines for the optimal method to secure the airway in patients with cervical spine injuries, with the exception that the head and neck must be kept in neutral position throughout the intubation procedure. Numerous approaches and devices to secure an airway in patients with an unstable spine have been suggested and were often presented in small series with high success rates. That said, it is essential that an anesthesiologist master a couple of these alternative approaches in addition to the standard intubation techniques with direct laryngoscopy, fiberoptic intubation, and blind nasal intubation. The goal is to facilitate endotracheal intubation without causing further injury to the unstable spine. Intubation while the patient wears the semirigid collar and the head is strapped down between the foam blocks is often impossible. The anterior part of the collar and the straps and blocks may be removed as long as head movement is avoided. This is accomplished with manual in-line axial stabilization (MIAS); note that the recommendation has changed *so traction (MIAT) is not recommended*. MIAS is applied by holding the sides of the neck and mastoid processes and exerting a gentle downward (posterior) pressure. During the intubation process, the person who provides MIAS must counteract the forces applied by the person who performs the intubation. Rapid sequence induction/intubation with cricoid pressure application should be used whenever indicated. Patients with cervical cord injury should be treated with glycopyrrolate prior to intubation to prevent the bradycardia that often occurs from unopposed parasympathetic stimulation during airway manipulation in these patients. The risk of failed intubation with inability to ventilate the patient must always be considered; it usually necessitates a surgical airway.

The patients with an unstable spine but otherwise stable vital signs who present for urgent or semi-elective procedures are commonly intubated with the use of fiberoptic techniques. Fiberoptic intubation of an awake, minimally sedated patient can often be achieved after adequate topical anesthesia of the airway. This method is preferred because the patient can immediately afterwards follow commands and demonstrate that postintubation movement of the extremities is unchanged from before.

For very anxious patients and for those where movement to command is desired after final positioning on the operation table, fiberoptic facilitated intubation may be preferable while they are under anesthesia. An ultrashort anesthetic provides analgesia and will keep the patient appropriately controlled while the intubation and positioning is accomplished, yet it wears off rapidly and the patient can demonstrate movement to command. The extremely unstable patients additionally may have somatosensory evoked potentials monitored both before and after intubation and positioning to document that neither procedure caused noticeable compromise. Team work, cooperation, and collaboration between the anesthesia, monitoring, and surgical teams are essential.

Rapid and accurate assessment of the patient's hemodynamic status is critical. Immediate replenishment of intravascular volume is followed with continued maintenance of an adequate intravascular volume and appropriate blood pressure to assure spinal cord perfusion. Anemia must be avoided. The bladder must be kept decompressed, and an NG tube is used to decompress the stomach.

Key Points

- Primary survey with ABCDE while the spine is stabilized
- General management considerations
  - Neurogenic shock
    (a) Traumatically induced sympathectomy with spinal cord injury.
    (b) Symptoms include bradycardia and hypotension.
    (c) Treatment: volume resuscitation to maintain systolic BP >90 mmHg (euvolemia).
    (d) May need phenylephrine (50–300 μg/min) or norepinephrine maintain BP
  - Gastrointestinal tract
    (a) Ileus is common and requires use of a nasogastric tube.
    (b) Stress ulcer prevention using medical prophylaxis.
    (c) Bowel training includes a schedule of suppositories and may be initiated within 1 week of injury.
  - Deep vein thrombosis
    (a) Start mechanical prophylaxis immediately.
    (b) Initiate chemical prophylaxis after acute bleeding has stopped.
  - Bladder dysfunction
    (a) Failure to decompress the bladder may lead to autonomic dysreflexia and a hypertensive crisis.
    (b) The bladder is emptied by intermittent or indwelling catheterization.
    (c) Antibiotic prophylaxis for the urinary tract is not advised.
  - Decubitus ulcers
    (a) Skin breakdown begins within 30 min in the immobilized hypotensive patient.
    (b) For prolonged transport, the injured patient must be removed from the hard spine board and placed on a padded litter.
    (c) Frequent turning and padding of prominences and diligence on the part of caretakers are essential to protect the insensate limbs.
    (d) All bony prominences are inspected daily.
    (e) Physical therapy is started early to maintain range of motion in all joints to make seating and perineal care easier.

Suggested Reading

American College of Surgeons. Advanced trauma life support student manual. Chicago: American College of Surgeons; 1997.

Deogaonkar M. Spinal cord injuries concepts of surgical management and rehabilitation. http://www.rehabindia.com/spinal-cord-injuries.htm. Accessed Jan 2009.

Desjardins G. Injuries to the cervical spine. http://www.trauma.org/archive/anaesthesia/cspineanaes.html. Accessed Jan 2009.

Grande CM, editor. Textbook of trauma anesthesia and critical care. St. Louis: Mosby; 1993.

Smith C. Cervical spine injury and tracheal intubation: a never ending conflict. Trauma Care. 2000;10:20–6.

Wounds and Injuries of the Spinal Column and Cord. http://www.usaisr.amedd.army.mil/ewsh/Chp20SpinalWounds&Injuries.pdf. Accessed Jan 2009.

Airway Crisis Associated with Cervical Spine Surgery

36

Edward Crosby

Overview

Airway problems encountered in anesthesia for cervical spinal surgery cluster into two major categories: the underlying spinal pathology increases the likelihood of *difficult airway* or surgery and prone positioning result in soft tissue swelling and acute *airway compromise postoperatively*. Less commonly, *intraoperative difficulties* arise, typically related to endotracheal tube migration or kinking resulting from surgical positioning.

Surgeries on the cervical spine can be divided into two broad categories, decompressive and reconstructive interventions. Simple decompression of a nerve foramen or discectomy is usually done via an anterolateral approach with the patient in the supine position. More extensive decompression of the canal itself is commonly done via a posterior approach with the patient in a prone position, although anterior approaches are used. Reconstruction procedures (with instrumentation) may be carried out after decompression to stabilize a spine compromised by the surgical intervention or done primarily to treat a spine rendered unstable by disease or injury. They may involve an anterior or posterior approach (or rarely both); the posterior approach is again carried out with the patient in the prone position.

Preoperative Airway Complications

Patients presenting for cervical spine surgery have a higher incidence of difficult laryngoscopy and intubation than is seen in the general surgical population; the likelihood of difficulties increases as movement becomes more restricted, and patients with occipito-atlantoaxial complex disease have the highest prevalence of difficulty. In patients <60 years, limitations in cervical spine movement are also associated with an increased likelihood of difficult mask ventilation. Other patient factors such as obesity, diabetes mellitus, and obstructive sleep apnea are common in this patient cohort and increase the incidence of anticipated difficult airway.

Intraoperative Airway Complications

Intraoperative airway complications are usually related to either migration or kinking of the tube. The head may be flexed on the neck to improve surgical access for posterior cervical operations in the prone position. This shortens the trachea and may result in migration of the tube into a main stem bronchus. Aggressively flexing the head may also force the jaw closed; if the patient has full dentition, this may result in the tube being kinked or crushed by the teeth and an obstructed airway. Compromise of the tube lumen may not be immediately evident but can manifest intraoperatively with increasing airway pressures and difficulty with ventilation resulting in decreased tidal volumes and hypercarbia. If the method to secure the tube becomes compromised in a prone-positioned patient, the tube may incrementally migrate out of the trachea – a recurrent cuff leak may indicate such migration.

Postoperative Airway Complications

Airway complications are common after anterior cervical spine surgery and range from acute airway obstruction to chronic vocal cord dysfunction. Variables associated with an increased likelihood of postoperative airway complications are included in Table 36.1. Unilateral vocal cord paralysis resulting from recurrent laryngeal nerve palsy is the most common airway complication after anterior cervical spine surgery; it should rarely result in any important degree of

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Table 36.1 Variables associated with airway complications after spinal surgery

Rheumatoid arthritis
Difficult intubation
Surgical exposure involving >3 levels
Surgical exposure involving C2, C3, C4
Occipito-cervical fusions
Combined anterior-posterior approach
Blood loss >300 ml
Operative time >5 h
Surgical use of bone morphogenetic protein

airway compromise. Pharyngeal and prevertebral edema is also common after cervical spine surgery, is most prominent at the C2–C4 levels, peaks on the second and third postoperative day, and may be associated with airway compromise. Surgical traction and dissection are implicated, and both prolonged surgery and difficult dissection increase the severity of the resulting edema. Patients with rheumatoid arthritis seem particularly susceptible to postoperative edema.

Decreased venous and lymphatic drainage of the head and upper airway is also implicated as an etiological factor for postoperative airway edema; prolonged operations and extreme flexed positioning may increase the risk. A hematoma in the soft tissues of the neck is common after cervical spine surgery but rarely results in clinically important airway compromise. However, larger hematoma may result in laryngeal and supraglottic edema, necessitating reintubation of the trachea on an urgent basis. Airway compromise resulting primarily from hematoma typically occurs earlier in the postoperative course ($\leq$12 h) than does that resulting from prevertebral and pharyngeal edema. Airway complications also occur after spine surgery performed in the prone position; these result primarily from supraglottic and laryngeal edema and to a lesser degree from macroglossia.

Prevention

Preoperative Airway Complications

A careful preoperative review will allow for the identification of many patients at risk for difficult intubation. Particularly relevant in the history is the presence of rheumatoid arthritis or ankylosing spondylitis, especially with disease which is longstanding and severe. Previous difficulties with laryngoscopy and intubation are also common in this population and likely predictive of repeat difficulties if the same strategy for airway management is chosen. The airway examination should emphasize evaluation of the usual features, but the Mallampati classification is a particularly useful predictor of difficult laryngoscopy in patients with cervical spine disease and restricted neck movement; a high score provides evidence of poor craniocervical extension and predicts difficulty. Although sophisticated imaging techniques can provide detailed information about the airway, even simple radiographs may be useful. Reduced separation of the posterior elements of the first and second cervical vertebrae on lateral radiographs is associated with difficult laryngoscopy. Once the evaluation is complete, a decision should be made as to whether the evaluation is reassuring regarding the ease of direct laryngoscopy. In the event that the evaluation is not reassuring, a plan for both intubation and extubation should be formulated which address the non-reassuring elements of the evaluation.

Intraoperative Airway Complications

Endotracheal tubes should be well secured and protected after correct placement has been confirmed. The use of a bite block or oral airway will provide protection to the tube intraoperatively and protect it from being crushed between the teeth with aggressive flexion of the head on the neck to afford surgical access to the upper cervical spine; the use of an armored tube alone will not prevent this from occurring. The circuit should be supported so as to reduce the dependent weight acting on the endotracheal tube in a prone-positioned patient to prevent outward migration of the tube; this may be done by securing the circuit to the operating table or the apparatus supporting the head.

Postoperative Airway Complications

Extubation is as risky a proposition as intubation in these patients; the airway will be no less difficult to manage than at intubation and will possibly be more so. A strategy should be in place to anticipate, monitor for, and manage postoperative edema (Table 36.2). Consideration should be given to a

Table 36.2 An approach to postoperative airway care after cervical spine surgery

Anticipate postoperative complications in at-risk patients
Consider postoperative ventilation in high-risk surgical scenarios
Employ tube exchangers for higher-risk extubations
Observe patients in high-surveillance units postoperatively
Aggressively evaluate complaints of respiratory distress
Administer drying agents if respiratory symptoms are present
Ensure the immediate availability of difficult intubation cart
Perform or arrange for endoscopic evaluation of the airway if airway symptoms persist
Maintain a low threshold for airway intervention if symptoms seem progressive
Arrange for timely notification of surgeon if airway interventions anticipated

period of postoperative ventilation to allow the swelling to subside, if high-risk characteristics are evident. If a decision has been made to extubate the trachea of a high-risk patient immediately postoperatively, a period of observation in a high-surveillance unit is the most prudent management strategy; placement of an airway exchange catheter may also be considered. Signs and symptoms of respiratory distress often herald the development of airway edema and should prompt immediate evaluation of the airway. The development of a quiet or muffled voice is an ominous sign and should be dealt with as an airway emergency.

Airway compromise associated with a wound hematoma is often a result of supraglottic edema, and, although frequently recommended, releasing the staple or suture line to evacuate the hematoma may have little apparent and immediate effect on the degree of compromise and the symptoms of distress. Consideration should be given to urgent tracheal intubation to stent the airway open, and, once the airway is secured and protected, a decision may be made regarding subsequent wound management.

Crisis Management

Pathophysiology and Clinical Presentation of Airway Complications

Preoperative Airway Complications

Difficulties with airway management at induction typically result from a combination of disease-related anatomical derangements, limitations in safe cervical spinal movement, and individual patient characteristics (e.g., obesity). It may not be possible to safely and optimally position a patient for direct laryngoscopy, and an alternate strategy for tracheal intubation is advisable. Extreme extension should be avoided as it may result in canal compromise and cord ischemia, especially if prolonged. Intraoperative complications more commonly are technical in nature and related to displacement of the tracheal tube or compromise of its lumen. Ensuring that the endotracheal tube is appropriately placed, well secured, and protected from kinking and crushing will reduce the potential for technical difficulties. A circuit leak should prompt immediate evaluation of tube integrity and placement; a fiberoptic bronchoscope (FOB) is indispensable in this regard. Increasing airway pressures and a concomitant reduction in the ventilation volumes should also trigger evaluation of the tracheal tube in addition to the usual review of the patient and apparatus.

Postoperative Airway Complications

Operative procedures performed upon patients in the prone position predispose to the development of airway edema. Venous drainage of the tongue, face, and airway is via veins which enter the internal jugular vein (IJV); the IJV is liable to kinking when the neck is maximally flexed. This may lead to partial or complete obstruction of the vessel and edema in the tissues drained by this system. Anatomical abnormalities of the skull base may predispose patients to venous obstruction at lesser degrees of flexion; the extreme flexion required obtaining surgical access to the posterior skull base and upper cervical spine may increase the risk of this complication. Postoperative edema and hematoma formation may also be associated with airway compromise through similar mechanisms. The amount of prevertebral edema formation is influenced by the duration of surgery, the difficulty of dissection, and the levels of ossification of the spinal ligaments.

Patient Assessment

Preoperative Airway Complications

Preoperative airway assessment should consist of both a history and physical examination. The occurrence of prior airway difficulties is predictive of recurrent difficulties during the new intervention being planned. Physical examination should review the usual features, but a detailed assessment of neck mobility is advised. The Mallampati evaluation may be particularly useful in this population as an assessment of neck movement and predictor of difficult laryngoscopy. Detailed imaging is often available for these patients and should be reviewed. Loss of the gaps between the occiput and posterior arch of C1 and the posterior arches of C1 and C2 are associated with difficult direct laryngoscopy.

Postoperative Airway Complications

Postoperative airway compromise as a result of either hematoma or edema is often subtle in its initial presentation. Compromise related to hematoma is more likely to present earlier, whereas that resulting from edema may be delayed, presenting up to 24–36 h or longer after surgery. Patient symptoms are common and may be present in the absence of clear signs of hematoma or airway compromise. However, complaints of dyspnea and insistence on either semi-recumbent or sitting positions are concerning; these should result in the continued observation of the patient in a high-surveillance unit and immediate evaluation of the state of the airway; an FOB facilitates this evaluation. A change in the quality of the voice should prompt immediate airway evaluation and consideration of tracheal intubation. This evaluation may be easily done with the patient in the sitting position; a nasal approach is useful and well tolerated. Early administration of drying agents (e.g., glycopyrolate 0.4–0.6 mg sc or IV) may facilitate subsequent airway evaluations and interventions.

Intervention and Treatment

Preoperative Airway Complications

Airway management is not predicted to be difficult in patients presenting for cervical spinal surgery who have reassuring airway assessments and well-preserved spinal mobility. However, patients for whom the assessments are not reassuring require management plans for both intubation and extubation which account for the anticipated difficulties; techniques employing devices other than the direct laryngoscope feature prominently in these plans. Awake intubation is more commonly chosen for patients with severe limitations in movement, myelopathy, unstable or fractured spines, and spinal stenosis with neurological symptoms or sequelae. The FOB is prominently featured in the management of these patients and may be used in both awake and asleep patients. However, a multitude of devices have been demonstrated to provide safe and effective airway care in these patients, including lighted stylets, rigid fiberoptic endoscopes, a range of videoscopes, the intubating laryngeal mask airway, and fiberoptic stylets, and experience rather than dogma should dictate choice.

Postoperative Airway Complications

Patients who present with airway compromise postoperatively require assessment on an urgent basis. Symptoms of respiratory distress may be out of proportion to observed signs of hematoma, swelling, and edema and should prompt early airway evaluation. It is also possible that symptoms of airway compromise in the setting of an obvious hematoma may be masked by administration of analgesics and sedatives in the early postoperative period, and the index of suspicion and surveillance should be raised accordingly. If supraglottic or laryngeal edema is present on examination, continued observation in a high-surveillance unit is mandatory, and consideration should be given to early tracheal intubation to protect the airway. Patients may progress to severe degrees of edema and airway compromise before the condition is recognized; it is likely that they will insist on sitting, and both position and agitation may complicate airway interventions. Awake intubation with an FOB may be attempted but will likely be complicated by the degree of airway distortion. If the patient is in extremis or has already suffered a respiratory arrest at the time of intervention, the observed degree of distortion will be extreme. Surgical establishment of an infraglottic airway may be lifesaving for a patient in extremis, but the surgical approach will be compromised by swelling in the neck and distortion of the anatomy. An urgent call for both a surgeon and the surgical kit should be made in a timely fashion. If respiratory arrest is imminent or apparent, airway interventions should not be delayed awaiting the arrival of a surgeon. Emergency intervention with the use of a direct laryngoscope and a gum elastic bougie to probe for the tracheal lumen may allow for successful tracheal intubation despite the lack of recognizable anatomy. Evacuation of a hematoma may not result in obvious or immediate improvement in the airway but may reduce the degree of tracheal deviation and reduce the difficulty of tracheal intubation.

Key Points

- Patients presenting for cervical spine surgery have an increased incidence of difficult airway.
- Significant limitations in cervical spine movement are predictive of difficult airway.
- Prolonged or extensive cervical spine surgery and the use of the prone position are associated with postoperative airway compromise.
- Extubation should be considered a high-risk intervention in these patients and planned accordingly.
- The use of an airway exchange catheter should be considered in high-risk extubations.
- At-risk patients should be monitored in high-surveillance nursing units postoperatively.
- Symptoms of respiratory distress may be out of proportion to observed signs of airway compromise.
- Airway distortion may be severe by the time assessment of symptoms occurs.
- The use of a gum elastic bougie during direct laryngoscopy may be useful in a severely distorted airway.

Suggested Reading

Preoperative Assessment and Management of the Airway

Manninen PH, Jose GB, Lukitto K, Venkatraghavan L, El Beheiry H. Management of the airway in patients undergoing cervical spine injury. J Neurosurg Anesthesiol. 2007;19:190–4.

Mashour GA, Stallmer ML, Kheterpal S, Shanks A. Predictors of difficult intubation in patients with cervical spine limitations. J Neurosurg Anesthesiol. 2008;20:110–5.

Postoperative Respiratory Complications

Sagi HC, Beutler W, Carroll E, Connolly PJ. Airway complications associated with surgery on the anterior cervical spine. Spine. 2002;27:949–53.

Palumbo MA, Aidlen JP, Daniels AH, Bianco A, Caiati JM. Airway compromise due to laryngopharyngeal edema after anterior cervical spine surgery. J Clin Anesth. 2013;25:66–72.

Management of Postoperative Respiratory Complications

Combes X, Dumerat M, Dhonneur G. Emergency gum elastic bougie-assisted tracheal intubation in four patients with upper airway distortion. Can J Anesth. 2004;51:1022–4.

Shakespeare WA, Lanier WL, Perkins WJ, Paternak JJ. Airway management in patients who develop neck hematomas after carotid endarterectomy. Anesth Analg. 2010;110:588–93.

Spinal Cord Injury During Spinal Surgery

37

Hironobu Hayashi and Masahiko Kawaguchi

Overview

Perioperative spinal cord injury (SCI) is a devastating complication, and its reported incidence based on primary diagnosis for adult patients can vary from 0% to 3%, depending on the pathological profiles and surgical approach. Its incidence seems to be especially high after spinal surgery for kyphosis, spondylolisthesis, and scoliosis. The neuronal/axonal injury can result in motor, sensory, and/or autonomic impairment. In addition to a direct insult to the spinal cord by the surgical procedure, anesthesia-related factors can also worsen SCI, which is pre- and intraoperatively developed. In order to improve neurological outcome after spine surgery, prevention, identification, and treatment of SCI is critical. Intraoperative neuromonitoring, cardiopulmonary management, and pharmacological therapy would be important general management of SCI. Multimodal intraoperative neuromonitoring with somatosensory-evoked potential (SSEP), motor-evoked potential (MEP), and/or electromyography (EMG) provides a higher specificity and sensitivity for detecting SCI than any modality used in isolation. However, anesthetic and neuromuscular blocking agents and physiological alterations can affect the results of neuromonitoring, which may interfere with an early detection of impending SCI and consequently delay its treatment. Therefore, proper understanding of its influences on each neuromonitor can be a key for anesthetic management to reduce the incidence and severity of SCI after spinal surgery.

Prevention

In the setting of an underlying pathological entity of the spinal cord at risk for injury and ischemia, careful anesthetic management is required. Hyperextension of the neck during intubation in patients with cervical stenosis and potentially unstable cervical spines should be avoided. Transfer and positioning of the patients should be performed with a careful control of spine. Hypotension should be avoided because it can lead to a decrease of spinal cord perfusion. Vasopressors should be used to maintain the MAP >80 mmHg, although no ideal MAP has been determined. The maintenance of hematocrit may also be required. Administration of methylprednisolone for the treatment of acute SCI is not recommended. High-dose steroids are associated with harmful side effects including death.

Successful neuromonitoring is one of the most important strategies to prevent permanent SCI. Early recognition of impending SCI can help to identify and promptly reverse the precipitating cause. Types of intraoperative neuromonitors to be used and each technique may vary depending on the pathological profiles, surgical procedures, and availability of electrophysiological monitoring staff and equipment. However, current evidence indicates that MEP is the most valuable tool to monitor functional integrity of descending motor pathways, although it may be combined with SSEP and wake-up test. A schema on MEP is described in Fig. 37.1. Spinal MEP can be recorded through epidural electrodes, and D-wave is used for monitoring because it is not affected by the anesthetic agents and neuromuscular blocking agents. Myogenic MEP can be recorded from the muscles as compound muscle action potentials (CMAPs). Since the myogenic MEP is very sensitive to suppression by most anesthetic agents, a choice of anesthetic agents should be carefully performed. Intravenous anesthesia using propofol and fentanyl/remifentanil seems to be a good choice to obtain reliable myogenic MEPs. In patients with preoperative motor deficits, the use of ketamine with minimum influences on myogenic MEP may be considered when a proper control MEP is difficult to obtain under propofol-based anesthesia. In contrast, inhalational anesthetic agents are suboptimal for myogenic MEP monitoring unless medically necessary because inhalational anesthetics suppress myogenic MEP amplitude

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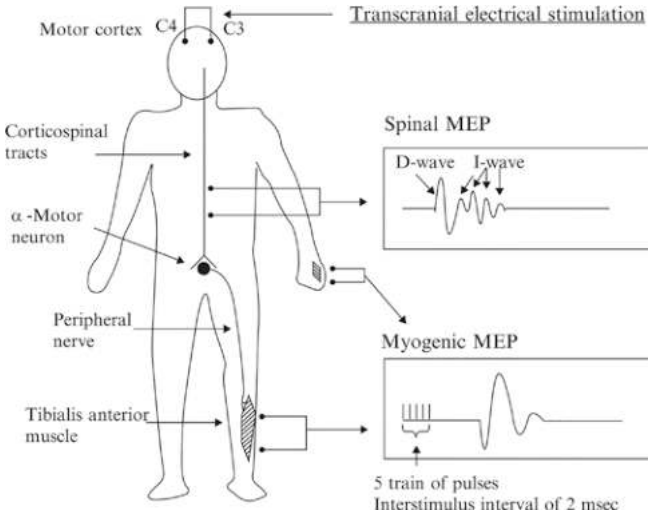

Fig. 37.1 Schema of spinal and myogenic MEPs

in a dose-dependent manner. However, it has been reported that low doses of desflurane up to 0.5 MAC can provide successful myogenic MEP monitoring when it is combined with propofol-remifentanil intravenous anesthesia, as a regimen of balanced anesthesia. Neuromuscular blocking agents should be avoided for myogenic MEP except for intubation. Otherwise, it may be used at the level of partial muscular blocking, which may complicate interpretation. No use of neuromuscular blocking agents to augment muscle contractions during transcranial stimulation for myogenic MEP may increase the risk of bite injury.

SSEP monitoring is commonly recorded on scalp after electrical stimulation of peripheral nerves. For recording SSEP, ulnar or median nerve for the upper limb and tibial or peroneal nerve for the lower limb are stimulated. Inhalational agents tend to suppress SSEP by decreasing the amplitude and increasing the latency in a dose-dependent manner. Total intravenous anesthesia using propofol delivers the most ideal condition for SSEP monitoring. Neuromuscular blocking agents do not affect SSEP.

Crisis Management

Pathophysiology and Clinical Presentation

Perioperative SCI involves a direct and indirect physiological insult to the spinal cord. A direct insult may include compression, impaction, laceration, distraction, and ischemia, which can develop during the induction of anesthesia, positioning of patients, and postoperative course, as well as during the surgical procedure. An indirect insult may result from reduction of spinal cord blood flow and oxygen delivery, edema, and inflammation and may be secondary to a cascade of biochemical and cellular processes initiated by a direct insult. Postoperative causes of SCI include an epidural hematoma and infection, which can initially present with symptoms such as back pain, radicular pain, sensory disturbances, weakness, and paralysis.

Patient Assessment

To recognize the intraoperative development of SCI under general anesthesia, the use of neuromonitoring is critical. Although still debated in detail, examples of the criteria for significant MEP and SSEP changes, which signal impending or manifest SCI, are shown in Table 37.1.

Usually myogenic MEP can be reduced or abolished in an early phase of SCI. In such situations, it is important to check whether changes in myogenic MEPs can truly be attributed to ongoing SCI or whether anesthesia-related factors are impairing the signal quality. Before initiating SCI-targeted treatment, other factors that may attenuate myogenic MEPs should be checked. Confounding variables that may affect the recording of myogenic MEPs and their appropriate managements are shown in Table 37.2.

Table 37.1 Criteria for significant MEP and SEP changes

Neuromonitor	Significant changes as an alarm
Myogenic MEP (CMAPs)	A reduction in amplitude to less than 20% of control or the complete lost
Spinal MEP (D-wave)	A reduction in amplitude to less than 50% of control
SSEP	A reduction of amplitude to less than 50% of control
	An increase in latency by 10% of control
Wake-up test	Motor weakness or paralysis

Table 37.2 Variables affecting myogenic MEPs

Factors affecting myogenic MEPs	Management
Electrodes failure	Check electrodes
Stimulus parameters	Check stimulus parameters
Anesthetics	Check the depth of anesthesia
	Keep the level of anesthesia constant
	Avoid inhalational anesthetics
	Avoid nitrous oxide >50%
Neuromuscular blockade	Check the level of neuromuscular blockade
	Keep the level of neuromuscular blockade constant
	Avoid the use of neuromuscular blocking agents
Hypothermia	Maintain normothermia
MAP reduction	Maintain MAP >80 mmHg
Reduction of hematocrit (anemia)	Maintain hematocrit > 30%

Intervention/Treatment

Once the development of SCI has been recognized by neuromonitoring, prompt and aggressive intervention is warranted. First, the concerns regarding impending or manifest SCI, based on the results of electrophysiological monitoring, should be immediately communicated to the surgeons. If surgical interventions such as particular instruments, screws, or deformity correction can be identified, these causes must be reversed immediately. If MAP is less than 80 mmHg or significantly below the preoperative value, the MAP should be corrected to levels at least above 80 mmHg using vasopressors. If profound perioperative blood loss has resulted in anemia and hypovolemia, means to correct the hematocrit and achieve normovolemia must be initiated. The use of methylprednisolone to prevent secondary injury in the setting of acute SCI has been considered as effective according to the beneficial results of the National Acute Spinal Cord Injury Study (NASCIS) trials. Recently, the 2013 guidelines indicated that high-dose methylprednisolone administration is associated with a variety of complications including infection, respiratory compromise, gastrointestinal hemorrhage, and death. There is no consistent or compelling medical evidence of any class to justify the administration of methylprednisolone for acute SCI. Methylprednisolone should not be routinely used in the treatment of patients with acute SCI.

Key Points

- Hyperextension of the neck during intubation, transfer and positioning of the patients, hypotension, and anemia can be causes of SCI, so that careful anesthetic management is required.
- Electrophysiological monitoring such as MEP and SEP is critical in the detection of SCI during spinal surgery.
- Understanding of the effects of anesthetic agents and physiologic alterations on electrophysiological monitoring is imperative for successful neuromonitoring.
- Maintenance of the MAP>80 mmHg and of the hematocrit >30% appears important for minimizing the risk of SCI.
- Administration of methylprednisolone for the treatment of acute SCI is not recommended. High-dose methylprednisolone are associated with harmful side effects, including death.

Suggested Reading

Hadley MN, Walters BC. Introduction to the guidelines for the management of acute cervical spine and spinal cord injuries. Neurosurgery. 2013;72(Suppl 2):5–16.

Hamilton DK, Smith JS, Sansur CA, Glassman SD, Ames CP, Berven SH, Polly DW Jr, Perra JH, Knapp DR, Boachie-Adjei O, McCarthy RE, Shaffrey CI. Scoliosis Research Society Morbidity and Mortality Committee. Rates of new neurological deficit associated with spine surgery based on 108,419 procedures: a report of the scoliosis research society morbidity and mortality committee. Spine. 2011;36(15):1218–28.

Hurlbert RJ, Hadley MN, Walters BC, Aarabi B, Dhall SS, Gelb DE, Rozzelle CJ, Ryken TC, Theodore N. Pharmacological therapy for acute spinal cord injury. Neurosurgery. 2013;72(Suppl 2):93–105.

Macdonald DB, Skinner S, Shils J, Yingling C, American Society of Neurophysiological Monitoring. Intraoperative motor evoked potential monitoring – a position statement by the American Society of Neurophysiological Monitoring. Clin Neurophysiol. 2013;124(12):2291–316.

Sloan TB, Toleikis JR, Toleikis SC, Koht A. Intraoperative neurophysiological monitoring during spine surgery with total intravenous anesthesia or balanced anesthesia with 3% desflurane. J Clin Monit Comput. 2015;29(1):77–85.

Tamkus AA, Rice KS, Kim HL. Differential rates of false-positive findings in transcranial electric motor evoked potential monitoring when using inhalational anesthesia versus total intravenous anesthesia during spine surgeries. Spine J. 2014;14(8):1440–6.

Zhuang Q, Wang S, Zhang J, Zhao H, Wang Y, Tian Y, Zhao Y, Li S, Weng X, Qiu G, Shen J. How to make the best use of intraoperative motor evoked potential monitoring? Experience in 1162 consecutive spinal deformity surgical procedures. Spine. 2014;39(24):E1425–32.

Blood Loss During Spine Surgery

38

Matthew T. V. Chan and Patricia K. Y. Kan

Overview

Blood loss during surgery of the spine varies enormously. Although the experience of surgeons is often considered as a major determining factor, there are other risk factors that may predict excessive blood loss during surgery (Table 38.1). Intuitively, substantial blood loss is expected in a prolonged, multilevel procedure that requires extensive decortication of the vertebrae, osteotomy, and stripping of paravertebral muscles for surgical exposure and instrumentation. However, bleeding could be significant even in a single-level laminectomy during revision surgery, surgery for tumor excision, traumatic injury, or infective diseases. Bleeding is also more likely in elderly, because the vascular channels are wide open due to osteoporosis and the epidural venous plexus is more fragile.

Clearly, the consequences are related to the extent of blood loss and the underlying physiologic condition of the patient. In general, the mechanisms of adverse effects are due to:

- Hemodynamic changes associated with fluid shift
- Anemia
- Depletion of platelets and clotting factors resulting in consumptive coagulopathy
- Adverse reactions related to the treatment administered, especially associated with transfusion of blood or blood products (Table 38.2)

In addition, bleeding will obscure operative field and may adversely affect surgical outcome. The associated coagulopathy and hyperfibrinolysis may lead to postoperative hematoma and thus predisposing patients to infection and potentially compressive neurologic injury (e.g., epidural hematoma).

Table 38.1 Risk factors for substantial blood loss after spine surgery

Procedure characteristics	Surgery for tumor excision
	Surgery for fracture of the spine
	Surgery for infection (such as tuberculosis, osteomyelitis)
	Revision surgery
	≥3 vertebral segments fusion
	Instrumentation
	Lumbar spine (compared with cervical spine) surgery
	Posterior and lateral approaches
Patient characteristics	Age >70 years
	Obese patients
	Patients with known clotting defects
	Children with neuromuscular scoliosis

Perioperative management should therefore aim to control the source of bleeding, to restore hemodynamic stability, to ensure tissue perfusion with sufficient delivery of oxygen and nutrients, and to enhance hemostasis. However, at the same time, it would be important to minimize exposure to allogenic blood and blood products.

Prevention

Minimizing Blood Loss

Preventing hemorrhage during surgery requires communication and close collaboration between the spine surgeons and anesthesiologists throughout the perioperative period. The following strategies may be adopted:

- A detail preoperative evaluation to identify patients with potential bleeding diathesis. This is particularly important to patients receiving nonsteroidal anti-inflammatory drugs. These agents are known to impair platelet function and are

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Table 38.2 Complications associated with transfusion of allogenic blood products

Mechanism	Adverse effects	Incidence per unit blood transfused
Immunologic	*Acute reaction*	
	Urticaria	1:50–100
	Febrile, nonhemolytic transfusion reaction	1:300
	Anaphylaxis	1:150,000
	Acute hemolysis	1:25,000
	Transfusion-related acute lung injury	1:5000
	Delayed reaction	
	Red cell alloimmunization	1:100
	Immune modulation/ suppression	Extremely rare
	Delayed hemolysis	Extremely rare
	Graft-versus-host disease	Extremely rare
Non-immunologic	*Acute reaction*	
	Hypothermia	1:100
	Hypervolemia	1:200
	Coagulopathy	1:200
	Delayed reaction	
	Human immunodeficiency virus	1:1,000,000–2,000,000
	Human T-lymphotropic virus I and II	1:625,000
	Bacterial contamination	1:5,000,000
	Hepatitis C, hepatitis B	1:100,000–2,000,000

best avoided or switched to selective COX-II blockers during the week prior to surgery. Patients with coronary artery disease, valvular replacement, atrial fibrillation, and stroke are often taking potent antiplatelet agents (such as aspirin and clopidogrel), heparin, and other novel oral anticoagulants. Although these agents may prevent major cardiac event in the non-operative setting, there are uncertainty whether the risk of perioperative bleeding will outweigh the benefits. It is therefore important to consider the timing to stop these agents prior to elective spine surgery (Table 38.3). The other drugs that should receive equal attention are those "over-the-counter" herbal products and traditional Chinese medicine. Many of them, such as ginkgo and ginseng, are known to affect coagulation and should be discontinued long before surgery. It is also important to ensure patients with known clotting defects actually received the appropriate treatment before surgery (e.g., desmopressin for von Willebrand disease). In urgent or emergent surgery, or when unexpected major blood loss occurs, it may be necessary to reverse the antithrombotic or antiplatelet effects (Table 38.3).

- In patients with vascular tumors, one should consider prophylactic embolization prior to invasive surgery.
- Where feasible, minimally invasive spine surgery should be considered. Compared with conventional open procedure, minimally invasive surgery avoids disruption of surrounding tissue and therefore minimizes approach-related bleeding.
- In the operating room, patient must be carefully positioned to avoid impediment of venous drainage and subsequent engorgement of epidural veins.
- Acute normovolemic hemodilution (ANH) may decrease loss of hemoglobin during surgery. In this technique, blood is removed (down to a hematocrit value of 20–30%), and circulating volume is restored with crystalloids or colloids prior to an anticipated episode of bleeding. The blood collected is then returned to the patient after hemostasis is achieved. Therefore, only diluted blood with lower hematocrit is being lost during surgery. Additional advantages of ANH are that it uses patient's own blood and that the clotting factors and platelets in it will improve hemostasis.
- Controlled hypotension, aiming to reduce systolic arterial pressure between 60 and 80 mmHg, has been advocated to decrease intraoperative blood loss. However, both controlled hypotension and ANH are contraindicated in patients with significant cardiac morbidity. Unfortunately, activity of spine patients is often limited because of pain and deformity. It is therefore difficult to predict the individual who may not be able to tolerate these maneuvers. Given the prevalence of coronary artery disease in the general population and the emerging cases of postoperative visual loss after spine surgery (see Chap. 40: Postoperative blindness), the risk of controlled hypotension and ANH should not be overlooked.
- Meticulous hemostasis is always required to decrease blood loss. Vasoconstrictors, bone wax, fibrin sealants, and hemostatic collagen and cellulose are commonly used for local control of bleeding. Hemostasis may also be enhanced with administration of hemostatic drugs. Table 38.4 summarizes the clinical uses, mechanisms of action, and potential side effects of these agents. In the literature, prophylactic use of tranexamic acid, aprotinin, or recombinant activated factor VII (rFVIIa) significantly decreases blood loss and the need for allogenic blood transfusion. However, they also increase the risk of thromboembolism, especially in patients with proven history or at risk of atherosclerosis or thrombosis. Aprotinin also increases the risk of other serious side effects, such as heart failure, renal failure, acute coronary syndrome, and stroke. Because of these adverse reactions, aprotinin is currently withdrawn from the market and is only restricted to investigational use under a limited user agreement. The efficacy data on epsilon-

Table 38.3 Characteristics of common anticoagulant and antiplatelet agents

Agents	Mechanism of action	Half-life	Timing of cessation before spine surgery	Antidote
Anticoagulants				
Dabigatran	Direct thrombin inhibitor	12–14 h (80% renal elimination; 20% fecal route)	3–5 days (depending on glomerular filtration rate)	Idarucizumab 5 g IVI; prothrombin complex concentrates 3000 U; hemodialysis or charcoal hemoperfusion to increase drug clearance
Apixaban	Direct factor Xa inhibitor	8–15 h (25% elimination via renal; 70% via hepatic)	3–5 day	Prothrombin complex concentrates 3000 U
Rivaroxaban	As above	5–13 h (65% renal elimination; 35% hepatic metabolism)	3 days	Prothrombin complex concentrates 3000 U
Warfarin	Inhibition of vitamin K–dependent factors II, VII, IX, and X for γ-carboxylation; proteins C and S	Metabolized by liver cytochrome P450; half-life 20–60 h	1–8 days (depending on INR; INR decreases to ≤1.5 in 90% of patients after 5 days)	Vitamin K; fresh frozen plasma transfusion or prothrombin complex concentrates
Unfractionated heparin	Anti-thrombin activation	60–90 min	IVI: 2–6 h	Protamine 25–30 mg (1 mg per 100 anti-Xa units in the last 2 h)
Low-molecular weight heparin	As above	4 h	Prophylactic dose: 12 h Therapeutic dose: 24 h	Protamine 25–30 mg (partial reversal, 1 mg per 100 anti-Xa units in the last 8–12 h)
Antiplatelets				
Aspirin	Irreversible inhibition of COX-1 in platelets and megakaryocyte, causing a decrease in TxA2	15–20 min	5–7 days	Desmopressin 0.3–0.4 μg/kg; Platelet concentrate transfusion
Prasugrel	Irreversible inhibition of ADP receptor $P2Y_{12}$	7 h (range 2–15 h)	7–10 days	As above
Clopidogrel	As above	7–9 h	7–10 days	As above
Ticagrelor	Reversible modification of ADP receptor $P2Y_{12}$	9 h (range 6.7–9.1 h)	5–7 days	As above
Abciximab	Glycoprotein IIb/IIIa inhibitor – prevents platelet aggregation and thrombus formation	10–30 min	2–5 days	As above
Eptifiban	As above	2.5 h	8–24 h	As above
Tirogiban	As above	2 h	8–24 h	As above

ADP Adenosine diphosphate, *INR* international normalized ratio, *COX* cyclooxygenase, *TxA* thromboxane

aminocaproic acid (EACA) and desmopressin are however less consistent, owing to the small number of patients in the trials. Desmopressin is a specific treatment for von Willebrand disease and mild hemophilia A. Other than this, there is no evidence that desmopressin will decrease blood loss or rate of transfusion after spinal surgery. Currently, tranexamic acid and rFVIIa should only be given to patients when massive hemorrhage is anticipated.

Minimizing Allogenic Blood Transfusion

Despite the best attempt to reduce intraoperative blood loss, a substantial proportion of patients undergoing complex spine surgery will require blood transfusion. The following techniques have been advocated to minimize the potential risk of allogenic transfusion (Table 38.2).

- There are ample of evidence to suggest that preoperative anemia predicts perioperative blood transfusion. It is important to identify and correct nutrient deficiency with supplemental iron, vitamin B, and folate therapy. Preoperative recombinant human erythropoietin (rHuEPO) administration (weekly subcutaneous injection 40,000 IU for 3 weeks) elevates hemoglobin and thus reduces allogenic transfusion. Thromboembolism and red cell aplasia (due to the development of autoantibodies) are the potential adverse effects of rHuEPO. Fortunately, these events are uncommon.
- Liberal transfusion should be avoided. Current evidence suggested that a hemoglobin concentration above 8 g/dL has little effect on perioperative morbidity. However, the

actual decision to transfuse should also consider cardiac and cerebrovascular status of the patient. The use of noninvasive pulse co-oximeter to estimate total hemoglobin concentration may help to avoid excessive transfusion.

- In preoperative autologous donation program, patients donate several units of blood before surgery. During and after surgery, patients received their own stored blood when clinically indicated. The major drawback of this technique is that it only applies to elective surgery when procedures are planned weeks ahead. It should also be clear that the risk of clerical error, bacterial contamination, and complications associated with stored blood is not modified.
- Perioperative red cell salvage involves collection of blood shed during surgery and reinfused to the patients following appropriate filtering and treatment. The technique could be applied to emergency surgery and has been shown to reduce allogenic transfusion, but the effect is small. It remains controversial whether perioperative red cell salvage can be used in surgery for infective or malignant disease.

Crisis Management

The cardinal signs for acute hemorrhage during spine surgery are hypotension, tachycardia, and oliguria (Table 38.5). Given its non-specific nature, a number of events may mimic acute hemorrhage. Table 38.6 summarizes the potential differential diagnoses, patient assessment, and management of major blood loss during spine surgery. While it is easy to identify sudden massive hemorrhage, insidious concealed bleeding may be difficult to recognize. The treatment priority is to control the source of bleeding and then to replace blood volume, hemoglobin, and clotting factors.

Hypothermia, electrolyte abnormalities, acidosis, and coagulopathy must be seriously considered when large amount of blood has been transfused (>10 units of red cell). Table 38.7 shows the causes, assessment, and treatment for the adverse events associated with massive transfusion.

In the most uncommon event when hemolytic reaction is suspect during blood transfusion, an outline of treatment is listed in Table 38.8. When coagulopathy is suspected, the use of point-of-care hemostatic assays, such as throm-

Table 38.4 Clinical uses and mechanisms of action of hemostatic agents

Drug	Dosage	Mechanism of action	Side effects	Results of clinical investigations
Tranexamic acid	Loading dose 10 mg/kg during induction of anesthesia Maintenance dose 1–2 mg/kg/h	Lysine analogue that inhibits the binding of plasmin to fibrin	Thromboembolism	Study results support its prophylactic use
Epsilon-aminocaproic acid (EACA)	Loading dose 150 mg/kg during induction of anesthesia Maintenance dose 10–15 mg/kg/h	As above	As above	Mixed results, most studies do not support its use
Aprotinin	Loading dose 1–2 × 10^6 KIU during induction of anesthesia Maintenance dose 0.25–0.5 × 10^6 KIU/h	Direct inhibition of plasmin, kallikrein, trypsin, and factor XIIa	Renal failure, coronary ischemia, cerebrovascular thromboembolism	Aprotinin has been withdrawn recently due to an increase in adverse events
Desmopressin (Deamino-8-d-arginine-vasopressin, DDAVP)	Slow infusion 0.3 μg/kg over 30 min	Release of von Willebrand factor	Possible increase in myocardial infarction	Useful in specific disease (type 1 von Willebrand disease and mild hemophilia A), may be effective in chronic renal failure
Recombinant activated factor VII (rFVIIa)	30–120 μg/kg every 2 h for three doses	rFVIIa binds with subendothelial tissue factor that is in the exposed vessel wall. The binding complexes subsequently generate thrombin that in turn facilitates conversion of fibrinogen to fibrin	Thromboembolism	Approved for the treatment of bleeding in patients with hemophilia. Limited data on its use for prophylaxis and treatment of bleeding during surgery

Table 38.5 Classes of the American College of Surgeons for acute hemorrhage

	Class I	Class II	Class III	Class IV
Blood loss				
Volume	≤750	750–1500	1500–2000	≥2000
Percent of total blood volume	≤15%	15–30%	31–40%	≥40%
Arterial pressure[a]	Normal	Normal	Decreased	Decreased
Pulse pressure	Normal/increased	Decreased	Decreased	Decreased
Pulse rate (beats per minute)	>100	>100	>120	≥140
Urine output (ml/h)	>30	20–30	5–10	Negligible

[a]Pulse pressure = systolic – diastolic arterial pressure

Table 38.6 Patients with acute intraoperative bleeding

Differential diagnoses	Assessment	Treatment/intervention
Inadvertent overdose of anesthetic and/or vasodilator therapy	Confirm the vital signs	Communicate with the surgeons of the problem and severity of blood loss
Pulmonary embolism	Exclude other causes of hemodynamic disturbances	Ensure adequate vascular access if not already secured
Other forms of obstructive shock (e.g., pneumothorax, cardiac tamponade)	Estimate blood loss (blood in suction bottle, surgical sponges, under the drape, and on the floor; see Table 38.4)	Communicate with blood bank for adequate supply of blood and component therapy
Anaphylaxis (including transfusion reaction)	Check hemoglobin concentration	Avoid hypertension to facilitate surgical control of bleeding (consider wound packing while preparing for transfusion or establishing equipments for cell salvage)
Always consider bleeding from other sites, especially in patients with multiple trauma (e.g., ruptured spleen)	Check coagulation status (both clinical, oozing from the wound, and laboratory parameters – platelet count, activated partial thromboplastin time, prothrombin time, fibrinogen, and thromboelastography)	Restore blood volume and maintain perfusion pressure with vasopressors as soon as hemostasis is achieved
	Check responses to therapy (including plasma electrolytes and arterial blood gas)	Reverse prior anticoagulation therapy (e.g., protamine for prophylactic heparin administration)
		Start transfusion when hemoglobin concentration <8 g/dl and there is evidence of ongoing bleeding
		Prevent and promptly treat the complications associated with massive transfusion (acidosis, hypothermia, and coagulopathy)

Table 38.7 Complications associated with massive transfusion

Complications	Causes/consequences/assessment	Treatment/intervention
Hypothermia	Heat loss due to exposure to refrigerated blood and cold operating room environment	Use only warmed fluids, blood, and blood products
	Decrease clotting factor activity by 10%/°C decease in core temperature	Apply forced air warming devices, heated blankets
	Depressed myocardial contractility when core temperature <32 °C	
Electrolyte disorders		
Hyperkalemia	Infusion of aged stored blood in large amount	Stop potassium containing
	Tissue hypoperfusion	Solution
		Administer dextrose 50%, 100 ml with actrapid 10 units *ivi*
	Tall peaked T wave when plasma potassium concentration >6 mmol/l	Calcium gluconate 10%, 10 ml *ivi*
Hypocalcemia	Consequence of citrate toxicity when large amount of blood is infused (>1 unit every 10 min)	Calcium gluconate 10%, 10 ml *ivi*
	Prolonged QT interval	
Metabolic acidosis	Tissue hypoperfusion	Fluid resuscitation and vasopressor therapy is required to improve tissue perfusion
	Hyperchloremic acidosis as a result of excessive saline infusion	Temporary measures included:
		Hyperventilation to maintain arterial carbon dioxide tension between 28 and 30 mmHg
		Sodium bicarbonate 8.4%, 50–100 ml infusion *ivi* to maintain pH >7.2
Coagulopathy	Dilutional coagulopathy and hyperfibrinolysis	Administer fresh frozen plasma 10 ml/kg, platelet concentrates 10 ml/kg, cryoprecipitate 10 units when PT >1.5, platelet count $<50\times10^9$/l, and fibrinogen concentration <1 g/l, respectively
		Consider other hemostatic agents (see Table 38.3; e.g., tranexamic acid 10 mg/kg, rFVIIa 90 μg/kg)

Table 38.8 Treatment for acute hemolytic reaction after blood transfusion

Causes	Assessments	Treatment/intervention
Infected blood transfusion	Many of the signs are concealed during general anesthesia, but the following should raise the possibility of hemolytic reactions:	Stop transfusion
Transfusion-related acute lung injury	Hypotension, tachycardia	Maintain arterial pressure and intravascular volume with fluid and vasopressor
Mismatched (incompatible) blood transfusion	Bronchospasm, urticaria	Treat bronchospasm with bronchodilator
	Bleeding diathesis	Maintain urine output with mannitol 20%, 0.5 g/kg over 10–30 min, frusemide 10–20 mg *ivi* if urine output remains unsatisfactory
	Hemoglobinuria due to an elevated plasma-free hemoglobin	Force alkaline diuresis with sodium bicarbonate 8.4%, 50–100 ml infusion
		Avoid further transfusion, if feasible
		Check hemoglobin concentration and coagulation status, correct clotting defects promptly
		Return unused blood, and send blood samples from the patients to the laboratory for further investigations

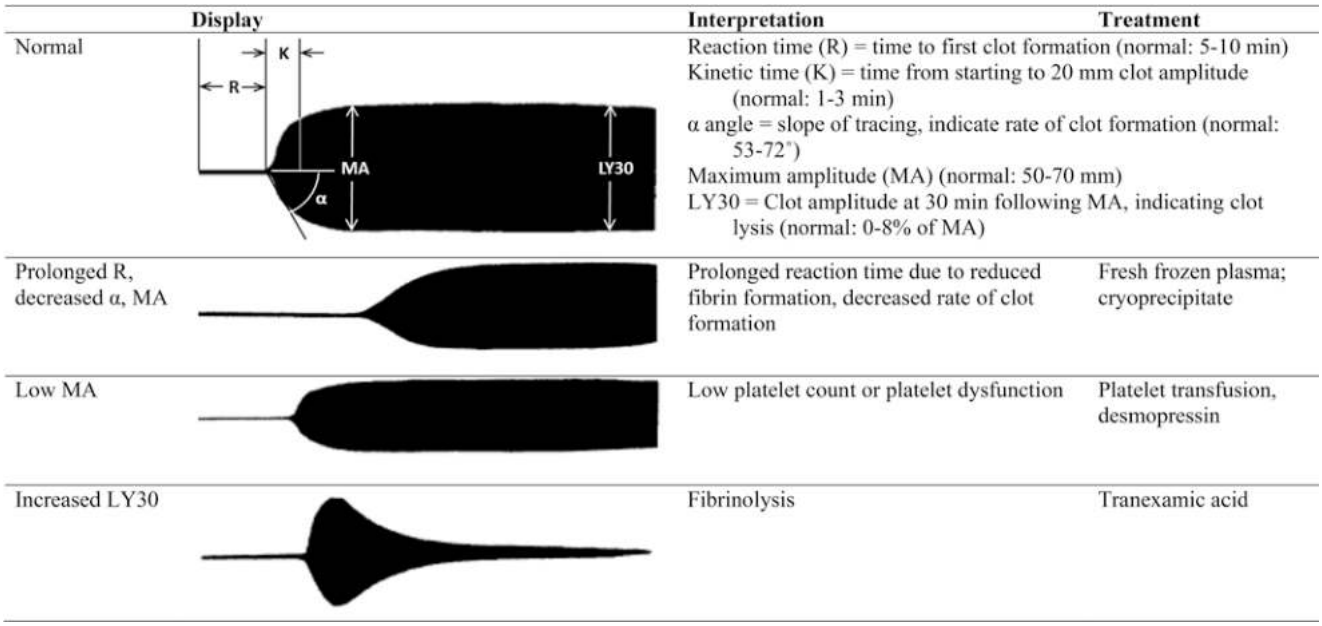

Fig. 38.1 Thromboelastographic features of hemostatic abnormalities

boelastography (TEG) and rotational thromboelastometry (ROTEM), provides useful displays of various causes of coagulation deficits and may help to rationalize transfusion of coagulation factors and cellular components (Fig. 38.1).

Key Points

- Detail preoperative preparation to identify patients at risk of massive hemorrhage during spine surgery, correct anemia, and stop agents that may impair coagulation.
- In patients at high risk of massive bleeding during surgery, preoperative autologous donation should be considered.
- During surgery, hypertension should be avoided. Acute normovolemic hemodilution is safe down to a hematocrit value of 30%. Lower hematocrit or controlled hypotension is considered risky in patients with known or at risk of coronary artery disease.
- Tranexamic acid may be used prophylactically to decrease blood loss. When bleeding becomes massive, consider giving rFVIIa.
- During an episode of massive bleeding, the treatment priority is to control the source of bleeding. When bleeding slows down, blood volume and hemodynamic stability should be restored.
- During massive transfusion, hypothermia, acidosis, and coagulopathy must be treated promptly.

Suggested Reading

Carabini LM, Zeeni C, Moreland NC, Gould RW, Avram MJ, Hemmer LB, Bebawy JF, Sugrue PA, Koski TR, Koht A, Gupta DK. Development and validation of a generalizable model for predicting major transfusion during spine fusion surgery. J Neurosurg Anesthesiol. 2014;26:205–15.

Levi M, Eerenberg E, Kamphuisen PW. Bleeding risk and reversal strategies for old and new anticoagulants and antiplatelet agents. J Thromb Haemost. 2011;9:1705–12.

Mannucci PM, Levi M. Prevention and treatment of major blood loss. N Engl J Med. 2007;356:2301–11.

Muñoz M, García-Erce JA, Villar I, Thomas D. Blood conservation strategies in major orthopaedic surgery: efficacy, safety and European regulations. Vox Sang. 2009;96:1–13.

Narouze S, Benzon HT, Provenzano DA, Buvanendran A, De Andres J, Deer TR, Rauck R, Huntoon MA. Interventional spine and pain procedures in patients on antiplatelet and anticoagulant medications: guidelines from the American Society of Regional Anesthesia and Pain Medicine, the European Society of Regional Anaesthesia and Pain Therapy, the American Academy of Pain Medicine, the International Neuromodulation Society, the North American Neuromodulation Society, and the World Institute of Pain. Reg Anesth Pain Med. 2015;40:182–212.

Pham HP, Shaz BH. Update on massive transfusion. Br J Anaesth. 2013;111(Suppl 1):i71–82.

Waters JH. Role of the massive transfusion protocol in the management of haemorrhagic shock. Br J Anaesth. 2014;113(Suppl 2):ii3–8.

Coagulopathy in Spinal Surgery

39

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Overview

More than 500,000 spinal operations are performed annually in the USA. Unanticipated coagulopathy during spine surgery is uncommon; however, substantial blood loss remains a feared complication of increasingly complex and longer-duration procedures. Significant intraoperative coagulopathy, defined as recurrent microvascular bleeding despite local hemostatic measures or decreased clot formation of blood pooled within the surgical field, has been reported in up to 16% of patients undergoing major spinal surgery. This bleeding can result in serious consequences including early termination of the procedure, postoperative hematoma formation, and increased in-hospital mortality. Therefore, it is imperative to identify risk factors for coagulopathy during preoperative assessment and take appropriate preventative action (Table 39.1).

While congenital bleeding disorders cannot be overlooked, those with severe manifestations are likely to be detected prior to adulthood. As the vast majority of patients will have undergone routine preoperative evaluation of PT, aPTT, and platelet count, coagulopathy during spinal surgery is generally due to some preexisting platelet dysfunction (i.e., known or unidentified use of platelet inhibitors) or an acquired problem with coagulation during the surgery such as dilutional coagulopathy. Other comorbid conditions with systemic impacts on coagulation may include hepatic or renal failure, malignancy, and collagen vascular disorders. In addition, there is evidence to suggest that certain spinal conditions, such as idiopathic scoliosis, may be associated with a degree of intrinsic platelet dysfunction.

Table 39.1 Risk factors and prevention strategies for coagulopathy in spine surgery

Risk factor	Prevention strategy
Common preexisting pharmacotherapy	Aspirin/NSAIDs/Plavix: discontinuation 5–7 days prior to surgery
Blood loss and fluid/blood product replacement	"Goal-directed" resuscitation (see text), use of colloid-containing fluids
Operative time	Planned staging of procedure
Hypothermia	Fluid warming, humidifier use, forced-air body warmers, serum calcium monitoring
Vascularized tumor resection	Preoperative embolization

An acquired problem with coagulation during surgery, such as a dilutional coagulopathy, can contribute to significant bleeding. Blood loss in large instrumented spine cases or resections of vascular spinal metastases can approach a patient's estimated blood volume. This loss is typically replaced with a combination of crystalloid, intraoperative autotransfused blood, and/or allogenic blood products. Continuing crystalloid administration without appropriate replacement of clotting factors and/or platelets can lead to severe coagulopathy over the course of long procedures. Coagulation factors typically remain functional down to concentrations approximately one-third of normal. However, this threshold is reached upon replacement of an entire blood volume. Of note, though coagulopathy may occur secondary to dilution of either coagulation factors or platelets, there is evidence suggesting that coagulation factor dilution and disturbed fibrin polymerization are of greater concern than thrombocytopenia.

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It is extremely important to prevent hypothermia, especially in the setting of a concurrent acidosis, as both factors are strongly associated with coagulopathy. Other severe but uncommon causes of coagulopathy include allergic and immunologic reactions (e.g., transfusion, drug reaction) or disseminated intravascular coagulation (DIC). DIC is of particular concern in patients with multiple traumatic injuries, especially severe head injury, and in patients with widespread metastases. During spine surgery, exposed bone may act as a source of tissue plasminogen activator and urokinase which may lead to activation of the fibrinolytic system and subsequent DIC.

Possible platelet dysfunction as a cause of coagulopathy is often difficult to assess preoperatively and is even more difficult to assess intraoperatively. Platelet aggregation studies and bleeding times have variable predictive value preoperatively and are not useful in the intraoperative setting. Assessment of surgical bleeding by measuring the viscoelastic properties of whole blood by techniques such as thromboelastography (TEG) has not been well described other than in cardiac and liver transplant surgery, though they have potential for application in spine surgery. This technique measures the entire clotting process from fibrin formation to fibrinolysis. Because whole blood is used, the plasmatic coagulation system interacts with platelets and red cells, providing useful information on platelet function at the patient's temperature. However, there is a difference between in vitro and in vivo coagulation as viscoelastic coagulation tests measure coagulation under static conditions (no flow) in a cuvette (not an endothelialized blood vessel).

A certain percentage of coagulopathy cannot be anticipated or avoided. Significant intraoperative bleeding mandates rapid assessment and treatment. This requires close communication between the anesthesia and surgery teams, including the decision to delay or abort further surgery for resuscitation as necessary.

Prevention

A complete review and reassessment, including obtaining a past medical history, current and recent medication use, family history, and surgical and anesthesia history, is essential to avoid intraoperative bleeding difficulties. Excessive bruising and/or unusual bleeding with attempts at intravenous or arterial access may suggest the possibility of clotting difficulties. Baseline studies typically include coagulation labs (PT/INR, aPTT), hemoglobin (Hb) levels, and platelet count. Bleeding times and other studies of platelet aggregation are of questionable utility in the preoperative setting. There must also be direct discussion between the surgical and anesthetic team prior to beginning complex cases, as the consent or booking description may not completely convey the complexity, length, or potential for blood loss. This discussion will help determine the need for large-bore vascular access, arterial line monitoring, blood products, and/or cell saver. Consideration should also be given to staging procedures, especially if combined anterior and posterior approaches are planned.

Intraoperative fluid replacement strategies are highly controversial. Restrictive, "goal-directed" fluid administration has been increasingly advocated as a means to prevent dilutional coagulopathy, as opposed to a solely formula-based approach. Suggested parameters include a rate of 4 mL/kg/h, with additional goal-directed boluses of 250 mL (up to a total of 1500 mL) given for periods of hypotension and tachycardia and for urine output dropping below 0.5 mL/kg/h for 2 or more hours. Vasopressors and/or furosemide may be used in patients not responding to these boluses. There is controversy regarding the value of administering fluids as colloid or crystalloid. Concerns exist over an increased risk of coagulopathy with the use of hetastarch in normal saline. Regardless of the fluid replacement strategy employed, the use of warming devices and the exclusive infusion of warmed fluids are recommended to maintain normothermia in long cases.

Further measures can be taken preoperatively and intraoperatively to help minimize the risk of significant blood loss. When positioning a patient prone, it is important to avoid abdominal compression that may cause engorgement of epidural veins, potentially exacerbating blood loss and contributing to a coagulopathy. It is advisable to have patients with vascular spinal metastases such as renal cell carcinoma undergo preoperative embolization to potentially reduce intraoperative blood loss. In these patients it is our practice to place the pedicle screws and contour the rods prior to proceeding with tumor resection. This allows for provisional stabilization of the spine in the event that massive bleeding necessitates premature termination of the case. With large incisions it is also important to use packing to control local bleeding in portions of the incision not immediately being addressed to avoid continuous blood loss. The use of vasopressor agents during surgery for the purpose of maintaining cord perfusion in cases of spinal cord compression, for example, may mask reduced intravascular volume. Indirect measures of adequate perfusion such as urine output and possibly lactate levels should be assessed. Regular reassessment of hemoglobin levels is advised, as a loss of RBC mass may have adverse effects on coagulation due to altered blood rheology. Periodic monitoring of electrolytes is also warranted, as coagulopathy can occur in the setting of electrolyte derangements. Of these, hypocalcemia is of particular concern given the complex interactions between ionized calcium and the negatively charged vitamin K-dependent clotting factors. Hypocalcemia may also be worsened by volume replacement with colloid solutions or infusion of citrated blood products.

The preoperative and/or intraoperative administration of antifibrinolytic agents, such as aprotinin and lysine analogs

tranexamic acid (TXA) and epsilon aminocaproic acid (EACA), has become increasingly widespread in elective spinal surgery. There is a growing body of evidence to support their routine use in a variety of orthopedic and neurosurgical procedures. These agents have been most extensively studied in the cardiovascular surgical literature, wherein all three have been found to significantly reduce intraoperative blood loss and postoperative transfusion rates. However, despite slightly superior efficacy, aprotinin has been associated with a higher risk of cardiovascular complications and death when compared to the lysine analogs, accounting for the increasingly widespread use of the latter. Dosing regimens and medical contraindications for antifibrinolytic agents remain variable and institution-dependent. While these agents show considerable promise and are the subject of further study, it must be noted that their use in spinal procedures remains off-label at this time.

Crisis Management

Once an intraoperative bleeding issue is identified, it is imperative that there is rapid assessment and treatment (Table 39.2). This requires close communication between the anesthesia and surgical teams.

Pathophysiology and Clinical Presentation

Rapid blood loss can be both the cause and result of coagulopathy. Intraoperative emergencies such as laceration of a large artery or vein can be life threatening and require immediate packing and vascular repair. Rapid blood loss can lead to hypotension and possibly DIC. Blood loss with vascular spinal lesions such as renal cell metastasis can be substantial despite preoperative embolization. Nevertheless, aggressive fluid resuscitation can cause a dilutional coagulopathy. Strong consideration should be given to aborting the originally intended procedure even if the injury is rapidly repaired and the patient is physiologically stable.

The development of excessive bleeding in complex cases can also be a gradual process with the development of recurrent microvascular bleeding. Sometimes, this is a subjective response by the surgical teams that comes with experience as "things just seem oozy." Well-established communication between anesthesia and surgery teams will allow early identification and intervention in such circumstances. New-onset bleeding in previously hemostatic areas is most frequently dilutional in nature. Paradoxically, this is may be more likely to occur in cases where large-volume resuscitation has been required following rapid bleeding from other etiologies, such as a vascular injury. In these situations it is often advisable to stop and reassess before continuing.

General anesthesia masks symptoms of end-organ dysfunction, and many signs (hypotension, tachycardia, oliguria/hemoglobinuria) may be wrongly explained by other causes. DIC should be suspected at the first potential sign of end-organ dysfunction, as clinically apparent bleeding is a late manifestation that occurs only after consumption of coagulation factors. While exceedingly rare, consideration must also be given to the possibility of a transfusion reaction in all patients receiving blood products.

Table 39.2 Diagnostic and therapeutic approach to intraoperative coagulopathy during spine surgery

Initial presentation	Potential etiology	Assessment	Treatment response
Mildly increased microvascular bleeding from case onset (esp. in emergent cases)	Preexisting use of platelet-inhibitor or anticoagulant medication	Clinical impression	Platelet transfusion regardless of platelet count
			FFP administration if anticoagulation with warfarin suspected
Gradual-onset microvascular bleeding in previously hemostatic areas	Dilutional coagulopathy	PT/INR	FFP administration (cryoprecipitate if additional volume undesirable and/or fibrinogen <80–100)
		aPTT	Platelet transfusion if <50,000/μL
		Hemoglobin (Hb)	
		Platelet count	
		Fibrinogen	
Severe bleeding and/or evidence of end-organ dysfunction (changes in vital signs, urine output)	Hypoperfusion with or without DIC	(Above), plus:	(Above), plus:
		ABG	Correction of acidosis, hypothermia, electrolyte abnormalities
		Lactate	
		D-dimer	RBC transfusion if Hb <10 g/dL[a]
			Consider termination of procedure to allow for stabilization of patient
			Consider administration of rFVIIa if unstable and refractory to above measures

[a]Higher Hb than typical transfusion threshold may be necessary to restore clotting function during ongoing bleeding

Patient Assessment

Any response to an intraoperative bleeding crisis must begin with an airway, breathing, and circulation assessment. Sites of intravenous or arterial access should be examined for evidence of new-onset bleeding and extremities examined for possible signs of ischemia or thrombosis. There should also be a simultaneous assessment of patient's intake and output balance, especially with regard to estimated blood loss and volume replacement. Initial laboratory evaluation should include Hb level, platelet count, and coagulation labs (PT/INR, aPTT). While PT and aPTT may often be mildly abnormal, values in excess of 1.5 times controls are most sensitive for clinically evident coagulopathy.

Periods of hypoperfusion or hypotension (i.e., patient requiring pressor agents to maintain blood pressure) should prompt an immediate blood gas to check for acidosis. Lactate levels may be useful in the assessment of systemic hypoperfusion, as lactic acidosis can preclude the restoration of normal coagulation. Additional laboratory evaluation may require levels of lactate dehydrogenase (LDH), fibrinogen, and fibrin split products (D-dimer) to evaluate for hemolysis or DIC. While elevations are nonspecific, a D-dimer within normal limits along with a normal platelet count renders DIC highly unlikely. An adequate concentration of fibrinogen is critical for clot formation. Concern for a transfusion reaction should prompt retesting and cross-matching of blood samples for major incompatibility.

Intervention/Treatment

Treatment decisions must be based on the extent and etiology of coagulopathy. Temporary suspension of surgical activity is advised in order to achieve adequate hemostasis and resuscitation before proceeding with the operation.

All homeostatic parameters affecting coagulation must be addressed. Buffering to physiologic pH is required at a pH less than 7.1 or a base deficit of 12.5. Optimal Hb for restoration of coagulation is higher than the one required for oxygen delivery, and transfusion to values of 10–11 g/dL may be necessary to support platelet function. Aggressive warming must also be pursued for core temperatures less than 34 °C.

Administration of fresh frozen plasma (FFP) is indicated for active bleeding following massive blood transfusion (more than one blood volume). Early implementation of a balanced transfusion protocol with both FFP and PRBC may limit the extent of transfusion-related coagulopathy. The extent of PT and/or aPTT elevations may be used to guide coagulation factor replacement, as they have been found to positively correlate with volumes of FFP required to maintain hemostasis. Cryoprecipitate or packed factor concentrates may be used, when available, if additional volume is undesirable or at fibrinogen concentrations less than 80–100 mg/dL. Platelets are often given prophylactically with normal counts even without documented coagulopathy on the presumption of altered platelet function; however, consideration must be given to the added expense, infectious risk, and risk of developing antibodies which could affect future transfusions.

Termination of the procedure to allow for optimal medical management of the coagulopathy is a complex decision that must be made in collaboration between the surgeon and the anesthesiologist. Factors to be considered include the patient's overall medical condition, acuity of the condition for which the patient is undergoing surgery, anticipated length of remaining procedure, response to treatment thus far, and availability of critical care services in the immediate postoperative period. This decision will be highly individualized to the clinical scenario and requires communication between both teams to arrive at the best decision for the overall health and safety of the patient.

Key Points

- Preoperative clinical and laboratory assessment, as well as close communication between the surgical and anesthetic teams, is essential to avoiding coagulation difficulties, as well as dealing with them effectively when they arise.
- Early recognition of intraoperative bleeding difficulties should prompt a simultaneous and systematic evaluation and initiation of therapy and may require either temporarily or permanently stopping the surgical procedure to allow re-establishment of physiologic homeostasis.

Suggested Reading

Cheriyan T, Maier SP 2nd, Bianco K, Slobodyanyuk K, Rattenni RN, Lafage V, Schwab FJ, Lonner BS, Errico TJ. Efficacy of tranexamic acid on surgical bleeding in spine surgery: a meta-analysis. Spine J. 2015;15:752–61.

Drews RE. Critical issues in hematology: anemia, thrombocytopenia, coagulopathy, and blood product transfusions in critically ill patients. Clin Chest Med. 2003;24:607–22.

Lier H, Krep H, Schroeder S, et al. Preconditions of hemostasis in trauma: a review. The influence of acidosis, hypocalcemia, anemia, and hypothermia on functional hemostasis in trauma. J Trauma. 2008;65:951–60.

Ornstein E, Berko R. Anesthesia techniques in complex spine surgery. Neurosurg Clin N Am. 2006;17:191–203, v.

Practice guidelines for blood component therapy: a report by the American Society of Anesthesiologists Task Force on Blood Component Therapy. Anesthesiology. 1996;84:732–47.

Shen Y, Silverstein JC, Roth S. In-hospital complications and mortality after elective spinal fusion surgery in the United States: a study of the nationwide inpatient sample from 2001 to 2005. J Neurosurg Anesthesiol. 2009;21:21–30.

Postoperative Visual Loss Following Spinal Surgery

40

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Overview

Incidence and Epidemiology

Postoperative visual loss (POVL) is a catastrophic perioperative complication that has come to the forefront of anesthesiologists' attention in the last 20 years. The extent of visual loss from POVL can be minimal unilateral visual field loss to complete blindness in both eyes. The incidence of symptomatic POVL varies from 0% to 4.5% depending on the institution and the type of cases studied. The highest reported incidence of symptomatic visual loss is 4.5% in cardiac cases and 0.2% in spinal fusion surgery. A recently published study utilizing data from the Nationwide Inpatient Sample (Rubin et al., 2016) documented an approximate 63% decrease in ischemic optic neuropathy (ION) associated with spinal fusion surgery from 1998 to 2012.

The most common types of surgical procedures associated with POVL include prone spinal fusion surgery, cardiopulmonary bypass procedures, head and neck procedures, and major vascular procedures. Though robotic prostatectomies that utilize an exaggerated steep Trendelenburg position were previously anticipated to be a high-risk procedure for ischemic optic neuropathy (ION) because of the elevated venous pressure in the head, very few ION cases have been reported with this procedure in comparison to cardiac or prone spinal fusion surgery. These differences in outcomes between cases may be partially attributable to decreased hemodynamic perturbations, smaller fluid shifts and shorter procedure durations in robotic prostatectomies compared to cardiac and prone spinal fusion surgery.

A wide variety of other miscellaneous procedures have also been associated with POVL including cholecystectomy, liposuction, supine spine surgery, nephrectomy, thoracotomy, and many others. Moreover, visual loss is known to occur in the critically ill in the absence of any surgical procedure, and it can affect any age of patient. Given this heterogeneous group of procedures and patients, it is not surprising that there are many different ophthalmologic diagnoses possible with POVL (Table 40.1) and many different suspected etiologies, most of which remain unproven (Table 40.2). The most common ophthalmologic diagnoses associated with POVL are central retinal artery occlusion (CRAO), cortical blindness which is more recently called cerebral visual loss, and anterior and posterior ION (AION, PION).

There is significant overlap in the procedures and the type of POVL. This table represents the most commonly associated procedures with each POVL diagnosis, respectively. Other rare causes of POVL include pituitary apoplexy, glycine toxicity, and posterior reversible encephalopathy syndrome (PRES).

Table 40.1 Postoperative visual loss (POVL) diagnoses and associated procedures/events

Ophthalmologic diagnosis	Associated procedures/events
Central retinal artery occlusion (CRAO)	Prone spine surgery, nasal and sinus procedures, cardiac bypass
Cortical blindness (cerebral visual loss)	Cardiac bypass, profound circulatory shock, emboli, major vascular surgery
Anterior ischemic optic neuropathy (AION)	Cardiac bypass, prone spine surgery, major vascular procedures, radical prostatectomy, abdominal compartment syndrome, liposuction, bilateral radical neck dissection
Posterior ischemic optic neuropathy (PION)	Prone spine surgery, bilateral radical neck dissection, cardiac bypass, nasal and sinus procedures
Acute angle closure glaucoma	Stress – no associated anesthetic technique or surgical procedure; many drugs utilized in the perioperative period have been suggested as contributory
Retrobulbar hemorrhage	Nasal or sinus procedures; trauma

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Table 40.2 Suggested associated factors with most common types of postoperative visual loss (POVL)

Ophthalmologic diagnosis	Suggested associated factor (most common)
Central retinal artery occlusion (CRAO)	Globe compression, emboli
Cortical blindness (cerebral visual loss)	Emboli, profound hypotension, cerebral artery thrombosis
Anterior ischemic optic neuropathy (AION)	Hypotension, anemia, atherosclerosis, major blood loss, large fluid resuscitation, high-dose vasopressors, patient-specific anatomic/physiologic aberrancies
Posterior ischemic optic neuropathy (PION)	Venous congestion/elevated venous pressure, prolonged duration in prone position, major blood loss, large fluid resuscitation, type of fluid (crystalloid vs. colloid), hypotension, anemia, high-dose vasopressors, patient-specific anatomic/physiologic aberrancies, obesity (in the prone position), male sex

Etiology

Each type of POVL can be associated with more than one etiology. Globe compression with periorbital trauma is the most common cause of perioperative CRAO, though embolic causation is also possible. Cortical blindness (cerebral visual loss) can be caused by either thromboemboli or profound circulatory shock (Table 40.2).

The etiologies of AION and PION remain unknown and may be multifactorial with both intrinsic and extrinsic risk factors. AION is more commonly associated with patients with atherosclerotic risk factors and their related surgical procedures in the supine position (e.g., cardiac bypass surgery and major vascular surgery). PION is more commonly associated with procedures with elevated venous pressure (e.g., prone position, bilateral radical head and neck surgery) and frequently occurs in relatively healthy patients. However, there is significant crossover with diagnoses, patient populations, and suggested risk factors.

The relatively low incidence of ION (both AION and PION) suggests that the patients themselves may have some unique anatomical or physiologic differences that promote its development. A small cup to disk ratio on fundoscopic exam has been described as an anatomic risk factor for spontaneously occurring AION. Many ophthalmologists believe that the small cup to disk ratio correlates with a narrow passage for the optic nerve and vessels as they pass through the semirigid sieve-like connective tissue (lamina cribrosa) on the way to the retina. Any swelling in this area in these individuals would impede flow through the blood vessels supplying the optic nerve. A recently published case-control study (Holy et al., 2009) of perioperative ION did not demonstrate a small cup to disk ratio as a risk factor, but this study was limited by a small number of affected cases from a wide range of different surgical procedures and a mixture of both AION and PION diagnoses. Pillunat demonstrated that 20% of healthy volunteers have a reduced ability to autoregulate blood flow in the anterior optic nerve with an intraocular pressure of 25 mmHg – a value typically reached during prolonged prone spine surgery. Other studies in humans suggest that the ophthalmic artery may behave extracranially with respect to carbon dioxide reactivity and its ability to reverse flow with tight carotid stenoses. Because of the location and size of the optic nerve and its vasculature, definitive studies in humans regarding autoregulation, vasoreactivity, and the effect of various physiologic perturbations on optic nerve blood flow are not technically feasible at this time.

Atherosclerotic-related diseases have been associated with spontaneously occurring AION. However, certain high-risk surgical procedures such as cardiopulmonary bypass and major vascular procedures have concomitant coexisting atherosclerotic disease, making it unclear whether the atherosclerosis is contributory to the ION complication in these cases. In contrast, the American Society of Anesthesiologists (ASA) Postoperative Visual Loss Registry study (Lee et al., 2006) demonstrated that two-thirds of 83 patients with ION after spine surgery were relatively healthy (ASA Physical Status I–II). Perioperative ION after spine surgery has also been reported in 10–16-year-old children. These findings suggest that ION after spine surgery is more likely associated with prolonged physiologic perturbations in the prone position, rather than an atherosclerotic-induced disease. Anesthetic duration was ≥6 h in 94% of the ASA POVL Registry cases, and estimated blood loss was ≥1000 ml in 82% of cases. Animal studies indicate that the optic nerve is more sensitive to physiologic perturbations than the brain. Clinically, perioperative ION rarely occurs in association with cerebral infarction. Unfortunately, there is no reliable intraoperative monitor of optic nerve function to guide therapeutic interventions at this time.

Currently there are five case-control studies on POVL. Two of these studies (Holy et al., 2009 and Myers et al., 1997) with detailed data collection failed to demonstrate any association with POVL and lowest blood pressure or lowest hematocrit, though numerous case reports and case series frequently speculate that these two factors are causative. These studies were limited by either cases with different ophthalmologic diagnoses or by cases from multiple different types of surgical procedures. Two other studies utilized the Nationwide Inpatient Sample to examine POVL associated with spine surgery. Patil and colleagues study (2008) on spinal fusion surgery found an association between ION and hypotension (OR 10.1), peripheral vascular disease (OR 6.3), and anemia (OR 5.3). Without detailed data consistently available from cases and controls, it is unclear that how hypotension and anemia were defined in this study and when it occurred in the perioperative course. Accuracy of data cannot be validated. Further, the Nationwide Inpatient Sample database is maintained for administrative purposes

and cannot be used for comparison of non-routinely collected data between cases and controls. For example, the presence of perioperative hypotension is not routinely evaluated unless there is a complication. Therefore, the control group (without complication) is unlikely to have hypotension diagnosed. A second study (Shen et al., 2009) utilizing the same database for all procedures examined variables entered into the database more consistently in both cases and controls. They found a significant multivariable association between ION and male sex, age >50 years old, non-fusion orthopedic surgery, spinal fusion surgery, and cardiac surgery. The lack of detailed perioperative data such as operative duration, blood loss, and type of fluid administered prevented assessment of potential confounding factors.

The fifth and most recent case-control study (The Postoperative Visual Loss Study Group., 2012) compared 80 cases of ION associated with prone spinal fusion surgery from the ASA POVL Registry to 315 controls that underwent similar spine procedures but did not develop POVL. Detailed collection of data from medical records allowed comparison of multiple variables between cases and controls. This study identified six significant and independent risk factors associated with ION including male sex, obesity, use of the Wilson frame (which makes the head very dependent relative to the heart and increases venous congestion in the head), longer duration, higher blood loss, and a lower percentage of colloid administered for fluid resuscitation (Table 40.3).

Table 40.3 Risk factors associated with ischemic optic neuropathy and prone spinal fusion surgery

Male sex
Obesity
Use of the Wilson frame
Duration
Estimated blood loss
Lower percentage of colloid used in non-blood fluid administration

Prevention

Given the short list of known etiologies and the relatively long list of suspected but unproven etiologies (Table 40.2), prevention of POVL is somewhat limited and speculative (Table 40.4). The POVL diagnosis most easily prevented is CRAO caused by globe compression. This complication is most commonly associated with prone spine operations and can be prevented by frequent checking of the eyes to ensure that they are free from direct pressure and appropriate head-positioning devices. Although all headrests have been associated with CRAO, devices that have a narrow margin between the eyes and the headrest edge (e.g., horseshoe headrest) may make checking of the eyes problematic. Emboli caused by cardiopulmonary bypass may be decreased with the use of special filters and epiaortic scanning but are not completely eliminated. Emboli from major orthopedic procedures are not currently preventable.

Other preventative measures are speculative as the etiology is thought to be multifactorial. Conditions which promote extreme physiologic stress (e.g., prone position, deliberate hypotension, severe anemia, etc.) for prolonged periods should be assessed with careful consideration of the risk to benefit profile, as their effect on optic nerve blood flow remains undetermined.

In the absence of class I evidence, the ASA has developed an advisory and second update for the prevention of blindness associated with major spine surgery (Table 40.5), based on expert opinion, case reports, case series, and case-control studies. Briefly, it recommends to consider consenting patients at risk for POVL, continually monitor blood pressure, minimize use of deliberate hypotension and treat prolonged significant decreases in blood pressure, periodically monitor hemoglobin

Table 40.4 Prevention of postoperative visual loss (POVL)

Ophthalmologic diagnosis	Preventative measures	Suggested (unproven) preventative measures
CRAO	1. Frequent eye checks	
	2. Avoid headrests with narrow margin between the eyes and headrest	
Cortical blindness (cerebral visual loss)	1. Devices or maneuvers that reduce emboli	
	2. Avoid extreme hypotension when possible	
AION and PION	Unknown	1. Avoid prolonged duration in the prone position with major blood loss
		2. Minimize blood loss with modifications in both surgical and anesthetic techniques (e.g., topical hemostatic agents, minimally invasive surgery, antifibrinolytic agents, replacement of depleted blood products needed for coagulation, and others)
		3. Treat prolonged significant decreases in blood pressure; avoid deliberate hypotension when possible.
		4. Monitor hemoglobin and hematocrit periodically and transfuse blood as appropriate
		5. Keep the head at or above the heart level to minimize venous congestion, and avoid surgical frames (e.g., Wilson) that promote venous congestion in the head for these high-risk procedures

and hematocrit and transfuse blood as appropriate, maintain the head equal to or higher than the heart, and consider staging very prolonged procedures. The update also recommends avoiding direct compression of the globe which can cause CRAO. It is unclear if the significant decrease in the incidence of ION associated with prone spine surgery found over the last decade is related to these practice advisories, studies, and other educational efforts for the prevention of ION.

Table 40.5 The American Society of Anesthesiologists Practice Advisory for perioperative blindness associated with spine surgery[a]

For patients undergoing major spine surgery:
1. Consider consenting patients undergoing major spine surgery for the risk of POVL
2. Continually monitor blood pressure. Minimize use of deliberate hypotension when possible and treat prolonged significant decreases in blood pressure
3. Keep head at or above the heart level
4. Periodically monitor hemoglobin and hematocrit and transfuse blood as appropriate
5. Avoid direct compression of the globe
6. Consider staging procedure

[a]Because of the low incidence of postoperative visual loss after spine surgery, prospective clinical trials are not currently feasible. With the lack of class I evidence, this Practice Advisory was based primarily on expert opinion, case reports, case report series, and one case-control study (Practice Advisory for Perioperative Visual Loss Associated with Spine Surgery 2019 Anesthesiology 2019)

Crisis Management

Pathophysiology and Clinical Presentation (Table 40.6)

Findings noted above are for typical presentations of postoperative visual loss. An ophthalmology consultation is an essential component of the diagnostic workup where rarer causes of postoperative visual loss or those cases with atypical presentations can be evaluated.

CRAO is most commonly associated with physical compression of the globe and typically has ipsilateral signs of periorbital trauma. In the absence of periorbital trauma, embolic causation is a possibility as CRAO can also occur spontaneously in the community in individuals who are hypercoagulable. The most common type of operation associated with CRAO is prone spine surgery, and specific head support devices that leave little room between the eyes and the headrest support margin (e.g., horseshoe headrest) may predispose to this injury. A complaint of visual loss is typically immediate on awakening from anesthesia. It is almost always unilateral and without a pupillary light reflex. It has a fundoscopic finding of a cherry red spot at the macula. This cherry red spot represents an island of well-perfused blood supply to the macula from the choriocapillaris, made prominent by the surrounding pale, ischemic retina that is devoid

Table 40.6 Patient findings for postoperative visual loss diagnoses

Diagnosis	Symptom onset	# of affected eyes	Pupillary light reflex	Visual fields	Visual acuity	Fundus	Diagnostic tests	Recovery
CRAO	Immediate	Unilateral (usually signs of ipsilateral periorbital trauma)	Absent in affected eye	Absent in affected eye	Usually blind in affected eye	Cherry red spot at macula; ischemic retina; attenuated retinal arteries	Fundoscopic exam alone is diagnostic; ERG and VEP abnormal (flattened)	Poor
Cortical blindness (cerebral visual loss)	Immediate	Bilateral	Normal	Usually absent; may have hemianopsia	Usually blind; may be normal in unaffected area with hemianopsia	Normal	CT, MRI to evaluate infarct; VEP abnormal (flattened); ERG normal	Better than ION (~2/3 patients get some recovery)
AION	Immediate to several days postoperatively – can be progressive over several days	Usually bilateral; can be unilateral	RAPD or absent	Altitudinal field cut or scotoma; may be blind	Usually decreased to blind; may be normal in unaffected area	*Early exam*: edema/swelling of the optic disk, peripapillary flame-shaped hemorrhages; *late exam*: optic nerve pallor after several weeks to months	VEP abnormal (flattened); ERG normal	Poor
PION	Immediate	Usually bilateral; can be unilateral	RAPD or absent	Altitudinal field cut or scotoma; may be blind	Usually decreased to blind; may be normal in unaffected area	*Early exam*: normal; *late exam*: optic nerve pallor after several weeks to months	VEP abnormal (flattened); ERG normal	Poor

CRAO Central retinal artery occlusion, *AION* anterior ischemic optic neuropathy, *PION* posterior ischemic optic neuropathy, *RAPD* relative afferent pupillary defect, *ERG* electroretinogram, *VEP* visual evoked potential, *CT* computed tomography, *MRI* magnetic resonance imaging

of blood supply from the central retinal artery. It may occur in association with AION, whose optic nerve pallor may not manifest until months later. There is no known beneficial treatment for CRAO, and recovery of vision is typically poor.

Cortical blindness (cerebral visual loss) is typically associated with emboli (air or particulate) or severe physiologic derangements. The most common procedure associated with the release of large numbers of emboli is cardiopulmonary bypass, but major orthopedic procedures such as femoral nailing and spinal fusion with instrumentation are also known to release large embolic loads. Because the retina has high blood flow, it serves as a repository for emboli that can be easily detected if emboli are suspected on the arterial side. Profound hypotension, as seen in cardiopulmonary resuscitation, has also been associated with cortical blindness. Patients will typically have bilateral involvement with a normal light reflex and fundoscopic exam. Recovery from cortical blindness is much better than either CRAO or ION with some significant improvement reported in approximately two-thirds of cases.

ION that occurs perioperatively is typically nonarteritic and consists of two types, AION and PION. Arteritic AION (e.g., temporal arteritis) almost never arises perioperatively. Patients most commonly complain of visual loss from PION immediately upon awakening or when they are first cognizant and able to communicate. It does not typically worsen from the time of the initial complaint. In contrast AION can present either immediately on awakening or up to several days postoperatively. It can have a more progressive onset and may worsen over the course of several days. Both AION and PION have an abnormal light reflex with either a relative afferent pupillary defect or absent light reflex. For ION cases with incomplete visual loss, there is either an altitudinal field cut and/or scotoma in one or both eyes, while visual acuity may be relatively normal in the unaffected portion of the visual field. Two-thirds of the ASA POVL Registry patients with ION had bilateral involvement, consistent with the theory that this injury is caused by systemic physiologic perturbations. The fundoscopic exam in PION is completely normal, whereas AION will demonstrate optic disk edema with or without peripapillary flame-shaped hemorrhages. The edema in AION eventually resolves and the peripheral heme gets absorbed. AION and PION are identical several months after the onset with only optic disk pallor. Recovery from perioperative ION is very poor. Some patients may get some mild improvement in vision but rarely return to baseline.

Patient Assessment

For any complaint of visual loss, consultation with the ophthalmology service should be obtained as soon as possible, preferably by a neuro-ophthalmologist if available. The ophthalmologic diagnosis is primarily based on physical exam, pupillary light reflexes, and dilated fundoscopic findings. It may be helpful in eliminating specific etiologies. Acute angle closure glaucoma is a very rare cause of POVL. It is typically painful, but this finding may be blunted with residual anesthesia and narcotics. It can be ruled out by the measurement of the intraocular pressures and is easily treatable with a lateral canthotomy. It is less common than the other four types of ophthalmologic diagnoses perioperatively but is the only complication that has a defined and effective treatment. Computed tomography or magnetic resonance imaging (MRI) is frequently used to eliminate the possibility of cortical infarction or other intracranial pathology. Small punctuate lesions on these studies are consistent with embolic events. Larger strokes in watershed areas from hypoperfusion may also be detectable for cases with profound circulatory shock.

Diagnosis of CRAO can be made by the cherry red spot on fundoscopic exam. Electroretinograms (ERGs) in the presence of CRAO will be highly abnormal but are superfluous in the presence of an absent pupillary light reflex and a cherry red spot. ERGs will be normal in the presence of ION and cortical blindness, as the retina maintains normal function. Visual evoked potentials will be abnormal in CRAO, ION, and cortical blindness. Definitive diagnosis of ION can be made several months later with the appearance of a pale optic disk though the ability to distinguish AION from PION will be lost.

Intervention/Treatment

Because the incidence of each of these causes of POVL is low, randomized trials with proven benefit are lacking. Further, there is no proven effective treatment for the spontaneously occurring forms of CRAO or ION. Experimental selective thrombolysis for spontaneous CRAO has had mixed results. Case reports of hyperbaric oxygen therapy, mannitol, and steroids have also had inconsistent results. Normalization of the blood pressure and transfusion to a hematocrit of 30% or more is frequently recommended by consultants and also lacks proven efficacy.

Key Points

- POVL can occur after a wide variety of surgical procedures but is most commonly associated with prone spine surgery, cardiac bypass surgery, and head and neck operations.
- The most common POVL diagnoses are CRAO, AION, PION, and cortical blindness.
- CRAO is most commonly caused by pressure on the globe, and this cause of CRAO is preventable with frequent eye checks and use of appropriate head-positioning devices.

- The etiologies of AION and PION are unknown but are associated with operations and positions that impart significant physiologic perturbations for prolonged durations. Patient-specific risk factors may also contribute to this complication.
- The largest case-control study to date on ION associated with prone spinal fusion surgery identified six risk factors including male sex, obesity, use of the Wilson frame, duration, estimated blood loss, and a decreased percentage of colloid in the non-blood fluid administration. The ASA practice advisory for the prevention of this complication was updated in 2012.
- Consent for POVL should be considered for high-risk procedures.
- Recent evidence from a national database indicates that the incidence of ION associated with spinal fusion surgery is decreasing.

Suggested Reading

American Society of Anesthesiologists Task Force on Perioperative Visual Loss. Practice advisory for perioperative visual loss associated with spine surgery: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Visual Loss. Anesthesiology. 2012;116(2):274–85.

Holy SE, Tsai JH, McAllister RK, Smith KH. Perioperative ischemic optic neuropathy: a case control analysis of 126,666 surgical procedures at a single institution. Anesthesiology. 2009;110:246–53.

Lee LA, Nathens AB, Sires BS, McMurray MK, Lam AM. Blindness in the ICU: possible role for vasopressors? Anesth Analg. 2005;100:192–5.

Lee LA, Roth S, Posner KL, Cheney FW, Caplan RA, Newman NJ, et al. The American Society of Anesthesiologists' Postoperative Visual Loss Registry: analysis of 93 spine surgery cases with postoperative visual loss. Anesthesiology. 2006;105:652–9.

Lee LA, Deem S, Glenny R, Townsend I, Moulding J, An D, et al. The effects of anemia and hypotension on porcine optic nerve blood flow and oxygen delivery. Anesthesiology. 2008;108:864–72.

Myers MA, Hamilton SR, Bogosian AJ, Smith CH, Wagner TA. Visual loss as a complication of spine surgery: a review of 37 cases. Spine. 1997;22:1325–9.

Patil CJ, Lad EM, Lad SP, Ho C, Boakye M. Visual loss after spine surgery: a population based study. Spine. 2008;33:1491–6.

Postoperative Visual Loss Study Group. Risk factors associated with ischemic optic neuropathy after spinal fusion surgery. Anesthesiology. 2012;116(1):15–24.

Roth S. In: Miller RD, editor. Postoperative blindness, anesthesia. 6th ed. New York: Elsevier/Churchill Livingstone; 2005. p. 2991–3020.

Rubin DS, Parakati I, Lee LA, Moss HE, Joslin CE, Roth S. Perioperative visual loss in spine fusion surgery: ischemic optic neuropathy in the United States from 1998 to 2012 in the nationwide inpatient sample. Anesthesiology. 2016. [Epub ahead of print].

Shen Y, Drum M, Roth S. The prevalence of perioperative visual loss in the United States: a 10-year study from 1996 to 2005 of spinal, orthopedic, cardiac, and general surgery. Anesth Analg. 2009;109:1534–45.

Practice Advisory for Perioperative Visual Loss Associated with Spine Surgery. An updated report by the American Society of Anesthesiologists task force on perioperative visual loss, the North American Neuro-Ophthalmology Society, and the society for Neuroscience in Anesthesiology and Critical Care. Anesthesiology. 2019;130(1):12–30.

Rubin DS, Parakati I, Lee LA, Moss HE, Joslin CE, Roth S. Perioperative visual loss in spine fusion surgery: ischemic optic neuropathy in the United States from 1998 to 2012 in the Nationwide Inpatient Sample. Anesthesiology. 2016;125(3):457–64.

Part VI

Critical Situations During Anesthesia for Other Procedures in Adult Neurosurgery

Perioperative Challenges During Diagnostic and Perioperative Magnetic Resonance Imaging (MRI)

41

Girija Prasad Rath and Deepak Sharma

Overview

Magnetic resonance imaging (MRI) is a non-invasive diagnostic procedure which is particularly useful for imaging the soft tissues with its unique ability to delineate different tissue characteristics. Majority of neurologically injured patients undergo diagnostic MRI at different stages of their clinical management. Anaesthesia or sedation ensures immobility of the patient during this procedure, hence acquiring an acceptable quality of image. MRI is also the imaging modality utilised for acquiring intraoperative images with acceptable spatial and contrast resolution. Risks associated with the MRI procedure apart from the specific problems inherent to the patient condition during provision of sedation and anaesthesia at places away from the operating room (OR) complicate the management strategy. This chapter revisits all such perioperative concerns in the patients with neurological abnormalities who need sedation or anaesthesia to undergo MRI.

Principle of MRI

MRI is based on the concept of nuclear magnetic resonance (NMR). Protons of water molecule present in the body have intrinsic magnetic properties. They are excited by a combination of strong and static magnetic field and extrinsic radiofrequency (RF) pulses. External magnetic fields are applied to create a magnetic gradient and excite the protons in different orientations within the basic magnetic field. The protons gain energy in an excited state, and shift from low-energy to high-energy state known as 'resonance'. When the RF pulse is turned off, the protons lose energy (relax); the energy released is used to create MR imaging. The hydrogen atom is most often used for imaging and is present in body tissue as water and fat. Relaxation rates vary for specific body tissues, thereby allowing differentiation of body structures in the images. There are two distinct mechanisms for relaxation with separate time constants, T1 and T2. Accordingly, the standard magnetic resonance (MR) image sequences include T1-weighted images, T2-weighted images, and contrast (gadolinium)-enhanced T1 images. Additional MRI sequences are also performed based on the diagnostic requirements. The flow-sensitive MR angiography and venography (MRA and MRV) provide images for blood flow; the diffusion-weighted sequence provides insight into tumour (increased cellularity), cell swelling (e.g. ischaemia), and oedema; and the functional MRI helps in detecting alterations in eloquent cortical activity in response to stimuli (speech area localisation).

Contrast Agent

Intravenous (IV) contrast agents are administered to alter relaxation rates of the hydrogen nuclei. Gadolinium is most commonly used for MRI which may cause mild side effects such as nausea, vomiting, headache, and pain on injection. Patients with renal failure who receive gadolinium are at risk of a life-threatening condition called nephrogenic systemic fibrosis. Hence, in these patients an estimated glomerular filtration rate (GFR) should be measured. The risk-benefit ratio must be assessed before the administration of this agent if the GFR is less than 30 ml/min/m^2.

The MRI Scanner and Environment

The medical MRI scanners use static magnetic field strengths generated by superconductor magnets that are cooled by liquid helium. The scanner also uses pulses of RF energy generated by

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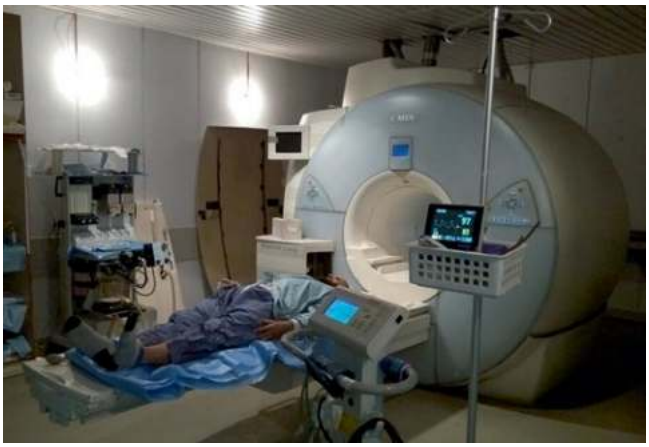

Fig. 41.1 A typical magnetic resonance imaging (MRI) suite

Table 41.1 MRI access zones

Zones	Activity/restriction of access
Zone I	The area freely accessible to general public
Zone II	Patients are greeted, interviewed, and screened by MR personnel
Zone III	Access strictly restricted; an unscreened access of non-MR personnel or ferromagnetic objects can result in serious injury owing to strong magnetic field
Zone IV	Location of MRI scanner; generates the existence of zone III

power delivery unit and application of superimposed gradient magnetic fields for spatial encoding. The body part being scanned is usually placed at the centre of the field in a standard cylindrical-bore designed scanner. A fringe field normally extends around the scanner. Field strength is measured in units of *Tesla* (T) or *Gauss* (G). The magnetic field strength of the MR system is maximal at the bore of the magnet, with the field strength of most modern scanners in clinical use being between 1 and 3 T. This field strength reduces exponentially with increasing distance from the magnet, so the danger of magnetic field increases as one move closer to the magnet (Fig. 41.1). Normally, the field strength at the scanner bore is quantified as Tesla, whereas the smaller values associated with safety limits around the fringe fields are described in Gauss, where 1 T = 10,000 G.

The MRI suites are designed to restrict access and limit exposure to the powerful magnetic field by four conceptual access zones (Table 41.1). Inside the MRI suite, the five gauss (5 G) line of the magnetic field is marked on the floor and wall for safety. It is the point where the magnetic field starts affecting the electromagnetic substances such as cardiac pacemakers, and hence, access to unscreened personnel is restricted.

Challenges for the Anaesthesiologist

The goal of anaesthesiologist for MRI is to provide immobility, safety, and comfort to the patient while acquiring best possible image. It can be achieved with sedation or anaesthesia based on the patient condition and the acceptability. The specific concerns for the anaesthesiologists are mentioned in Table 41.2.

Table 41.2 Anaesthetic concerns of MRI

The risks of MR procedures
Anaesthesia outside OR
Compatible anaesthesia monitors and equipment
Inaccessibility patients in MRI suite
Anaesthetic technique
Sedation vs. general anaesthesia
Patient related factors
Children
Adult claustrophobic patients
Movement disorder
Intensive care patients
Prolonged studies

Risks Involved with MRI Procedures

The strong physical processes responsible for producing high resolution MR images have the potential for injury to the patients, if specific precautions are not undertaken.

Static Magnetic Field Hazards

The static magnetic field in MR systems is the most important field hazard because it poses a constant invisible danger as the magnet remains switched on continuously. Ferromagnetic substances within the 30 G line will experience both an attractive force being pulled towards the centre of magnet and a torque (makes substances line up with the magnetic field). The major risks of the static field include pacemaker malfunction, projectile effect, implant dislodgement, and malfunction of the medical equipment (Table 41.3).

The long-term effects of strong magnetic fields on the developing foetus are unknown. Hence, MRI should be avoided during first trimester of pregnancy in view of possible teratogenicity.

Hazards from RF Pulses and Magnetic Gradient Fields

The pulses of RF energy and time-varying magnetic gradient fields are superimposed on the powerful static magnetic field for generation of spatial images. During the process current is induced in the biological tissue and electrical conductors (e.g. cable wiring). As the human body is conductive by nature, RF pulse-generated current gets absorbed as heat. The RF heating is more prominent in the periphery of the body than its core. Moreover, direct

Table 41.3 Risks of the intense static magnetic field

Risk of magnetic field	Precautions
Projectile or 'missile' effect	
Ferromagnetic objects in the zone III are attracted by the strong magnetic field and rendered projectile. Collisions can result in injury and death to patient and staff, as well as potential damage to the scanner	Access to zone III/IV is restricted and all persons must be medically screened before admission
Ferromagnetic objects include many pieces of essential anaesthetic equipment, e.g. laryngoscopes, gas cylinders, defibrillators, and pulse oximeters	A dedicated area adjacent to the magnet room and outside the strong magnetic field (zone II) is provided for anaesthesia
	Only non-ferromagnetic (*MR safe* or *MR conditional*) equipment is permitted within the *zone III*, e.g. fibre-optic pulse oximeter, aluminium gas cylinders, etc.
Pacemaker malfunction	
Pacemakers malfunction where magnetic field strength exceeds 5G, with reported fatalities	A robust screening procedure is required to identify and prohibit persons with pacemakers and defibrillators entering the *zone III*
Implant dislodgement	
Ferromagnetic objects implanted in the patient may dislodge with potential for devastating internal injury	A robust screening procedure is essential. Ferromagnetic implants are a contraindication to MR procedures
Medical implants include aneurysm clips, stents, prosthetic heart valves, internal defibrillators, intrauterine contraceptive devices, and cochlear implants	Non-ferromagnetic implants are safe, e.g. general surgical clips, many joint prostheses, artificial heart valves, and sternal wires
Metal shrapnel and intra-ocular foreign bodies from welding or penetrating eye injury	Access to zone III is denied in the event of any uncertainty
Equipment malfunction	
Malfunction of standard equipment may lead to device failure. Malfunction of infusion device may result in incorrect drug delivery	Standard equipment should only be used outside the 5G line
	Only equipment designated *MR safe* or *MR conditional* is safe to use inside it

MR safe: No known MR hazards in any MR environment; MR conditional: no hazard in specified MR environment during specific condition of use; MR unsafe: pose a hazard in all MR environment

contact of conductive materials to the skin creates a risk of thermal burn to the patient. Hence, contact of metallic objects in the clothing, cables, ECG leads, and other equipment must be avoided; it can be ensured with robust screening procedures.

The switching of magnetic gradient fields cause mechanical vibrations and loud acoustic noises typically above the safe limit of 85 dB with potential for auditory damage. Hence, earplugs should be used for protection in both awake or anaesthetised patients and staffs.

Helium Escape and Emergency MRI Shutdown

All modern high-tesla MRIs have superconducting magnets that are maintained at extremely low temperature. Liquid helium is used as the cooling fluid. In the event of spontaneous or emergency shutdown of magnetic field (quench), liquid helium boils rapidly and expands to gaseous state. The cryogenic gas is released to the atmosphere and must be vented rapidly outside the building by a quench pipe. In case the quench pipe is blocked or leaked gas enters into the suite, the atmosphere is rendered hypoxic and high-pressure. It is an emergency situation and necessitates immediate evacuation of patient and MRI staff. MRI suites usually have oxygenation sensors; attention should be given to the zone IV with regard to oxygen monitoring and alarm. Release of the cryogenic gas causes fogging and condensation of the room. Within the machine frame near the quench pipe, condensed oxygen may be formed which creates a localised oxygen-rich environment, increasing the risk of fire. Ventilation of the zone IV may minimise this hazard.

The potential danger of quenching is the reason why in the event of a medical emergency, the patient should be removed from the magnetic field rather than causing an emergency magnetic shut down.

Anaesthetic Equipment and Monitoring

Anaesthetic equipment used within the MR suite is often different from the conventional ones used elsewhere in the hospital. They may be MR safe, MR conditional, or MR unsafe (known to pose a hazard in all MR environments). Practitioners of MR anaesthesia should be fully familiar with the MR equipment used in the suite. An ideal equipment for the use within zone IV should pose no hazard to the patient and function normally in the strong magnetic field, and its presence does not degrade MR image.

The monitoring in the patients undergoing MRI must have the same standards as in the OR consistent with the ASA 'Standard for basic anaesthesia monitoring'. The monitors should be MR safe or MR conditional in zone IV for the scan. Use of standard pulse oximeter may result in severe burn owing to induction of current, and hence, fiber-optic MRI-safe probes may be used. ECG is also prone to

interference resulting in spikes on the trace and ST-T changes. Hence, arrhythmias and morphological changes in ECG are difficult to be detected. The effects of induction currents on ECG are reduced by using high impedance, short leads, and MRI-safe electrodes placed in a narrow triangle on the chest of the patient. MR safe ECG electrodes use fiber-optic cables, transmit the ECG signal by means of light rather than electric current, and are more resilient to electromagnetic effects. Non-invasive blood pressure monitoring can be safely used by changing ferrous connections to nylon. Length of invasive pressure lines are minimised to reduce damping. Capnography with long sampling line increases the time delay for waveform display by 20s. A monitor should be available at zone III when the anaesthesiologist is not present in zone IV.

Table 41.4 Sedative agents for MRI in children

Agent	Dose	Route	Onset (min)	Duration (min)
Chloral hydrate	50–100 mg/kg (max 2 g)	Oral	15–30	60–120
Pentobarbital	4 mg/kg (maximum 8 mg/kg)	Oral	20–60	60–240
Midazolam	0.5–1 mg/kg (max 15 mg)	Oral	20–30	60–90
	0.02–0.1 mg/kg	IV	5–10	30–60
Propofol	1–2 mg/kg bolus followed by 50–150 mcg/kg/min	IV	1–2	5–10 (after bolus)
Ketamine	3–5 mg/kg	IM	3–6	30–180
Dexmedetomidine	1 mcg/kg over10 min (bolus) followed by 0.5 mcg/kg/min	IV	15–30	120–180

Screening of Patient and Personnel

Thorough screening of the patients and MR personnel is essential to prevent any mishap. Contraindications to MRI are directly related to the major risks discussed above (Table 41.3). The patient screening should include patient- and equipment-related risk factors. The anaesthesiologist should determine whether the patient presents with high-risk medical conditions like (prematurity or infancy, ICU status, respiratory abnormality, haemodynamic instability and on vasopressor medication or other co-morbidities such as obesity and sleep apnoea); implanted devices (e.g. Pacemakers, cardiac defibrillators, or nerve stimulators, surgical clips/stents, prosthetic heart valves); or foreign bodies embedded (orbital iron filling, tattoos) and pierced (pierced jewellery and rings).

Anaesthesia Techniques

An MRI study usually consists of a combination of multiple imaging sequences. Each sequence may take 5–10 min to acquire. The duration of a particular MRI study may vary depending on the number of scanning sequences required with certain studies lasting for more than 2–3 hours. Immobility is the most crucial aspect to acquire optimal image. Nevertheless, safety of the patient is of paramount importance as the anaesthesiologist does not have direct access to the patient. The anaesthetic techniques most commonly utilised include sedation and general anaesthesia with IV or inhalational anaesthetics.

Sedation Most often the MRI is carried out under sedation by non-anaesthesiologists (radiologists, nurses, technicians, etc.) as many hospitals do not have availability of anaesthesiologists. The goals of sedation are to guard the safety of patient, minimise physical discomfort and pain, control anxiety, provide amnesia, and control movements. All the patients should be evaluated before sedation for appropriate fasting (as ensured before an elective procedure) and an airway examination, to secure it in case of adversity. Airway equipment should be kept ready, routine physiological monitors should be attached, and an IV access will have to be secured for safe delivery of sedation. If hypoventilation or other problems occur during the procedure, the procedure has to be halted, and the patient needs to be managed after pulling out of the magnetic field. It requires special expertise for the caregiver to save time yet provide optimum safety to the patient.

A number of medications (oral/IV) are described to provide sedation (Table 41.4) in children undergoing MRI. An appropriate understanding of pharmacological properties is required to choose the agent based on a particular patient or scenario. The ideal agent should be safe and reliable with rapid onset and offset of action, minimal respiratory depression, maintain haemodynamic stability, and allow rapid awakening. Infants under 6 months of age can be managed with chloral hydrate or triclofos, whereas older infants and toddler can be sedated with oral pentobarbital. However, these sedatives are rarely used, in the current scenario. Midazolam as a sole agent may not be effective all the time, for sedation. In cooperative children without an IV access, sedation is still provided in some centres with intramuscular (IM) ketamine. Propofol infusion is one of the most popular techniques for MRI procedures. It provides effective sedation, easy titration to achieve desired level of hypnosis, with a short recovery time. Currently, dexmedetomidine also has been tried for MRI sedation in different routes (IV and intranasal); however, the exact dose is yet to be defined. *Conscious sedation* has been described for adult patients with moderate

Table 41.5 Patients requiring general anaesthesia for MRI

Infants and children with associated neurological diseases, neural tube defects, intracranial tumours, vascular malformations
Uncooperative patients
Patients with movement disorders
Claustrophobia
Patients undergoing stereotactic neurosurgical procedures
Intensive care patients; ventilated patients
Prolonged procedure of MRI
Patients undergoing intraoperative MRI during surgery

anxiety who may require an anxiolytic (e.g. benzodiazepines) before entering into the MRI suite.

General Anaesthesia A certain group of patients require general anaesthesia during MRI (Table 41.5); children are most common among them. A lighter level of anaesthesia may be appropriate for MRI procedures as these are painless. However, the lighter plane may lead to airway complications (bronchospasm and coughing) and may necessitate alterations in anaesthetic depth. It is important to discuss about the possible duration of the procedure, as it would also help determine spontaneous ventilation via a laryngeal mask airway (LMA) or tracheal intubation and subsequent mechanical ventilation.

Induction of anaesthesia should be carried out in an anaesthesia room or an area adjacent to MRI suite outside 5 G line, earmarked for the anaesthetic procedures. This area/room should also be utilised for resuscitation in case of an emergency after the patient is immediately pulled out of the magnetic field. The patient transfer between this room and the magnetic field (zone IV) is made by non-ferromagnetic trolleys. After the patient placed in the scanner, the head becomes inaccessible. Moreover, placement of a receiver coil for head scan further restricts the access to the airway which must be secured, adequately. The pilot balloon of the cuffed endotracheal tubes (ETT) may contain ferromagnetic spring which must be taped away from the magnetic field in order to prevent artefacts.

Monitoring of end-tidal carbon-dioxide ($EtCO_2$) should be considered in all patients requiring deep sedation. Oxygenation monitoring by pulse oximeter should not be considered as a substitute of monitoring of ventilator function. MRI safe/conditional anaesthesia machines are always to be preferred in the MRI suite. In case of non-availability, inhalational anaesthetic agents can be administered with standard anaesthesia machines from zone III via an elongated circuit with a waveguide. Alternatively, total intravenous anaesthesia (TIVA) may be used with MRI safe/conditional infusion pumps from zone IV or traditional pumps with IV tubing passed through a waveguide. Whatever may be the anaesthetic technique, a speedy recovery from anaesthesia is expected after the MR procedure with a minimal side effect.

Paediatric Patients

Children are the most common patient group requiring anaesthesia for MRI. Hence, it is imperative that the anaesthesia team is adequately trained, equipped, and prepared for the challenges of paediatric anaesthesia. Young infants often sleep after feeding and may allow a small duration scan to be carried out. Otherwise a sedative agent may be tried to achieve immobility during the procedure. However, for administration of sedative or anaesthesia, an IV access must be secured. Children without an IV access must be induced with inhalation agents followed by continuation of inhalational anaesthesia or propofol infusion for the maintenance. LMA is commonly utilised in uncomplicated children for securing the airway during MRI procedures along with spontaneous ventilation in order to prevent the pitfalls of intermittent positive pressure ventilation (IPPV) with long circuit tubing.

Intensive Care Patients

MRI is a complicated procedure for the intensive care unit (ICU) patients as the patient may have associated critical neurological condition such as coma or spinal cord compression along with cardiovascular instability and might be on vasopressor infusions. MR imaging is contraindicated in the unstable patient. The risk-benefit ratio must be analysed before transferring the patient from the ICU to MRI suite which is usually located at distant place. Proper medical history on implanted foreign bodies must be obtained from the relatives or else a plain radiography of the body should be carried out before scan. Metallic implants and incompatible monitoring devices (e.g. ICP bolt) should be removed or changed with MR conditional monitors and equipment. Similar precaution should be taken for infusion pumps before the patient enters zone IV. Current induction in lines or wires in direct contact with the heart muscle may cause micro-shocks and may lead to ventricular fibrillation and cardiac arrest. Temporary pacing wires and pulmonary catheter should be removed before MR procedures.

Crisis Management During MRI

Safe practice in the MRI under sedation and anaesthesia requires robust screening, adequately trained staff, multidisciplinary teamwork, and eternal vigilance. Table 41.6

Table 41.6 Management of possible complications during MRI

Complication	Assessment	Intervention
Loss of airway (Regurgitation, hypoxia, disconnection)	Confirm airway position and patency	Correct abnormality
	Assess breathing	If not possible to correct immediately, remove patient from zone III/IV, shift to the resuscitation area
	Circulation	Do not bring anaesthetic equipment into zone III/IV, e.g. laryngoscope
Cardiorespiratory arrest	Airway (A)	Initiate basic life support
	Breathing (B)	Immediate removal of patient from the magnetic field before beginning advanced life support
	Circulation (C)	
Object stuck in the MR scanner	Assess patient safety	Remove patient from zone IV
		Remove the object
Quenching emergency	Hypoxic alarm	Evacuation of patient and staff magnetic field
	Helium present	Quenching procedure (see text)
Contrast reaction	ABC	Stop administration of contrast
	Anaphylaxis management	Assess patient and remove zone IV for resuscitation
		Institute anaphylaxis management protocol – oxygen, adrenaline, IV fluids, etc.

summarises the immediate management of some potential catastrophic complications during MR anaesthesia.

Intraoperative MRI (iMRI)

Intraoperative MRI (iMRI) allows the patient to be scanned at regular intervals during the surgery so that exact location and near-complete resection of the lesion is possible. It has also been used to identify eloquent areas of the brain and hence, known as intraoperative functional MRI (fMRI). iMRI also reduces the necessity of a postoperative scan with improved clinical outcome of the patients. This procedure has been successfully used for intracranial tumour surgery (pituitary tumour, intraventricular tumours, and benign gliomas), epilepsy surgery, and deep brain stimulation. iMRI is also used during awake craniotomy to maximise the excision of intracranial tumour present adjacent to the eloquent areas of the cortex.

The current high-field iMRI system, constructed by the cooperation of Siemens and Brain Lab (Brain Suite), consists of a standard 1.5T magnet scanner, implemented in a dedicated OR with a computer-assisted neuronavigation system, and digitised image transfer and projection system to form a comprehensive unit (Fig. 41.2). The typical iMRI

Fig. 41.2 Intraoperative magnetic resonance imaging (MRI) set-up showing magnetic scanner and computer-assisted neuronavigation system

suite comprises of an inner controlled area. The red line (inner) represents the region where the magnetic field is 50 G and higher, and the yellow line (outer) demarcates the region beyond which the magnetic field strength is less than 5 G. Any ferromagnetic object within 5G line can be attracted to the magnet. The areas for imaging and surgery are separate in many clinical circumstances; either the patient is transferred to the MRI, or the MRI is brought to the patient. If the operating table is located inside the 5 G area, all the surgical instruments should be MRI safe/conditional. However, if the table is located outside 5 G line, full range of surgical and anaesthetic equipment may be used with its transfer into magnetic console to obtain images whenever indicated during surgery.

Management of patients in the iMRI suite creates great challenges to the anaesthesiologist. The concerns of patient safety and compatibility of monitors and equipments remain similar to that of a standard MR environment. The neuroanaesthetic concerns are further complicated by repeated intraoperative scan, cold intraoperative condition leading to hypothermia, appropriate positioning of patient during transfer to the magnetic field, and prolonged operative times. Both TIVA and inhalational anaesthetic techniques for general anaesthesia, and monitored anaesthesia care (MAC) for awake craniotomy have been used successfully in iMRI condition.

Suggested Reading

Association of Anaesthetists of Great Britain and Ireland. Provision of anaesthetic services in magnetic resonance units. The Association of Anaesthetists of Great Britain and Ireland; 2002. http://www.aagbi.org/publications/guidelines/docs/mri02.pdf.

Farling PA, McBrien ME, Winder RJ. Magnetic resonance compatible equipment: read the small print! Anaesthesia. 2003;58:86.

Gupta N, Rath GP. Intraoperative magnetic resonance imaging in neurosurgery and anesthetic considerations. World J Anesthesiol. 2014;3(2):174–80.

Osborne IP. Magnetic resonance imaging: new challenge and techniques. Curr Opin Anaesthiol. 2002;15:443–8.

Practice advisory on anesthetic care for magnetic resonance imaging. An updated report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. Anesthesiology. 2015;122:459–79.

Reddy U, White MJ, Wilson SR. Anaesthesia for magnetic resonance imaging. Contin Educ Anaesth Crit Care Pain. https://doi.org/10.1093/bjaceaccp/mks002. First published online: February 26, 2012.

Safety guidelines for magnetic resonance imaging equipment in clinical use. London: Medicines and Healthcare Products Regulatory Agency (HPRA). March 2015. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/476931/MRI_guidance_2015_-_4-02d1.pdf.

Serafini G1, Ongaro L, Mori A, Rossi C, Cavalloro F, Tagliaferri C, Mencherini S, Braschi A. Anaesthesia for MRI in paediatric patients. Minerva Anestesiol. 2005;71:361–6.

Shellock FG, Spinazzi A. MRI safety update 2008: part 1, MRI contrast agents and nephrogenic systemic fibrosis. AJR Am J Roentgenol. 2008;191:1129–39.

Perioperative Challenges During Electro Convulsive Therapy (ECT)

42

Carrie Bowman-Dalley and James G. Hilliard

Since 1938, electroconvulsive therapy (ECT) has been used in the treatment of severe and refractory depression, catatonia, schizophrenia, and suicidal ideation. ECT has also been studied recently as a potential treatment to improve post-traumatic stress disorder (PTSD) symptoms and reduce mortality in this patient population. Although ECT was performed without anesthesia for almost 30 years, the collaboration between anesthesia practitioners and our psychiatric colleagues has resulted in safer techniques, improved patient comfort, and more efficacious therapy. The anesthesia practitioner must anticipate the physiologic response to the electrical stimulus and understand the effect of anesthetic drugs on the treatment to minimize the risks and increase the effectiveness of ECT.

Several recent reports indicate a decline in the incidence of ECT-related adverse events. However, the anesthetic management of ECT continues to be associated with many potential complications (see Table 42.1). Among the most commonly reported causes of ECT-related morbidity and mortality are cardiovascular events including dysrhythmia, myocardial infarction, congestive heart failure, and cardiac arrest. This chapter will focus on the cardiovascular complications associated with ECT, along with pulmonary, neurological, and musculoskeletal consequences of ECT.

Table 42.1 Complications associated with ECT

Pulmonary
Aspiration
Obstruction
Laryngospasm
Pulmonary edema
Cardiovascular
Dysrhythmia
Hypertension
Myocardial infarction
CHF
Cardiac arrest
Neurological
Pretreatment anxiety
Status epilepticus
Convulsive
Nonconvulsive
Delirium and agitation
Inadequate seizure length
Headache
Intracranial hemorrhage
Musculoskeletal
Long-bone fractures
Dislocations
Dental damage
Oral lacerations
Myalgia
Other
PONV
Recall

Cardiovascular Complications

Overview

Electroconvulsive therapy stimulates the parasympathetic and sympathetic branches of the autonomic nervous system. Following application of the electrical current to the brain, a vagal reflex occurs, and parasympathetic dominance is generally observed for 10–60 seconds. The patient's hemody-

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Table 42.2 Management of cardiovascular complications associated with ECT

Patient risk factors	Potential complications	Prevention strategies
Cardiovascular disease	Myocardial ischemia	Pretreatment with beta-blockers
Previous myocardial infarction	Myocardial infarction	Optimize outcomes by controlling hypertension, diabetes mellitus, CHF, angina and dysrhythmias
LVEF <50%	Dysrhythmias (ventricular tachycardia)	
>10 PVC an hour	Cardiac rupture	
Pacemaker or implanted cardioverter defibrillator (ICD)	Dysrhythmias	Pre- and post-ECT device interrogation
		Proper grounding of all equipment
		Consider having a cardiology specialist present for the first ECT
		Have magnet available
		Pacemaker: follow the recommendation of the manufacturer and cardiologist[a]
		ICD: deactivate defibrillator function during ECT, turn back on after procedure[a]
Monoamine oxidase inhibitor therapy	Hypertensive crisis	Consult psychiatrist for risk/benefit analysis of discontinuing for 2 weeks before ECT
	Dysrhythmias	Avoid meperidine
		Avoid indirect sympathomimetics
Tricyclic antidepressants	Dysrhythmias	Consult psychiatrist for risk/benefit analysis of discontinuing for 2 weeks before ECT
	Synergistic with anticholinergic drugs	Titrate sympathomimetic drugs carefully
	Synergistic with sympathomimetic drugs	Avoid preemptive anticholinergic drugs
Serotonin-norepinephrine reuptake inhibitors (SNRIs)	Dysrhythmias (SNRIs)	Consult psychiatrist for risk/benefit analysis of discontinuing before ECT
Bupropion	Asystole (SNRIs)	
	Prolonged seizure activity	
Hyperkalemia	Dysrhythmias with succinylcholine administration	Avoid succinylcholine
		Consider small dose of atracurium or *cis*-atracurium
Atrial fibrillation	Thromboembolism following conversion to sinus rhythm with ECT stimulation	Recommend anticoagulation therapy prior to ECT for all patients with concurrent atrial fibrillation
Cerebral aneurysm	Enlargement or rupture of aneurysm from increased wall stress	Complete pharmacologic suppression of sympathetic nervous system response
		In patients with known coronary artery disease, reduced ejection fraction, or aortic insufficiency, consider nitroprusside 30 mcg/minutes IV with atenolol 50 mg PO and arterial-line monitoring
Hypertension	Intracranial hemorrhage	Maintain BP within 20% of patient's baseline. See Table 42.3 for preferred agents and ECT related considerations
Brady-dysrhythmias and cardiac conduction delays	Profound bradycardia	Pretreat with anticholinergic agent
	Asystole	Avoid repeat dosing of succinylcholine

[a]No randomized controlled clinical trials are available to direct practice. Recent case series/case reports suggest pacemaker function does not usually require modification (i.e., placement into asynchronous mode)

namic profile then quickly changes as catecholamines are released from postganglionic sympathetic nerves and the adrenal medulla (period of sympathetic dominance). The hemodynamic impact of this sympathetic stimulation is generally observed for approximately 5–10 minutes, with peak heart rate and systemic blood pressure readings observed 3–5 minutes after the electrical stimulation. Profound bradycardia and asystole have been observed during the parasympathetic phase, and cardiac rhythms ranging from transient sinus tachycardia to ventricular tachycardia have been reported in the sympathetic phase. In addition, hypertension is common with the average increase in systolic blood pressure of 30–40%. While studies have demonstrated that most patients experience impairment in left ventricular systolic and diastolic function for up to 6 hours following ECT, the majority of patients tolerate the cardiovascular alterations well. Patients with increased risk for the development of life-threatening cardiovascular complications during ECT and respective associated prevention strategies are summarized in Table 42.2.

Prevention

Standard monitors (as defined by the American Society of Anesthesiologists) are generally sufficient during anesthesia for an ECT procedure. Hemodynamic and respiratory derangement requires prompt intervention to prevent

cardiovascular crisis with ECT. Hypoxemia secondary to compromised airway patency or hypoventilation must be prevented with adequate bag-mask ventilation. The patient should be pretreated with an anticholinergic agent (e.g., glycopyrrolate or atropine). This is especially important if the psychiatrist is using subthreshold stimuli or repeated stimuli to determine the seizure threshold, if the patient is taking a beta-adrenergic antagonist medication, or if there is a history of failure to induce a seizure following electrical stimulation. In any of these situations, there is a much higher risk of clinically significant bradycardia and asystole. The sympathetic response may be diminished or absent, with unopposed vagal discharge following the induced seizure. Glycopyrrolate may be superior to atropine because it offers a stronger antisialagogue effect with less tachycardia and does not have central nervous system side effects.

In high-risk patients, additional suppression of the hyperdynamic response is desirable to prevent cardiovascular crisis such as myocardial infarction arising from tachycardia, other significant arrhythmias, and hypertension. Table 42.3 summarizes agents that have been effectively used to minimize autonomic nervous system effects of ECT and their effect on seizure duration. When using antihypertensive agents during ECT, one must be cautious that cerebral perfusion pressure is maintained. Adequate cerebral blood flow is crucial during ECT because the induced seizure will increase cerebral oxygen demand by 200%.

Table 42.3 Intravenous antihypertensive agents and effect on seizure duration

Preemptive medication	Effect on seizure duration	ECT-related considerations
Esmolol Up to 1 mg/kg	Mildly decreased	Short duration of action desirable
Labetalol 0.1–0.2 mg/kg	Decreased	Effect on seizure duration controversial
Nicardipine 1.25–2.5 mg	No change	Used in combination with labetalol to avoid rebound ↑ HR
Diltiazem 10 mg	Decreased	Nicardipine preferred for ECT
Nitroglycerin 3 mcg/kg	No change	Advised if at risk for myocardial ischemia
Nitroprusside 0.1–5 mcg/kg/minutes	No change	Advised for coexisting aneurysms and aortic stenosis; arterial line required
Dexmedetomidine 1 mcg/kg over 10 minutes (pre-induction)	No change	Administration with propofol 1 mg/kg may augment antihypertensive effect
Remifentanil 100 mcg	No change	Anesthetic sparing effect may be helpful to improve suboptimal seizure duration

Crisis Management

In the event of a life-threatening cardiovascular complication, the anesthesia provider must be prepared to intervene with ACLS protocols. Emergency medications and resuscitative equipment must be immediately available.

If myocardial ischemia is suspected, oxygenation and hemodynamic parameters should be optimized immediately following current evidence based protocols. The patient should be admitted to a monitored setting with continuation of supportive therapies. Serial cardiac markers including troponin should be followed to quantify myocardial damage.

Key Points

- Following electrical brain stimulation with ECT, patients will predictably experience a vagal reflex followed 15–60 seconds later by sympathetic discharge.
- Patients at risk for cardiovascular complications from ECT-related autonomic nervous system stimulation include those with coronary artery disease, cerebral vascular disease, hypertension, congestive heart failure, aneurysms, and pre-existing arrhythmias or those currently taking a tricyclic antidepressant (TCA), serotonin-norepinephrine reuptake inhibitor (SNRI), bupropion, or monoamine oxidase inhibitor (MAOI).
- Premedication with an anticholinergic agent is recommended particularly if the patient is taking beta-blockers or in cases where repeated electrical stimulation or subthreshold stimulation are being used.
- Premedication to attenuate the hyperdynamic responses to ECT can be considered for patients at high risk for cardiovascular complications.
- Cardiovascular complications are the leading cause of ECT-related mortality. Complications include bradycardia, asystole, severe hypertension, severe sinus tachycardia, ventricular tachycardia, myocardial ischemia, and infarction.
- Anesthesia for ECT should only be administered in an environment which is equipped and trained for immediate delivery of ACLS.

Pulmonary Complications

Overview

ECT treatment regimens commonly require patients to receive treatments three to four times per week. A mask

Table 42.4 Management of pulmonary complications associated with EC

Complication	Adverse effects of complication	Treatment	Potential adverse effects of treatments
Aspiration of gastric contents	Airway obstruction by solid particulate matter leading to hypoxemia/neurologic injury/death	Trendelenburg position	Injury to teeth and soft tissue structures; sore throat
	Immediate pulmonary tissue injury (pH related) and secondary inflammatory injury	Suction oral pharynx	
	Pneumonia	Support oxygenation and ventilation	
	Acute respiratory distress syndrome (ARDS)	Secure airway	
Laryngospasm	Hypoxia	Positive pressure ventilation	Bradycardia, hyperkalemia
	Hypercarbia	Succinylcholine	
	Pulmonary edema		
Upper airway obstruction	Hypoxia	Reposition airway	Epistaxis
	Hypercarbia	Insert oral/nasal airway	
		Consider LMA or ETT	
Pulmonary edema	Inadequate gas exchange	Support oxygenation and ventilation	Hypovolemia, hypotension
	Hypoxemia	Confirm diagnosis	
	Hypercarbia	Restrict IV fluids and consider diuretics	

anesthetic is the treatment of choice, unless contraindicated because of known difficult ventilation, significant gastroesophageal reflux disease, or late-term pregnancy.

Most of the pulmonary complications associated with ECT are similar to those of any mask anesthetic: aspiration, airway obstruction, laryngospasm, hypoxia, or hypoventilation. Aspiration is rare (fewer than 1 of 2000 patients) but can be life-threatening.

Pulmonary edema is a rare complication of ECT. The sympathetic output after the electrical stimulus increases afterload over a short period of time. In patients with myocardial dysfunction, the increase in afterload may cause transient decompensated heart failure.

Prevention

The prevention of pulmonary complications begins with a thorough preoperative assessment. When gastroesophageal reflux disease (GERD) is identified, the patient's condition can be optimized with prophylactic medications. The preoperative administration of H_2 receptor blockers (ranitidine), prokinetic agents (metoclopramide), and antacids (sodium citrate) can increase the pH and reduce the volume of stomach contents, which may prevent or reduce the negative impact of a clinically significant aspiration event. Furthermore, in patients with severe GERD, rapid sequence induction and intubation should be considered to protect the patient's airway. In all patients, proper positioning, with the head of bed elevated 15–30°, reduces the chance of passive aspiration and improves pulmonary compliance.

Preparation of airway resuscitation equipment is imperative. The anesthesia provider must be able to support oxygenation and ventilation quickly and effectively.

Patients at risk for pulmonary edema should be identified early. In these patients, normovolemia should be maintained, and medications can be administered throughout the procedure to optimize hemodynamic parameters such as heart rate (beta-adrenergic antagonists), preload (venodilators), and afterload (direct acting vasodilators).

Crisis Management

Treatment strategies for pulmonary complications are summarized below in Table 42.4.

Key Points

- A thorough preoperative assessment and preparation of airway equipment is paramount.
- Patients at risk for aspiration should receive H_2 blockers, prokinetic agents, and sodium citrate, and endotracheal intubation should be considered.

Neurological Complications

Overview

Neurological complications result from the effects of the electrical stimulus on extracranial and intracranial structures, as well as mental status changes associated with the postictal state.

Headaches (HA) are a common complaint after ECT, occurring in about 45% of patients. When the electrodes deliver a direct stimulus, the muscles of the head and face contract for the duration of the stimulus. The contraction of the temporalis and masseter muscles, along with ECT-related vascular changes, are proposed etiologies. The incidence of headache has been associated with increased duration of seizure.

Intracranial hemorrhage is a reported complication of ECT; however, it is extremely rare. The acute hyperdynamic response can cause increased cerebral blood flow, transient neurologic deficits, cortical blindness, and damage to vascular structures. Patients with undiagnosed underlying vascular malformations such as aneurysm or arteriovenous malformations may be at increased risk for post-ECT intracranial hemorrhage.

Tonic-clonic seizures of adequate length are consistent with efficacious treatment. Although rare, a seizure lasting more than 5 minutes, or multiple seizures within a short period, despite no additional electrical stimulus, may be precipitated by ECT. Status epilepticus (SE) must be recognized and treated immediately and may be convulsive or nonconvulsive. Convulsive SE is characterized by focal or generalized sustained tonic-clonic movements, such as rhythmic contraction followed by relaxation of flexor and extensor muscles of the elbow, knee, and hip joints. Nonconvulsive SE requires EEG to confirm diagnosis and should be suspected in patients with significantly delayed emergence or emergence delirium, not explained by the usual postictal state. Patients who may be tapering their antipsychotic medications or patients currently on aminophylline are at risk for this complication. Propofol and thiopental can inhibit the ECT seizure, rendering it ineffective. Etomidate, in comparison to propofol, can result in longer motor and electroencephalogram seizure duration. Most sedatives or anxiolytics will decrease the efficacy of the ECT.

While most patients recover quickly from their ECT, some patients develop confusion, agitation, and violent behavior post-procedure. These patients may require premedication (see below), increased vigilance in the recovery room, or sedation post-ECT.

Prevention

A thorough preoperative assessment is crucial to reducing the incidence of neurological complications during ECT. A careful examination of the patient's health history and medications may reveal coexisting disease and medications that can influence seizure activity. For example, mediations used to control epilepsy (lamotrigine, valproate, and carbamazepine), and anxiety (benzodiazepines), may attenuate seizure activity, whereas medications used to treat bipolar disease (lithium) and schizophrenia (phenothiazines and clozapine) have been reported to prolong seizure activity. Therefore, consultation with an appropriate specialist (e.g., neurologist for a patient with epilepsy, etc.) should be considered. In addition, the choice of anesthetic agent can influence ECT seizure length. For example, methohexital and etomidate have been reported to promote a longer ECT seizure duration compared with propofol.

Patients who report HA can receive pretreatment in the form of oral NSAIDS unless contraindicated.

The incidence of post-procedure agitation can be reduced with premedication of low dose midazolam (0.025 mg/kg) or dexmedetomidine (0.5 mcg/kg) without adverse effects. Administration of a half dose of the induction agent (typically methohexital) after the stimulus has also been described. Efforts by the staff to reduce stimulation and provide reassurance may be helpful.

Crisis Management

Crisis management for neurological complications of ECT is summarized in Table 42.5.

Key Points

- Headaches are common and can be avoided by premedicating with NSAIDS.
- Intracranial hemorrhage is an important differential diagnosis if LOC is inadequate following ECT.
- Status epilepticus results in increased cerebral metabolic demand and an unprotected airway.
- Pharmacologic and non-pharmacologic methods can be employed to reduce post-ECT agitation.

Table 42.5 Management of neurological complications associated with ECT

Complication	Adverse effects of complication	Treatment	Potential adverse effects of treatments
Headache	Patient discomfort	NSAIDs	Gastric ulcers
			Renal failure
			Platelet inhibition
Intracranial hemorrhage	Increased intracranial pressure	Support oxygenation and ventilation	Excessive hypercarbia resulting in cerebral vasoconstriction and reduced flow through collateral vasculature
	Decreased cerebral perfusion pressure	Maintain MAP to ensure adequate CBF	
	Neuronal hypoxia	Monitor for signs of intracranial hypertension	
	Brain herniation	Reduce ICP	
	Death	Hyperventilation	
		Osmotic diuresis	
		HOB elevated	
		Ventriculostomy	
		Consult neurosurgeon	
		Confirm diagnosis (STAT head CT)	
		Consider emergency surgery	
Status epilepticus	Neuronal hypermetabolism resulting in central nervous system hypoxia, potential cell death, and central nervous system injury	Support oxygenation and ventilation	Sedation, respiratory depression and airway obstruction
Convulsive		Administer benzodiazepines, barbiturates or propofol	Bradycardia
		Consider administration of other anticonvulsants (e.g., levetiracetam or phenytoin)	Sedation, respiratory depression, and airway obstruction
Nonconvulsive		Confirm diagnosis with EEG	
		Administer benzodiazepines or other anticonvulsants as necessary (consult neurologist)	
Agitation and delirium	Potential physical and psychological trauma	Reduce stimulation during the postictal phase	Sedation, prolonged recovery times, bradycardia
		Provide verbal reassurance	
		Premedication with midazolam or dexmedetomidine	

Musculoskeletal Complications

Overview

Musculoskeletal injuries caused by ECT were commonplace prior to the application of anesthesia to the procedure. Now long-bone fracture and dislocations are extremely rare. These complications can be a result of inadequate dosing of muscle relaxants or delivery of the stimulus prior to complete paralysis. Patients with a history of osteoporosis are at greater risk for skeletal injury.

Damage to the teeth and soft tissues of the mouth remain a concern. Direct electrical stimulation causes sustained contraction of the masseter muscle despite profound muscle relaxation. Anesthesia and psychiatric personnel must take measures to prevent injury to the teeth, tongue, and lips.

Myalgia continues to be a relatively common complication. The etiology is unclear; both the fasciculations from succinylcholine and the motor activity during convulsions may be responsible. Severity of myalgia is not predicted by degree of fasciculation or motor activity but appears to be worse in patients younger than 45 years.

Prevention

Accurate dosing of muscle relaxants and careful timing by the psychiatrist can prevent long-bone fractures and dislocations. Deep tendon reflexes are a reliable indicator of muscle tone and can be used to determine the optimal time for stimulation. Meticulous care and vigilance ensure minimal injury to the teeth and mouth. A bite guard with an opening to allow for continued ventilation placed between the teeth from molars to incisors provides adequate protection. The lips are at risk for laceration and should be free of the teeth prior to the stimulus.

The prevention of myalgias remains controversial. Success has been reported with reduced succinylcholine doses, defasciculation with non-depolarizing muscle relaxants, and premedication of a variety of drugs including sodium channel blockers (lidocaine), calcium gluconate, pregabalin, enteric-coated aspirin (650 mg orally), acetaminophen (650 mg orally), or ketorolac (30 mg IV).

Crisis Management

Crisis management for musculoskeletal complications of ECT is summarized in Table 42.6.

Table 42.6 Management of musculoskeletal complications associated with ECT

Complication	Adverse effects of complication	Treatment	Potential adverse events of treatments
Long-bone fractures and dislocations	Pain	Stabilize fracture	Fat embolism
	Disability	Control pain with opioids	Respiratory depression, nausea, vomiting, pruritus
		Administer IV fluids	
		Consult orthopedic specialist	
Dental damage and oral lacerations	Pain	Remove any broken teeth to prevent aspiration	Aspiration of teeth, blood
	Disability	Consult oral surgery	
Myalgia	Pain	IV NSAIDS (ketorolac 30 mg)	Gastric ulcers
			Renal failure
			Platelet inhibition

Key Points

- Accurate dosing of muscle relaxants and a well-timed electrical stimulus reduce the incidence of fractures and dislocations.
- Structures of the mouth require careful attention in order to prevent damage and aspiration of foreign bodies.
- A bite guard should be considered to provide protection for the teeth and lips.
- Premedication with NSAIDS can reduce to incidence of myalgia.

References

Ahmadi N, Moss L, Simon E, Nemeroff CB, Atre-Vaidya N. Efficacy and long-term clinical outcome of comorbid posttraumatic stress disorder and major depressive disorder after electroconvulsive therapy. Depress Anxiety. 2015;33:640–7.

Aydogan MS, Yucel A, Begec Z, Colak YZ, Durmus M. The hemodynamic effects of dexmedetomidine and esmolol in electroconvulsive therapy: a retrospective comparison. J ECT. 2013;29(4):308–11.

Begec Z, Toprak H, Demirbilek S, Erdil F, Onal D, Ersoy M. Dexmedetomidine blunts acute hyperdynamic responses to electroconvulsive therapy without altering seizure duration. Acta Anaesthesiol Scand. 2008;52(2):302–6.

Dersch R, Zwernemann S, Voderholzer U. Partial status epilepticus after electroconvulsive therapy and medical treatment with bupropion. Pharmacopsychiatry. 2011;44(7):344–6.

Ding Z, White PF. Anesthesia for electroconvulsive therapy. Anesth Analg. 2002;94:1351–64.

Dinwiddie SH, Hou D, Gottlieb O. The course of myalgia and headache after electroconvulsive therapy. J ECT. 2010;26(2):116–20.

Kadar AG, Caleb HI, White PF, Wakefield CA, Kramer BA, Clark K. Anesthesia for electroconvulsive therapy in obese patients. Anesth Analg. 2002;94:360–1.

Kurup V, Ostroff R. When cardiac patients need ECT – challenges for the anesthesiologist. Int Anesthesiol Clin. 2012;50(2):128–40.

Mizrak A, Koruk S, Ganidagli S, Bulut M, Oner U. Premedication with dexmedetomidine and midazolam attenuates agitation after electroconvulsive therapy. J Anesth. 2009;23(1):6–10.

Recart A, Rawal S, White PF, Byerly S, Thornton L. The effect of remifentanil on seizure duration and acute hemodynamic responses to electroconvulsive therapy. Anesth Analg. 2003;96(4):1047–50.

Saito S. Anesthesia management for electroconvulsive therapy: hemodynamic and respiratory management. J Anesth. 2005;19:142–9.

Tecoult E, Nathan N. Morbidity in electroconvulsive therapy. Eur J Anaesthesiol. 2001;18:511–8.

Tess VJ, Smetana GW. Medical evaluation of patients undergoing electroconvulsive therapy. N Engl J Med. 2009;360:1437–44.

Watts BV, Groft A, Bagian JP, Mills PD. An examination of mortality and other adverse events related to electroconvulsive therapy using a national adverse event report system. J ECT. 2011;27(2):105–8.

Perioperative Challenges During Carotid Artery Revascularization

43

Ursula G. Schulz

Introduction: Carotid Revascularization Procedures

Carotid stenosis is an important cause of ischemic stroke. About 10–15% of patients with carotid territory strokes and transient ischemic attacks (TIA) have a carotid stenosis >50%. If not treated appropriately, these patients have a high risk of further, potentially disabling, cerebral ischemic events, which may be as high as 10% in the 1st week and 15% in the 1st month following the initial presentation. Urgent treatment of the carotid stenosis to prevent recurrent strokes is therefore mandatory and will in most cases consist of a revascularization procedure in addition to medical management.

The most widely used procedure to treat carotid stenosis is carotid endarterectomy (CEA), which very effectively reduces the long-term risk of stroke. A pooled analysis of the largest trials showed that the 5-year absolute risk of any stroke or death was reduced by 15.3% (95% CI 9.8–20.7) in patients with 70–99% stenosis and by 7.8% (3.1–12.5) in patients with 50–69% stenosis. Surgery has no benefit in patients with <50% stenosis. Because the risk of recurrent stroke is highest in the first few days after the initial event, this is also when the benefit from CEA is highest. Benefit from surgery rapidly diminishes over time, and surgery within 2 weeks after the initial event is recommended in patients with a TIA or nondisabling stroke who are neurologically stable and medically fit to tolerate the procedure.

While the benefit of surgery for recently symptomatic carotid stenosis is uncontested, there is more debate about the benefit from surgery for asymptomatic carotid stenosis. The risk of stroke from an asymptomatic carotid stenosis is lower than from a recently symptomatic stenosis, and the benefit from surgery is therefore smaller. Two large trials showed an absolute risk reduction of about 5% over 5 years. However, medical treatment has become more aggressive since these trials were done, and the risk from surgery in the trials was probably lower than in "real life." Hence, the actual benefit from CEA in asymptomatic stenosis may well be lower. Overall, the quality of medical treatment has improved since the carotid surgery trials for symptomatic and for asymptomatic stenosis were done, and at the same time, the operative risk has decreased. The risk reduction from surgery in recently symptomatic high-grade stenosis was so large in the original trials that it is likely that the benefit of surgery will have been maintained even compared to current aggressive medical management. However, the benefit of surgery in comparison to current medical management is less certain for patients with asymptomatic carotid stenosis, and potentially even for patients with lower risk symptomatic stenosis, such as those with moderate (50–69%) stenosis, or with delayed presentation. Trials to determine if intervention is still beneficial in this group are ongoing.

In recent years, carotid artery stenting (CAS) has been increasingly used as an alternative to CEA. While it is generally more convenient, may avoid some of the complications associated with open surgery, and the hospital stay may be shorter, there are also specific risks of CAS. These include stroke caused by dislodged atherothrombotic debris, arterial wall dissection, arterial rupture, and, in the longer term, restenosis. The debate whether CEA or CAS is the preferable intervention for treating carotid artery stenosis is, to some extent, still ongoing. Recent data from two large studies (International Carotid Stenting Study – ICSS and the Carotid Revascularization Endarterectomy vs. Stenting Trial – CREST) suggest that the periprocedural risk of stroke and death is higher for carotid stenting, whereas the risk of periprocedural myocardial infarction, and of cranial nerve deficits, is higher in patients undergoing carotid endarterectomy. Long-term follow-up data from the ICSS showed similar benefit of CEA and CAS, with a similar risk of recurrent

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stroke for both treatment modalities. The decision on whether CEA or CAS is offered will therefore often also depend on local preference. However, CAS is usually the preferred option where CEA is technically difficult, for example, in stenosis related to previous neck irradiation, in patients with restenosis following previous CEA, in surgically poorly accessible stenosis, and in patients with contralateral carotid occlusion, as the vessel occlusion time during CAS tends to be shorter. In contrast, CAS appears to be higher risk in patients who are more than 70 years of age, and CEA is the preferred option here.

One further revascularization procedure, which is far less commonly used, is *extra-intracranial bypass surgery*, in which a branch of the superficial temporal artery is anastomosed with a cortical branch of the middle cerebral artery via a cranial burr hole. This surgery is sometimes used in recurrently symptomatic carotid occlusion or in stenosis of the distal carotid or middle cerebral artery. There has only been one randomized trial in symptomatic carotid occlusion due to atheromatous disease, which showed no benefit.

Complications of Carotid Revascularization Procedures

Complications arising during and after carotid revascularization can be classified as follows:

- General complications arising from general anesthesia and from cerebral angiography
- Complications arising from manipulation and recanalization of the carotid artery
- Procedure-specific complications associated with CEA or CAS

The complications arising from general anesthesia and neuroradiological interventional procedures are dealt with elsewhere in this book (see Chap. 73: Anesthesiological Challenges During Neuroradiological Interventions). In this chapter, we focus on complications specifically associated with carotid revascularization procedures.

Stroke Associated with Carotid Revascularization Procedures

Background

Periprocedural stroke is the main neurological risk associated with both CEA and CAS. The reported risks vary widely but in patients with symptomatic stenosis are generally about 5–6% for CEA and 4–8% for CAS. During surgery, ischemic stroke may occur from embolization of atheromatous material or low flow associated with temporary vessel occlusion and insufficient collateral vessels. Surface thrombus or atheromatous material may also be dislodged during CAS, but in addition stroke may be caused by vessel wall dissection with subsequent thrombus formation and embolization, thrombus formation on the guide wire, or air embolism. Postprocedural stroke may occur from thrombus formation on the endarterectomized surface, on suture lines, on the inserted stent, or from embolization from residual atheromatous plaque.

Prevention of Periprocedural Stroke

Carotid Endarterectomy

- *Antiplatelet therapy*: Patients should be on an antiplatelet agent, usually either aspirin or clopidogrel, before and, for secondary stroke prevention, indefinitely after the procedure. From a secondary prevention point of view, clopidogrel may be slightly more effective than aspirin in reducing the risk of recurrent stroke, but it may also be associated with a higher rate of operative bleeding, which is why many surgeons prefer patients to be on aspirin rather than clopidogrel prior to CEA. There is evidence that treatment with a combination of aspirin and clopidogrel reduces the number of emboli from a recently symptomatic carotid plaque. Short-term use of dual antiplatelet therapy to reduce the risk of recurrent ischemic event is currently investigated in a clinical trial. However, dual antiplatelet therapy also increases the overall risk of hemorrhage, and there is currently insufficient evidence to recommend its use prior to or following CEA.
- *Anticoagulation*: A heparin bolus is usually given before clamping the carotid artery.
- *Shunting* during surgery maintains blood flow through the internal carotid artery, while it is clamped. However, this procedure carries a risk of dislodging thrombus, and routine shunting has not been found to be associated with a reduced risk of stroke, although it may be helpful in individual cases.
- *Intraoperative monitoring*: The gold standard is to assess the patient's functional status clinically during the procedure. This is possible when using local anesthesia and one of the advantages of this anesthetic modality. If there is any deterioration, for example, if the patient develops a focal deficit after clamping of the carotid artery, shunting can be performed. Under general anesthetic, other monitoring methods, such as transcranial Doppler (TCD), EEG, or sensory evoked potentials, have been used to help decide if shunting is indicated.

Carotid Artery Angioplasty and Stenting

- *Antiplatelet therapy*: Generally patients should be on dual antiplatelet therapy (aspirin and clopidogrel) at least 3 days prior to the procedure, and this should be continued for 1–3 months postprocedure. Indefinite antiplatelet therapy for secondary stroke prevention then continues according to local guidelines.
- *Anticoagulation*: Patients are generally anticoagulated with heparin throughout the procedure to prevent thrombus formation on the catheter and guidewire. Anticoagulation is not routinely used after the procedure.
- *Protection devices*: These are deployed prior to angioplasty and stenting to prevent any debris that may be dislodged during the procedure from embolizing distally. There are several types of device available. Largely, they can be divided into distal filter or occlusion devices, which need to be passed through the stenosis prior to being deployed, and into proximal occlusion devices, which prevent blood flow through the artery, while the stent is inserted, with subsequent aspiration of debris. Even though the use of these devices is recommended as standard in some countries, they also have inherent risks. There is currently no conclusive evidence that any one type of protection is superior to the other in preventing complications during CAS, or indeed if the use of any protection devices is beneficial.

How to Recognize and Investigate a Periprocedural Stroke

Consider a periprocedural stroke if the patient develops a new focal neurological deficit during or after the procedure or – less frequently – becomes restless and develops a decreased level of consciousness.

During the Procedure

If done under local anesthetic, exclude other possible causes for agitation, for example, pain or urinary retention. Assess the patient's vital signs, neurological status, and blood sugar. If the patient is undergoing a stenting procedure and the angiography catheter is still in place, the neuroradiologist will be able to check blood vessels for patency, and – if a vessel occlusion is present – it may be appropriate to perform clot retrieval or to give intra-arterial thrombolysis. Endovascular salvage may also be feasible if a stroke occurs during endarterectomy and the patient can quickly be transferred to an angiography suite.

After the Procedure

After a general anesthetic, the patient may awake with a new neurological deficit. In this case, the therapeutic options will depend on the care provider's best estimate of time of onset of the deficit. In addition, a patient may develop a neurological deficit several hours or days after the procedure. In this situation proceed as follows:

- Try to ascertain as precisely as possible when the deficit developed.
- Quickly assess the patient to determine the extent of the deficit (vital signs, quick neurological examination – probably most easily and rapidly done by using the NIH Stroke Scale, a standardized scale for assessing and classifying stroke severity).
- Urgently contact the responsible neurologist/stroke physician and the neuroradiologist for further assessment and brain imaging (intracerebral hemorrhage after carotid revascularization is not uncommon), and repeat vascular imaging. In case of a recent ischemic event, intervention may be appropriate (e.g., endovascular clot retrieval).

The potential for salvaging brain tissue after vessel occlusion decreases rapidly with increasing time since onset even within the first few hours, and intra-arterial intervention might only be feasible within the first 6 h after onset. However, this will have to be decided on an individual basis, so urgent discussion with the stroke team and neuroradiologist or surgeon who has done the procedure is mandatory.

Treatment of a Periprocedural Stroke

Any interventional treatment will be decided on and done by the stroke team/neuroradiologist.

Any further treatment will follow the general guidelines for treatment of ischemic stroke outlined in Table 43.1.

Cerebral Hyperperfusion Syndrome

Background

Cerebral hyperperfusion syndrome (CHS) is a complication that occurs in 0–3% of patients following carotid revascularization. It usually occurs within a few hours or days after revascularization but may occur up to 28 days later. The exact pathophysiology is incompletely understood. Generally, it is thought to be due to sudden restoration of blood flow in a chronically hypoperfused area of the brain. Autoregulation in that part of the brain is impaired, and the cerebral blood vessels fail to constrict fully in response to increased perfusion, which is therefore

Table 43.1 General management of acute ischemic stroke

Blood pressure (hyper- and hypotension)
Hypertension in acute stroke usually settles spontaneously and should not be treated unless systolic BP is >220 mmHg or diastolic BP is >120 mmHg or there is acute ischemic heart disease, heart failure, aortic dissection, renal failure, hypertensive encephalopathy, or preeclampsia/eclampsia
Causes of hypertension, such as pain, anxiety, or urinary retention, should be treated
If systolic BP >220 mmHg or diastolic BP >120 mmHg, lower BP very cautiously, for example, with labetalol 10–20 mg IV over 1–2 min. Aim to lower the blood pressure by 15% over the first 24 h
Hypotension after stroke is rare. Any causes should be sought and corrected. Treatment includes volume replacement, correction of arrhythmias, and the use of vasopressors
Blood glucose
Hyperglycemia is associated with a worse outcome after stroke
Blood glucose should be kept at <10 mmol/l
Body temperature
A raised temperature may lead to a worse outcome in ischemic stroke
Temperature should be kept within normal limits
Oxygen saturations
Maintaining adequate tissue oxygenation is important to prevent hypoxia and worsening of brain injury. Maintain O_2-saturations in the normal range, aiming for >92%
Prophylaxis of venous thromboembolism
Early mobilization and use of compression stockings
Low-dose heparin is safe in patients with ischemic stroke and should be used
Adequate hydration and nutrition, swallowing assessment
Stroke patients are at increased risk of aspiration and require a swallowing assessment before they can be allowed to eat and drink
Adequate hydration will improve cerebral perfusion and help prevent venous thrombosis
Stroke patients are at high risk of malnutrition and may require enteral feeding

markedly increased compared to before the revascularization procedure. Generally, cerebral perfusion increases by at least 100%, although more recently CHS has also been reported in patients showing perfusion increases of only 40–60%.

Clinical Presentation

- Hypertension
- Headache, usually ipsilateral, often throbbing, frontal, or periorbital
- Seizures: focal with secondary generalization
- Focal neurological deficits
- Cerebral hemorrhage

Investigations

One of the main diagnostic questions in a patient who develops a new neurological deficit after a revascularization procedure is whether the patient has had an ischemic event due to vessel occlusion or embolization from the procedure site or has CHS. The main investigations are therefore:

- Brain imaging: CT or preferably MRI. MRI should be done with diffusion and perfusion-weighted imaging (DWI and PWI). The aim is to look for new infarction or for a cerebral hemorrhage. CHS may show diffuse cerebral edema in one hemisphere and, if severe, may show an intracerebral hemorrhage.
- Vascular imaging: to rule out restenosis or occlusion of the operated vessel. In CHS the carotid arteries are patent.
- Perfusion imaging: with SPECT, MRI, or CT. This should show markedly increased perfusion (≥100%) in the affected hemisphere compared to baseline or, perhaps to a lesser extent, in comparison to the contralateral hemisphere. Transcranial Doppler (TCD) shows a flow velocity increase of 150–300% in the ipsilateral middle cerebral artery and may be the most convenient way of monitoring the patient's progress.

Treatment

This should occur in a Neuro Intensive Care Unit or High Dependency Unit. The mainstay of treatment is aggressive blood pressure management with the goal of reducing cerebral hyperperfusion. Management is outlined in Table 43.2.

Prognosis

The few studies that are available suggest that mortality in CHS may be as high as 50% and that 30% of the surviving patients remain disabled.

Table 43.2 Management of cerebral hyperperfusion syndrome

Blood pressure control
There are no trial data to give the optimum blood pressure range for patients with CHS. General recommendations are that systolic blood pressure should not exceed 90–140 mmHg. Blood pressure control may be very difficult to achieve
Recommended drugs for blood pressure lowering are labetalol and clonidine. Vasodilating antihypertensive agents and ACE inhibitors should be avoided, because they can lead to further increases in cerebral blood flow and worsening of CHS
Seizures
If a patient develops seizures, these should be treated with anticonvulsants, which can be given intravenously, and with a loading dose, for example, levetiracetam or phenytoin
There is no evidence that prophylactic anticonvulsants are helpful
Cerebral edema
There are no specific data on how this should be managed in CHS. Reduction in perfusion pressure remains the main aim of treatment
Monitoring of treatment
Monitoring of treatment effect is clinical
Monitoring of flow velocities in the middle cerebral artery with transcranial Doppler may be helpful
Duration of treatment
Tight blood pressure control is recommended until cerebral autoregulation is restored, which can be monitored with transcranial Doppler. As all patients will have atheromatous disease, close blood pressure control should continue indefinitely as a secondary prevention measure for further vascular events

Cardiovascular Complications

Hypotension and Bradycardia

Carotid plaque is usually located close to the carotid baroreceptors. Manipulation during surgery or distension of the artery during angioplasty and stenting may therefore produce a hypotensive response. The reported incidence varies widely between 12% and 60%. This tends to be more frequent and more prolonged after CAS and can rarely also occur with a delay of several hours after the procedure. It may be associated with an increased risk of stroke and is of concern in ischemic heart disease, which is highly prevalent in patients with carotid atheromatous disease. More rarely, in 10–15% of cases, patients may also develop a hypertensive response.

Prevention

- Some centers withhold the patient's usual antihypertensives before the procedure and for 12 h afterward. However, because hypertension may be associated with a higher risk of CHS and perioperative stroke, this is not a generally accepted practice.

Table 43.3 Cardiovascular complications after carotid revascularization

Cardiovascular complication	Management
Hypotension	Intravenous fluids
	Consider starting vasopressors if BP is persistently <90 mmHg systolic
Bradycardia	Atropine or glycopyrrolate
	Temporary pacing is only rarely required
Hypertension	No specific antihypertensives are recommended. Given the danger of bradycardia, beta-blockers should probably be avoided. Continuous infusion of calcium antagonists, for example, nicardipine, has been used

- Before CAS some centers premedicate with atropine or glycopyrrolate.
- Before CEA some surgeons inject the area around the carotid baroreceptors with local anesthetic, although definite evidence that this reduces the risk of procedural hypotensive episodes is lacking.

Myocardial Infarction

Myocardial infarction during, or in the early days, after surgery occurs in 1–2% of patients, more often if there is a history of symptomatic coronary heart disease, and particularly if myocardial infarction has occurred in the previous few months or if the patient has unstable angina. Perioperative myocardial infarction can be painless, so clues to the diagnosis are unexplained hypotension, tachycardia, and dysrhythmias. Congestive cardiac failure, angina, and cardiac dysrhythmias are also occasional concerns following surgery. The management of cardiovascular complications associated with carotid revascularisation procedures is summarized in Table 43.3.

Cranial Nerve Injuries

Cranial nerve injuries may occur in up to 20% of patients following CEA and are caused by traction, pressure, or transection of a cranial nerve. These injuries tend to recover spontaneously and rarely have any long-term consequences but may cause short-term complications, particularly if a bilateral endarterectomy is done and bilateral damage occurs. Because of the danger of serious bulbar dysfunction with bilateral cranial nerve damage, if a patient has symptoms referable to both severely stenosed carotid arteries which require bilateral CEA, it is probably safer to do the operations a few weeks apart. Furthermore, a permanent nerve injury may be as disabling as a mild

stroke, which needs to be taken into account when considering the risks and benefits of surgery. Table 43.4 shows which cranial nerves may be damaged during endarterectomy and which deficits this may cause.

Table 43.4 Cranial nerve damage after carotid endarterectomy

Affected cranial nerve	Deficit caused by nerve damage
Recurrent and superior laryngeal nerve, vagus nerve	Change of voice quality, hoarseness, difficulty coughing, and sometimes dyspnea due to vocal cord paralysis
	Bilateral damage during a bilateral endarterectomy may cause airway obstruction and require temporary airway support
Hypoglossal nerve	Ipsilateral tongue weakness, leading to dysarthria, dysphagia, and difficulty chewing. Bilateral damage may lead to airway obstruction
Spinal accessory nerve	Shoulder and neck pain and stiffness
	Weakness of sternomastoid and trapezius muscles
Facial nerve (marginal mandibular branch)	Mild weakness of the corner of the mouth
Greater auricular nerve	Numbness of ear lobe and angle of jaw
Transverse cervical nerves	Numbness of scar area

Key Points

- Carotid Endarterectomy and Carotid Artery Stenting are the two most commonly used carotid revascularization procedures. While endarterectomy is still the established standard procedure, stenting is increasingly used, particularly in patients with high surgical risk or a poorly accessible stenosis.
- While the benefit of revascularization in recently symptomatic stenosis ≥70% is well established, the benefit of intervention in asymptomatic stenosis is less clear.
- The main risks specific to carotid revascularization procedures are periprocedural stroke and Cerebral Hyperperfusion Syndrome. Cardiovascular complications, especially hypotension and bradycardia, and, in endarterectomy, cranial nerve injuries may also occur.
- In periprocedural ischemic stroke, it is important to determine the time of onset as accurately as possible. Urgent discussion with the responsible stroke team and neuroradiologist is mandatory, as endovascular intervention to treat a new vessel occlusion may be possible.
- Cerebral Hyperperfusion Syndrome is thought to be due to sudden restoration of blood flow in a hypoperfused area of the brain. It presents with headache, seizures, focal deficits, and hypertension. Mainstay of treatment is aggressive blood pressure control.
- Manipulation and stretching of the carotid baroreceptors may cause hypotension and bradycardia during the procedure.
- Cranial nerve injuries mainly occur after endarterectomy. They rarely have long-term consequences but may be problematic in the short term, especially if bilateral.

Suggested Reading

Arnold M, Fischer U, Schroth G, Nedeltchev K, Isenegger J, Remonda L, et al. Intra-arterial thrombolysis of acute Iatrogenic intracranial arterial occlusion attributable to neuroendovascular procedures or coronary angiography. Stroke. 2008;39:1491–5. (i.a. thrombolysis after angiography associated stroke may be helpful).

Augoustides J, Gutsche JT. Anesthesia for carotid endarterectomy and carotid stenting. www.uptodate.com. Last accessed 1 Feb 2016. (Review of anesthetic management of carotid revascularization procedures).

Bonati LH, Dobson J, Featherstone RL, for International Carotid Stenting Study investigators, et al. Long-term outcomes after stenting versus endarterectomy for treatment of symptomatic carotid stenosis: the International Carotid Stenting Study (ICSS) randomised trial. Lancet. 2015;385:529–38. (Long term outcomes of RCT of carotid endarterectomy versus carotid stenting).

Jauch EC, Saver JL, Adams HP Jr, Bruno A, Connors JJ, Demaerschalk BM, Khatri P, McMullan PW Jr, Qureshi AI, Rosenfield K, Scott PA, Summers DR, Wang DZ, Wintermark M, Yonas H, American Heart Association Stroke Council, Council on Cardiovascular Nursing, Council on Peripheral Vascular Disease, Council on Clinical Cardiology. Guidelines for the early management of patients with ischemic stroke. A scientific statement from the Stroke Council of the American Stroke Association. Stroke. 2013;44:870–947. (A good overview over current recommended management of ischemic stroke).

Mantese VA, Timaran CH, Chiu D, Begg RJ, Brott TG, CREST Investigators. The Carotid Revascularization Endarterectomy versus Stenting Trial (CREST): stenting versus carotid endarterectomy for carotid disease. Stroke. 2010;41(10 Suppl):S31–4.

Rothwell PM, Eliasziw M, Gutnikov SA, et al. Analysis of pooled data from the randomised controlled trials of endarterectomy for symptomatic carotid stenosis. Lancet. 2003;361:107–16. (Individual patient data meta-analysis of the carotid endarterectomy trials for symptomatic stenosis).

Spence JD. Management of asymptomatic carotid stenosis. Neurol Clin. 2015;33:443–57.

Stoneham MD, Thompson JP. Arterial pressure management and carotid endarterectomy. Br J Anesth. 2009;102:442–52.

van Mook WNKA, Rennenberg RJMW, Schurink GW, van Oostenbrugge RJ, Mess WH, Hofman PAM, et al. Cerebral hyperperfusion syndrome. Lancet Neurol. 2005;4:877–88. Good review of cerebral hyperperfusion syndrome.

Wu TY, Anderson NE, Barber PA. Neurological complications of carotid revascularisation. J Neurol Neurosurg Psychiatry. 2012;83:543–50. (Summary review of potential complications from carotid revascularization procedures).

www.nihstrokescale.org. Website explaining and detailing the NIH Stroke Scale, which is widely used for standardized assessment of stroke severity.

Zhang L, Zhao Z, Ouyang Y, et al. Systematic review and meta-analysis of carotid artery stenting versus endarterectomy for carotid stenosis. Medicine (Baltimore). 2015;94:e1060. (Review of the currently available trials comparing carotid endarterectomy and stenting).

Part VII

Specific Perioperative Concerns in Adult Neuroanesthesia

Venous Air Embolism During Neurosurgery

44

Chris C. Lee, Anshi Wu, and Min Li

Overview

The reported incidence of VAE in neurosurgery varies according to the sensitivity of detection methods, the type of the procedures, and the positioning of the patients. The surgeries in the sitting position have the highest rate of occurrence of VAE, with an incidence of 10–80%. The common sources of critical VAE are the major cerebral venous sinuses which may be noncollapsible, including the transverse and the sigmoid. The air from the operative field may enter the venous vasculature whenever the open vein is above the level of the right side of the heart. This is the reason why VAE is most often associated with sitting position. VAE may also occur in neurosurgical procedures performed in the lateral, prone, or supine positions with reported incidence from 10% to 25%. Table 44.1 lists the neurosurgical procedures with VAE risk.

Besides the type of surgery, there are other contributing factors, both procedure-related and patient-related, which may have an impact on the occurrence of air entrainment during neurosurgery (Table 44.2).

Table 44.1 Neurosurgical procedures associated with venous air embolism (VAE)

Procedure	Known incidence (%)	Relative risk
Sitting position craniotomies	9.3, 27.4, 43	High
Posterior fossa procedures	76	High
Craniosynostosis repair	8–82.6	High
Cervical laminectomy	23–25	Medium
Posterior spinal fusion	10	Medium
Deep brain stimulator placement	6	Low
Peripheral denervation	2	Low
Torticollis corrective surgery		Low

Table 44.2 Factors contributing to the occurrence of venous air embolism (VAE)

Factors
Procedure-related
Surgical site relative to the level of right heart
Extensive operation field exposure
Investigational procedures which requires injection of gas
Decompression of the abdomen
Hydrogen peroxide for wound irrigation
Patient-related
Preexisting hypovolemia
Spontaneous ventilation (with the attendant intermittent negative intrathoracic pressure)

Prevention

Since VAE can be lethal, its prevention and having a high index of suspicion are crucial in clinical practice. Various measures have been taken to reduce the incidence of VAE in neurosurgery (Table 44.3).

Positioning

Avoid sitting position if possible. In fact, with the awareness of the VAE risk associated with sitting position and the

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Table 44.3 Prevention of venous air embolism (VAE)

Avoid sitting position if possible
Elevate the legs/wrap the legs
Maintain adequate intravascular volume
Controlled positive pressure ventilation
Avoid nitrous oxide in high-risk patients if possible
Avoid drugs that dilate the venous capacitance vessels, such as nitroglycerin (NTG)

improvement of surgical technique, the popularity of the sitting position has greatly declined. If sitting position is strongly recommended, try to place the patient in a more semi-recumbent position than sitting up. The legs elevated to the level of the heart can also help to reduce the pressure gradient between the right atrium and the surgical site.

Hydration

Ensure adequate intravascular volume to maintain the right atrial pressure. This method can not only reduce the negative pressure gradient between the surgical site and the right heart but also reduces the right-left atrial pressure gradient, which is then beneficial in reducing the incidence of VAE and paradoxical air embolism. It has been proposed that the right atrial pressure be maintained between 10 and 15 cm H_2O. However, hydration should be applied cautiously in patients with elevated intracranial pressure or those with either preexisting or borderline cardiopulmonary disease.

Controlled Ventilation

Since spontaneous ventilation is related to the increased negative intrathoracic pressure and greater pressure gradient between the surgical site and right atrium, general anesthesia with controlled positive pressure ventilation is recommended in high-risk surgery. The advocating mechanical ventilation with positive end-expiratory pressure (PEEP) during anesthesia is controversial. Some studies state that PEEP induces a reliable and sustained increase in right atrial pressure, which is sufficient to increase venous pressure above atmospheric level. Others suggest that PEEP may facilitate the occurrence of paradoxical air emboli (PAE) in a patient with a patent foramen ovale (PFO) and also potentially result in hemodynamic deterioration by impeding venous return and reducing right ventricular preload. Therefore, although controversial, some clinicians suggest that PEEP should not be routinely used in craniotomies unless there is a strong indication.

Avoiding the Use of Nitrous Oxide (N_2O)

Since nitrous oxide expands the size of embolized air bubbles tremendously, it is reasonable to avoid its use in high-risk surgeries and patients at high risk, especially in those with known intracardiac septal defects, preexisting pneumocephalus, during acute venous air embolism, disorders of folate metabolism, and abnormal SSEP (somatosensory evoked potential) monitoring intraoperatively. Paradoxical air emboli (PAE) phenomenon adds an additional reason for avoiding N_2O use after the occurrence of VAE.

Crisis Management

Pathophysiologic Manifestation of VAE

If the embolism is large (>5 ml/kg), the obstruction to the right ventricular outflow tract may immediately occur and subsequently result in acute right heart failure and cardiovascular collapse. The lethal dose of intravascular air in adult has been estimated as 200–300 ml or 3–5 ml/kg. Small amount of air can be dissipated and absorbed by the lungs. The embolization of pulmonary circulation may cause pulmonary vasoconstriction, pulmonary hypertension, V/Q mismatch, and the release of inflammatory mediators (e.g., endothelin 1 and platelet activator inhibitor). This, in turn, may result in pulmonary capillary injury, bronchoconstriction, and pulmonary edema. The V/Q mismatch is characterized by decreased $P_{ET}CO_2$, decreased PaO_2, and increased $PaCO_2$.

The release of vasoactive mediators, such as thromboxane, leukotrienes, and 5-Hydroxytryptamine (5-HT, serotonin), into systemic circulation will cause intense vasoconstriction and thromboembolism of other organs. In a patient with a PFO, right to left shunting may develop due to major VAE, leading to an actively increased risk of paradoxical air embolus (PAE) with catastrophic cardiac and cerebral events.

Clinical Presentation

The clinical manifestation and the severity of the pathophysiologic effects of a VAE are directly proportional to the rate of air entrainment and volume of accumulation of air in the right atrium. A small amount of air entrained may be of little consequence. However, if the air is entrained rapidly or if the cumulative volume is large, hypoxemia and acute right heart failure may be present (Table 44.4).

Respiratory System

The awake patients may experience coughing as the first symptom, followed by chest pain, dyspnea, tachypnea, and a sense of "impending doom." A "gasp" leads to further decrease of intrathoracic pressure, resulting in more air entrainment. For anesthetized patients under mechanical ventilation, the major changes in respiratory system are the decreased $P_{ET}CO_2$, decreased PaO_2, and increased

Table 44.4 Clinical presentations of venous air embolism (VAE)

Clinical presentations
Respiratory (early signs)
Awake patient
Coughing
Chest pain
Dyspnea
Tachypnea
Anesthetized patient
Decreased $P_{ET}CO_2$
Hypercarbia
Hypoxemia
Wheezing
Cardiovascular (late signs)
EKG: Tachycardia or bradycardia, arrhythmias, ST-T changes, and myocardial ischemia
Hypotension
Elevated PAP, CVP or RAP-LAP gradient
Jugular venous distension (JVD)
"Mill-wheel" murmur
Acute right heart failure
Cardiac arrest
Neurological
Altered mental status (in awake patients)
Neurological deficit

$PaCO_2$. If patients develop bronchoconstriction, wheezing may be present.

Cardiovascular System

There may be several EKG changes, including sinus tachycardia or bradycardia, arrhythmias, right heart strain pattern, ST-T changes, and myocardial ischemia. Other hemodynamic responses include hypotension, elevated CVP, PA pressure or RAP-LAP gradient, and jugular vein distension. In the most devastating cases, cardiac arrest may occur. The "mill-wheel" murmur may be detected by auscultation, indicating a significant amount of air has entered the right heart.

Central Nervous System

Low cerebral perfusion may result from hypotension and hypoxemia. Altered mental status, convulsion, and even coma may develop in awake patients. Brain damage is exacerbated by cerebral (arterial) air embolism with possible long-term neurologic deficits.

Patient Assessment

In neurosurgical procedures with high VAE risk, routine monitoring such as EKG, SpO_2, $P_{ET}CO_2$, direct measurement of arterial pressure, and arterial blood gases is essential. In addition, specific monitoring such as transesophageal echocardiography and precordial Doppler has enabled earlier diagnosis of VAE. The current available monitoring devices for VAE are listed in Table 44.5.

Table 44.5 Monitors for detection of venous air embolism (VAE)

Monitor	Advantages	Disadvantages
TEE	High level of sensitivity (0.02 ml/kg)	Moderate invasive
	High level of specificity	Expensive
		Need experienced operator to monitor continuously
Precordial Doppler	High level of sensitivity (0.05 ml/kg)	Correct placement of the probe can be hard in obese patients and those in prone or lateral positions
	Noninvasive	
		The auditory signal gives no indication of the size of the bubble
		Subjective, false-negative rate reported to be 3%
Capnography	Noninvasive	Less sensitive (sensitivity as 0.5 ml/kg)
	Most convenient	
	Routinely used for any surgery	Not specific for air embolism
Pulmonary artery catheter	Provide intensive hemodynamic monitor for patients with significant cardiopulmonary comorbidities	Less sensitive (sensitivity as 0.5 ml/kg)
		Invasive

Transesophageal Echocardiography (TEE)

TEE is currently the most sensitive monitoring device for VAE. It can detect as little as 0.02 ml/kg of air given by bolus injection. However, TEE has to be inserted orally, which may cause injury. Also, it is expensive and requires expertise for continuous monitoring, limiting its use in neuroanesthesia.

Precordial Doppler

Precordial Doppler is the most sensitive noninvasive monitor for VAE and is able to detect as little as 0.05 ml/kg of air. The performance of the Doppler is related to the correct placement of the transducer. Placing the probe over the right side of the sternum may provide better detection than along the left sternal border. In high-risk neurosurgical procedures, precordial Doppler is strongly recommended. It is the most cost-effective and relatively easy to use. However, precordial Doppler is nonquantitative and can be difficult to place in obese patients and those in prone or lateral positions.

Capnography

End-expiratory CO_2 ($P_{ET}CO_2$) is an effective and convenient method of detecting VAE. Its use is required as a standard intraoperative monitor by ASA, and it can be used in any position. However, it is less sensitive than precordial Doppler and a decreased $P_{ET}CO_2$ may have alternative etiologies. Nevertheless, a sudden decrease in $P_{ET}CO_2$ with hypotension in high-risk patients should always alert the anesthesiologist to the diagnosis of VAE.

Pulmonary Artery Catheter (PAC)

VAE results in an increase in pulmonary arterial pressure. The degree of the increase is proportional to the amount of air entrainment. PA pressure monitoring has a sensitivity similar to $P_{ET}CO_2$. It can measure the pressure gradient between the left and right atria, which may be useful in assessing the risk of paradoxical air embolism. Nevertheless, it is an invasive procedure and should not be used as a routine monitor.

Transcranial Doppler

Transcranial Doppler has demonstrated its ability in detecting air bubbles in the cerebral artery with a sensitivity of 91.3% and specificity of 93.8%. Transcranial Doppler is suitable for monitoring intracranial VAE in a patient with a PFO.

Treatment

Early detection of VAE during neurosurgery, early diagnosis, and rapid intervention are the key elements in decreasing the severity of its complications and improving the patient's outcome. If possible, the entrapped air should be aspirated as much as possible. Fortunately, most cases of VAE are clinically mild. Table 44.6 lists the elements of treatment.

Prevent Further Air Entrainment

If a VAE is suspected, then the surgeon should be immediately informed to inspect the possibility of air entrainment into the open veins. The field should be flooded with saline or covered by saline-soaked dressings. Closing the open vessels as soon as possible should stop the source of the gas embolism.

Reposition the Patient

Immediate change to Trendelenburg position will increase venous pressure at the operative site and reduce air entrainment. Rotating the patient to the left side with head-down position helps to localize air into the right heart, which prohibits the air entering the orifice of pulmonary artery and facilitates the aspiration through a central catheter. However, it may be difficult to change the position of the patient in some situations.

Table 44.6 Treatment of venous air embolism (VAE)

Prevent further air entrainment
Inform surgeon (flood the wound and close open vein)
Lower the head (Trendelenburg position), and compress jugular veins
Discontinue nitrous oxide (N_2O) if used
Start controlled ventilation if the patient is spontaneously breathing
Treat VAE
Aspirate air from a CVP or PA catheter
Switch to 100% O_2
Hemodynamic support: pressors, inotropes, and IV fluids
Resuscitation (CPR and ACLS) and abandon surgery

Institute 100% Oxygen

Nitrous oxide (N_2O) should be turned off immediately if used. Controlled positive ventilation enhances the intrathoracic pressure which is beneficial for both oxygenation and prevention of further air entrainment.

If a central venous catheter is in place, aspirating air from the right atrium should be attempted promptly. This maneuver is diagnostic and therapeutic. It has been reported that air could be best aspirated with multiorificed catheter placed with the tip at or 2 cm below the sinoatrial node. Blood should be withdrawn until no air bubbles are seen. Emergent catheterization takes time and is not routinely recommended to date.

Hemodynamic Support

IVF, ephedrine, dobutamine, norepinephrine, and/or epinephrine have been recommended.

If cardiac arrest occurs, advanced cardiac life support (ACLS) protocol should be followed and cardiopulmonary resuscitation (CPR) initiated immediately. A thoracotomy may be necessary to aspirate the air from the right ventricle.

If possible, the patient should be taken to a hyperbaric chamber, and the treatment should be started as soon as possible to prevent severe and possible long-lasting brain damage. For VAE patients, especially for those with cerebral embolism, the hyperbaric oxygenation therapy has many advantages. The best outcome results from early recognition and prompt treatment.

Key Points

- Venous air embolism (VAE) is most commonly seen in neurosurgeries in sitting position.
- Prevention from its occurrence and having a high index of suspicion are crucial in clinical practice.
- Constant vigilance and inclusion of VAE in the differential diagnosis of intraoperative cardiovascular collapse, especially in the high-risk procedures and patients at high risk, are the best preparation for this lethal complication.
- Early diagnosis of VAE and prompt intervention are critical to avoid further associated complications and the key elements in improving the patient's outcome.
- Capnography ($P_{ET}CO_2$) and precordial Doppler are the most convenient and practical detection methods for VAE. Their combination is the current standard of care.

- Once the diagnosis is made, prevention of further air entrainment and expansion of the air embolus with nitrous oxide (N_2O), 100% O_2, lowering the height of the surgical site, aspiration of air from right heart, and maintenance of cardiac output are essential.

Suggested Reading

Archer DP, Pash MP, MacRae ME. Successful management of venous air embolism with inotropic support. Can J Anaesth. 2001;48:204–8.

Gale T, Leslie K. Anaesthesia for neurosurgery in the sitting position. J Clin Neurosci. 2004;11:693–6.

Gracia I, Fabregas N. Craniotomy in sitting position: anesthesiology management. Curr Opin Anaesthesiol. 2014;27(5):474–83. https://doi.org/10.1097/ACO.0000000000000104.

Hervías A, Valero R, Hurtado P, Gracia I, Perelló L, Tercero FJ, González JJ, Fàbregas N. Detection of venous air embolism and patent foramen ovale in neurosurgery patients in sitting position. Neurocirugia (Astur). 2014;25(3):108–15. https://doi.org/10.1016/j.neucir.2013.12.002. Epub 2014 Mar 12.

Leslie K, Hui R, Kaye AH. Venous air embolism and the sitting position: a case series. J Clin Neurosci. 2006;13:419–22.

Miller RD. Venous air embolism. In: Miller RD, editor. Miller's anesthesia. 8th ed. New York: Elsevier Churchill Livingstone; 2015. p. 2169–72.

Mirski MA, Lele AV, Fitzsimmons L, Toung TJ. Diagnosis and treatment of vascular air embolism. Anesthesiology. 2007;106:164–77.

Palmon SC, Moore LE, Lundberg J, Toung T. Venous air embolism: a review. J Clin Anesth. 1997;9:251–7.

Rozet I, Vavilala MS. Risks and benefits of patient positioning during neurosurgical care. Anesthesiol Clin. 2007;25:631–53.

Arterial Hypotension and Hypertension

45

Kirstin M. Erickson and Daniel J. Cole

Carotid Endarterectomy (CEA)

Overview

Atherosclerosis is a systemic disease, and, accordingly, patients with carotid plaque also often have coronary artery disease. Moreover, long-standing essential hypertension is frequently a comorbidity along with its effects on cardiac function (e.g., diastolic dysfunction or left ventricular hypertrophy). Both hypertension and hypotension are common.

In patients with poorly controlled hypertension, the blood pressure range for normal cerebral autoregulation is shifted to the right (Fig. 45.1). Moreover, in patients with advanced carotid artery disease, cerebral autoregulation is often impaired, making regional cerebral blood flow (CBF) exquisitely sensitive to perfusion pressure. Carotid sinus baroreceptor manipulation can cause bradycardia and hypotension.

Severe hypertension (>180/110 mmHg) increases overall morbidity and mortality. The most common complication of hypertension is myocardial ischemia. Hypotension can worsen ischemic neurologic deficits. Postoperative hypertension can lead to hyperperfusion syndrome. Active blood pressure management is essential.

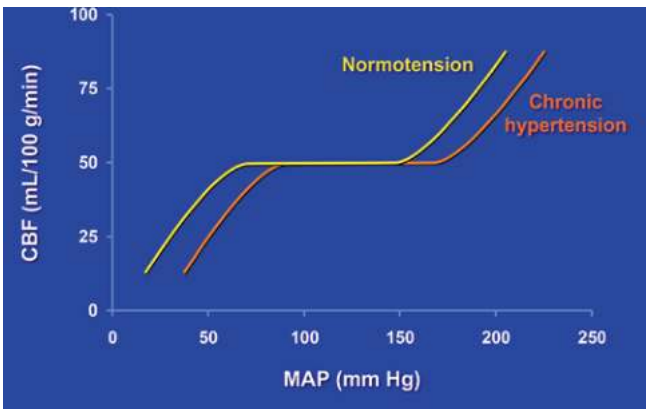

Fig. 45.1 The relationship between cerebral perfusion pressure (CPP) and mean arterial pressure (MAP) shows autoregulation of CPP across a range of MAP. The curve is shifted to the right in patients with chronic hypertension

Hypertension and Hypotension in CEA: Prevention

Chronic hypertension should be well controlled before CEA. Ordinary intraoperative alterations in the level of stimulation should be anticipated and treated early with small doses of therapeutic medication. An arterial line is recommended for beat-to-beat assessment and precise control of blood pressure.

Blood pressure is maintained at preoperative, awake values until the carotid artery is cross-clamped. If there are no contraindications, blood pressure is then increased by as much as 20% during cross-clamping to improve perfusion *via* collateral vessels. Small doses of phenylephrine or ephedrine are appropriate. Careful phenylephrine infusion is often used although it is associated with a higher risk of myocardial ischemia compared to lightened anesthesia. Coughing and other causes of blood pressure spikes during emergence should be averted to minimize stress on the freshly repaired artery and the potential complication of neck hematoma.

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Hypertension and Hypotension in CEA: Crisis Management

Table 45.1 summarizes intraoperative events requiring blood pressure management, signs or indications for treatment, and suggested therapy for hypertension and hypotension during CEA.

Table 45.1 Intraoperative events requiring blood pressure management, signs or indications for treatment, and suggested therapy for hypertension and hypotension during CEA

Event/pathology	Signs/indications for treatment	Suggested therapy
Direct laryngoscopy, intubation, incision	Hypertension, tachycardia	Deepen anesthetic
		Lidocaine
		Fentanyl/remifentanil
		Esmolol/metoprolol
		Nicardipine/clevidipine
		Nitroglycerin
Post-induction	Hypotension	Lighten anesthetic
		Phenylephrine
		Ephedrine
Chronic untreated hypertension	Severe or refractory intraoperative hypertension	Nitroprusside
		Nitroglycerin
		Esmolol
Intravascular volume depletion, hemorrhage	Hypotension, tachycardia, systolic pressure variation	Intravenous fluid
		Blood
		Phenylephrine
		Ephedrine
Carotid cross-clamping	Blood pressure low or low-normal	Increase baseline blood pressure by 10–20% (phenylephrine, decreased anesthetic dose)
Carotid sinus baroreceptor manipulation	Hypotension, bradycardia	Vagolytic (atropine, glycopyrrolate)
Decrement in neurologic monitoring (e.g., EEG slowing)	Hypotension	Raise blood pressure with phenylephrine, ephedrine, lighten anesthetic
Emergence, coughing	Hypertension	Beta-blocker (labetalol, esmolol)
		Lidocaine
		Remifentanil

Hypertension and Hypotension in CEA: Key Points

- The autoregulation curve is shifted to the right in patients with chronic hypertension.
- Prevention of blood pressure lability is achieved by anticipating stimuli and using small doses of therapeutic drugs.
- Normotension is the goal during CEA before and after cross-clamping of the carotid artery. During cross-clamping, blood pressure should be mildly elevated from baseline (approximately 20% is appropriate).

Aneurysm/AVM Repair

Overview

Tight control of blood pressure during aneurysm repair or arteriovenous malformation (AVM) resection is essential. Hypertension increases transmural pressure and risks vessel rupture and subarachnoid hemorrhage, brain edema, and postoperative cerebral hyperperfusion. Conversely, hypotension lowers cerebral perfusion pressure (CPP) and risks ischemia, especially in areas of vasospasm. Moreover, acute hypertension may be a sign of aneurysm rupture and intracranial hypertension.

Hypertension and Hypotension in Aneurysm/AVM Repair: Prevention

Anticipation of stimulating events prevents abrupt blood pressure changes. A preinduction arterial line is routinely used. Small doses of pressors guard against marked reductions in blood pressure following induction of anesthesia. Dramatic blood pressure increases may occur with laryngoscopy, pinion placement, incision, dural opening, and surgical manipulation. Lidocaine, esmolol, or short-acting opioids will diminish hemodynamic stimulation from these events. Nimodipine and nicardipine, calcium channel blockers, may improve neurologic outcome by preventing the development of vasospasm after aneurysmal hemorrhage.

Hypertension and Hypotension in Aneurysm/AVM Repair: Crisis Management

If an aneurysm ruptures intraoperatively, immediate temporary proximal occlusion of the culprit vessel by the surgeon is necessary. Maintaining cerebral perfusion should continue to be the goal while the surgeon gains control.

If vasospasm develops, more aggressive therapy combining hemodynamic augmentation ("triple-H therapy"), angioplasty, and intra-arterial infusion of vasodilator drugs is used. Excessive hypertension risks rebleeding.

Table 45.2 summarizes intraoperative events requiring blood pressure management, goal of intervention, and suggested therapies.

Hypertension and Hypotension in Aneurysm/AVM Repair: Key Points

- Strict maintenance of normotension minimizes abrupt changes in transmural pressure and optimizes collateral circulation.

- Anticipation of stimulating events is key to optimal blood pressure management.
- If rupture occurs, blood pressure should be kept in the high normal range to maintain CPP and minimize ischemia.
- Inducing mild hypertension following subarachnoid hemorrhage improves neurologic outcome, but marked hypertension increases the risk of rebleeding.

Table 45.2 Intraoperative events requiring blood pressure management, goal of intervention, and suggested therapies

Event	Goal of blood pressure management	Suggested therapy
Dissection, manipulation of the aneurysm or AVM, placement of temporary clips on the parent vessel, aneurysmal clip ligation, and closure	Normotension	Deepen anesthetic
		Lidocaine
		Fentanyl
		Labetalol, esmolol
		Nicardipine
		Phenylephrine
		Ephedrine
Following temporary clipping of parent artery	Normotension, or may need to increase blood pressure approximately 20% to maintain CPP	Phenylephrine
		Ephedrine
Rupture	Normotension; may need to increase blood pressure to maintain adequate CPP if intracranial pressure rises, balance with need to control hemorrhage	Maintain intravascular volume
		Phenylephrine
		Ephedrine
Vasospasm	Induced hypertension as part of "triple-H" therapy (hypervolemia, hypertension, hemodilution)	Volume expansion
		Phenylephrine
		Dopamine

Acute Traumatic Brain Injury (TBI)

Overview

Traumatic brain injury (TBI) per se is associated with hypertension either due to increased circulating catecholamines or as a response to intracranial hypertension. Cerebral autoregulation is impaired which increases the risk of hypertension causing hyperemia, vasogenic edema, and intracranial hypertension. In the setting of intracranial hemorrhage (ICH), minimizing hypertension has been shown to reduce hematoma growth. Hypotension can develop when TBI is severe or accompanied by systemic injuries and significant blood loss.

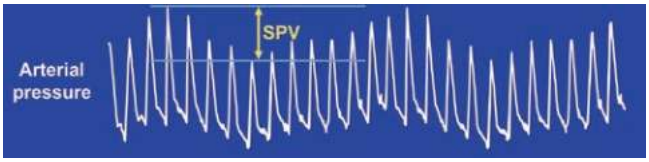

Fig. 45.2 Systolic pressure variation (SPV) is the measured difference between minimum and maximum systolic pressure within one respiratory cycle. Increased SPV reflects volume-sensitive hypotension

Hypertension and Hypotension in Acute TBI: Prevention

Intra-arterial pressure monitoring is customary, although lines may need to be placed during or after surgical incision to facilitate immediate surgical intervention and thereby limit secondary brain injury.

Hypotension is usually a sign of hypovolemia from other injuries. Hypovolemia is best assessed by clinical signs including arterial blood pressure and systolic pressure variation (Fig. 45.2). Urinary output may be confounded as a guide if mannitol has been given.

Hemorrhage should be treated with immediate and aggressive volume resuscitation. Glucose-containing solutions should be avoided because they are associated with worsened neurologic outcomes. To prevent hypotension in the patient receiving large amounts of mannitol, diuresed fluid should be replaced. Control of bleeding and volume resuscitation takes precedence over immediate surgical intervention, as systolic pressure of less than 80 mmHg leads to poor outcomes.

Hypertension and Hypotension in Acute TBI: Crisis Management

Targets for treating hypertension are based on intracranial pressure (ICP) and CPP. Although controversial, CPP should be 70 mmHg or greater. Overaggressive fluid administration may worsen intracranial edema and ICP.

The 2007 guidelines set a systolic blood pressure target of less than or equal to 180 mmHg. Recent data strongly suggest that a lower systolic pressure of 140 mmHg reduces hemorrhagic growth and risk of poor outcomes. No specific agents have been shown to be superior.

Table 45.3 summarizes differential diagnoses and suggested therapeutic approaches to hypertension and hypotension in TBI.

Table 45.3 Differential diagnoses and suggested therapeutic approaches to hypertension and hypotension in TBI

Sign	Differential diagnosis	Therapeutic approach
Hypertension, tachycardia	Catecholamine release	1. Lower ICP
	Increasing ICP	2. Ensure adequate anesthesia, oxygenation, ventilation
	Inadequate anesthesia	
	Coughing, bucking	3. Avoid hypocapnia unless herniation evident
		4. Beta-blocker (avoid vasodilators in a closed cranium)
Hypertension, bradycardia, irregular respiration	Impending herniation (Cushing phenomenon)	Manage blood pressure based strictly on direct ICP monitoring
Hypotension, tachycardia	Hypovolemia	1. Isoosmolar colloid or crystalloid solutions
	Hemorrhage from systemic injuries	2. Transfusion
	Acute mannitol diuresis,	3. Vasopressor or inotrope
	Central diabetes insipidus	1.1.4. Vasopressin for diabetes insipidus
	Chronic diuretic therapy	
	Severe traumatic brain injury (variable heart rate)	

Hypertension and Hypotension in Acute TBI: Key Points

- TBI alone is associated with increased catecholamines and arterial hypertension.
- Arterial hypertension may be a marker of intracranial hypertension and impending herniation.
- Limiting hypertension after ICH reduces hematoma formation.
- Hypotension should be treated as hypovolemia, until proven otherwise.

Suggested Reading

Carotid Endarterectomy

Biller J, Feinberg WM, Castaldo JE, et al. Guidelines for carotid endarterectomy: a statement for healthcare professionals from a special writing group of the Stroke Council, American Heart Association. Stroke. 1998;29(2):554–62.

Herrick IA, Higashida RT, Gelb AW. Occlusive cerebrovascular disease: anesthetic considerations. In: Cottrell JE, Young WL, editors. Cottrell and Young's neuroanesthesia. 5th ed. Philadelphia: Mosby Elsevier; 2010. p. 278–95.

Yastrebov K. Intraoperative management: carotid endarterectomies. Anesthesiol Clin N Am. 2004;22(2):265–87, vi–vii.

Aneurysm/Arteriovenous Malformation Repair

Drummond JC, Patel PM, Lemkuil BP. Neurosurgical anesthesia. In: Miller RD, editor. Miller's anesthesia. 8th ed. Philadelphia: Elsevier Saunders; 2015. p. 2158–99.

Butterworth J, Mackey DC. Anesthesia for neurosurgery. In: Morgan and Mikhail's clinical anesthesiology. 5th ed. New York: McGraw-Hill; 2013. p. 593–612.

Pong RP, Lam A. Anesthetic management of cerebral aneurysm surgery. In: Cottrell JE, Young WL, editors. Cottrell and Young's neuroanesthesia. 5th ed. Philadelphia: Mosby Elsevier; 2010. p. 218–46.

Traumatic Brain Injury

Anderson CS, Heeley E, Huang Y, INTERACT2 Investigators, et al. Rapid blood-pressure lowering in patients with acute intracerebral hemorrhage. N Engl J Med. 2013;368:2355–65.

Bendo AA. Management of severe head injury. In: Cottrell JE, Young WL, editors. Cottrell and Young's neuroanesthesia. 5th ed. Philadelphia: Mosby Elsevier; 2010. p. 317–26.

Dagal A, Lam AM. Head trauma–anesthetic considerations and management. In: Smith CE, editor. Trauma anesthesia. 2nd ed. New York: Cambridge University Press; 2015. p. 364–81.

Hyperthermia and Hypothermia During Neurosurgical Procedures

46

Eric Tesoriero, Evgeni Brotfain, and Akiva Leibowitz

Overview

Humans are euthermic beings, that is, critical physiologic functions must be maintained within a fixed temperature range. Any shifts from a body core temperature of 36.6 ± 0.2 °C result in either hyperthermia or hypothermia, causing pathophysiologic reactions. Normal thermoregulation is a highly complex process with positive and negative feedback systems depending on input from nearly every tissue of the body and several well-identified response mechanisms. While the hypothalamus and skin are identified as having the major role in thermal regulation, nearly every tissue of the body is involved in the process. When thermal stresses arise from the environment, changes in skin temperature occur prior to changes in core temperature. When thermal stresses arise from alterations in heat production by the body, changes in core temperature occur prior to changes in skin temperature. In either case, thermal gradients are established between the skin and the body core. In the neurosurgical patient, a combination of environmental factors and endogenous thermal dysregulation may result in hypothermia. When hyperthermia occurs, it must be quickly addressed, particularly in patients with neurological injury or disease.

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Processing of thermoregulatory information occurs in three phases:

- Afferent input: Temperature-sensitive neurons in the anterior hypothalamic-preoptic area and the spinal cord transmit and integrate afferent sensory inputs from the core and the skin, in response to excessive cold and heat. Information is transmitted in distinct neural fibers via multiple spinal tracts to the hypothalamus.
- Central control: Most of the processing takes place in the hypothalamus, where input from different sites is compared and integrated, and responses are regulated when deviation from threshold appears. Many factors influence the absolute threshold and normal core temperatures in humans. Distinguishing normal deviations from pathological states is of major importance. Table 46.1 lists some of the major contributors to threshold and core temperature variation. The interthreshold range is bounded by sweating on the upper end and shivering on the lower end; perturbations of 0.2 °C do not typically trigger an autonomic response.

Table 46.1 Factors influencing the threshold

Factor		Effect
Drugs and substances	Norepinephrine, dopamine, 5-hydroxytryptamine, acetylcholine, prostaglandin E1, neuropeptides, alcohol, sedatives, nicotine	Mediation of absolute threshold
Gender	Female > male	Female core temperature up to 1 °C > male
Menstrual cycle		Further rise in second half of menstrual cycle
Circadian rhythm	Daily variation in core temperature	Lowest temperatures in mornings
Systemic disease	Hypothyroidism, hyperthyroidism, infection	

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Table 46.2 Response mechanisms

Response	Mechanism	Other effects
Cutaneous vasoconstriction/ vasodilation	Metabolic heat is lost primarily through convection and radiation from the skin surface, and vasoconstriction reduces this loss. Thermoregulatory skin blood flow is comprised primarily of the cutaneous plexuses and capillary loop system which are abundant in most of the body surface and the arteriovenous shunt component which is found mainly in glabrous skin. Active vasodilation is not blocked by any known drugs	Variation in BP up to 15 mmHg
Sustained shivering	Augments heat production by 50–100%. Not fully developed in infants	Blocked by anesthetics and neuromuscular blocking agents
Nonshivering thermogenesis	Increases metabolic heat production without producing mechanical work	Activated by circulating norepinephrine. Blocked by β-blockers
Sweating	Dissipation of heat mediated by postganglionic cholinergic nerves	Blocked by anticholinergics (e.g., atropine)

- Efferent response: Thermal perturbations from normal limits activate effector responses that increase metabolic heat production or regulate heat convection and radiation to the environment. Each thermoregulatory effector has its own threshold and gain, so there is an orderly progression of responses and response intensities in proportion to need. Aside from autonomic responses, there are behavioral responses that are absent in anesthetized patients. Table 46.2 summarizes the major autonomic effector responses.

Thermoregulation During Anesthesia

Thermoregulation during anesthesia – general or regional – is often significantly impaired. Anesthetics may modulate thermoregulatory thresholds and influence effector responses. Other factors prevalent in the OR environment and in surgical procedures, such as cool environment, exposed body surface, cold IV fluid replacement, cold surgical irrigation fluids, and mechanical ventilation, further contribute to the difficulty in maintaining normothermia. Incidence of perioperative hypothermia is reported to be as high as 70% and is of major concern particularly in lengthy procedures. Hyperthermia is a less frequent intraoperative complication, but – when occurring – may have devastating effects in the context of central nervous system injury. Later in this section, mild hypothermia will be discussed as a controversial treatment modality in neurosurgery (see Table 46.3).

Prevention: Hypothermia

Body heat redistribution following anesthesia follows a specific pattern, extensively studied by Sessler et al. (1991). A gross summary of this pattern is represented in Fig. 46.1.

Table 46.3 Summary of thermoregulatory alterations during general anesthesia

Influences of anesthesia on thermoregulation	
Behavioral responses	Abolished
Thermoregulatory threshold	Significantly altered. Reduced from 37 to 34.5 °C, interthreshold range widened to ±4 °C, sweating threshold slightly elevated, and vasoconstriction threshold markedly lowered
Vasoconstriction	Impairment of vasoconstriction response, primarily in AV shunts, affects redistribution of body heat
Shivering thermogenesis	Impaired by all general anesthetics, even without muscle blockade
Nonshivering thermogenesis	Primarily affects infants who depend on this mechanism. In adults, an insignificant mechanism

The physician's role is crucial in intervening in each of these phases, minimizing the development and extent of hypothermia.

Phase 1

Redistribution hypothermia, once initiated, is extremely difficult to treat, since it is a result of heat flow from core to periphery (rather than cutaneous heat loss) and warming the core compartments is a lengthy procedure. Endogenous reflex mechanisms, reducing skin blood flow, and conserving heat production are effective in maintaining core body temperature within a certain temperature range. Redistribution may be further minimized (but is not necessarily required) by the following means:

- Increasing body heat content by prewarming the patient preoperatively.
- Pharmacologic vasodilation preoperatively, inducing redistribution prior to anesthesia.

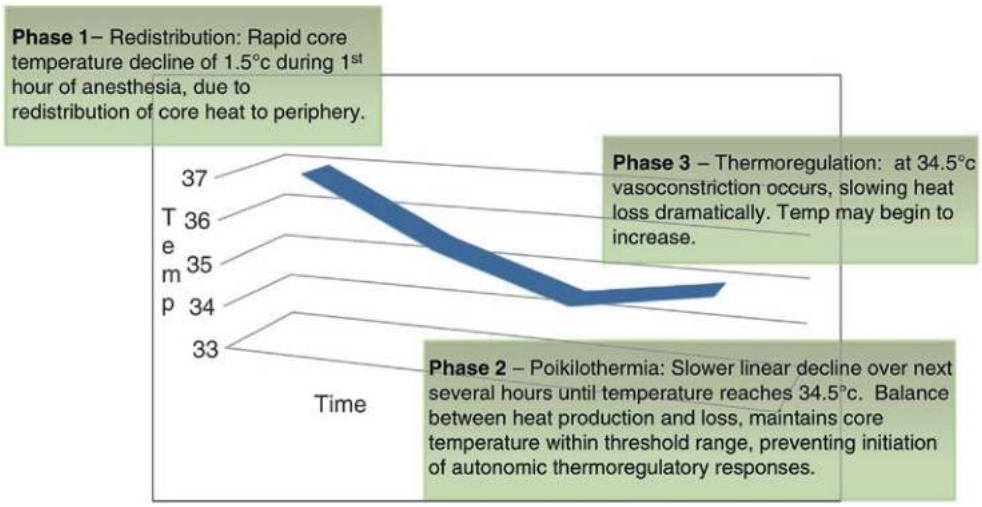

Fig. 46.1 Phases of intraoperative heat loss

- Phenylephrine-induced vasoconstriction during the first hour of anesthesia has been shown to decrease the extent of redistribution hypothermia.

Phase 2

Most of the heat lost during this stage is due to radiation or convection. Endogenous mechanisms are overwhelmed and are no longer able to offset the redistribution. Thus, effectively interrupting these pathways has been found to be effective in minimizing heat loss. Approximately 90% of body heat is lost via the skin surface. The remaining body heat is mostly lost via surgical incisions and cold IV fluid administration. Another source of heat loss is through respiration, although it is not of clinical significance. In neurosurgical cases involving large incisions or massive fluid shifts, heating IV fluids has a greater significance. Cutaneous insulation and warming remain the mainstay of preventing perioperative hypothermia and include the following:

- Raising ambient temperature: This minimizes heat lost to radiation. Often, controlling ambient temperature may be impractical, as the ambient temperature necessary may reach levels uncomfortable to the scrubbed-in surgical team (e.g., 23–26 °C for an infant patient and >30 °C for burn surgery).
- Cutaneous warming: Passive insulation is highly effective. A single layer of cotton blankets or surgical drapes reduces heat loss by as much as 30%, while the effectiveness of subsequent layers decreases. Heat preservation is proportional to the body surface area insulated. This is important with respect to infants whose proportions are different from those of adults (i.e., covering the head may be of significance.).
- Active warming: Two main methods are used clinically for active warming – forced warm air and circulating heated water. Since 90% of heat loss is via skin surface, cutaneous heating is an efficient way of elevating core body temperature. Thermoregulatory vasoconstriction impairs heat flow from the periphery to core and poses a difficulty in warming unanesthetized hypothermic patients efficiently. Therefore, active warming is best when applied to vasodilated anesthetized patients. Numerous studies have shown use of forced warm air to be superior to circulating hot water systems, albeit some studies demonstrate quicker heating with circulating water systems. When used, circulating hot water systems should be applied on top of the patient rather than underneath, as most foam mattresses provide good insulation and patient weight impairs cutaneous blood flow and increases risk of burns.
- Heated IV fluids: Heated IV fluids (limited to 40 °C) are not sufficient to maintain normothermia in anesthetized patients. Nevertheless, in cases involving large fluid shifts, extensive blood loss, or extremely long procedures, heated IV fluids provide some protection against development of hypothermia associated with cool IV fluid administration.
- Warmed and humidified gasses: As this route of heat loss is negligible in adults, there is no significant benefit of warming inspired gasses. Infants might have some benefit, as this route is somewhat more significant for them.

Crisis Management: Hypothermia

Managing hypothermia, once initiated in the intraoperative period, includes temperature monitoring and adequate warming. Complications of hypothermia should be sought and treated as indicated.

Monitoring Sites

Temperature can be measured from a variety of sites. The gold standard of temperature measurement is intravascular measurement (pulmonary artery catheter or central arterial catheter). Other sites where temperature can be measured include central (urinary bladder, esophageal, rectal, nasopharyngeal) or peripheral (tympanic, temporal artery thermometer, axillary, oral, forehead). The accuracy of peripheral temperature monitoring sites is less accurate in both hypothermia and hyperthermia.

Table 46.4 summarizes the different temperature monitoring sites.

Complications of Perioperative Hypothermia

Perianesthetic hypothermia produces potentially severe complications. The controversial benefits of mild hypothermia in the neurosurgical setting will be discussed further below.

Wound Infection and Healing

Wound infection and impairment of healing are among the most common serious complications of anesthesia and surgery, known to increase morbidity and lengthen hospital stay, and have been shown to be reduced when normothermia is maintained.

Coagulation

Coagulation is impaired in hypothermic patients and is thought to be mainly a result of a decrease in activity of clot-activating factors. Other mechanisms shown to be impaired include platelet function and the fibrinolytic system. Two points should be kept in mind:

- Platelet count is not affected.
- Routine coagulation studies will usually result in normal coagulation function, as these tests are performed routinely in an environment of 37 °C.

Adverse Myocardial Events

Mild hypothermia has been shown in some studies, to increase the risk of postoperative adverse myocardial events threefold. Particular care should be taken with patients suffering from preexisting cardiac ischemic disease and elderly patients.

Drug Metabolism

Drug metabolism is decreased by hypothermia, and postanesthetic recovery is prolonged. The effect of hypothermia differs from drug to drug and is listed in Table 46.5.

Postoperative Shivering

Patients report shivering and thermal discomfort as their worst experience of the perioperative period, even worse than surgical pain. Of particular interest in neurosurgery, shivering increases ICP and intraocular pressure, in addition to stretching surgical incisions and interrupting moni-

Table 46.5 Effect of hypothermia on drug metabolism

Drug class	Effect
Neuromuscular blocking agents	Mainly pharmacokinetic effect. Onset of action delayed. Prolonged duration. Recovery minimally affected. Vecuronium affected more than atracurium. Efficacy of neostigmine not altered
Inhaled anesthetics	Pharmacodynamic effect. Solubility increases. Decrease in MAC of 5% for every °C
Propofol	Increase in plasma concentration of 30% when temperature decreased by 3 °C

Table 46.4 Major temperature monitoring sites

Monitoring site	Reliability	Advantages	Disadvantages
Pulmonary artery catheter	Gold standard. Reflects core blood temperature	Accurate	Highly invasive Impractical in most clinical scenarios
Distal esophagus	Reliable, accurate	Reliable, easy to use, accessible	Sensitive to site of placement. Malpositioning leads to false recordings
Nasopharynx and tympanic membrane	Reflects core brain temperature. Infrared aural canal thermometers inaccurate	If properly placed – reflects temperature reliably. Accessible	Tympanic membrane thermometer must be directly parallel to tympanic membrane. Positioning might be difficult. Risk of eardrum perforation
Bladder	Close approximation to core temperature	Tolerable by awake patients	Accuracy varies with urine output
Rectal	Close approximation to core temperature	Tolerable by awake patients. Easily accessible site	Presence of stool and bacteria may falsely elevate temperature. Temperature changes lag behind core temperature changes
Skin	Inaccurate. Many confounding conditions	Simple, accessible	Confounded by ambient temperature, redistribution, and vasomotor tone

toring devices. Incidence is as high as 40%, but decreases when patients are normothermic and larger doses of opioids are used intraoperatively. Shivering may increase metabolic rate and oxygen consumption by 200%, but currently is not thought to contribute significantly to the adverse myocardial events.

The approach to postoperative shivering should include the following:

- Skin surface warming: Shivering threshold is dependent on core and mean skin temperature. Thus increasing the skin temperature will decrease shivering through augmentation of the cutaneous warm input. Skin warmers increase mean skin temperature by only a few degrees, and thus it is important to raise core temperature >35 °C, for augmentation of warm input to be efficient and to prevent shivering.
- Drugs: Meperidine (25–50 mg IV) is considerably more effective in treating shivering than equianalgesic doses of other μ-agonists, and this may be attributed to its effect on κ receptors and other non-opioid sites of action. Other proposed treatments include clonidine (75–150 μg IV, most probably by reducing vasoconstriction and shivering thresholds), ketanserin (10 mg IV), tramadol (1–2 mg/kg), physostigmine (0.04 mg/kg), and magnesium sulfate (30 mg/kg).

Therapeutic Hypothermia in Neurosurgery

The decrease in metabolic rate and oxygen demand has led researchers and clinicians to postulate that hypothermia might have beneficial effects on neurological outcomes, in a vast array of situations involving cerebral ischemia and brain trauma. While numerous studies have shown mild hypothermia to provide protection against cerebral ischemia and hypoxemia in animal species, the only benefit proven in humans, in some studies, is on the neurological outcomes following ventricular fibrillation cardiac arrest.

Global Ischemia

Early studies had shown improved neurologic outcomes and reduced mortality in comatose survivors of ventricular fibrillation cardiac arrest treated with mild hypothermia (32–34 °C) for a period of 12–72 h. More recently the Targeted Temperature Management trial demonstrated that hypothermia at 33 °C compared to 36 °C for 36 h did not alter mortality or neurologic outcome. The benefits of therapeutic hypothermia may not have been from hypothermia per se but rather from avoidance of hyperthermia. Thus, current literature supports limiting therapeutic hypothermia to 36 °C, following cardiac arrest.

Intracranial Aneurysms

A randomized trial found no benefit to intraoperative hypothermia in patients undergoing craniotomy for aneurysm clipping (Todd et al. 2005). A number of studies show some possible benefit of hypothermia as a last resort treatment for carefully selected subgroups of patients suffering from refractory intracranial hypertension and/or cerebral vasospasm following aneurysmal subarachnoid hemorrhage. However, the complications of hypothermia are very common including increased rates of nosocomial infections and septic shock, hypernatremia, hyperkalemia, and thrombocytopenia. Upon rewarming, one must be diligent to monitor for further complications including vasodilatory shock and hyperkalemia. Thus, therapeutic hypothermia is not a recommended treatment in this group of patients.

Traumatic Brain Injury

Hypothermia as a protective mechanism in traumatic brain injury is under debate. It has been shown to decrease ICP. Some studies have been able to show some benefit in particular subgroups of the study. Recent investigations have not demonstrated overall beneficial effect of hypothermia on outcomes of traumatic brain injury.

Utilizing Therapeutic Hypothermia

While therapeutic hypothermia in neurosurgery is not generally indicated, should the risk benefit profile of therapeutic hypothermia be appropriate, there are several important considerations.

Opposing thermoregulatory responses to hypothermia: This means providing adequate sedation, anesthesia, and potentially neuromuscular blockade to prevent shivering.

- Cooling techniques: There is a wide variety of techniques, invasive and noninvasive. The most appropriate technique should be selected.
- Rewarming: While there is no consensus on the ideal time or rate for rewarming patients, an accepted rate of rewarming is 0.5 °C/h. When hypothermia is prolonged, rewarming may be as gradual as 1 °C/day.
- Increased diligence for potential complications of hypothermia.

Key Points

- Shifts from a body core temperature of 36.6 ± 0.2 °C result in hyperthermia or hypothermia, causing pathophysiologic reactions, setting off a variety of response mechanisms. General anesthesia impairs normal regulation significantly.
- Effector mechanisms preventing hypothermia include vasoconstriction, shivering thermogenesis, and nonshivering thermogenesis.
- Factors contributing to hypothermia which may be modified include OR ambient temperature, drugs, exposure, and duration.
- Core body temperature monitoring is extremely important and is reliable when monitored in one of the five sites – pulmonary artery, distal esophagus, nasopharynx, tympanic membrane, and bladder.
- Intervention in three phases of hypothermia is crucial: Phase 1, minimizing redistribution hypothermia; Phase 2, minimizing heat loss due to radiation or convection; and Phase 3, monitoring and prevention of hyperthermia in the vasoconstriction phase.
- Passive insulation and active warming are the mainstay of maintaining normothermia.
- Perioperative hypothermia causes a variety of systemic complications and should be avoided. Evidence advocating permissive hypothermia in neurosurgery is limited.
- Meperidine is the opioid of choice for treatment of postoperative shivering.

Overview: Hyperthermia

Even a mild elevation in brain temperature may be detrimental to the hypoxic, ischemic, and injured brain. Hyperthermic states may be caused by a wide variety of clinical disorders which can be divided into two major groups: (1) controlled hyperthermia, resulting from a deviation of thermoregulatory set points and thresholds, and (2) uncontrolled hyperthermia, resulting from impaired thermoregulatory responses or excessive heat production. Table 46.6 lists major causes of hyperthermia.

Numerous studies have found pyrexia to be associated with increased mortality and morbidity after stroke. Early fever is associated with a poor Glasgow Coma Scale score in traumatic brain injury patients. Hyperthermia may potentially worsen vasospasm-mediated brain injury, in patients suffering from subarachnoid hemorrhage. Several studies have shown hyperpyrexia to be an independent risk factor, predicting worse outcomes in TBI, SAH, and ischemia. Blood in the cerebrospinal fluid induces fever in experimental models, and temperature is thus a possible marker for the primary severity of the hemorrhage. The harm associated with hyperthermia is a result of direct cellular toxicity (i.e., deterioration of mitochondrial activity and alterations of enzymatic reactions and cell membrane instability). Cellular effects may progress to widespread organ pathophysiologic reactions. Muscle damage, degeneration, and necrosis are direct results of extreme heat production and are associated with significant elevation in muscle enzymes. Cardiovascular effects caused by elevated core body temperature are associated with elevated

Table 46.6 Major causes of hyperthermia

Increased heat production	Impaired heat loss	Surgical and medical conditions	Drugs
↑Metabolic rate	Environmental (high ambient temperature and humidity)	Hypothalamic bleeding	Anticholinergics
Fever			Monoamine oxidase inhibitors
Heat stroke			
Thyrotoxicosis, thyroid storm	Excessive heating	Fourth ventricle bleeding	Serotonin releasers
	Cardiovascular disease	CNS lesions	
Pheochromocytoma		Hemispherectomy	Serotonin reuptake inhibitors
Drugs: amphetamines, hallucinogens	Hypokalemia	Infectious etiology	
	Dehydration	Meningitis	Amphetamines
Malignant hyperthermia	Old age	Encephalitis	MDMA
	Skin disease	Cerebral abscess	LSD
Neuroleptic malignant syndrome	Cystic fibrosis	Subdural empyema	Tricyclic antidepressants
		Medullary abscess	
		Sepsis	Analgesics
		Intraparenchymal hemorrhage	Antihistamines
			Phenothiazines
		Subarachnoid hemorrhage	Butyrophenones
			Thiothixenes
			Anti-Parkinsonian agents
			β-Blockers
			Alcohol

cardiac output due to a several fold increase in skin blood flow, leading to an increase in demand and diminished peripheral vascular resistance (secondary to vasodilation and dehydration) and tachyarrhythmias (sinus tachycardia, SVT, and also VT/VF). High-output cardiac failure and heat-induced myocardial damage often lead to various degrees of systemic hypotension.

CBF and CMR are increased by elevated body temperature (between 37 and 42 °C), but above 42 °C cerebral oxygen consumption decreases due to cellular enzymatic degradation. Uncoupling of CNS metabolism may lead to further damage if CBF is compromised and may have deleterious effects on the noncompliant brain by raising ICP. Other effects of hyperthermia on the injured and ischemic brain include direct brain and spinal cord toxicity associated with cell death, alterations in membrane stability, enzyme function and neurotransmitter release, blood-brain barrier disruption, cerebral edema and local hemorrhage, seizure/epileptiform discharges, and increased peritumoral edema. These processes may lead to stupor or coma. In conscious patients, ataxia, dysmetria, and dysarthria may be seen. Hyperthermia and impaired brain autoregulation may increase the risk for cerebral hypoperfusion during periods of hypotension and likewise in the setting of hypertension, development of vasogenic edema, vascular engorgement, and worsening of intracranial hypertension during periods of hypertension.

Hyperthermia can cause acute renal failure (incidence 5%) secondary to dehydration, hypotension, and rhabdomyolysis. Acute tubular necrosis with moderate proteinuria is more common. In the gastrointestinal tract, hyperthermia frequently leads to ischemic ulcerations that may result in bleeding, elevated liver enzymes, cholestasis, and hepatic necrosis. Table 46.7 summarizes the major clinical and laboratory manifestations of hyperthermia.

Table 46.7 Clinical and laboratory manifestations of hyperthermia

Clinical manifestations	
Cardiovascular effects	Tachyarrhythmia, various degree of systemic hypotension
Neurologic effects	Ataxia, dysmetria, dysarthria, profound stupor, coma, and seizures
Respiratory	Pulmonary edema, ARDS
Renal failure	Acute tubular necrosis, renal failure
Muscle	Degeneration and necrosis, rhabdomyolysis
Gastrointestinal	Bleeding, elevated liver enzymes, cholestasis, and hepatic necrosis
Laboratory tests	
White blood cell count	Elevated
Coagulation	DIC
Electrolytes, chemistry, hormones	Hyperglycemia, elevated serum cortisol, growth hormone, and aldosterone levels
	Hypokalemia, mild hypophosphatemia, and hypocalcemia

Prevention: Hyperthermia

Core body temperature should be measured continuously throughout the entire perioperative period. Core temperature is best reflected by monitoring in a site that reflects central temperature: intravascular, distal esophagus, nasopharynx, and bladder. Rectal temperature tends to lag behind core body temperature.

Crisis Management: Hyperthermia

Hyperthermia is suggested by recording above normal core temperature. The diagnosis is confirmed by history and physical examination of the patient. A thorough examination and diagnostic evaluation for all vital signs (pulse, blood pressure, oxygenation, $ETCO_2$, arterial blood gas analysis) should be conducted to identify the cause of hyperthermia. Differential diagnosis must include the most common causes of hyperthermic state (Table 46.7). While the most common cause of hyperthermia is benign, caused by excessive insulation and heating, the more sinister etiologies must be considered as well.

Hypothalamic tumors or intraoperative brain hemorrhage may produce hyperthermia by elevating core body temperature and may be distinguished from heat stroke or severe infection, by noting associated clinical conditions such as diabetes insipidus and anhydrosis. Central nervous system infections are characterized by relevant history, clinical signs, and elevated enzyme and white cell count in CSF.

While the underlying cause of hyperthermia should be sought, symptomatically correcting fever in the brain-damaged patient is warranted, minimizing damage and improving outcomes. While the ideal method of cooling is not known, treating pyrexia with antipyretics and external cooling is recommended. Disadvantages of physical cooling include patient discomfort, limited effectiveness, and elevation of CMR and catecholamine levels – particularly in instances of "controlled" fever. Some evidence exists, demonstrating advantages in pharmacologic control of hyperpyrexia in brain-injured patients.

Malignant hyperthermia is a rare but fatal phenomena encountered in anesthesia. Most commonly, it occurs under severe stress and after administration of triggering anesthetic agents (most notable – volatile anesthetics and succinylcholine). Several reports have associated brainstem hemorrhage with MH like symptoms. Hyperthermia is usually a late sign and is preceded by masseter muscle contraction, tachyarrhythmia, combined respiratory and metabolic acidosis, muscle rigidity, and hypertension. Aberrations in calcium homeostasis may contribute to increased neuronal damage. The cerebellum has been noted to be particularly vulnerable. Neuroleptic malignant syndrome may be diagnosed by

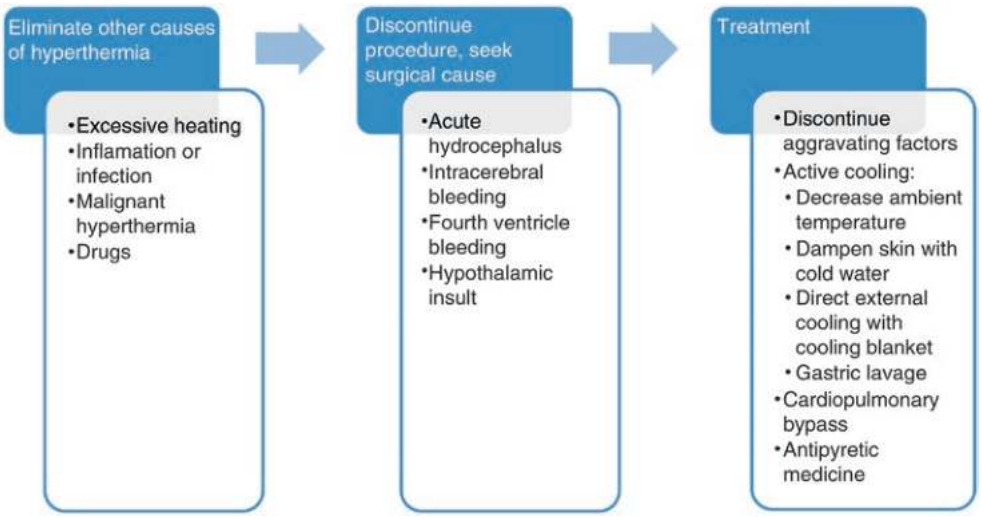

Fig. 46.2 Treatment approach for hyperthermia

history of use of neuroleptic agents (butyrophenones, phenothiazines, thioxanthenes, dopamine-depleting agents, and others). A wide variety of other drugs not included in this category have been suspected to cause hyperthermia as well. Several reports have shown TBI patients to have greater risk of developing NMS following treatment with haloperidol, and particular attention should be given to early detection. If malignant hyperthermia is suspected, discontinue the triggering agent, and dantrolene must be administered as soon as possible (IV dantrolene sodium 1–10 mg/kg). Forced diuresis and hemodialysis may be indicated to treat rhabdomyolysis and renal failure. Supportive therapy aimed at treating systemic disturbances (tachyarrhythmias, hypotension, decreased urine output, and metabolic acidosis) associated with hyperthermia should be initiated. Continuously monitoring arterial blood gas analysis, urine output, and serum electrolytes are critical in the management of the acute crisis.

Treatment of hyperthermic disorders depends on the etiology of underlying cause. The following approach is suggested (Fig. 46.2).

Key Points

- Hyperthermia is caused by a variety of clinical states. It is important to differentiate controlled and uncontrolled hyperthermia and evaluate the underlying cause.
- Continuous temperature monitoring is essential and may be an indicator of a life-threatening syndrome.
- Malignant hyperthermia is life-threatening and must be treated promptly. Elevated core temperature lags behind other signs and symptoms. When suspected, discontinue causative agents, treat with IV dantrolene, cool patient, and provide supportive care.
- Surgical intraoperative causes of hyperthermia include acute hydrocephalus, fourth intraventricular hemorrhage, hypothalamic insult, and intracerebral bleeding.
- Treatment depends on etiology and includes active cooling and pharmacologic antipyretic therapy and is warranted particularly in the injured brain.

Suggested Reading

Hypothermia

Andrews P, Sinclair HL, Rodriguezm A, et al. Hypothermia for intracranial hypertension after traumatic brain injury. N Engl J Med. 2015;373:2403–12.

Hutchison JS, Ward RE, Lacroix J, Hebert PC, Barnes MA, Bohn DJ, et al. Hypothermia therapy after traumatic brain injury in children. N Engl J Med. 2008;358:2447–56.

Kurz A. Thermal care in the perioperative period. Best Pract Res Clin Anaesthesiol. 2008;22:39–62.

Marion DW. Moderate hypothermia in severe head injuries: the present and the future. Curr Opin Crit Care. 2002;8:111–4.

Matsukawa T, Sessler DI, Sessler AM, Schroeder M, Ozaki M, Kurz A, et al. Heat flow and distribution during induction of general anesthesia. Anesthesiology. 1995;82:662–73.

Nielsen N, Wetterslev J, Cronberg T, et al. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med. 2013;369:2197–206.

Niven DJ, Gaudet JE, Laupland KB, et al. Accuracy of peripheral thermometers for estimating temperature: a systematic review and meta-analysis. Ann Intern Med. 2015;163(10):768–77.

Sessler DI. Temperature monitoring and perioperative thermoregulation. Anesthesiology. 2008;109:318–38.

Sessler DI, McGuire J, Sessler AM. Perioperative thermal insulation. Anesthesiology. 1991;74:875–9.

Seule MA, Muroi C, Mink S, Yonekawa Y, Keller E. Therapeutic hypothermia in patients with aneurysmal subarachnoid hemorrhage, refractory intracranial hypertension, or cerebral vasospasm. Neurosurgery. 2008;64(1):86–92; discussion 92–3.

Todd MM, Hindman BJ, Clarke WR, Torner JC. Mild intraoperative hypothermia during surgery for intracranial aneurysm. N Engl J Med. 2005;352:135–45.

Hyperthermia

Badjatia N. Hyperthermia and fever control in brain injury. Crit Care Med. 2009;37(7 Suppl):S250–7.

Cairns CJ, Andrews PJ. Management of hyperthermia in traumatic brain injury. Curr Opin Crit Care. 2002;8:106–10.

Cormio M, Citerio G, Portella G, Patruno A, Pesenti A. Treatment of fever in neurosurgical patients. Minerva Anestesiol. 2003;69:214–22.

Grogan H, Hopkins PM. Heat stroke: implications for critical care and anaesthesia. Br J Anaesth. 2002;88:700–7.

Johnson JM, Minson CT, Kellogg DL Jr. Cutaneous vasodilator and vasoconstrictor mechanisms in temperature regulation. Compr Physiol. 2014;4(1):33–89.

Lenhardt R, Grady M, Kurz A. Hyperthermia during anaesthesia and intensive care unit stay. Best Pract Res Clin Anaesthesiol. 2008;22:669–94.

Roth J, Rummel C, Barth SW, Gerstberger R, Hubschle T. Molecular aspects of fever and hyperthermia. Neurol Clin. 2006;24:421–39.

Washington DE, Sessler DI, Moayeri A, Merrifield B, McGuire J, Prager M, et al. Thermoregulatory responses to hyperthermia during isoflurane anesthesia in humans. J Appl Physiol. 1993;74:82–7.

47 Challenges Associated with Perioperative Monitoring During Neurosurgery

Viraat Harsh, Shankar P. Gopinath, and Claudia S. Robertson

Overview

The Monro-Kellie doctrine states that the sum of volume of the brain, blood, and cerebrospinal fluid (CSF) is constant and an increase in one should cause a decrease of either or both of the remaining two. An increase in any intracranial constituent or development of a mass lesion beyond the ability of the other components to acclimate in volume will result in raised ICP. Early recognition of intracranial hypertension and timely intervention significantly decreases the morbidity and mortality in these patients. Ventriculostomy or intraparenchymal catheters may be used to monitor ICP in such patients.

Measures of cerebral oxygenation, such as jugular venous oxygen saturation ($SjvO_2$) or brain tissue pO_2 ($PbtO_2$) help in estimating the adequacy of cerebral blood flow (CBF) relative to cerebral metabolic requirements. These parameters of cerebral oxygenation assist in distinguishing between low CBF (25–30 ml/100 g/min) from hypoperfusion (decreased oxygenation) and that from decreased metabolic requirement (normal oxygenation). $SjvO_2$ reflects the residual oxygen after oxygen has been extracted from the blood in the brain, whereas $PbtO_2$ gives an estimate of the average tissue pO_2 in the vicinity of the electrode. For neuromonitoring, change in the values of these parameters is more important than their isolated readings or the absolute values of CBF.

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Intracranial Pressure Monitoring

Background

ICP management is the cornerstone in the perioperative monitoring of a neurosurgical patient. Both invasive and noninvasive methods of ICP monitoring are available (Table 47.1). Challenges with ICP monitoring are summarized in Table 47.2.

Table 47.1 ICP monitoring techniques

Technique	Advantages	Disadvantages
Ventriculostomy	Allows for therapeutic drainage of cerebrospinal fluid	High risk of infection, hemorrhage and blockage
	Allows for drug administration	Difficult placement and chance of malpositioning
	Resetting and recalibration possible	
	Measure of global intracranial pressure	
Intraparenchymal catheter	Easier to place (in patient with small ventricles or midline shift)	Does not allow for therapeutic drainage and hence not indicated in hydrocephalus
	Reflects local intracranial pressure	Cannot withdraw cerebrospinal fluid for culture
	No chance of occlusion	
	Minimal neurological damage	Resetting and recalibration not possible; exhibit drift with time
		More expensive
		Inaccurate if intraparenchymal gradient exists
Noninvasive methods	Economical	Low accuracy
	No risk of infection or hemorrhage	High inter-examiner variability
	Good as screening technique	

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Table 47.2 Summary of challenges associated with common invasive neuromonitoring techniques, and their management

Procedure	Challenge	Management
Intracranial pressure	Placement (ventriculostomy)	Pre-procedure CT, stepwise insertion
	Over-/underdrainage (ventriculostomy)	Recalibration every time the device/patient is moved
	Infection (ventriculostomy/ intraparenchymal catheter)	Aseptic techniques during catheter placement, short duration of monitoring, longer tunneling below scalp, use of antibiotic-impregnated catheters, removal of catheter on the earliest sign of infection,
	Hemorrhage (ventriculostomy/ intraparenchymal catheter)	Conservative for small bleed, surgery for big bleeds
Jugular venous oxygenation saturation	False reading	Placement of catheter in dominant side vein, frequent calibration
	Carotid puncture and damage to nerves, pleura/lungs	Insertion of catheter lateral to carotid pulsation; apply local pressure for 10 min to stop bleeding. Ultrasound guidance helps protect nearby structures
	Infection	Sterile technique
Brain tissue pO_2	Infection	Sterile technique
	Hemorrhage	Conservative management, unless bleed is large enough for surgery

Ventriculostomy is considered as the gold standard of ICP monitoring as it may be used for therapeutic drainage as well, throughout the normal and pathologic ranges of ICP. The ventricular end of an external ventricular drainage device is positioned in the frontal horn of the lateral ventricle and is coupled with fluid-filled tubing to an external pressure transducer. This allows for resetting to zero when required and recalibration against an external standard. The alternative device, an intraparenchymal strain gauge catheter with transducer tip, is easier to insert especially in patients with compressed ventricles or those with a midline shift or brain swelling. Also, they provide more accurate measure of ICP as compared to fluid-coupled or pneumatic devices placed in the subarachnoid, subdural, or epidural spaces.

Noninvasive methods like fundoscopy, MRI (fat suppression sequences), transcranial Doppler ultrasound pulsatility index calculation, and tympanic membrane displacement estimation may give an idea about the ICP status but have not been found to be very reliable in quantifying it; still, they may find use in patients with coagulopathy. The low accuracy of noninvasive techniques of ICP monitoring makes them poor choice over their invasive counterparts. However, the method of choice for ICP monitoring must be individualized for every patient keeping in mind the advantage/disadvantage of every technique.

Measurement of ICP allows the calculation of cerebral perfusion pressure (CPP), which is the driving pressure for cerebral blood flow. CPP is calculated as the difference between the mean arterial pressure (MAP) and the ICP. Cerebral pressure autoregulation, which is the brain's ability to maintain a constant CBF over a range of blood pressures, can be assessed by calculating the cerebrovascular pressure reactivity index (PRx). PRx is the slope of a regression line comparing MAP and ICP. For patients with impaired pressure autoregulation (PRx > 0.13), a lower CPP target of 50–60 mm Hg may be considered, while if pressure autoregulation is intact, a higher CPP target may be beneficial and improve ICP control. An individualized CPP target can be assessed using this method.

Challenges and Management

The primary challenge in placement of a ventriculostomy catheter is in the localization of the ventricles. An immediate pre-procedure computed tomography (CT) scan will help in highlighting any change in the position of the ventricles or midline shift. In case of an intraventricular hemorrhage, the catheter should be placed in the contralateral lateral ventricle. The Kocher's point is the most preferred site of insertion of an external ventricular drain (EVD), although other ventriculostomy points have also been described and used. The stepwise procedure should be strictly followed for appropriate placement of the ventriculostomy catheter and should be known to all neurosurgeons as this is the single most important modifiable factor which may help in decreasing the complications of ICP monitoring.

When an external ventricular drainage device has been applied, it should be appropriately positioned to avoid over- or underdrainage. It is important that neither the patient nor the drainage device be accidently lowered or raised. It may be required to sedate a restless patient. Any obstruction in the CSF flow may lead to false ICP readings and should be avoided. Gentle saline flush may be attempted to clear clogged catheters.

In case of parenchymal catheters, they should be placed at locations where local pressure gradients will not adversely affect ICP measurement. Failure from mechanical complications (breakage/migration/displacement) may occur in up to

5% cases. Drifts are more common in strain gauge catheters than fiber-optic ones.

Infection is a prominent complication and may occur in up to 20% of the patients. Intraventricular or subarachnoid hemorrhage, open skull fracture, craniotomy, systemic infections, catheter manipulation, leak and frequent irrigation, and sampling predispose the patient to infection. Duration of catheterization correlates with an increasing risk of CSF infections which does not seem to be reduced by prophylactic catheter exchange or antibiotic use. Infection rates increase after 5 days of EVD placement. Modern-day antibiotic-impregnated ventriculostomy catheters have been shown to reduce the risk of CSF infection to around 1%. In addition, longer tunneling below the scalp before exteriorization of the catheter has been found to lower the infection rates. All patients need to be closely monitored for any signs of infection, including but not limited to fever, headache, neck rigidity, and deteriorating mental sensorium. CSF samples should be sent for culture and biochemical analysis for early diagnosis of infection. Appropriate antibiotics and removal of the catheter help in management of the infection.

Although not as frequent as ventriculitis, hemorrhage is an important complication of ICP monitoring. The incidence is higher with EVD as compared to parenchymal catheters and in children when compared with that in adults. Evidence suggests that INR $\leq$ 1.6 has a very low risk of hemorrhage, if a parenchymal catheter is placed. Most hemorrhages are small in size and may be managed conservatively, but large volume hematomas warrant urgent surgical evacuation.

Key Points About ICP Monitoring

- Ventriculostomy catheters are preferred because they have diagnostic as well as therapeutic value (by draining CSF).
- The rate of ventriculitis can be up to 10% with ICP monitoring.
- Factors that reduce the risk of developing ventriculitis include meticulous aseptic technique in placing the catheter, use of antibiotic-impregnated catheters, and minimizing the duration of monitoring.
- Practices that do not reduce the risk of developing ventriculitis include prophylactic antibiotics and prophylactic changing of the catheter.
- Treatment of catheter-induced ventriculitis is appropriate antibiotics and removal of the catheter.
- The risk of intracranial hemorrhage from ICP monitor placement is low (1–2%) but may require surgical evacuation if the hematoma is large.
- Normal resting value: <10 mmHg

Jugular Venous Oxygen Saturation Monitoring ($SjvO_2$)

Background

$SjvO_2$ is a measure of the saturation of oxygen in blood taken from a fiber-optic catheter placed in the jugular vein, with its tip in the jugular bulb. In an adequately perfused healthy brain, the $SjvO_2$ remains between 55% and 75%. It reflects the residual oxygen after oxygen has been extracted from the blood in the brain. Lower values imply that cerebral blood flow has been inadequate, leading to increased extraction of oxygen from the blood and hence the lower $SjvO_2$. Similarly, higher values indicate that the brain is not able to sufficiently extract the oxygen, leaving higher residual oxygen in the venous blood and hence the higher $SjvO_2$. Lower values indicate cerebral hypoperfusion, whereas higher values indicate compromised brain function and possible brain injury, although small regional abnormalities may be missed.

Challenges and Management

Owing to incomplete mixing of cerebral venous blood prior to where the sagittal sinus divides into right and left transverse sinuses, $SjvO_2$ values may significantly differ in internal jugular bulb of either side, and it is important to decide which bulb to cannulate. The dominant internal jugular vein is preferably catheterized and may be determined by the use of Doppler ultrasound or by comparing the ICP increase caused by temporary compression of either internal jugular vein. The side with the dominant flow will have greater ICP rise during compression. Frequent calibration is important to avoid fallacious readings.

Potential complications of $SjvO_2$ monitoring can be divided into those associated with insertion of the catheter, including carotid artery puncture, injury to nerves in the neck and pneumothorax, and those associated with the catheter remaining in the jugular vein, including infection, an increase in ICP, and venous thrombosis.

Carotid puncture is the most common complication associated with internal jugular vein catheterization. However, it rarely has serious consequences, and the risk can be minimized by making certain that the puncture is lateral to the carotid pulsation and through the use of ultrasound to guide insertion. Most arterial punctures can be managed conservatively by applying local pressure for 10 min. Other insertion complications, such as pneumothorax, are relatively rarer when inserting jugular bulb catheters but might pose serious risk.

Line sepsis is a complication that is commonly associated with all types of indwelling catheters. Most studies have reported an overall rate of 0–5 episodes of infection per 100 catheters. Proper sterile technique in the placement and maintenance of the jugular bulb catheter should be observed to minimize this risk.

ICP can be increased by maneuvers that obstruct venous return from the brain, and concerns that a catheter in the jugular vein might raise ICP have been addressed. The 4F or 5F catheter used for $SjvO_2$ monitoring is quite small relative to the lumen of the internal jugular vein, especially when the dominant vein is cannulated and does not significantly raise ICP.

Non-obstructive, subclinical thrombus in the internal jugular vein has been observed in up to 40% of patients undergoing bulb catheterization. Symptomatic thrombosis of the internal jugular vein is very uncommon with jugular bulb catheters but could have serious consequences. Depending on the normal flow to the thrombosed internal jugular vein, the obstruction could impair venous return from the head and elevate ICP.

Key Points About $SjvO_2$ Monitoring

- $SjvO_2$ monitoring provides a continuous measure of the adequacy of cerebral perfusion relative to cerebral metabolic requirements.
- The dominant internal jugular vein should be cannulated for $SjvO_2$ monitoring.
- Insertion complications, such as carotid puncture and pneumothorax, can be minimized by the use of ultrasound guidance.
- Nonocclusive thrombosis of the internal jugular vein occurs in up to 40% with jugular bulb catheters but is rarely symptomatic.
- Normal value: 55–75%

Brain Tissue pO_2 Monitoring

Background

Monitoring of partial pressure of brain tissue oxygen ($PbtO_2$) is now increasingly being used for early recognition and prevention of hypoxic cerebral events. An intraparenchymal Clark-type pO_2 sensitive electrode attached to a microcatheter measures pO_2 over an area of 13 mm^2 and gives an estimate of the average tissue pO_2 in the vicinity of the electrode. In the normal brain tissue, continuous or intermittent $PbtO_2$ values represent global brain oxygenation. In the injured brain, however, the $PbtO_2$ values may only represent the tissue pO_2 in the area of the brain surrounding the catheter, so it is important to understand the nature of the tissue where the catheter is placed. Normal $PbtO_2$ is said to be between 23 and 35 mmHg. Values less than 20 mmHg represent a compromised brain, and $PbtO_2$ values of <15 mm Hg often predict poor outcome. Preliminary evidence suggests that $PbtO_2$ may be used to guide therapy and gives accurate data for up to 10 days with measured response to interventions.

Challenges and Management

The most important factor while monitoring $PbtO_2$ is deciding where to position the catheter. In the normal brain, minute changes in the hypoxic area may be missed, while $PbtO_2$ values from a catheter placed in the injured brain will not be representative of the whole brain oxygenation. Temperature probe placed along with the $PbtO_2$ catheter helps in estimating the temperature-corrected values of $PbtO_2$.

Risks associated with $PbtO_2$ monitoring are those integral to any intracranial catheter placement, i.e., infection and hemorrhage; however, owing to their smaller diameter (<0.5 mm), $PbtO_2$ catheters pose lower risk of hemorrhage than do EVDs. Shorter duration of catheter placement and use of aseptic measures while catheter placement decrease the risk of infection.

Key Points About $PbtO_2$ Monitoring

- $PbtO_2$ catheters give a local measure of tissue pO_2 in the brain around the tip of the catheter.
- When the $PbtO_2$ catheter is in relatively normal brain, the pO_2 values reflect global cerebral oxygenation.
- In the injured brain, the pO_2 values reflect the local tissue oxygenation near the tip of the catheter.
- Complications of $PbtO_2$ catheters are similar to ICP catheters, but the risk of hemorrhage is probably lower because of the smaller diameter of the catheter.
- Normal value: 23–35 mmHg

Suggested Reading

Bratton SL, Chestnut RM, Ghajar J, Connell Hammond FF, Harris OA, Hartl R, et al. Guidelines for the management of severe traumatic brain injury. VII. Intracranial pressure monitoring technology. J Neurotrauma. 2007;24(Suppl 1):S45–54.

Lazaridis C, DeSantis SM, Smielewski P, Menon DK, Hutchinson P, Pickard JD, Czosnyka M. Patient-specific thresholds of intracranial pressure in severe traumatic brain injury. J Neurosurg. 2014;120(4):893–900.

Lazaridis C, Yang M, DeSantis SM, Luo ST, Robertson CS. Predictors of intensive care unit length of stay and intracranial pressure in severe traumatic brain injury. J Crit Care. 2015;30(6):1258–62.

Le Roux P, Menon DK, Citerio G, Vespa P, Bader MK, Brophy GM, et al. Consensus summary statement of the international multidisciplinary consensus conference on multimodality monitoring in neurocritical care: a statement for healthcare professionals from the neurocritical care society and the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40(9):1189–209.

Ponce LL, Pillai S, Cruz J, Li X, Julia H, Gopinath S, Robertson CS. Position of probe determines prognostic information of brain tissue PO_2 in severe traumatic brain injury. Neurosurgery. 2012;70(6):1492–502; discussion 1502–3.

Stiefel MF, Spiotta A, Gracias VH, Garuffe AM, Guillamondegui O, Maloney-Wilenshky E, et al. Reduced mortality rate in patients with severe traumatic brain injury treated with brain tissue oxygen monitoring. J Neurosurg. 2005;103:805–11.

Zabramski JM, Whiting D, Darouiche RO, Horner TG, Olson J, Robertson C, et al. Efficacy of antimicrobial-impregnated external ventricular drain catheters: a prospective, randomized, controlled trial. J Neurosurg. 2003;98:725–30.

Unintended Wake-Up During Neurosurgery

48

Chris C. Lee, Tian-Long Wang, and Susan Ironstone

Overview

Neurosurgical patients are at increased risk for the occurrence of light anesthesia for several reasons. Many procedures wax between minimal and intense stimulation, given that the scalp, dura, and cranial nerves carry pain fibers, while the brain itself is insensate. Due to the desire for a prompt awakening, longer-acting agents and high dosages of anesthetic/analgesics are often avoided. However, these patients may also be at increased risk due to tolerance (from chronic benzodiazepine or opioid use) and/or enzymatic induction of the P450 system, such as caused by antiepileptic medications. Therefore, effect and duration of action of muscle relaxants, opioids, and other agents may be decreased.

The anesthesia provider must pay close attention to anesthetic depth, administration of analgesics, and level of stimulation in order to avoid unintended patient arousal. Prevention is key; however, early recognition and treatment of light anesthesia are important to minimize complications.

Prevention

Attention to anesthetic depth is critical. The provider must ensure that the patient is adequately anesthetized and has appropriate analgesia for the procedure being performed. Intraoperative hypertension and/or tachycardia should prompt an immediate reassessment of the patient with consideration toward light anesthesia.

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Stimulating events must be anticipated. Examples include:

- Laryngoscopy and intubation
- Pinning
- Surgical incision, manipulation of scalp wound
- Surgical manipulation of dura
- Manipulation of cranial nerves
- Request from surgeon for Valsalva maneuver.

Special care should be taken to confirm that the patient has adequate anesthesia and analgesia prior to these events. It is prudent to deepen the anesthetic and/or give a bolus of opioid (e.g., IV fentanyl 50–100 mcg or alfentanil 10 mcg/kg) prior to events such as pinning and start of surgery. Nerve blocks of the cutaneous nerves of the scalp administered preoperatively, or local anesthetic infiltration of pin sites may also be helpful in attenuating hemodynamic response.

Uses of proprietary EEG-based systems such as the BIS monitor have been studied extensively as devices to prevent intraoperative awareness. Although it appears that these monitors may not be as effective as adhering to end tidal anesthetic concentration monitoring protocols, they are still recommended when the patient is receiving a total intravenous anesthetic (TIVA), as the incidence of awareness is likely to be higher among patients undergoing this type of anesthesia. Because there is a 20–30 seconds lag time in conversion of EEG data to BIS index, these monitors should still not be relied upon exclusively to monitor anesthetic depth or to predict patient response to a nociceptive stimulus but may be useful for following trends. As movement by anesthetized patients in response to surgical stimulus is primarily mediated via the spinal cord, cortical EEG-based monitors are unable to effectively predict patient movement.

Adequate analgesia is essential for the prevention of hemodynamic responses, coughing/straining, and other movement. Short-acting opioids (remifentanil, alfentanil, and fentanyl) may be preferable for allowing a rapid

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emergence at the conclusion of surgery or a planned intraoperative wake-up. Continuous infusion of remifentanil has been demonstrated to decrease movement in non-paralyzed patients during craniotomy in a dose-dependent manner. Dexmedetomidine (0.2–0.7 mcg/kg/h) can also be a useful anesthesia adjunct for its sedative, sympatholytic, and opioid sparing properties. Dexmedetomidine has been demonstrated to improve perioperative hemodynamic stability in patients undergoing craniotomy.

Pharmacologic paralysis with non-depolarizing muscle relaxants is preferred for patients when pinned, especially for intracranial surgery, unless precluded by neuromonitoring techniques such as transcranial motor evoked potentials, EMG, or planned intraoperative wake-up. Due to the risk to the patient from coughing and movement in pins, paralytic drugs can provide an additional margin of safety. When paralytics must be avoided, adequate analgesia is imperative as is strict attention to detail. For non-paralyzed patients, especially while pinned, an intravenous anesthetic (such as a syringe of propofol) should be immediately available to deepen the depth of anesthesia.

Conclusion of surgery and emergence from anesthesia require special attention to timing to prevent an early wake-up. This is of particular importance when the patient is in pins, positioned other than supine, and/or the anesthesia provider has limited access to the patient's airway. Premature discontinuation of anesthetics and/or administration of neuromuscular reversal, especially before pins are removed, can place patients at risk.

Crisis Management

Pathophysiology and Clinical Presentation

Neurosurgical patients are at increased risk for complications secondary to unintended wake-ups due to multiple reasons:

- Positioning – Movement while in pins can result in cervical spine injury or dislocation of pins. Change in position can also interfere with neuroimaging/navigation systems such as STEALTH or intraoperative MRI. As the anesthesia provider often has limited access to the patient after surgery start, patient movement can risk loss of airway, lines, or monitors.
- Increased ICP – Coughing and straining result in increased ICP by the transmission of increased venous pressures. Increased ICP may lead to herniation syndromes within the closed skull or produce a bulging brain or frank herniation through a craniotomy.
- Bleeding – Perioperative hypertension has been shown to be associated with intracranial hemorrhage following craniotomy. Bulging or herniation through a craniotomy may also result in a hemorrhagic brain. Coughing/straining and hypertension can all increase the danger of aneurysmal rupture in at-risk patients.
- Cerebral hyperemia – Hypertension and tachycardia contribute to cerebral hyperemia which may worsen cerebral edema and contribute to bleeding risk.
- Direct tissue injury by in situ surgical instruments during unexpected movement.
- Cardiovascular complications.
- Intraoperative awareness.

Patient Assessment

Light anesthesia typically presents as hypertension, tachycardia, and possibly movement in patients without significant pharmacologic paralysis. The occurrence of any of the above should prompt an immediate reassessment of the patient and should be directed toward rapid differentiation of light anesthesia from other potential causes. As many patients receive beta-blockers and other antihypertensives, these early signs of light anesthesia may not be present in some patients, making it very difficult to predict when a patient may move. Other patients have exaggerated hemodynamic responses to anesthesia and may not maintain a reasonable blood pressure at target values of either intravenous or inhaled agents.

Differential Diagnoses

- Light anesthesia/pain
- Increased ICP (hypertension)
- Cerebral ischemia
- Drug effect
- Volume depletion/blood loss and anemia (tachycardia)
- Essential – hypertension
- VAE (tachycardia)
- Seizure
- Electrical stimulation of motor cortex.

Clinical suspicion of light anesthesia should trigger an assessment of the current anesthetic regimen/dosage, opioids administered, and level of stimulation.

- Check the vital signs. Hypertension and tachycardia generally accompany light anesthesia but should be limited due to risk of complications.

- Check that the patient is receiving the planned anesthetic regimen: vaporizer full and appropriate ET agent concentration for current setting, IV lines running, and intravenous anesthetics being received.
- Check progress of surgical procedure with attention toward recent changes in the level of stimulation and likelihood of intracranial hypertension and/or ischemia.
- Check train-of-four ratio or other assessment of neuromuscular blockade.

Intervention/Treatment

- Ask for temporary cessation of surgical stimulation and removal of surgical instruments (if possible).
- Intermittent mandatory ventilation can exacerbate coughing in a light patient. Consider changing to a synchronous breathing mode, or briefly discontinue the ventilator and open the pop-off valve.
- Deepen the anesthesia. This can be most rapidly accomplished with a bolus of an intravenous agent (e.g., propofol 50 mg).
- Ensure adequate analgesia. Consider additional fast-acting opioid administration, (e.g., fentanyl 100–200 mcg).
- Control hemodynamic response. Intravenous esmolol is well suited to this purpose as it is short acting and does not increase cerebral blood flow. Exercise caution with co-administration of antihypertensives and anesthetic bolus to avoid hypotension.
- After the patient is re-anesthetized, consider re-dosing of non-depolarizing muscle relaxant.
- In procedures where neuromuscular blocking agents would be contraindicated, the anesthesia provider may need to administer an infusion of a vasopressor (e.g., phenylephrine) so that a deeper depth of anesthesia may be achieved, in patients who become hypotensive from subanesthetic concentrations of inhaled or intravenous agents. Target MAP ranges should be discussed with the surgical team prior to the initiation of the procedure.
- Recheck patient positioning with specific attention to pressure points, airway, monitors, and IV access.
- Evaluate and treat for potential neurologic sequelae.
- Assess the patient postoperatively for recall. Intraoperative awareness has the potential to cause prolonged psychological and emotional distress. When intraoperative recall is deemed likely, it is important to provide explanation and reassurance. Follow-up and consider referral to a psychologist.

Key Points

- Prevention is key. Maintain an adequate depth of anesthesia, and anticipate stimulating events
- Anticipate higher anesthetic requirements in at-risk patients
- Ensure adequate analgesia for the procedure being performed
- Pharmacologic paralysis is preferred for craniotomies and patients in pins
- Rapid intervention in cases of light anesthesia can limit complications from movement, coughing, and hypertension
- Support hemodynamics pharmacologically when patient's blood pressure will not tolerate target concentrations of inhaled or intravenous anesthetic agents.

Suggested Reading

Avidan MS, Mashour GA. Prevention of intraoperative awareness with explicit recall: making sense of the evidence. Anesthesiology. 2013;118:449–56.

Basali A, Mascha EJ, Kalfas I, Schubert A. Relation between perioperative hypertension and intracranial hemorrhage after craniotomy. Anesthesiology. 2000;93(1):48–54.

Bekker A, Sturaitis M, Bloom M, Moric M, Golfinos J, Parker E, et al. The effect of dexmedetomidine on perioperative hemodynamics in patients undergoing craniotomy. Anesth Analg. 2008;107:1340–7.

Brown EN, Solt K, Purdon PL, Johnson-Akeju O. Chapter 50: monitoring brain state during general anesthesia and sedation. In: Miller's anesthesia. Philadelphia: Elsevier/Saunders; 2015. p. 1524–40.

Drummond JC, Patel PM, Lemkuil BP. Chapter 70: anesthesia for neurologic surgery. In: Miller's anesthesia. Philadelphia: Elsevier/Saunders; 2015. p. 2158–99.

Grillo P, Bruder N, Auquier P, Pellissier D, Gouin F. Esmolol blunts the cerebral blood flow velocity increase during emergence from anesthesia in neurosurgical patients. Anesth Analg. 2003;96:1145–9.

Jameson LC, Sloan TB. Using EEG to monitor anesthesia drug effects during surgery. J Clin Monit Comput. 2006;20:445–72.

Rose JC, Mayer SA. Optimizing blood pressure in neurological emergencies. Neurocrit Care. 2004;1:287–99.

Cardiac Arrest/Code

49

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Introduction

It is not known how many patients suffer cardiac arrest and need to be resuscitated while in the hospital. However, fewer than 20% of patients who suffer from cardiocirculatory arrest in the hospital survive. In-hospital cardiac arrest is preventable in most cases. Often patients suffer from hypoxia or hypotension that is not recognized and treated in time and leads to cardiac arrest. During and around surgery, 2 out of 1000 patients develop myocardial infarction – one of the most important causes of cardiac arrest (Table 49.1). Successful cardiopulmonary resuscitation (CPR) requires intensive practical instruction and training and good teamwork as well.

Prevention

There is no sure means of preventing cardiocirculatory arrest. Thus, it is all the more important to preoperatively identify those patients who are at risk (e.g., coronary artery disease, diabetes associated with renal insufficiency) or who present with risk factors (e.g., perioperative myocardial infarction, electrolytic disturbance, Table 49.1) and to monitor these individuals intensively and give appropriate treatment.

Table 49.1 Causes of cardiocirculatory arrest

Etiology	Cause
Cardiac: 70–90%	Myocardial infarction
	Cardiac arrhythmia
	Pericardial tamponade
	Pulmonary embolism
Noncardiac: 10–30%	Bleeding
	Intoxication
	Metabolic lapse/electrolytic disturbance
	Suffocation
	Central respiratory depression
	Tension pneumothorax
	Severe hypovolemia
	Anaphylaxis

Furthermore, establishment of rapid response teams (RRTs) – including physicians and nurses – is recommended. These teams should be alerted by hospital staff at the bedside on the normal ward as soon as vital signs or the global clinical impression of a patient deteriorates. This early intervention reduces the incidence of in-hospital cardiocirculatory arrest.

Crisis Management

Patients undergoing surgery and intensive care patients who are intubated and ventilated comprise special circumstances. In the following we present procedures for standard situations, particularly in the operating room and in the intensive care unit; however, patients are often being monitored continuously so that cardiocirculatory arrest is detected sooner and the appropriate treatment can be implemented earlier. In Europe CPR measures are carried out according to the Guidelines of the European Resuscitation Council (ERC) (Fig. 49.1). In North America, CPR measures are carried out according to the Basic and Advanced Cardiovascular Life Support, American Heart Guidelines.

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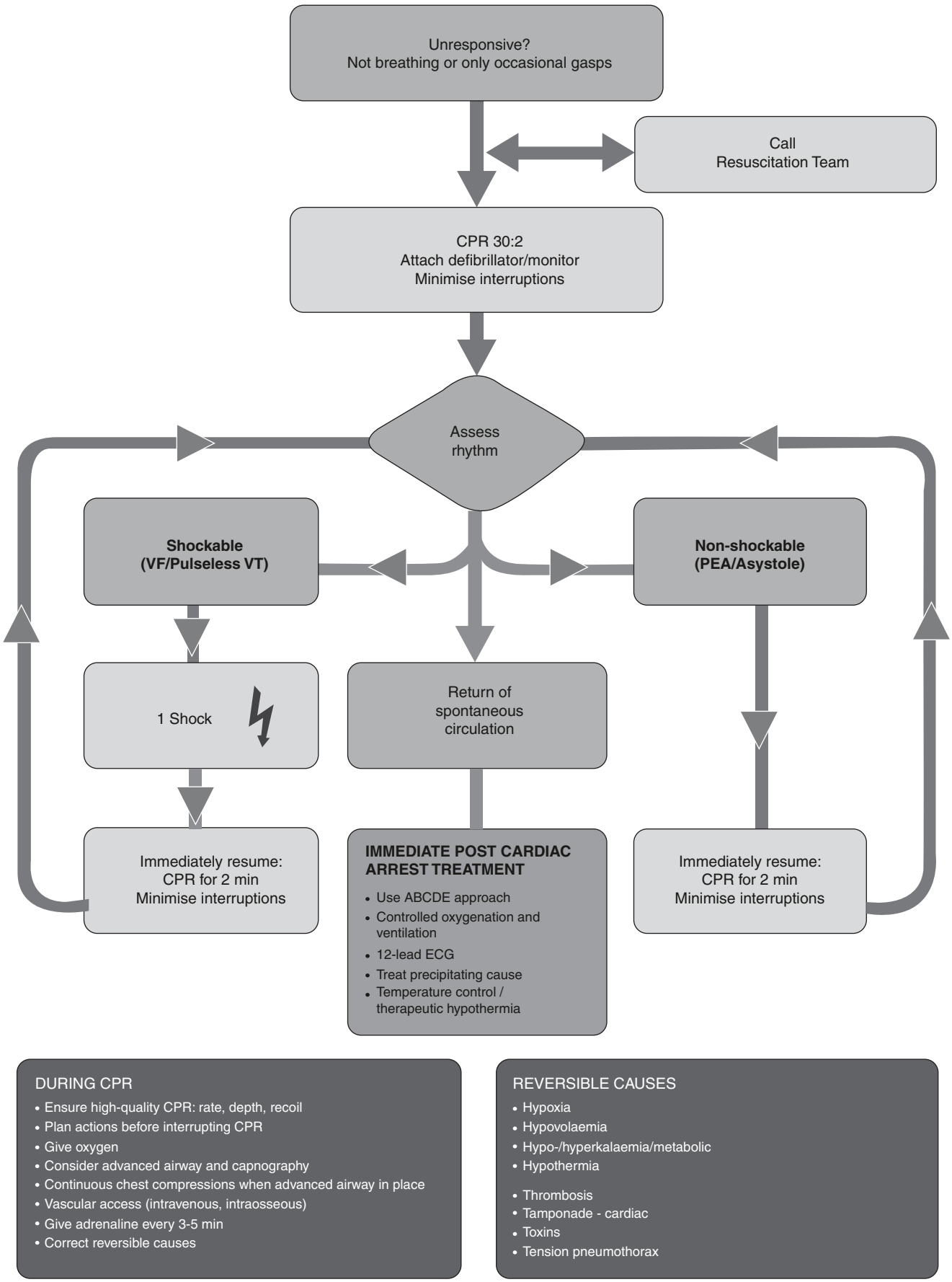

Fig. 49.1 CRP Algorithm of the Guideline of the European Resuscitation Council

Clinical Presentation of Cardiac Arrest

- After 10–15 s patient is unconscious (collapse).
- After 15–45 s cerebral convulsions may develop. Cerebral convulsion is quite common after the occurrence of cardiac arrest.
- After 30–120 s pupils are dilated, and the skin color is pale to cyanotic.
- Patient may show symptoms of the underlying disease (Table 49.1).

Patient Assessment

Checking State of Consciousness, If the Patient Is Not Intubated

- Speak loudly and clearly to the patient (if the patient is not sedated or anesthetized).
- Use tactile stimulation (e.g., shake, pain stimulus).
- Call additional personnel for help.

Check Breathing

- Check breathing for no longer than 10 s.
- Do not mistake gasping for adequate breathing. Gasping is a typical sign of cardiac arrest.
- When in doubt, assume that breathing is inadequate and start resuscitation.
- If the patient is intubated: check the ventilation, airway patency, and the ventilator.

Checking for "Signs of Life"

- Look for "signs of life" (e.g., coughing, pressing, and spontaneous movement).
- Providers trained in advanced cardiac life support may manually palpate the carotid artery (total time for checking the pulse, max. 10 s). Never palpate the two carotid vessels at the same time.
- If the patient shows no "signs of life" and/or no pulse can be felt: immediately start chest compression and face mask ventilation (compression–ventilation ratio: 30:2).
- If a pulse can be felt: secure airway and measure blood pressure.
- If the patient has invasive arterial blood pressure monitoring: check monitor and arterial access.

Medical History from Third Party

- Without delaying resuscitation measures, obtain the patient's medical history from a third party in order to gain additional information that may reveal potentially reversible conditions [electrolytic disorder, intoxication (Table 49.2)].

Table 49.2 Potentially reversible causes and specific treatment options during CPR

Cause	Treatment option
Hypoxia	Intubation and ventilation with 100% oxygen, check position of the tube and exclude malpositioning
Hypovolemia	Blood volume support and possibly surgical repair of the cause of bleeding
Hyperkalemia	Administration of glucose and insulin (while monitoring serum glucose concentration and electrolytes), administration of calcium (while monitoring electrolytes)
Hypokalemia	Administration of potassium (while monitoring electrolytes)
Hypocalcemia	Administration of calcium (while monitoring electrolytes)
Acidosis	Administer sodium bicarbonate buffer (while monitoring electrolytes and blood gases)
Severe hypothermia	CPR and immediate extracorporeal circulation
Tension pneumothorax	Relieve, thoracic drainage
Pericardial tamponade	Pericardiocentesis (ultrasonographically guided)
Pulmonary embolism and myocardial infarction	Thrombolysis and/or PTCA, if necessary
Intoxication	Administration of antidote, gastric lavage, hemodialysis, etc.

- Use ultrasonography (especially echocardiography) to detect potentially reversible causes.
- Review the ICU documentation; check for recently performed interventions (e.g., central venous catheter placement).

Treatment

- Call for additional help (optimize manpower).
- Immediately start chest compressions.
- Treat potentially reversible causes.

ECG Diagnosis

As soon as an ECG/defibrillator is available, the heart rhythm should be analyzed. When circulatory collapse occurs in the operating room or intensive care unit, monitoring is already established and the check can be performed immediately. Four different forms of cardiocirculatory arrest are considered:

- *Ventricular fibrillation* (VF) is marked on the ECG by chaotic electrical activity and not clearly identifiable QRS complexes of alternating amplitude and frequency.

- *Pulseless ventricular tachycardia* (pulseless VT) is marked by tachycardia with wide QRS complexes but no palpable pulse because there is no cardiac ejection.
- *Asystole* is marked by the complete lack of QRS complexes on the ECG. Artifacts may be mistaken for VF. Lead defects must be excluded by changing leads, controlling amplitude, and controlling the cables and electrodes.
- *Pulseless electrical activity* (PEA) is characterized by presence of QRS complexes on the ECG and absence of palpable pulses (cardiac ejections).

In in-hospital emergencies asystole and pulseless electrical activity represent 80% of the cases of cardiocirculatory arrest.

Airway and Ventilation

- Open the airway by tilting the patient's head back and using the Esmarch maneuver (head tilt, chin lift maneuver).
- Remove any foreign bodies and regurgitated fluid from the mouth and throat.
- Perform synchronized face mask ventilation: after compressing the chest 30 times ventilate twice.
- Providers trained in endotracheal intubation should intubate the patient as soon as reasonable to secure the airway and prevent aspiration. The time for endotracheal intubation should not be any longer than 30 s; if the procedure exceeds 30 s, it should be aborted, and face mask ventilation should resume. Endotracheal intubation can be attempted again at the earliest after another 2 min CPR cycle. If the second attempt is also unsuccessful, alternative methods to secure the airways should be chosen, e.g., laryngeal mask.
- The basic parameters for ventilation can be found in Table 49.3.
- Immediately after endotracheal tube placement chest compression should be resumed, and the position of the tube must be verified by auscultation and obligatory by capnometry/capnography. Secure the endotracheal tube properly.

Table 49.3 Ventilation for resuscitation

Ventilation parameters	
Tidal volume	Goal: "visible chest movement"
Duration of inspiration	1.0 s
Ventilation frequency	10/min
Concentration of inspired oxygen (F_iO_2)	1.0

Circulation

Chest Compression

Only if chest compressions are continuously performed, adequate cerebral and myocardial perfusion is achieved (Table 49.4). Depth of compression must be 5 cm, maximal 6 cm.

Because chest compression is a physically very strenuous activity, helpers should switch with one another every 2 min.

Defibrillation

Defibrillation represents the only effective treatment if the electrocardiogram indicates VF or pulseless VT. While a defibrillator is retrieved, applied, and charged, CPR must be performed. Defibrillation should be commenced as soon as the defibrillator is available. Self-adhesive electrodes (so-called patches) should be preferred.

It is important that the mechanical CPR is resumed immediately after defibrillation and that the heart rhythm is not analyzed until after a subsequent 2 min cycle of CPR has been performed. The defibrillator should be charged at the end of the 2 min cycle of CPR, so that delivery of another shock would be possible with only a very brief interruption of chest compressions (<5 s) if VF/pulseless VT persist. In the case of witnessed, monitored VF or pulseless VT give up to three quick successive (stacked) shocks. During defibrillation, the person who is defibrillating must ensure that no one touches the patient ("clear – all clear").

Administering Medications

When emergency medications are injected intravenously, each dose of drug should be followed by a bolus injection of 20 ml of a 0.9% saline solution ("flush").

Table 49.4 Chest compression

Compression parameters	
Compression frequency	100–120/min
Pressure point	Center of the chest
Depth of chest compression	5–6 cm
Compression–decompression ratio	1:1
Compression–ventilation ratio for face mask ventilation	30:2 synchronized = interrupted for ventilation
Compression–ventilation ratio after intubation of the trachea or securing the airways using an alternative method (LT, CT, LM)	30:2 nonsynchronized

Drug Administration During Resuscitation

For CPR a venous access should be established. In intensive care patients or in patients undergoing an intervention, a central venous access has often already been placed before cardiac arrest ensued, and this access should be preferred during CPR. If a central venous access is not available, a secure peripheral vascular access is sufficient.

If only an intraosseous access is available, administration of CPR medications follows the same guidelines that are established for the intravenous route. An intraosseous access (medial proximal tibia or distal tibia) is preferred particularly in infants and young children if an intravenous access cannot be established. The rate of successfully placing this access in pediatric patients is very high, and in rare cases an intraosseous access may be the only viable option in an adult patient. The endotracheal application of drugs is not recommended. Subcutaneous or intramuscular administration of drugs is obsolete during CPR secondary to the profoundly reduced regional blood flow.

Medications

Oxygen is the most important medication. An overview of the most common emergency drugs for CPR is presented in Table 49.5.

In general, blood volume substitution or fluid resuscitation is not indicated, except for hemorrhagic or anaphylactic shock, diabetic coma, or in patients with burns.

In case of cardiovascular collapse or cardiac arrest secondary to an intoxication with local anesthetics, an initial intravenous bolus of 1.5 ml/kg 20% lipid emulsion is recommended in addition to standard advanced life support. The bolus dose can be repeated up to three times at 5 min intervals and can be followed by an infusion of 15 ml/kg/h until ROSC is achieved, or the patient has received the maximum of 12 ml/kg.

Table 49.5 Emergency mediations for resuscitation

Medication	Effect	Dosage	Special features
Epinephrine	Sympathomimetic, α- and β-receptors, increases coronary and cerebral perfusion pressure	1 mg i.v. after the third unsuccessful defibrillation attempt	Can be administered for all forms of cardiocirculatory arrest
		1 mg i.v. as quickly as possible in cases of asystole or pulseless electrical activity repeated every 3–5 min	
Amiodarone	Class III antiarrhythmic	300 mg once i.v. after the third unsuccessful defibrillation attempt. Possibly repeated at 150 mg i.v. and subsequent chronic infusion at 900 mg/24 h	First-line antiarrhythmic drug for VF and pulseless VT
Lidocaine	Class Ib antiarrhythmic	1–1.5 mg/kg body weight i.v. after the third unsuccessful defibrillation attempt	Max. dosage 3 mg/kg body weight. Higher doses decrease possibility to defibrillate
			Second line, only when amiodarone is not available. Do not use when amiodarone was given to start with
Magnesium	Membrane stabilization	8 mmol = 2 g 50% magnesium sulfate solution i.v.	Administration for hypomagnesemia (e.g., diuretic treatment and torsade-de-pointes tachycardia)
Sodium bicarbonate	Chemical alkalization and buffer for acidic valence	50 mval (=50 ml sodium bicarbonate 8.4%) i.v.	Consider for hyperkalaemia and tricyclic overdose in case of prolonged resuscitation use only based on blood gas analysis
			Catecholamine flakes with concomitant administration via an infusion system and is inactivated. Thus a separate venous access is needed
Calcium	Calcium replacement	2–4 mg/kg body weight i.v.	Generally, administration of calcium is not recommended for CPR and only suitable in special circumstances
			Administration for hypocalcemia, hyperkalemia, and intoxication with calcium antagonists
Thrombolytics (e.g., urokinase, rt-PA, tenecteplase)	Lysis for a thromboembolic event	Depending on the thrombolytic drug	Administer to treat pulmonary embolism and other thromboembolic events on a case-by-case basis. For thrombolytic treatment under CPR, continue CPR for 60–90 min

Key Points

During cardiocirculatory arrest we distinguish fundamentally between ECG rhythms with a defibrillation indication (VF/pulseless VT) and without a defibrillation indication (asystole/PEA). The former requires defibrillation and administration of antiarrhythmic drugs to reestablish a survivable heart rhythm. Otherwise, the two groups are managed in the same way.

- First importance:
  - Perform high-quality and uninterrupted chest compressions.
  - Electrical defibrillation attempt as soon as possible.
  - Minimize the delay before and after delivery of a shock, ventilation, and rhythm assessment. Maximum of 5–10 s.
  - Push hard and fast: 5–6 cm of compression depth and 100–120 chest compressions per minute, only interrupted for ventilation (if no advanced airway is in place).
  - Search for reversible causes for cardiac arrest.
- Second importance:
  - Secure the airway.
  - Establish venous access.
  - Administer epinephrine.

For patients in whom pulmonary embolism is the suspected cause of cardiac arrest, thrombolysis can be indicated if the intra- or postoperative situation permits this.

Resuscitation Protocol for Asystole and PEA

Asystole and PEA represent the two ECG manifestations of cardiocirculatory arrest without an indication for electrical defibrillation.

Proceed as follows for both asystole and PEA (Fig. 49.2):

- Perform chest compression and ventilation (30:2).
- Establish i.v. access, and administer 1 mg epinephrine as quickly as possible.
- Secure the airway.
- Check the ECG rhythm after performing a 2 min CPR cycle.
- If asystole/PEA persists, continue CPR.
- Administer 1 mg epinephrine.
- Every 3–5 min.

If an ECG rhythm is detected that could be associated with cardiac ejection, check for a pulse, but no longer than 10 s. If no pulse can be detected, perform another 2 min CPR cycle followed by another check of the ECG and, if indicated, of the pulse. If a pulse is detected without doubt, the patient's blood pressure is measured and the cardiovascular system stabilized; furthermore, electrolytes and blood pH should be optimized. If the rhythm changes to a VF/pulseless VT, proceed accordingly.

If there is doubt from the ECG as to whether asystole or a subtle VF is present, assume asystole and do not defibrillate.

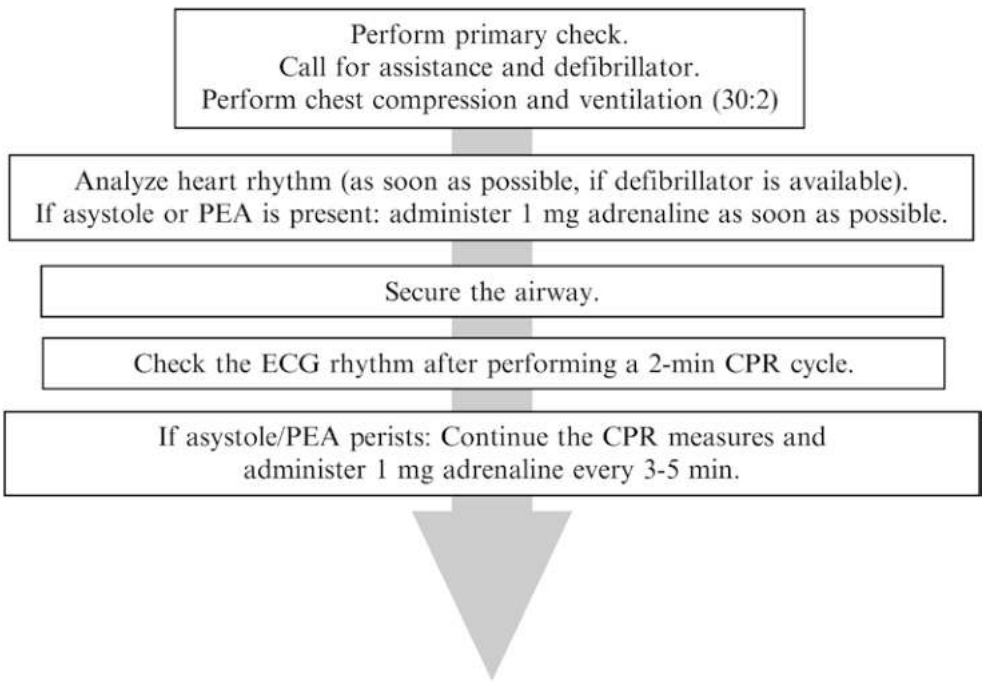

Fig. 49.2 CPR measures for asystole and PEA

Resuscitation Protocol for Ventricular Fibrillation and Pulseless Ventricular Tachycardia

For ventricular fibrillation (VF) and pulseless ventricular tachycardia (pulseless VT), defibrillation represents the key therapeutic measure in addition to chest compression and ventilation (30:2). CPR measures for VF and pulseless VT should be carried out in the following order (Fig. 49.3):

- Primary check.
- Call for assistance and, if not readily available, a defibrillator.
- Perform chest compression and ventilation (30:2).
- Analyze heart rhythm as soon as a defibrillator is available.
- Perform single biphasic defibrillation at 150–200 J, alternatively single monophasic defibrillation at 360 J.

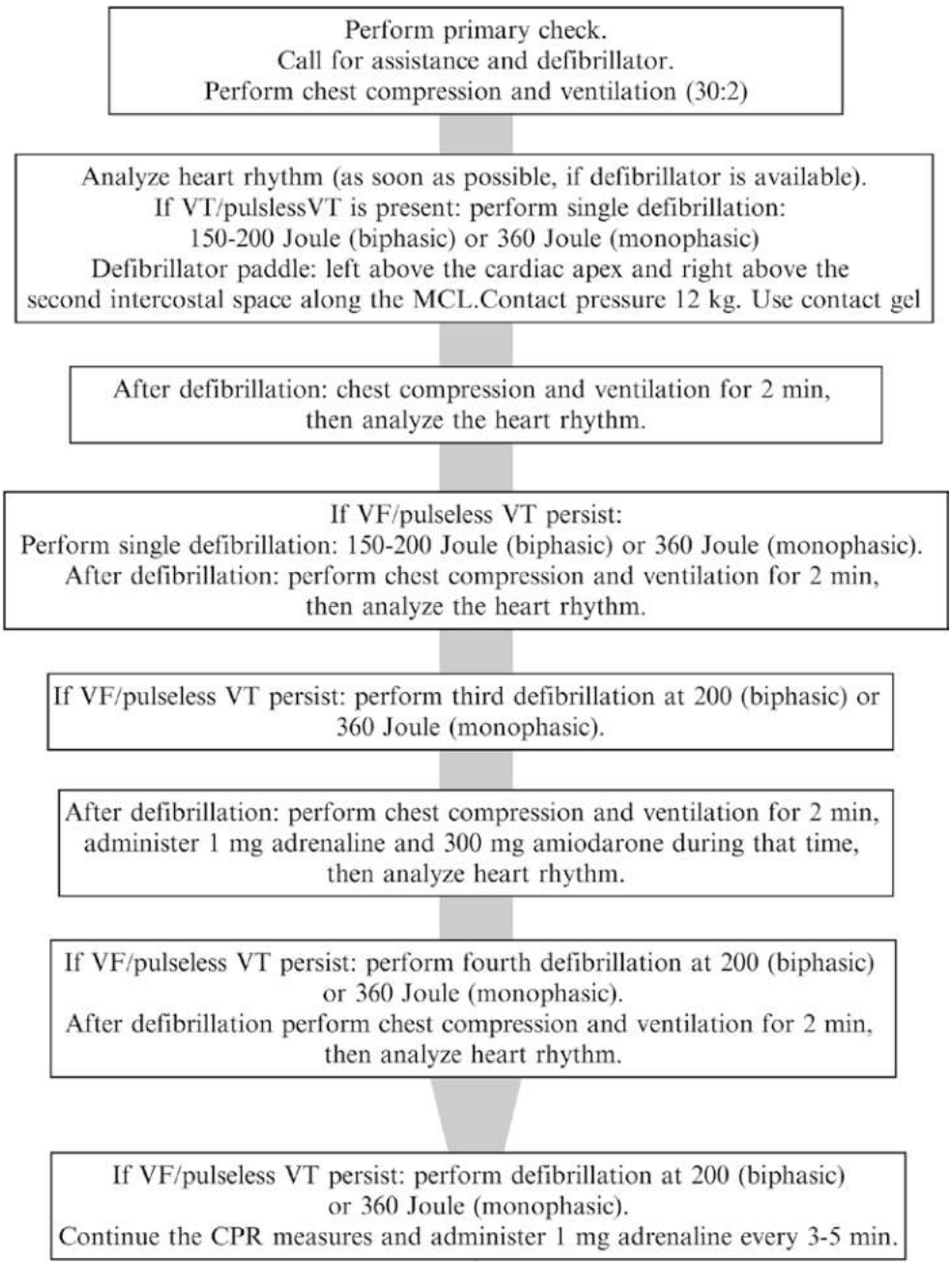

Fig. 49.3 CPR measures for VT and pulseless VT

  - Position the defibrillator patches on the left above the cardiac apex and on the right above the second intercostal space along the medioclavicular line.
  - If defibrillator paddles are used: Contact pressure for the paddle on the chest should be about 12 kg, and contact gel must be used.
- After defibrillation, chest compression and ventilation should be initiated again immediately and performed for 2 min; then the heart rhythm is analyzed again.
- If VF/pulseless VT persist, a second single biphasic defibrillation at 200 J, alternatively single monophasic defibrillation at 360 J is performed.
- After defibrillation chest compressions and ventilation should be initiated again immediately and performed for 2 min, and then the heart rhythm is analyzed again.
- If VF/pulseless VT continue to persist: perform a third single defibrillation at 200 or 360 J.
- After chest compressions have restarted, administer 1 mg epinephrine after the third unsuccessful defibrillation attempt.
- If ROSC is suspected on the basis of a significant increase of end-tidal CO_2 in waveform capnography, withhold epinephrine. Give epinephrine if cardiac arrest is confirmed at the next rhythm analysis.
- Three hundred milligrams amiodarone is also given after the third unsuccessful shock.
- After each defibrillation, chest compression and ventilation should be initiated again immediately and performed for 2 min, and then the heart rhythm is analyzed again.

If VF/pulseless VT still continue to persist, administer 1 mg epinephrine every 3–5 min, i.e., immediately after every other additional defibrillation attempt. If a rhythm potentially indicating perfusion develops during the heart rhythm analysis, check the pulse. If a pulse cannot be felt, perform another 2 min CPR cycle followed by another rhythm analysis and, if necessary, pulse check. When a pulse clearly can be identified, the patient's blood pressure is measured and the cardiovascular system stabilized; furthermore, electrolytes and blood pH should be optimized. If the rhythm changes to asystole/PEA, manage this accordingly.

Post-resuscitation Care

After ROSC post-resuscitation care on the basis of standardized protocols is essential:

- Use ABCDE approach.
- Inspiratory oxygen fraction should be reduced aiming an arterial oxygen saturation of 94–98%.
- Aim for normocapnia.
- Perform a 12-lead ECG.
- If a cardiac cause of cardiac arrest is suspected: perform coronary catheter intervention.
- If a noncardiac cause is suspected: treat precipitating cause accordingly.
- All comatose patients should be treated with therapeutic hypothermia (constant temperature at 32–34 °C or 36 °C core body temperature) for at least 24 h aimed at improving the neurological outcome.
- Fever should be prevented for at least 72 h.

Prognostication

Prognostication should not be performed earlier than 72 h after ROSC. If the patient remains unconscious 72 h after ROSC:

- Exclude confounders: residual sedation or neuromuscular blockade, hypothermia, hypotension, hypoglycemia, etc.
- If pupillary and corneal reflexes or somatosensory evoked potentials are bilaterally absent, poor outcome is very likely (false positive rate <5%).
- If not, wait for at least another 24 h before a multimodal prognostication approach should be performed (EEG, MRI/CT).
- Under no circumstances only a single marker (e.g., serum levels of neuron-specific enolase) should be used.

Suggested Reading

Neumar RW, Shuster M, Callaway CW, et al. Part 1: executive summary: 2015 American Heart Association guidelines update for cardiopulmonary resuscitation and emergency cardiovascular care. Circulation. 2015;132:315–67.

Nielsen N, Wetterslev J, Cronberg T, et al. Targeted temperature management at 33°C versus 36°C after cardiac arrest. N Engl J Med. 2013;369:2197–206.

Nolan JP, Soar J, Cariou A, et al. European resuscitation council and European Society of Intensive Care Medicine guidelines for post resuscitation care 2015. Section 5 of the European Resuscitation Council guidelines for resuscitation 2015. Resuscitation. 2015;95:202–22.

Soar J, Nolan JP, Böttiger BW, et al. European Resuscitation Council guidelines for resuscitation 2015. Section 3. Adult advanced life support. Resuscitation. 2015;95:100–47.

Arousal from Anesthesia: Failure to Emerge

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W. Scott Jellish

Overview: Surgical Area and Size of Tumor

The effect of the surgical excision, brain retraction, frontal pathology, and abnormal elastance has been blamed for delayed emergence after intracranial surgery. Frontal brain resection and posterior fossa tumors produce a higher incidence of delayed emergence compared to supratentorial tumors. The ability to predict which patients will awaken slowly after intracranial surgery is advantageous for clinical management. Decisions concerning the need for postoperative tracheal intubation and intensive care observation can be facilitated.

Mass effect of intracerebral lesions will also affect emergence. Tumor size >30 mm or a midline shift of >3 mm with cerebral edema is a good predictor for delayed emergence after surgery. Subtle brain shifts may occur, particularly when a large amount of tissue is surgically removed. Brain edema associated with large masses may lead to slower washout of anesthetic agents. In addition, single structure lesions such as an infarction or tumor, if especially close to the ascending reticular activating system, will cause lethargy preoperatively and result in delayed emergence from anesthesia.

Cerebral edema and increased brain size may increase the amount of retraction needed to resect the lesion. This could produce ischemia to the retracted structure and diminish perfusion with increased local acidosis. If temporary occlusion of cerebral arteries is required to affect surgical repair, the patient could develop ischemic/reperfusion cerebral injury after restoration of blood flow. Depending on the type of tumor resected and its vascularity, postoperative intracerebral bleeding could occur after closure of the dura. A large surface area and vascular bed from which the tumor was resected could predispose the patient to bleeding after the surgery. A cerebral hematoma exceeding 2–3 cm in diameter or large lobar hematomas often will produce coma and require surgical evacuation.

Prevention

Little can be done to prevent the effects of tumor size or the area of resection on emergence from anesthesia after the surgical procedure. However, meticulous control of fluids and blood pressure are important to avoid cerebral edema and possible postoperative subdural bleeding. Control of emergence hypertension is complex but key to reducing the possibility of postoperative cerebral edema, bleeding, or increased ICP. The size of the lesion is important in producing emergence hypertension with a shift in midline structure of more than 5 mm on cerebral imaging, an independent risk factor for hypertension at the end of the procedure. Coughing, bucking, or straining on the endotracheal tube may also cause increased ICP and postoperative bleeding. Thus, an anesthetic technique should be used with antitussive effects to reduce the incidence of this occurrence. After intracranial surgery, there is an increase in oxygen consumption, catecholamine blood concentrations, blood pressure, and heart rate. These systemic metabolic changes induce alterations in cerebral perfusions or cerebral metabolic rate which could produce cerebral hyperemia with an increased risk of intracranial hemorrhage. Hypercapnia or return to normocapnia after hyperventilation may increase blood flow in the middle cerebral artery. With termination of hyperventilation, CBF increases above levels measured before hyperventilation begins. Studies have shown that middle cerebral artery blood flow changes from 2.5% to 4% per mmHg change in $PaCO_2$. A $PaCO_2$ increase from 33 to 40 mmHg could produce a 21% increase in cerebral blood flow. In addition, during neurosurgical recovery an increase in blood catecholamine concentration has been noted.

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On emergence from anesthesia, catecholamine activation in the vasomotor center could, coupled with normocapnia, increase cerebral blood flow and metabolism. This postoperative cerebral hyperemia may promote vasogenic edema and intracranial hypertension and the risk of intracranial hemorrhage. Hemodynamic control during emergence from anesthesia is imperative for optimal outcome after neurosurgical procedures.

Other causes of delayed emergence with major brain resection must also be anticipated and prevented. Possible cerebral thromboembolism and related neurological dysfunction is highest with vascular procedures involving the carotid or cerebral vasculature. Entrainment of air, especially in neurological procedures where the surgical field is higher than the heart, could migrate into the cerebral circulation and cause profound disruption of CNS function. Monitoring with a precordial Doppler to detect air entrainment along with placement of a multi-orifice catheter will help to extract air from the central circulation should it be suspected or documented during the surgical resection.

Finally, maintenance of cerebral perfusion and elevation of blood pressure should always be considered in cases where temporary disruption of blood flow occurs during resection of vascular tumors, aneurysms, or ablation of arteriovenous malformations.

Crisis Management

If delayed emergence is suspected and believed to be secondary to postsurgical cerebral edema or hemorrhage, hemodynamic perturbations must be limited and meticulous control of blood pressure maintained. Many anesthetics have been used during intracranial surgery, but it is impossible to judge which agent or combination is preferable. Anesthetic regimen with isoflurane-fentanyl and, more recently, sevoflurane-fentanyl has been the most frequently used for neurosurgical procedures since it allows for rapid recovery and prompt neurologic assessment. A total intravenous technique with propofol and remifentanil is a useful technique, effectively preserving autoregulation and controlling responses to tracheal stimulation while allowing for rapid emergence. The difference between an inhalational technique and TIVA with propofol/fentanyl is observed in hemodynamics. Several studies reported a large percentage of patients receiving propofol-remifentanil needed antihypertensive therapy in the postoperative period.

Hemodynamic control of hypertension with the use of short-acting beta-blockers such as esmolol, administered by bolus or infusion, has been utilized with success. Labetalol or calcium channel blockers such as nicardipine may be important in controlling blood pressure and avoiding bleeding. This is especially important in surgical resections of large vascular tumors during the latter stages of the procedure, when anesthetic levels are reduced. If the patient is hypotensive from a large loss of blood, hemodynamic support should be initiated with fluids (colloid or crystalloid) and vasopressors, such as ephedrine or Neo-Synephrine. Hypotension, due to an arrhythmia, should be corrected with the use of beta-blockers or adenosine, especially if the patient is in supraventricular or paroxysmal atrial tachycardia. If postsurgical cerebral ischemia is suspected secondary to vasospasm, nicardipine treatment has been shown to reduce neurologic impairment if started in less than 6 h after onset. Cerebral perfusion can also be improved by reducing blood viscosity with hemodilution. Hypervolemic hemodilution with dextran produces a small but significant improvement in cerebral blood flow. If blood pressure is also artificially elevated, increased cerebral perfusion can be maintained and improved.

On an emergent basis, intracranial hypertension is quickly treated by reducing cerebral blood volume by acute hyperventilation. However, attention must be paid to not hyperventilate to an extreme because of the possible risk of cerebral ischemia. If hyperventilation is needed to reduce ICP, F_1O_2 should be increased to 100%. Mannitol and other osmotic diuretics are also used to reduce brain volume by osmotically removing water from the uninjured brain. Dosages of 1–1.5 gm/kg are used which usually are effective for 3–4 h. Furosemide may also be added to reduce brain volume and also inhibit the formation of CSF.

In addition to hypertension, a very high rate of blood gas abnormalities is also noted in the early postoperative period for craniotomy, regardless of anesthetic technique used. Respiratory impairment after craniotomy has been noted to be as high as 28%. PaO_2 <90 mmHg and a $PaCO_2$ >45 mmHg are considered as thresholds for hypoxia and hypoventilation. Coupled with hypoxia and hyperventilation is the overall incidence of pain medication administration. The administration of opioids to control pain could further add to hypoventilation, increased ICP, and delayed emergence. Some centers prefer not to use any opioids postoperatively and instead administer ketorolac 30 mg IV. In several studies, ketorolac provided adequate pain relief in a majority of patients. Neurologic examination did not deteriorate during the following 48 h.

Key Points #1

- Frontal brain resection and posterior fossa procedures have a higher incidence of delayed emergence.
- A tumor >30 mm in size with a midline shift of >3 mm with cerebral edema preoperatively is a good predictor of delayed emergence.
- The size of the cerebral lesion is important in producing emergence hypertension with a midline shift >5 mm an independent risk factor for hypertension. Blood pressure control is key during emergence from anesthesia. Several studies have noted that the addition of a fentanyl infusion is the most effective technique to assure early awakening after craniotomy with prevention of emergence hypertension.

Overview: Anesthetic Effects

Rapid emergence from anesthesia with control of blood pressure is paramount when devising a neuroanesthetic plan. Patients with larger intracranial lesions may have procedures that last for prolonged periods of time. This could result in prolonged administration of opioids or inhalational agents that could delay emergence, depending on the agent or opioid used. Hyperventilation during the procedure to reduce brain size and improve surgical resection may also result in prolonged emergence from anesthesia. An increase in pH may result in a higher total volume of distribution and longer elimination half-life for sufentanil. Similarly, fentanyl brain concentrations may also be prolonged in hyperventilated individuals presumably because of reduced brain washout from a change in the drug lipid/plasma distribution. In addition, intraoperative hypocapnia has also been linked to postoperative impairment in reaction time and short-term memory.

Opioids are frequently implicated in producing a prolonged state of unconsciousness with the degree and duration of postoperative sedation related to the timing, route, and total dosage of the drug administered. Prolonged depression is especially common after intraoperative administration of long-acting opioids such as morphine, meperidine, or hydromorphone. Shorter-acting opioids, such as fentanyl or sufentanil, may also exhibit a prolonged sedative effect when given in high doses or infusions for prolonged periods of time. Remifentanil, with its metabolism linked to plasma cholinesterase, has the shortest half-life and is the least likely contributor to postoperative unconsciousness. Some opioids like meperidine are metabolized to active metabolites, which prolong and add to central neural depression. In addition, these drugs will also decrease spontaneous minute ventilation slowing the washout of residual inhalational anesthetics prolonging sedation. The intense analgesic component of opioids also minimizes the arousal generated by postoperative pain.

The administration of sedative premedications to achieve anxiolysis or amnesia may also contribute to prolonged unconsciousness, particularly if long-acting sedatives (hydroxyzine, promethazine, or lorazepam) were administered. The administration of certain antiemetics or anticonvulsants, as part of an anesthetic regimen, may have a profound effect on depression of consciousness in the PACU, especially if they are given toward the end of surgery. Antiemetics such as droperidol, prochlorperazine, or scopolamine have sedative side effects that can augment sedation from anesthesia. Other parenteral medications such as propofol, short-acting barbiturates, or etomidate, especially if used as a continuous infusion during the surgery, could result in redistribution of high concentrations of drug into the tissue and accentuate delayed awakening.

Both the length of exposure to the volatile agent and the solubility of the agent must be considered to prevent buildup of agent in tissues that have lower perfusion, which would lead to a prolonged washout of anesthetic after discontinuation. Obese patients may be particularly prone to prolonged emergence after extensive intracranial procedures because of their relatively high proportion of body fat. Lower solubility agents such as sevoflurane or desflurane are unlikely to cause prolonged emergence after anesthesia because they are eliminated rapidly after discontinuation. However, if these agents are combined with other longer-acting parenteral medications, sedation may be prolonged. Overall, TIVA is similar to volatile anesthetics with regard to emergence times, early cognitive function, and adverse events. In several prospective randomized studies, evidence suggests that ICP is decreased and MAP is increased in patients receiving TIVA relative to those receiving volatile anesthetics in elective craniotomy procedures.

The patient could have residual paralysis from an infusion of neuromuscular blocking agents and be unable to move or respond to commands. The use of atropine intraoperatively, for treatment of bradycardia, could produce a central anticholinergic syndrome causing somnolence and unconsciousness, especially in older individuals.

Prevention

To prevent the possibility of delayed emergence after intracranial procedures related to anesthetic agents or medications, the practitioner should review the drugs that were administered perioperatively over the last 24 h period. Nonanesthetic drugs such as reserpine, methyldopa, clonidine, lidocaine, antihistamines, certain antiemetics, and anticonvulsants have sedative properties that may prolong emergence. Antiemetics such as droperidol, prochlorperazine, and scopolamine should not be part of the anesthetic regimen for intracranial procedures. If hyperventilation to reduce brain size is needed, care should be taken not to overventilate the patient which could change the pharmacokinetics of opioids, producing higher brain opioid concentrations. If the patient is hyperventilated, the patient should be as normocarbic as possible after dural closure.

A procedure estimated to last for a prolonged period of time should utilize a less soluble inhalation anesthetic. In addition, combination inhalational and opioid-based anesthetics reduce the overall concentration of inhalational anesthetics used and produce an early emergence. A fentanyl infusion in the presence of low-dose isoflurane has been noted to produce a more rapid emergence with much less hypertension when compared to a propofol total intravenous anesthetic. Desflurane, with similar effects as isoflurane on cerebral vasculature, can be used for prolonged intracranial procedures with minimal cumulative effect.

If opioids are administered, longer-acting ones should be avoided. In addition, IM administration, which leads to slower uptake and prolonged action, should be also be avoided. Remifentanil may be used for many neurosurgical procedures to avoid a delay in emergence, but postoperative management of pain and emergence hypertension are key factors that must be considered with its use. Opioid premedication should also be avoided to prevent preoperative hypoventilation, especially in patients with large intracranial masses where increased ICP could be a factor.

If propofol infusions are added to an opioid/inhalational anesthetic to improve neurophysiologic monitoring, discontinuation of the infusion should occur as soon as possible to avoid the accumulative effect of propofol on emergence from anesthesia. If antiemetics are to be used as part of the anesthetic regimen, dexamethasone and serotonin-blocking agents (i.e., ondansetron, dolasetron), which do not have sedative effects, should be administered. In many instances neuromuscular-blocking agents are not needed for intracranial procedures and in some instances (facial nerve or other cranial nerve monitoring) should be avoided altogether. If muscle relaxants are used, appropriate titration of intermediate neuromuscular-blocking agents will avoid the prolonged paralysis that may occur with multiple boluses or infusions of long-acting agents such as pancuronium. Finally, if bradycardia occurs during the intracranial procedure, glycopyrrolate can be substituted for atropine to increase heart rate. This drug does not cross the blood-brain barrier and will not produce a central anticholinergic syndrome.

Crisis Management

When determining the reason for prolonged unresponsiveness after intracranial surgery, the initiation of analgesia and sedation regimens should be delayed until the source of the unconsciousness is identified. Generally, a patient demonstrating signs of pain will also exhibit some degree of consciousness. To determine whether prolonged unconsciousness is related to residual opioids, small incremental doses of naloxone 40 mcg IV can be administered. Careful titration can reverse both ventilatory depression and sedation without precipitating excessive sympathetic activity, which may result from rapid reversal of narcosis. If benzodiazepines are suspected, flumazenil can be given in titrated incremental doses of 0.1 mg IV q 2 min to reverse the sedative effect. Its duration of action is short, however, and repeated doses may be needed to maintain consciousness.

There is no specific reversal for barbiturates, propofol, phenothiazines, or butyrophenones. However, the administration of physostigmine 1.25 mg generates a degree of arousal that may counter, but not reverse depression from sedatives, antiemetics, and other CNS depressants. Physostigmine can also be used to reverse the central nervous system effects associated with central anticholinergic syndrome.

Finally, unconsciousness or prolonged sedation after anesthesia could be simulated by a paralyzed patient. If the patient is totally unresponsive after the neurosurgical procedure and muscle relaxants were utilized, the patient's neuromuscular integrity should be assessed with the use of a neurostimulator. If no twitches are observed or if a minimal train of four is realized, the patient should be supported and reversal agents (neostigmine with glycopyrrolate) administered.

Key Points #2

- Hyperventilation and extreme hypocapnia could alter opioid pharmacokinetics and reduce brain washout of the drug, prolonging emergence from anesthesia.
- Long-acting sedatives should not be administered preoperatively for anxiolysis as they could prolong postoperative emergence.
- The administration of certain antiemetics and anticonvulsants, as part of an anesthetic regimen, may have a profound depressant effect at the end of surgery.
- Residual paralysis from neuromuscular-blocking agents as well as central anticholinergic syndrome, if atropine is used, should be considered in neurological procedures with delayed emergence.

Overview: Patient Factors

Individual patient factors, not related to the anesthetic or surgical procedure, could also affect emergence from anesthesia after an intracranial procedure. Physiologic abnormalities could exist in patients that would cause a prolonged return to consciousness. Patients with large intracranial masses may be on large doses of steroids especially dexamethasone. These patients may be hyperglycemic which could interfere with consciousness by increasing serum osmolarity. Acutely high glucose levels can produce a hyperglycemic hyperosmolar coma. Concomitant ketoacidosis and metabolic acidemia can compound the effect of hyperosmolarity on reduced consciousness. Patients may also be hypoglycemic if overtreated with bolus or insulin infusion. Severe hypoglycemia will also produce unconsciousness because of the loss of essential substrates necessary for neuronal function.

The level of consciousness can also be impacted by an acute hypo-osmolar state. A rapid drop in osmolarity of serum could occur after a neurosurgical procedure because of a sudden increase in antidiuretic hormone secretion, which has been noted to occur with certain tumor cell lines, after subarachnoid hemorrhage, and with postsurgical trauma, especially in the pituitary/hypothalamic regions. Serum sodium levels below 125 meq/L are especially troublesome and could lead to seizures or prolonged postoperative unconsciousness.

Hypernatremia produces a hyperosmolar state similar to that caused by hyperglycemia. Hypernatremia could occur after either marked dehydration from aggressive diuresis with either mannitol or furosemide or from postsurgical trauma to the neurohypophysis producing diabetes insipidus. This is characterized by insufficient secretion of antidiuretic hormone and loss of free water. Unconsciousness due to hypernatremia is rare but could occur if urine output and intake are not carefully monitored during the intraoperative period.

A reduction in core body temperature will decrease the level of arousal and increase the effect of anesthetics and muscle relaxants. Body temperatures below 34 °C impair consciousness, and extremely low body temperatures will produce fixed pupils and areflexia. Hypothermia is rarely the primary cause of postoperative unconsciousness. However, a moderately decreased body temperature will certainly augment the depression of unconsciousness or impair the clearance of anesthetic agents and muscle relaxants.

Delayed awakening may be caused by an array of benign or life-threatening conditions. However, because of its potentially severe consequences, brain injury should be at the top of the differential after neurosurgical procedures. In most instances, delayed awakening after general anesthesia may be attributed to the lingering effect of anesthetic drugs. Several etiologic mechanisms can be associated with delayed awakening. Residual neuromuscular blockade should be ruled out, along with anesthetic overdose. Hypothermia, hypercarbia, electrolyte disturbances, glucose, and arterial blood gas extreme abnormalities are other factors which could delay emergence. Various psychoactive substances, including alcohol, could also prolong emergence. Injection of local anesthetics in close proximity of nerve structures has been described as the cause of isolated postoperative neurologic deficits. In some instances, intra-arterial injections of local anesthetic during certain blocks could produce hemiparesis and loss of consciousness. Infusion of a large volume local anesthetics along suture lines, especially close to the brainstem, could cause diffusion of local anesthetics into the subarachnoid space causing paralysis and loss of consciousness.

Pre-existing patient conditions should also be ascertained since some could contribute to a prolonged emergence after anesthesia. Patients with porphyria will exhibit a prolonged state of unconsciousness with the use of barbiturates, propofol, and other medications. Hunter's syndrome and other mucopolysaccharide disease states may also produce prolonged unconsciousness. Patients who are hypothyroid, especially if not properly medicated, may be especially slow to emerge from anesthesia. In addition, patients with obstructive sleep apnea (OSA) will be particularly sensitive to the effects of opioids and inhalational agents. If the OSA is severe, the buildup of CO_2 could be particularly detrimental, especially after a recent craniotomy where control of cerebral edema is an important postoperative consideration.

Finally, the post craniotomy patient could be postictal, having had an unrecognized seizure under anesthesia or during emergence. It is a common practice to give anticonvulsant therapy to patients undergoing a supratentorial craniotomy. Seizures, in the early postoperative period, are not common if the patient has been administered the correct level of anticonvulsants. However, seizures have been noted to occur on emergence from anesthesia and may go undetected.

Ideally, recovery from neuroanesthesia should be smooth and progressive with no major hemodynamic fluctuations and should not have any thermogenic effects. It should not produce seizure activity and should facilitate rapid awakening for early neurologic assessment and follow-up.

Crisis Management

Alterations in patient physiologic parameters that could alter emergence from anesthesia after an intracranial procedure must be recognized quickly and treated appropriately to avoid neurologic injury. Cerebral blood flow of <20 ml/100 gm/min or a partial pressure of O2 at <40 mmHg leads to reduced consciousness. Brief periods of ischemia

from decreased cardiac output or decreased vascular resistance cause syncope. Four types of events could occur to produce delayed awakening and neurologic injury. The first is delayed hypoperfusion or no reflow phenomenon. This is reduced CBF associated with marked cerebrovascular resistance. This usually follows an anoxic ischemia event. The second is the production of cytotoxic metabolites of arachidonic acid. Another is production of oxygen-free radicals, and the final is neuronal influx of CA++ ions. Hypoxic ischemic injury also occurs in conditions of increased vascular resistance such as with hypertensive encephalopathy, disseminated intravascular coagulation, meningitis, and cerebral edema. If unconsciousness is suspected from hypoglycemia, an empiric trial of intravenous 50% dextrose solution should be initiated. Lethargy, confusion, agitation, or coma could all be signs of hypoglycemia occasionally complicated by seizures, focal neurologic signs, and hypothermia. It is inappropriate to delay the administration of dextrose until serum glucose is corroborated. If acute hyperglycemia is demonstrated with hyperglycemic hyperosmolar coma, hydration should be immediately initiated with saline and titration of IV regular insulin either in small incremental doses or by an infusion. This allows for adjustment of blood glucose without the delay to peak effect or uptake problems that occur with subcutaneous, longer-acting insulins. Potassium replacement and serial blood glucose measurements are essential.

Acute hypo-osmolar states can occur (<260 mmOSm/2) by a sudden increase in antidiuretic hormone secretion, especially in cases involving the pituitary or hypothalamus. If severe hyponatremia is recognized, care should be taken to restore the serum sodium gradually. Replacement of fluids with normal saline and IV administration of furosemide, to promote renal wasting of free water in excess of sodium, should be initiated. Infusions of hypertonic saline may be necessary, but care should be taken to avoid rapid overcorrection of electrolyte levels, which could predispose to the development of central pontine myelinolysis. Unconsciousness due to a hypernatremic, hyperosmolar state is rare in postoperative patients. If diminished antidiuretic hormone is secreted due to neurosurgical injury, the patient will develop hypernatremia with high output dilute urine. The treatment of diabetes insipidus consists of the administration of an isotonic crystalloid solution and infusion of aqueous ADH (100–200 milliunits/h). Serum sodium and plasma osmolarity are measured on a regular basis, and therapeutic changes are made accordingly.

Patients who do not awaken after neurosurgical procedures with a history of alcoholism, malnutrition, bariatric surgery, dialysis, or hyperemesis could have delayed emergence from thiamine deficiency. The syndrome, Wernicke's encephalopathy, would include impaired consciousness, disturbed memory, nystagmus, paralysis of lateral gaze, and impaired vestibular response. Though the complete syndrome may only be present in a few cases, thiamine deficiency should always be considered when delayed emergence from anesthesia is coupled with the other histories.

Hypothermic patients should be treated by rewarming with warm ambient air and the use of heated IV fluids. Covering the patient's head will also help retain heat. Surface or radiant warmers and humidification of inspired gases will also reduce heat loss. Patients with a temperature below 35 °C should be rewarmed using radiant lighting, heating blankets, warmed forced air, reflective coverings, and heated nebulized air. As the temperatures rise, patients should be carefully monitored for hypotension related to increasing venous capacitance. Resolution of metabolic acidemia usually accompanies rewarming.

Electrolyte and other osmolality abnormalities may be present after craniotomy, especially with the use of mannitol or brain tumors with possible SIADH. This syndrome may also be present with the use of thiazides, carbamazepine, and tricyclic antidepressants. The rate of change of sodium concentration is probably a more significant contributor to brain swelling. Decreased levels of conscious may occur when sodium levels reach 115–120 mEq/l. Rapid recorrection could cause control pontine myelinolysis which can lead to further deterioration of consciousness. Hypomagnesemia can occasionally present with delirium, nystagmus, and seizures. Hypophosphatemia with levels below 1 mg/dl may occur with hyperalimentation, vomiting, gastric suctioning, sepsis, or treatment of ketoacidosis. All of these can depress consciousness and mimic neurologic injury after neurosurgery. A complete electrolyte panel is warranted in someone who fails to emerge from anesthesia from an intracranial neurosurgical procedure.

Key Points #3

- Physiologic abnormalities could occur during intracranial neurosurgical procedures, which could lead to extremes in glucose concentrations, sodium levels, and serum osmolarity, all of which could affect emergence from anesthesia.
- Body temperature, especially hypothermia, could lead to prolonged anesthetic effects with delayed emergence from anesthesia.
- Always consider the possibility that the post-craniotomy patient may have had an intraoperative seizure and are in a postictal state, which could delay wakening after an intracranial procedure.

Suggested Reading

Bhagat H, Dash HH, Bithal PK, Chou han RS, Pandia MP. Planning for early emergence in neurosurgical patients: a randomized prospective trial of low-dose anesthetics. Anesth Analg. 2008;107(4):1348–55.

Bruder NJ. Awakening management after neurosurgery for intracranial tumours. Curr Opin Anesthesiol. 2002;15(5):477–82.

Grover VK, Tewari MK, Mahajav R. Cranial surgery: impact of tumour size and location on emergence from anaesthesia. J Anesth Clin Phamacol. 2007;23(3):263–8.

Himmelseher S, Pfenninger E. Anaesthetic management of neurosurgical patients. Curr Opin Anaesthesiol. PMID: 17019134. 2001;14(5):483–90.

Schubert A, Mascha E, Bloomfield EL, DeBoer FE, Gupta MK, Ebrahim ZY. Effect of cranial surgery and brain tumor size on emergence from anesthesia. Anesthesiology. 1996;85(3): 513–21.

Zelcer J, Wells DG. Anesthetic-related recovery room complications. Anaesth Intensive Care. 1996;15:168.

Communication Challenges During the Perioperative Period

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David J. Murray

Overview

Risk, Incidence, and Epidemiology

Communication failure is ubiquitous in human relationships, so the finding that miscommunication occurs in the perioperative period should not be surprising. Communication is required for health-care teams to provide safe patient care, so when communication fails, there is a potential for an adverse patient outcome. In the operating room environment, experts must possess task work skills and coordinate the delivery of these skills and activities with other team members. Each team member has a specific set of expert skills and a defined set of roles, tasks, and responsibilities. The majority of tasks are interdependent, where tasks performed by one member are dependent on tasks performed by other team members. The quality of the teamwork (and patient outcome) is often the result of how effectively the team manages the interdependent tasks and coordinates care. This coordination of care requires effective communication and a shared understanding of team goals. When a patient condition does not follow the typical trajectory and deviates from the routine due to an acute, uncommon, or infrequent event, the quality of teamwork becomes a key factor in patient outcome. Not surprisingly, in the specialized, high-acuity operating room and ICU environments where critical events are frequent, effective team function and communication is most likely to have a measurable impact on patient outcome.

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Etiology of Communication Failure

Communication, whether explicit or implicit, is how teams exchange information. When a communication failure occurs, the cause is often difficult to attribute to a single missed, communication opportunity. For example, communication failure is cited as the main factor causing the death of a 50-year-old man. His lethal myocardial infarction occurred less than 48 h following an uneventful outpatient procedure to replace a lead for his spinal nerve stimulator. Coronary stent thrombosis less than 48 h following the procedure was attributed to his failure to restart his antiplatelet therapy that he had been instructed to stop prior to the procedure. The communication failures that contributed to the lethal event included an inadequate history about the antiplatelet therapy, insufficient knowledge about the risks of stopping antiplatelet therapy, incomplete information transfer during multiple hand-offs of care, and failure to take responsibility for post-procedure instructions. While standardized protocols for medication reconciliation, hand-offs of care, and discharge instructions might have prevented this adverse patient outcome, the team's inadequate knowledge about the risks of stopping therapy would not be altered by this approach.

Many authors have defined teamwork as including five associated components. These team functions or components include leadership, mutual performance monitoring, backup behavior, adaptability, and orientation. In a health-care professional team composed of multiple experts, the expectation is that leadership may shift among the team members at various times in order to achieve the goal. Team members must coordinate activities and often manage tasks in a sequential and interdependent manner. In the perioperative routine, limited communication may be observed or required, as team members are cognizant of the team goal as well as engaged in specialized activities demanding their full attention.

In the operating room, task density (number of tasks X task difficulty) is often extremely high, and multiple professionals coordinate their expert skills with other team

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members. Such task interdependence, where tasks performed by one member are dependent on tasks performed by other members, is characteristic of the perioperative environment. A shared mental model and effective communication is key to accomplishing all of the tasks that lead to achieving an ideal perioperative outcome. In high functioning teams, progress toward the desired goal may be "on track" even in the absence of explicit communication. The team is monitoring mutual performance with multiple shifts in leadership among team members in order to achieve the goal. During a routine operation, explicit communication may not be necessary, however, when a deviation from a normal trajectory occurs then communication becomes imperative. In the majority of operating rooms, teamwork and many of the described teamwork behaviors to avert or manage a crisis are often readily observed. For example, an air embolus occurs during a craniotomy; the anesthesiologist recognizes the signs and adjusts anesthetic care but more importantly alerts the operating room team and leads the team to actions that counter the potential source of the embolus. The scrub nurse and neurosurgeon understand the likely cause and flood the operative field with saline. Similarly, if an intraventricular catheter inserted during a ventricular peritoneal shunt placement leads to brisk bleeding, the neurosurgeon leads the team and indicates the need for immediate craniotomy. The team members (anesthesiologist and OR nurses) would be expected to adapt to the changing circumstances and assume leadership for various activities that are needed to convert the operative procedure from ventricular catheter placement to craniotomy. In these examples, the team recognizes the "abnormal" and responds to correct the crisis either averting or mitigating an unfavorable outcome. An awareness of the roles and responsibilities of various team members, mutual performance monitoring, an ability to assume backup behaviors, and adapting to a changing clinical situation by team members are all essential teamwork activities to resolve a crisis.

Communication Assessment and Teamwork Complications

Communication and teamwork are widely recognized as important factors in patient safety. Effective teamwork, however, is not automatic. The most serious communication and teamwork failures are most often an error that results from the absence of a shared understanding or shared responsibility for the operative procedure.

Some of the most striking examples of morbidity attributed to communication failure are operative procedures conducted on the patient's wrong side. Despite the relatively low frequency of this obviously preventable and egregious error, "pre-briefs" and "time-out" procedures prior to surgery are expected to eliminate this type of error. The expectation is that this team communication will encourage teamwork rather than a "silo" approach to care and lead to a shared responsibility for all aspects of the procedure. Unfortunately, this regulatory approach will likely not reduce errors unless the team adopts the behaviors that the time-out is expected to encourage.

This shared responsibility is expected to reduce the types of egregious errors such as:

- Operations on the wrong side/level
- Operation guided by wrong MRI
- Error in preparing operative site (none, toxic solution for preparation)
- Contaminated OR equipment (sterilization failure)
- Positioning morbidity (position or equipment to position)
- Solutions on the surgical field
  - Concentration of epinephrine
  - Neurotoxicity from irrigation (formalin, chlorhexidine, alcohol, antibiotic irrigation instead of saline)
  - Flammable substances on the field (collodion/alcohol)
- Prophylactic antibiotic administration errors
  - Allergic, dosage, timing, and susceptibility
- Blood transfusion errors
- Pathologic specimen discarded/mislabeled

Clinical Presentation

The causes of communication breakdown are often multifaceted primarily because expert teams require both expertise and teamwork to accomplish goals.

Some of the potential causes of team failure include

- Team members do not understand roles and responsibilities both by profession and discipline (nursing, physician) and specialty (surgeon, anesthesiologist, internist).
- Few contingency plans are in place when a critical event occurs during the perioperative period.
- Team members unable or unwilling to support or crossover to help other team members when a work overload exists.
- Team members fail to recognize crisis or adapt to a changing situation.
- Changing expectations about performance exist among team members, and many of the actions are not clearly designated to individual members of the team (e.g., assuring donated blood is readily available for administration).

Many teamwork failures attributed to communication are due to expertise factors associated such as insufficient

experience, inadequate team knowledge, poor judgments, or issues of professional interactions such as accountability, behavior, and integrity.

Intervention/Prevention

An understanding of the causes of these types of adverse outcomes would suggest that no one method would likely correct communication failure. Checklists have been adopted as a novel solution to the numerous causes of communication failure. In anesthetic practice, checklists were long ago recognized as a necessary method to prepare and plan anesthesia equipment and supplies. Similarly, an operating room nurse would rarely, if ever, be unprepared for a planned operation. The checklist assures that often simple and repetitive items are not overlooked and readily available. Not surprisingly, checklists are likely to be lifesaving in settings that were previously associated with limited emphasis on advance planning and team coordination. This may explain why adopting checklists have proven to be most beneficial in settings where the availability of necessary supplies and resources are likely to vary daily.

The majority of strategies to decrease the frequency of communication failure are directed to improving teamwork function, yet most education continues to place more emphasis on developing the specialty expertise necessary to participate as a member of an expert team. This specialty training, whether during residency or advanced training in nursing, most commonly occurs with limited, if any, interaction with future team members. This training results in experts who have the knowledge and skills to accomplish the cognitive and technical skills expected but may not understand the need for teamwork. A combination of knowledge, skills, and attitudes is necessary for successful patient care. While considerable attention is directed to evaluating and remediating physicians with inadequate knowledge and skills, the evaluation and remediation of attitudes and behaviors that lead to teamwork failures have received less consideration. Disruptive behaviors that prevent effective teamwork are increasingly recognized as contributing factors to adverse patient outcomes.

There are a variety of strategies that are used to improve concepts of team function in health-care settings. These strategies are believed useful to improve attitudes and behaviors that contribute to communication failure. One of the global strategies applied by hospitals is through the use of surveys of the safety culture of the health-care professional team. The responses by the health-care professional team correlate with measures of patient safety. In hospitals that are perceived by health-care professionals as "safer" in terms of the environment and commitment to patient care, the measures of patient safety in terms of outcome are improved. In hospitals with a safety climate that is not favorable to safe patient care, the strategy to improve the environment is not clearly defined, but the majority of research suggests some form of team training. The nature of the team-training curriculum may not be as important as the involvement and engagement of the entire health-care professional team. These training paradigms recognize skill and expertise in safe care but also a climate and culture that encourages safe care.

A variety of team-training curriculum and strategies are available that potentially improve teamwork. The adaptations from the military and aviation industry (frequently referred to as "Crew Resource Management" strategies) are relatively directive in terms of the conduct of training and team member expectations. One example, the Team Strategies and Tools to Enhance Performance and Patient Safety (TeamSTEPPS) program includes an interactive curriculum for teaching teamwork concepts. The program is divided into four modules: communication, situation monitoring, mutual support, and leadership. In terms of communication between team members, the participants are instructed to use defined communication skills and structured opportunities for information exchange. The use of a variety of mnemonic such as Situation, Background, Assessment, and Recommendation (SBAR), "Check Back," and "Call Out" to convey communication about relevant patient information are ideal approaches that assure effective information exchange in crisis situations.

Overview of Communication in Teamwork (TeamSTEPPS) Curriculum

- SBAR eponym for communication of relevant patient information (Situation, Background, Assessment, Recommendation).
- DESC eponym indicates *d*escribe the behavior, *e*xpress concerns, *s*pecify a course of action, and assure *c*onsensus.
- Two-Challenge (the action of verbalizing a safety concern twice if no action is taken).
- Check Back (closed-loop communication between the sender to ensure that the receiver has heard and understands the message correctly).
- Call Out (calling out loud to staff important decision for anticipating next steps).

Benefits of Improvements in Teamwork and Communication

- Enhanced coordination of care
- Better initial as well as more comprehensive patient care plans
- Fewer adverse patient outcomes
- Increased patient satisfaction
- A reduction in frequency of medicolegal cases and decreased magnitude of claim settlements

Key Points

- Communication failure and miscommunication among health-care professional teams are serious, preventable causes of patient morbidity and mortality.
- The cumulative expertise of the health-care professional team does not necessarily translate into expert patient management. While the medical team requires individuals to possess the knowledge, skills, experiences, and attitudes to perform essential tasks, teamwork is also essential. Teamwork is not automatic.
- Checklists and other standardized protocols provide a method to transmit and receive information that can reduce the frequency of communication errors; however, the main benefit of checklists and protocols is to encourage teamwork and provide a framework for a shared mental model for the care of the patient.

Suggested Reading

Anthes E. The trouble with checklists. Nature. 2015;523:516–8.

Burke CS, Salas E, Wilson-Donnelly K, Priest H. How to turn a team of experts into an expert medical team: guidance from the aviation and military communities. Qual Saf Health Care. 2004;13(Suppl):i96–104.

Cohran A, et al. A model of disruptive surgeon behavior in the perioperative. Environ J Am C Surg. 2014;219:390–8.

Haynes AB, Weiser TG, Berry WR, et al. Safe Surgery Saves Lives Study Group: a surgical safety checklist to reduce morbidity and mortality in a global population. N Engl J Med. 2009;360:491–9.

Murray D, Enarson C. Communication and teamwork: essential to learn but difficult to measure. Anesthesiology. 2007;106:895–6.

Phitayakorn R, Minehart RD, Hemingway MW, Pian-Smith MCM, Petrusa E. The relationship between intraoperative teamwork and management skills in patient care. Surgery. 2015;158:1434–40.

Rosenstein AH, O'Daniel M. A survey of the impact of disruptive behaviors and communication defects on patient safety. Jt Comm J Qual Patient Saf. 2008;34:464–47.

Russ S, Rout S, Sevdalis N, Moorthy K, Darzi A. Do safety checklists improve teamwork and communication in the operating room? A Syst Rev Ann Surg. 2013;258:856–71.

Schmutz J, Manser T. Do team processes really have an effect on clinical performance? A systematic literature review. BJA. 2013;110:529–44.

Urbach DR, Govindarajan A, Saskin R, Wilton AS, Baxter NN. Introduction of surgical safety checklists in Ontario, Canada. N Engl J Med. 2014;370:1029–38.

Weiser TG, Berry WR. Review article: perioperative checklist methodologies. Can J Anaest. 2013;60:136–41.

Weldon SM, Korkiakangas T, Bezemer J, Kneebone R. Communication in the operating theatre. BJS. 2013;100:1677–88.

Part VIII

Fundamentals of Pediatric Neurosurgery and Neuroanesthesia

Anatomy and Physiology of the Central Nervous System in Children

52

Benjamin B. Bruins and Todd J. Kilbaugh

Overview

The perioperative care of the pediatric patient presenting for neurosurgical procedure presents a set of unique challenges to the neuroanesthesiologist and neurointensivist. The developing central nervous system anatomy and rapid physiologic changes require the practitioner to have a working knowledge of expected differences throughout the growth and maturation of the pediatric patient.

- The head of an infant is proportionately larger than the adult head, exacerbating heat loss and challenges with laryngoscopy.
- The boney growth of the calvarium occurs at fibrous suture lines, and premature closure of these sutures can lead to an abnormal shape: craniosynostosis.
- The junction of multiple suture lines creates the fontanels, a unique "window" into the developing child's intracranial vault.
- The pediatric cranial vault is much softer and more pliable than the adult due to the higher content of cartilage.
- The scalp and bone of the cranial vault have a rich vascular supply, especially in the youngest of pediatric patients.

The Fontanels

Infants at birth have two major fontanels, and understanding their natural course is critical to recognizing possible challenges for the practitioner.

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Table 52.1 Differential diagnosis of abnormal fontanel examination

Sunken fontanel	Persistently full or bulging fontanel
Over drainage of CSF (cerebrospinal fluid)	Increased CSF volume (hydrocephalus, shunt failure)
Dehydration	Cerebral edema (trauma, metabolic, infection)
	Intracranial bleed
	Mass lesion

- The anterior fontanel is diamond shaped, typically closing before 2 years of age.
- The posterior fontanel is smaller and triangular, typically closing by 2 months of age.
- The fontanel should be examined with the patient in the upright position and on palpation should feel slightly concave, and a pulse may be palpable.
- A slightly full fontanel can occur during vagal maneuvers such as crying, coughing, or emesis, but a persistently full fontanel is concerning for elevated intracranial pressure (Table 52.1).
- Infants with severe dehydration are at risk for sinus thrombosis which may lead to increased intracranial pressure. In this specific case, a full fontanel may be observed in the presence of severe dehydration.
- Delayed or early closure of sutures and the fontanels can be signs of systemic disease or genetic syndromes, such as trisomy 21, rickets, hypothyroidism, and craniosynostosis.

Intracranial Compartments

The intracranial compartments of the pediatric brain are similar to the adult, with volume accounted for as follows:

- Brain and interstitial fluid 80%
- Cerebrospinal fluid (CSF) 10%
- Blood 10%

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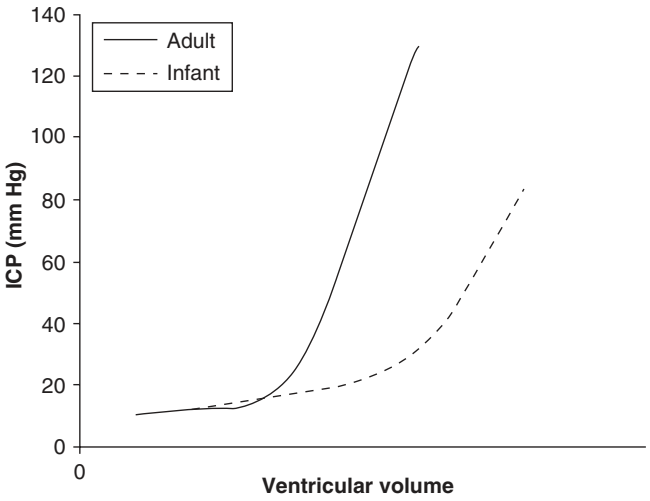

Fig. 52.1 Cranial vault compliance. Note the increased compliance of the infant cranial vault (dash line)

The presence of unfused sutures and an open fontanel alters the Monro-Kellie doctrine as it is applied to children (Fig. 52.1). The increased compliance of the cranial vault decreases the slope of the curve, allowing for larger increases in intracranial volume before rapid increases in intracranial pressure are observed. It is important to note that unfused sutures and open fontanels do not preclude the pediatric patient from herniation during rapid increases in intracranial volume and pressure.

Cerebrospinal Fluid

CSF occupies similar percentage of the intracranial volume in adults and children. Although actual CSF volume is smaller in the children, absolute CSF daily production approaches adult values. CSF is produced by the choroids plexus located in the ventricular system (lateral, third, and fourth ventricles). It then circulates and is absorbed by the arachnoid villi into the venous system. Hydrocephalus can be the result of three different conditions related to CSF regulation.

- Increased CSF production (choroid plexus papillomas)
- Obstruction to circulation through the ventricular system (aqueductal stenosis)
- Impaired absorption by the arachnoid villi (intracranial blood)

Cerebral Blood Flow and Autoregulation

Cerebral blood flow (CBF) has been observed to be age-dependent. Infants have been found to have CBF rates similar to adults (50 mL/100 g of brain tissue). Normal CBF increases with age and peaks around 70 mL/100 g of brain tissue between 3 and 8 years. It then decreases to adult levels by mid to late adolescence. Although CBF rates are similar in infants and adults, it should be noted that a much higher percentage of cardiac output is directed to the brain in the child (25%) compared with the adult (15%).

The maintenance of CBF to meet the metabolic needs of the brain is called autoregulation. There are several aspects to autoregulation.

- Pressure autoregulation refers to the maintenance of cerebral perfusion over a range of mean arterial pressures (MAP). The exact upper and lower limits are not well established in the developing human brain yet are known to exist within an age continuum. Preterm infants likely have such a narrow autoregulation zone that their CBF is passively dependent on MAP. This increases the propensity for ischemic injury with mild hypotension and increases the chances of vasogenic cerebral edema and intraventricular hemorrhage with hypertension. This must be taken into account when utilizing cerebral perfusion pressure-directed therapy in the pediatric patient with severe brain injury.
- Carbon dioxide (CO_2) vasoreactivity describes the implication of CO_2 changes upon CBF. A respiratory acidosis and resulting increased serum CO_2 will decrease cerebral interstitial pH which results in cerebral vessel dilation and increases in CBF and cerebral blood volume. In general, otherwise healthy children will tolerate the systemic effects of hypercarbia better than adults. The cerebral vascular effects in children, however, follow the same principles as in adults.
- CBF does not change in response to changes in differences in arterial oxygen until it reaches levels less than 50 Torr, below which, cerebral vessel dilation occurs.
- Flow-metabolism coupling describes the matching of neuronal metabolic demand with CBF. Clinical conditions such as hypothermia may decrease CBF and metabolism, while clinical seizures and hyperthermia may precipitate the opposite. Interestingly, some anesthetics are known to decouple the flow-metabolism relationship, most notably potent inhalation agents and ketamine. Other intravenous agents decrease neuronal metabolism and CBF in a similar magnitude, maintaining the coupled relationship. Opioids have very little effect on cerebral metabolism by themselves but are believed to maintain autoregulation of CBF.

Spinal Cord

The spinal cord anatomy also changes during childhood development. The conus medullaris (terminal end of the

spinal cord) is lower in infants (L3) and does not reach the adult stage (L1) until 1 year of life. In children, the sacrum is narrower and flatter allowing a much more direct approach to the subarachnoid space. A sacral dimple may be a sign of underlying spinal cord abnormalities requiring furthering diagnostic testing (ultrasound and magnetic resonance imaging). Children are also more prone to neck and cervical spinal cord injuries due to their weaker neck musculature.

Implications for the Neurosurgical Patient

In the pediatric patient, the mass ratio of head to body is much higher than adults. This, in combination with the weaker neck musculature, places the child at greater risk for head injuries than the adult. Due to the incomplete myelination of axons and the smaller astrocyte and oligodendrocyte populations, the pediatric brain also has a higher water content and different viscoelastic properties compared with the adult brain. These properties along with the more elastic skull and rich vascular supply of the subarachnoid space lead to predominance of diffuse axonal injury and subarachnoid hemorrhage in the younger pediatric population following traumatic brain injury. As the central nervous system matures, mass lesions such as epidural, subdural, and intraparenchymal hematomas become more prevalent following traumatic brain injury. Special consideration must be taken for the prematurely born infant, where the blood-brain barrier has not completely matured, and its fragility places the premature neonate at higher risk for intraventricular hemorrhage.

Besides increased head-to-body mass ratio, pediatric patients also have higher body surface area to mass ratios. This has important implications in the operating room, where pediatric patients are at higher risk for hypothermia, and care must be taken to regulate temperature carefully. Cooled cleaning solutions such as iodine and chlorhexidine can produce significant drops in body temperature in the pediatric patient compared with the adult.

Concerns and Risks

The increased vascularity of the cranial vault provides unique challenges to care of the pediatric patient. Large blood replacement requirements may be observed during cranial vault reconstructions. When the dura is breached and the blood-brain barrier is compromised, a disseminated intravascular coagulation cascade can be initiated intraoperatively and postoperatively requiring resuscitation with fresh frozen plasma, cryoprecipitate, and other component therapies. Cephalohematomas, which are subperiosteal hemorrhages, are common in infancy but when associated with linear skull fractures and/or coagulopathy may cause life-threatening hemorrhage.

Inflicted or non-accidental pediatric TBI (shaken-baby or shaken-impact syndrome) is a common cause of morbidity and mortality, especially in infants and young children. The practitioner must be familiar with the typical features of non-accidental head trauma and have a low threshold for further investigation.

- Non-accidental head trauma is most common in children under the age of 3 with the majority being less than 1 year.
- Typically the history is vague or varies over time and consists of a minor blunt impact of the head with a mechanism of injury that is not consistent.
- Presenting symptoms in the infant can also be vague. Lethargy, irritability, or poor feeding may be the initial complaint for seeking medical attention. Infants may also present with seizures, hyper- or hypotonia, or a full fontanel.
- Extracranial findings are not always present but may include bruising, burn marks, or fractures.
- Retinal hemorrhages are found in a majority of patients and may be unilateral or bilateral but are not specific for the diagnosis. For instance, vaginally delivered infants may have retinal hemorrhages up to 1 month after delivery.

Nontraumatic causes of retinal hemorrhages include sepsis, coagulopathy, galactosemia, osteogenesis imperfecta, and malignant hypertension which can be difficult to differentiate without considering the entire clinical picture. Intracranial bleeding should prompt a coagulation workup including fibrinogen, PT, INR, platelet count, and PTT. Isolated cardiopulmonary resuscitation without coagulopathy is thought not to be associated with retinal hemorrhages; however, this lacks definitive study. If non-accidental TBI is suspected, a skeletal survey should also be performed since extracranial abnormalities are detected in a large percentage of cases. Likewise, there are conditions such as osteogenesis imperfecta that can mimic non-accidental fractures. In addition, other occult injuries, such as blunt abdominal trauma, should be investigated with laboratory data and/or a CT and surgical consultation. Once there is a concern for possible non-accidental trauma, social services should be consulted.

Key Points

- Central nervous system anatomy and physiology of the pediatric patient are not static and vary with age.
- Open fontanel and unfused sutures do not preclude the pediatric patient to herniation.
- Cerebral blood flow rates change with age and peak in school-age children.
- The limits of pressure autoregulation vary with age, and infants have lower pressure thresholds compared with adults.
- Children have a rich vascular supply to the subarachnoid space and more compliant skull predisposing them to subarachnoid hemorrhage and diffuse axonal injury following traumatic brain injury.
- Control of the cerebral circulation changes with age and critical illness.
- Inflicted head trauma must always be considered in the pediatric patient where there is no clear history or mechanism of accidental trauma.

Suggested Reading

Cheng MI, Khairi S, Ritter AM. Pediatric head injury. In: Reilly PL, Bullock R, editors. Head injury pathophysiology and management. 2nd ed. New York: Oxford University Press; 2005.

Duhaime AC, Christian CW, Rorke LB, Zimmerman RA. Nonaccidental head injury in infants-the "shaken baby syndrome". N Engl J Med. 1998;338(25):1822–9.

Odom A, Christ E, Kerr N, Byrd K, Cochran J, Barr F, et al. Prevalence of retinal hemorrhages in pediatric patients after in-hospital cardiopulmonary resuscitation: a prospective study. Pediatrics. 1997;99(6):E3.

Soul JS, Hammer PE, Tsuji M, Saul JP, Bassan H, Limperopoulos C, et al. Fluctuating pressure-passivity is common in the cerebral circulation of sick premature infants. Pediatr Res. 2007;61(4):467–73.

Udomphorn Y, Armstead WM, Vavilala MS. Cerebral blood flow and autoregulation after pediatric traumatic brain injury. Pediatr Neurol. 2008;38(4):225–34.

Urlesberger B, Müller W, Ritschl E, Reiterer F. The influence of head position on the intracranial pressure in preterm infants with posthemorrhagic hydrocephalus. Childs Nerv Syst. 1991;7(2):85–7.

Pediatric Anesthetic Care Requirements

53

Mali Hetmaniuk and Gregory J. Latham

Overview

From the previously healthy child who receives the unfortunate diagnosis of a brain tumor to the medically complex child who arrives for better seizure control, the pediatric neurosurgical patient can present numerous challenges for the anesthesiologist. Providing age-appropriate, neuro-anesthetic care for children requires an understanding of both the neurologic and general developmental changes, the neurosurgical procedure, the existing neurologic deficits, the underlying comorbidities, and the effects of anesthesia on all of these factors.

The risk of perioperative morbidity and mortality increases as age decreases, with the neonatal group at the highest risk. As with adults, the American Society of Anesthesiology (ASA) physical status predicts the risk of anesthesia for children. Children who are less than 2 years of age or critically ill generally receive anesthetic care by providers with special training in pediatric anesthesiology. Similar to the way a cardiac anesthesiologist uses pre-load, contractility, and afterload as a framework for approaching the patient's pathology, the neuro-anesthesiologist views clinical scenarios based on intracranial perfusion, intraoperative injury, and postoperative function. One of the biggest challenges of neuro-anesthesia is how the operating conditions rendered possible by an anesthetic can immediately become a hindrance once the surgery is complete and an accurate neurological exam becomes desirable. As with any procedure, advanced communications with the surgical team is imperative. The following chapter reviews the general and neurosurgical-specific preoperative, intraoperative, and postoperative considerations of the pediatric patient.

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Table 53.1 General pediatric preoperative assessment

General	Developmental level, congenital abnormalities or syndromes, previous anesthetic problems, family history of malignant hyperthermia (MH)
Birth	Prematurity, anoxic injury, admission to intensive care unit, surfactant administration
Cardiac	Congenital heart disease, murmur, high output heart failure
Pulmonary	History of prolonged intubation, use of monitoring or oxygen at home, chronic lung disease (BPD), subglottic stenosis, reactive airway disease, obstructive sleep apnea (tonsillar hypertrophy), aspiration pneumonia
Neurologic	Seizures, myopathies, paralysis, gross motor deficits, visual defects, hydrocephalus, central apnea
Infectious	Recent upper respiratory infection (URI)
GI	Gastroesophageal reflux, dysphagia, prior abdominal surgery, bowel incontinence, liver dysfunction
GU	Kidney disease, bladder incontinence
Hematologic	Sickle cell disease, coagulopathy, anemia
Other	Endocrine imbalance, functional status

General Preoperative Assessment of Children

While the relatively healthy child may be evaluated immediately before surgery, most medically complex patients (and this comprises the majority of neurosurgical patients) benefit from a pre-anesthetic evaluation well prior to surgery. If the anesthesia team can participate in surgical planning conference, then care can be further optimized. The pediatric preoperative assessment should include diagnosis, history, physical examination, and NPO status. A list of highlights for the typical pediatric preoperative assessment is included in Table 53.1. A list of highlights for the preoperative assessment for the pediatric neurosurgical patient is included in Table 53.3.

Patients with intracardiac connections may be at risk for embolic events, subacute bacterial endocarditis (SBE), cardiovascular instability, hypoxia, or arrhythmias. Significant cardiac disease may warrant consultation with a pediatric

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cardiac anesthesiologist. Children with upper respiratory infection (URI) or reactive airway disease may be at increased risk of laryngospasm or bronchospasm. Children with myopathies or a positive family history may be at increased risk of malignant hyperthermia (MH). Children without any significant history or medications usually do not require any preoperative lab studies.

General Preoperative Sedation for Children

Parental separation and entrance into the operating room can provoke anxiety in a child, particularly toddlers. While many regimens exist for preoperative sedation, oral midazolam (0.25–1 mg/kg, maximum of 20 mg) is commonly used. If vascular access is in place, intravenous midazolam may be titrated to effect (approximately 0.05–0.1 mg/kg). Preoperative anxiety can be particularly severe in patients who have had multiple procedures. In these cases, parents may be helpful in identifying tactics that have been helpful in the past. Parental presence during induction can be a helpful substitute for sedatives if parents act appropriately and operating room staff are prepared for such an arrangement. Another approach to preoperative anxiolysis is to take advantage of a child's natural curiosity and love for play; allowing the child to examine or play with their facemask preoperatively (e.g., decorate with stickers) can be very effective. Lastly, utilization of a child life specialist may be beneficial prior to the day of surgery or during the preoperative period. These specialists are trained to provide age-appropriate preparation, distraction, and coping skills.

General Preparation of the Pediatric Operating Room

Much of the preparation for intraoperative anesthetic care is dictated by the specific procedure to be performed. Pediatric-specific preparations for all anesthetics have been suggested and endorsed by the American Society of Anesthesiologists (ASA) and American Academy of Pediatrics (AAP). Anesthetic personnel need to be trained to administer anesthetics and medications in appropriate doses and volumes appropriate for pediatrics and have experience in the airway management and ventilation of infants and children. Equipment necessary for the pediatric environment is listed in Table 53.2. Discussion of specific monitoring for pediatric neurosurgical procedures can be found in Chap. 47.

Table 53.2 General pediatric anesthetic preparation, equipment, and drugs

Airway equipment – in pediatric sizes	Masks
	Laryngeal mask airways (LMA)
	Endotracheal tubes
	Nasal and oral airways
	Laryngoscopes and blades
Pediatric positive pressure ventilator and circuit	
Temperature control	Patient warmers
	Fluid warmers
Fluid administration	Volumetric devices
	Pediatric size catheters
	Intraosseous needles
Monitors	Pulse oximetry probes – in pediatric sizes
	Blood pressure cuffs – in pediatric sizes
	ECG pads
	Temperature
	Capnography
Difficult airway equipment	Equipment for video laryngoscopy, fiber-optic intubation, and cricothyrotomy
Portable equipment for transport to ICU	To provide oxygenation and ventilation
	Portable monitoring
Resuscitation cart	Defibrillator with pediatric paddles or pads
	Vasoactive medications in dilutions appropriate for weight-based administration
	Dantrolene
	Pediatric dosing template

General Anesthesia for Children

The lack of patient cooperation is a fundamental characteristic of pediatric anesthesia. While an adult patient can often be convinced to hold still for multiple IV attempts, it is rare to meet such a child. However, the choice between an inhalational and intravenous induction is still dictated by safety, with the added caveat that there are risks to attempting to place an IV in a combative child for both the patient and the provider. The majority of children coming from home to the operating room may receive an inhalation induction; those with full stomachs, loss of airway reflexes, vomiting, decreased level of consciousness, or severe illness are best induced with aspiration precautions and intravenous medications.

Inhalation inductions in children are usually performed with sevoflurane with or without nitrous oxide. Sevoflurane is the least noxious and best tolerated potent inhalational agent for pediatric induction. Nitrous oxide is generally considered odorless and for the elective case may precede the application of sevoflurane to speed induction and minimize the initial impact of the more noxious smell. Children then can be maintained on sevoflurane or switched to isoflurane or desflurane after induction.

Classically, premedication with atropine IV (to prevent or treat bradycardia) is recommended for children less than 2 years, for children less than 6 years and receiving succinylcholine, or if bradycardia is present. However, given that the incidence of bradycardia and arrhythmia is

actually quite low, it may be appropriate to simply have atropine available (20 mcg/kg) in case bradycardia or arrhythmia occurs during induction. Repeat dosing of succinylcholine carries a significantly higher risk of causing bradycardia.

The US Food and Drug Administration (FDA) has issued a "boxed" warning about the use of succinylcholine in children. In summary, the use of succinylcholine for routine use in children has been abandoned except in cases of "emergent intubation or instances where immediate securing of the airway is necessary." High-dose rocuronium, 1.2 mg/kg, is an alternative for rapid sequence intubations. If succinylcholine is required (e.g., laryngospasm, suspected difficult airway, full stomach, no IV access, or concern that inadequate paralysis during laryngoscopy will cause a spike in ICP), then atropine 0.02 mg/kg IV/IM should precede succinylcholine.

Maintenance, emergence from anesthesia, and appropriate postoperative care of the general pediatric patient are dependent on the particular procedure and the patient's condition. With a higher risk for pressure-related injuries, it is beneficial to enlist the help of operating room nursing staff and surgical team in assessing the patient's position. If possible, intermittent and gentle repositioning of the head and limbs can help to decrease pressure during particularly long surgeries. Maintaining normothermia is also more challenging in the pediatric patient for a variety of reasons. The different anatomic and physiologic reasons behind this are discussed in detail in Chap. 47. Briefly, children have a larger body surface area to mass ratio and a relatively large head, and the head is usually fully exposed and wet during neurosurgical procedures. The exposed and anesthetized child is particularly vulnerable to hypothermia; thus, consideration should be given to raise ambient temperature, to use heating lamps and forced air warmers, and to minimize positioning and site prep time in order to drape the patient in a timely manner.

Emergence from anesthesia is a high-risk period for any patient, but the pediatric patient in particular must be watched for residual neuromuscular blockade, apnea, bronchospasm, and laryngospasm. It is worthwhile remembering that respiratory events are directly or indirectly responsible for the bulk of perioperative complications in children. Appropriate postoperative care of the general pediatric patient will depend on what procedure was performed, institutional practices, and patient-specific concerns. The specifics are beyond the scope of this chapter, but any receiving unit will need to be comfortable with assessing the airway, evaluating pain, recognizing delirium, and responding to the needs of recovery by administering medications, enlisting help of parents, or calling for the assistance of a qualified provider.

Implications for the Neurosurgical Patient

Preoperative Assessment of the Pediatric Neurosurgical Patient

In addition to the general pediatric preoperative evaluation, there should be particular emphasis on intracranial perfusion and pre-existing neurologic deficits in the pediatric neurosurgical patient. Documentation of the preexisting neurologic deficits and the child's developmental level will help with postoperative assessment. Patients with intracranial hypertension can have decreased levels of consciousness and carry a higher risk of complications from preoperative sedation, aspiration during induction, and delayed emergence. Lastly, the hydration status should be assessed prior to administering anesthetic agents that can cause hypotension and decrease cerebral blood flow (CBF) (Tables 53.3 and 53.5).

No specific laboratory tests are required for pediatric neurosurgical patients. However, measuring preoperative electrolytes may be important in children with a history of vomiting or the use of osmotic diuretics. Platelet number or coagulation studies may be affected by the use of some antiepileptic medications or a ketogenic diet. In general, risk for blood loss should be discussed preoperatively, and type and cross-matched blood should be available for high-risk cases such as open craniosynostosis repair.

Children with a history of chronic steroid treatment or replacement (hypopituitarism) may benefit from intraoperative replacement of stress dose steroid (1–2 mg/kg of hydrocortisone [Solu-Cortef] IM/IV or an equivalent dose of dexamethasone IV [0.05–0.1 mg/kg]). More than 3 weeks of exogenous corticosteroid therapy (>20 mg/day prednisone or equivalent) can produce measurable suppression and inability to mount a stress response for up to a year.

Table 53.3 Preoperative assessment of the pediatric neurosurgical patient

Assessment	Rationale
Presence of neurologic deficits	Determine a change in postoperative period
Developmental level	Appropriate induction techiques, anticipate recovery needs
Presence of elevated ICP	Cerebral perfusion, vomiting
Congenital abnormalities	Airway difficulty, SBE risk, embolism risk
Hydration status	Risk of hypotension, reduction of CPP
Use of diuretics or osmotic agents	Effect on volume status or electrolytes
Use of antiepileptic medications	Effect on platelets or coagulation factors, effect of large blood loss on blood levels, need for immediate postoperative continuation

CPP cerebral perfusion pressure, *ICP* intracranial pressure, *SBE* subacute bacterial endocarditis

Preoperative Pediatric Neurosurgical Sedation

Oversedation can lead to respiratory depression, hypercarbia, hypoxia, and resultant increases in ICP. Sedative premedications should never be given to children with symptomatic intracranial hypertension or central nervous system depression, unless directly monitored by the anesthesiologist. Calm reassurance or parental presence through the time of induction may be the better approach for such children.

Preparation of the Pediatric Neurosurgical Operating Room

If warranted for the specific patient and procedure, equipment for ICP monitoring, for detection of venous air embolism (VAE), and for evoked potentials may be needed. Mannitol and hypertonic solutions may be needed. Blood products may need to be in the room if large or sudden blood loss is likely.

Induction of Pediatric Neurosurgical Anesthesia

In children with intracranial hypertension, the goals of induction are protection of the airway, hemodynamic stability, and maintenance of cerebral perfusion. Maintaining hemodynamic stability during induction will entail frequent measurement of blood pressure, calculation of cerebral perfusion pressure (CPP) if ICP monitoring is available, careful titration of anesthetic agents, and the availability of appropriately diluted vasoactive drugs to tightly control blood pressure. Typical medications for intravenous induction are listed in Table 53.4.

A rapid-sequence induction should be performed for patients with a decreased level of consciousness or other risk factors for aspiration. When the rapid-sequence induction technique is used, increases in ICP will occur if hypoventilation is prolonged and hypercarbia develops. Lidocaine IV, 1 mg/kg, is an additional adjunct to laryngoscopy that is tolerated well in children to prevent ICP increases during laryngoscopy or suctioning of the trachea. Lidocaine works best if given 2–3 min before laryngoscopy.

If an inhalational induction is chosen when there may be a risk of elevated ICP, then slight hyperventilation can be used to help counter the cerebral vasodilatory properties of sevoflurane.

The use of intramuscular ketamine for induction of uncooperative children should be avoided when intracranial hypertension is a concern because it may increase cerebral metabolism, CBF, and ICP. These concerns are based on case reports and small studies, where ventilation may not have been controlled. There is emerging evidence in patients with traumatic brain injury that ketamine (as a component of sedation) does not negatively impact ICP and may in fact have neuroprotective properties. These benefits may come in part from ketamine's hemodynamic stability (assuming the patient is not catecholamine depleted) and subsequent protective effects on areas of the brain at risk for ischemic injury. It is important to know that there have been no high-quality studies on children to investigate the effects of ketamine for anesthetic *induction* on ICP.

Maintenance of Pediatric Neurosurgical Anesthesia

No single anesthetic technique has been shown to be superior for maintenance of anesthesia for children undergoing neurosurgery. The most important factor in choosing an anesthetic technique is to understand the pharmacokinetics of the agents, the effects of the agents on ICP and CBF (Table 53.5), and the needs of the surgical procedure.

Factors considered in the choice of anesthetics for the maintenance of anesthesia include impact on neuromonitoring, ability to titrate to rapid emergence, requirements of the specific surgical procedure, and cost. The volatile anesthetics isoflurane and sevoflurane vary in their use for induction, cost, rapidity of emergence, cerebral vasodilation, and auto-

Table 53.4 Pediatric induction drug dosages

Type of induction agent	Drug	IV dosage	Notes
Sedative/hypnotic	Propofol	2–4 mg/kg	Titrate to avoid systemic and cerebral hypotension
Blunt hyperdynamic response	Fentanyl	1–5 mcg/kg	Support ventilation and BP
	Lidocaine	1 mg/kg	2–3 min prior to laryngoscopy
Paralysis	Vecuronium	0.1 mg/kg	
Paralysis for rapid-sequence induction	Rocuronium	1.2 mg/kg	
	Succinylcholine	1–2 mg/kg	Consider contraindications
Vasoactive drugs to treat changes in CPP	Phenylephrine	3–10 mcg/kg	Titrate to effect
	Sevoflurane	1–2%	

Table 53.5 Cerebral effects of anesthetic agents

Drug	CBF	$CMRO_2$	ICP	Autoregulation
Propofol	↓↓	↓↓	↓↓	Preserved
Opioids	↔	↔	↔	Preserved
Thiopental	↓↓	↓↓	↓↓	Preserved
Dexmedetomidine	↓	↓	↓/↔	Preserved
Benzodiazepines	↓	↓↓	↓	Preserved
Ketamine	↑↑	↔	↑↑	Unknown
N_2O	↑	↔ or ↑	↑	Preserved
Sevoflurane	↑	↓↓	↑	Abolished[a]
Isoflurane	↑	↓↓	↑	Abolished[a]
Desflurane	↑	↓↓	↑	Abolished[a]
Halothane	↑↑	↓	↑	Abolished

↑, increase; ↑↑, significant increase; ↔, no change; ↓, decrease; ↓↓, significant decrease; *CBF* cerebral blood flow, $CMRO_2$ cerebral metabolic rate, ICP intracranial pressure, *N_2O* nitrous oxide
[a]Abolished in a dose-dependent fashion

regulation effect. Recent literature suggests that sevoflurane may lead to better preservation of CBF and autoregulation than isoflurane and, especially, desflurane. Nitrous oxide is an adjunct that may help speed induction and emergence. The use of nitrous oxide varies upon the user's experience with its effect on evoked potentials and upon the risk for expanding pneumocephaly or VAE.

Propofol can help preserve evoked potentials but may need to be titrated as the length of the case progresses because accumulation can lead to loss of signals. Because of concerns for propofol infusion syndrome, a continuous infusion should be limited to less than 6 h in children. Furthermore, the clinical duration of propofol after infusion is difficult to gauge if a wake-up test or rapid emergence is planned.

The short-acting opioids fentanyl and remifentanil are commonly employed during pediatric neurosurgery. The rapid metabolism of remifentanil aids rapid emergence, but experience is helpful in knowing when and how to add longer-acting opioids for postoperative pain relief. The greater cost of remifentanil is also a consideration.

Paralytics are often used to eliminate motion during surgery, prevent injury to patients in head pins, and allow low-dose anesthetic administration when critical for monitoring. Avoidance of paralytics may be needed if motor-evoked potentials are being used.

Antiemetics may be administered intraoperatively to reduce the risk of postoperative nausea and vomiting, which may exacerbate any elevated ICP. Ondansetron is an effective antiemetic with minimal side effects in children and can be given as 0.15 mg/kg IV, 30 min before emergence. Dexamethasone is also used in children for antiemetic effects and may also be requested by the neurosurgeons to minimize vasogenic edema from operative manipulation. Dexamethasone has been found to have antiemetic properties in doses of 0.0625–1.0 mg/kg IV, with some studies showing low doses as effective as high.

Specific pediatric neurosurgical procedures may have specific intraoperative needs and are discussed in Sect. 4.2.

Pain Management for Pediatric Neurosurgical Procedures

Scalp incisions, even for minimally invasive neurosurgical procedures, cause postoperative pain. Commonly, parenteral opiates are used intraoperatively and postoperatively. However, acetaminophen and NSAIDs have fewer effects on neurologic examination, less respiratory depression, and may be useful alone or as adjunct to opiates. The potential for bleeding or short-term renal dysfunction in children with renal insufficiency should be considered with NSAIDS. Typical postoperative analgesia pediatric dosages are listed in Table 53.6.

Scalp blocks may be used for supplemental analgesia of excisions of the scalp. These blocks usually need to be performed while children are anesthetized, and total dosages of local anesthetic need to be monitored to avoid neurologic or cardiovascular toxicity. Maximum recommended doses of commonly used local anesthetics include 7 mg/kg of lido-

Table 53.6 Pediatric analgesic dosages

Analgesic	Dosage	Notes
Acetaminophen (oral/IV)	10–15 mg/kg Q4-6h	Max: 75 mg/kg/24 h.; 60 mg/kg/24 h. in neonates; consult pharmacy for premature neonates
Acetaminophen (rectal)	30–40 mg/kg PR loading dose, then 20 mg/kg PR every 6 h	Max: 75 mg/kg/24 h.; 60 mg/kg/24 h. in neonates; neonates should receive Q12h dosing
Morphine	0.025–0.1 mg/kg increments IV in children >2 months of age	Half-life 2 ± 1.8 h after ~2 months of age
Hydromorphone	15–30 mcg/kg IV q 3 h	
	30–80 mcg/kg PO/PR q 3 h	
Fentanyl	0.5–1 mcg/kg IV	
Oxycodone	0.05–0.15 mg/kg PO	
Hydrocodone	0.05–0.15 mg/kg PO	
Morphine PCA	10–20 mcg/kg/dose, lock out 8–15 min, basal 0–30 mcg/kg/h, 250–400 mcg/kg 4 h limit	
Hydromorphone PCA	2–4 mcg/kg/dose, lock out 8–15 min, basal 0–5 mcg/kg/h, 50–80 mcg/kg 4 h limit	
Fentanyl PCA	0.5 mcg/kg/dose, lock out 6–10 min, basal 0–0.5 mcg/kg/h, 7–10 mcg/kg 4 h limit	

caine with epinephrine, 2.5 mg/kg of bupivacaine, and 3 mg/kg of ropivacaine; maximum doses should be decreased by 30% in infants younger than 6 months. Epinephrine is often included as a vascular marker because of the toxicity risk associated with inadvertent intravascular administration.

Supraorbital and supratrochlear nerve blocks provide analgesia of the anterior forehead and scalp, from the bridge of the nose to the apex of the head. Occipital nerve blocks provide analgesia to the occipital and temporal regions of the scalp, from the nuchal line to the apex of the head. Both blocks are easy to perform. The reader is directed to a textbook of pediatric regional anesthesia for further discussion of the technique of these blocks.

Postoperative Pediatric Neurosurgical Management

The recovery rooms or intensive care units responsible for children recovering from a neurosurgical procedure should have the same pediatric capabilities mentioned in Table 53.2. In addition to being familiar with pediatric respiratory and hemodynamic physiology, the staff needs to be familiar with the pediatric neurologic examination. Units taking care of children should be familiar with weight-based dosing for patients less than 40 kg and with pediatric advanced life support for patients less than 12 years (intraosseous access technique, appropriate defibrillator paddles, etc.).

Because of the sensitivity of children to pain medications, titration of medications is recommended to avoid hypotension and hypoventilation. The same basic goals of avoiding hypotension, hypoxia, hypoventilation, hyper- or hypoglycemia, and hypo- or hyperthermia apply. The staff needs to be aware that even without neurologic problems, neonates are at risk for periodic breathing and hypoventilation/hypoxia in the postanesthetic period. Children with adenotonsillar hypertrophy or congenital airway anomalies are at risk for postoperative obstructive apnea.

It is especially important for the postanesthetic staff to know the preoperative neurologic findings and the developmental level of the patient because postoperative neurologic changes may require immediate investigation and intervention. Depending on the procedure, the postoperative patient may also need to be closely monitored for sequelae of cranial nerve injury, especially injury to cranial nerves IX, X, and XII, as these can impair a patient's ability to protect his/her airway. Some abnormalities may be age appropriate such as Babinski reflexes, Moro reflexes, asymmetric tonic neck reflexes, and clonus in very young children. Additionally, a description of typical seizure patterns can be helpful to the postanesthetic care staff for recognition and appropriate response to postprocedure seizures. The postoperative neurologic examination in an ICU setting needs to be recorded serially and at regular intervals with age-appropriate measures so that subsequent examiners can review for changes in examination.

In addition to close neurologic monitoring, the postoperative staff should watch for related complications (such as fluid and electrolyte disturbances) and act proactively to prevent subsequent problems. Children need to have weight-based fluid administration and depending on age and health may need to have glucose added. The same postoperative disturbances in volume and sodium status that occur in adults can occur in children, such as syndrome of inappropriate antidiuretic hormone (SIADH), diabetes insipidus, or cerebral salt wasting. A common pediatric postoperative complication is hyponatremic seizures in a child who is NPO, having continuous CSF drained by ventriculostomy, and whose maintenance fluid only contains one-quarter normal saline.

Concerns and Risks

Preoperative Management

The hydration status should be assessed prior to administering anesthetic agents that can cause hypotension and decrease CBF. NPO guidelines must be followed (Table 53.7). If significant dehydration is a concern, preoperative intravenous hydration may be necessary.

Pediatric Intraoperative Cerebral Resuscitation

The same general guidelines for cerebral resuscitation apply to children and adults. Hypotension and hypoxemia have been shown to have a negative effect on the outcome of children with neurologic injury. Other general factors may have an impact on outcome and should be considered in the intraoperative management: avoid hyperthermia, seizures, and hypo- or hyperglycemia. Specific responses to concerns about brain edema are included in Table 53.8. It should be noted that while ICP may fall when the dura is open, brain swelling may continue during this time.

Table 53.7 Pediatric NPO guidelines

Solids (including Infant formula)	6 h
Breast milk	4 h
Clear liquids	2 h

Table 53.8 Methodologies to reduce or prevent cerebral edema

Promote venous drainage
Head elevation
Note: increased risk for VAE if burr holes or craniotomy underway
Head midline
Reduces venous outflow obstruction but may not be possible for surgical positioning
Minimize intrathoracic pressure (i.e., avoid excessive PEEP, allow adequate exhalation time)
CPP maintenance – age appropriate
No guidelines exist for a minimum CPP in children, either under anesthesia or not
Note: One study in healthy infants found that the lower limit of autoregulation was at 38 mmHg or more than 20% deviation from baseline. Another study observed postoperative intracranial hypertension in children with severe traumatic brain injury (TBI) (with ICP monitors) when CPP fell below 40 mmHg
Maintain adequate age-appropriate mean arterial pressure (MAP)
Note: Ideal blood pressure goals for children with brain injury are unknown. Some investigations have examined the use of cerebral near-infrared spectroscopy (NIRS) or transcranial Doppler (TCD) in concert with blood pressure monitoring to aid in maintaining the patient within the range of autoregulation
Minimize ICP
Hyperventilation
Avoiding hypoventilation is prudent ($PaCO_2$ 35–40 mmHg)
Mild hyperventilation with problematic ICP/edema management ($PaCO_2$ 30–35 mmHg)
More aggressive hyperventilation ($PaCO_2 < 30$ mmHg) has risks, and if needed for a prolonged period, monitoring of SjO_2, PbO_2, or CBF is suggested
Osmolar therapy
Mannitol
0.25–1 g/kg raises serum osmolarity by 10–20 mOsm/L
Furosemide
1 mg/kg
Hypertonic saline
12 cc/kg of 3% NaCl should raise serum Na 10 mEq/L and serum osmolarity by 20 mOsm/L
Urine output measurement.
Urinary catheter helps monitor diuresis caused by diuretic agents, and CVP helps monitor volume status, while increasing osmolarity may decrease edema, hypotension may decrease CBF and reduce CPP, volume shifts in children may be more dramatic than in adults
Barbiturate
Useful to reduce ICP/edema by cerebral vasoconstriction and reduction in $CMRO_2$
May impair neurologic examination and emergence from anesthesia
Dexamethasone
Useful for peri-tumor or peri-abscess vasogenic edema
Unclear if useful for vasogenic edema secondary to surgical manipulation
Not useful for traumatic edema
Complications include hyperglycemia and hypertension
Hypothermia
May reduce ICP/edema by reducing $CMRO_2$
Unclear if improves outcome from traumatic injuries
CSF drainage
May be useful when shunt or ventricular drain is available

Key Points

- Sedative premedications increase risk when given to children with symptomatic intracranial hypertension or central nervous system depression.
- Succinylcholine should be avoided in children, except in situations of emergent airway management.
- The choice of inhalation versus intravenous induction depends on several factors. Most importantly, patients with full stomachs, loss of airway reflexes, vomiting, intracranial hypertension, decreased level of consciousness, or severe illness are best induced with a balanced technique of intravenous drugs.
- No single anesthetic technique has been shown to be superior for maintenance of anesthesia for children undergoing neurosurgery. The most important factor in choosing an anesthetic technique is to understand the effects of the agents on ICP and CBF, intraoperative monitoring, rapidity of emergence, and the needs of the surgical procedure.
- It is imperative that the anesthesiologist is aware of the methodologies to reduce or prevent cerebral edema preoperatively, intraoperatively, and postoperatively.

Suggested Reading

Chang LC, Raty SR, Ortiz J, Bailard NS, Mathew SJ. The emerging use of ketamine for anesthesia and sedation in traumatic brain injuries. CNS Neurosci Ther. 2013;19(6):390–5.

Dinsmore J. Anaesthesia for elective neurosurgery. Br J Anaesth. 2007;99(1):68–74.

Drummond JC, Dao AV, Roth DM, Cheng CR, Atwater BI, Minokadeh A, Pasco LC, Patel PM. Effect of dexmedetomidine on cerebral blood flow velocity, cerebral metabolic rate, and carbon dioxide response in normal humans. Anesthesiology. 2008;108:225–32.

Hammer GB, Krane EJ. Perioperative care of the neurosurgical pediatric patient. Int Anesthesiol Clin. 1996;34(4):55–71.

McAuliffe G, Bissonnette B, Boutin C. Should the routine use of atropine before succinylcholine in children be reconsidered? Can J Anaesth. 1995;42(8):724–9.

McClain CD, Soriano SG. Anesthesia for intracranial surgery in infants and children. Curr Opin Anaesthesiol. 2014;27(5):465–9.

McClain CD, Soriano SG, Rockoff MA. Pediatric neurosurgical anesthesia. In: Cote CJ, Lerman J, Todres ID, editors. A practice of anesthesia for infants and children. 4th ed. Philadelphia: Saunders Elsevier; 2009. p. 509–34.

Soriano SG, Bozza P. Anesthesia for epilepsy surgery in children. Childs Nerv Syst. 2006;22(8):834–43.

Soriano SG, Eldredge EA, Rockoff MA. Pediatric neuroanesthesia. Neuroimaging Clin N Am. 2007;17(2):259–67.

Williams M, Lee JK. Intraoperative blood pressure and cerebral perfusion: strategies to clarify hemodynamic goals. Pediatr Anesth. 2014;24(7):657–67.

The Pediatric Airway in Neurosurgery

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Debra Elayne Morrison and Zeev N. Kain

Overview

Characteristics of the Pediatric Airway

The pediatric airway is characterized by smaller size and developmental anatomical differences.

1. *Smaller size* implies increased likelihood of soft tissue obstruction and resistance to airflow, especially if edema is present, as well as less technology available for airway management. Smaller size also necessitates a more subtle technique and predicates more immediate and disastrous consequences for failure to manage the airway:
   - Rapid desaturation with bradycardia
   - Laryngospasm
   - Distention of the stomach with mask ventilation, making it difficult to expand the lungs
2. *Developmental differences* include:
   - Relatively large occiput, which influences positioning
   - More pliable and collapsible tissue
   - Likely presence of relatively larger tongue and larger tonsils and adenoids, which contribute to airway obstruction
   - A more cephalad larynx, which usually makes a straight laryngoscope blade more practical
   - A shorter, narrower, and angled epiglottis, which can often be difficult to lift with a laryngoscope blade
   - The possibility of transitioning dentistry (unanticipated loose teeth)

The airway examination is mostly external, including the entire head and neck, and historical (previous anesthetic records, if existing) and is either normal or probably abnormal, based on suspected or known syndrome or diagnosis. Some pediatric patients who appear to be normal can be difficult to intubate.

Ventilation

The most effective technique for pediatric *mask ventilation*:

1. Gently place the mask below the lips over the *open* mouth and at the bridge of the nose with the thumb and forefinger using just enough pressure to create a seal.
2. The fourth and/or fifth fingers should grasp the angle of the mandible and gently pull the jaw upward into the mask (if fourth finger is on the mandible, spare fifth finger can also be used to manipulate the cricoid cartilage).
3. The middle finger should be free or touching only the bony portion of the mandible to avoid compression of midline soft tissue.
4. Care should be exercised to keep the middle finger away from the midline soft tissue and to avoid pressure on the mandible that forces the mouth to close.
5. A small roll may be placed under the shoulders to compensate for the large occiput, which may be stabilized by a small gel donut, or the entire body excluding the head may be elevated on a pad.
6. Gentle continuous positive airway pressure (CPAP) can be used to distend the pharynx and larynx during spontaneous or assisted ventilation while maintaining low peak inspiratory pressures (at no more than 15 cm H_2O) to avoid gastric distension.
7. Use of CPAP is preferable instead of an oral airway, since an oral airway, especially one of the wrong size, can compress or distort the anatomy and cause obstruction, trauma, or laryngospasm.
8. A lubricated nasal trumpet (if not contraindicated by choanal atresia, coagulopathy, neutropenia, or basilar skull fracture) approximately the diameter of the nasal opening can also be used to relieve airway obstruction during mask ventilation.

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9. If mask ventilation is at all difficult despite simple maneuvers, it is best to move on rather than to waste time struggling.
10. The patient with uncorrected meningomyelocele can be elevated above the table for induction and intubation with a donut around the "cele," a large roll under the shoulders, and support for the head adequate to maintain normal alignment of head and neck.

Alternative Methods of Ventilation if Difficult Mask

An appropriately sized, thermosoftened, *lubricated endotracheal tube (ETT)* placed nasally (if not contraindicated) can be used in lieu of mask ventilation.

The adult nasal passage can be vasoconstricted to minimize potential bleeding which could make fiber-optic intubation more problematic. It is hard to approximate a correct pediatric dose of nasal decongestant spray or to quickly dilute Neo-Synephrine; thus, it is imperative that nasal ETT be placed with minimal trauma.

1. Use a suction catheter as an ETT stylet positioned just past the distal tip of the standard ETT to blunt the edges of the ETT and lubricate the distal tip with water-soluble gel before insertion. A 6 F suction catheter fits in a 2.5 ETT, an 8 F fits in a 3.0 ETT, a 10 F fits in 3.5–4.5 ETT, and a 14 F catheter fits in larger ETTs.
2. Introduce ETT nasally just past the nasal passage and then (after optional suctioning) remove the suction catheter, leaving ETT in place.
3. Other techniques have been described using an esophageal stethoscope as stylet (works only in ETT sizes 4.5 and larger) or a red rubber catheter placed over the ETT tip, but the esophageal stethoscope method is more elaborate, and the red rubber catheter is made of latex.
4. A wire-reinforced ETT has a softer, symmetrical tip and may be less traumatic than a standard ETT, although thicker walls result in a smaller lumen for a given external diameter. A wire-reinforced ETT may not require a suction catheter to minimize mucosal trauma.
5. A Parker Flex-Tip™ tracheal tube, which comes in sizes 2.5 and larger, can be placed with less trauma to the naris.
6. Gently occlude both mouth and other naris, by laying a flattened hand over the mouth and using the forefinger to pinch the other naris, attach circuit, and ventilate.
7. If using lidocaine 1% to blunt response to intubation, use maximum of 1–2 mg/kg.
8. If considering use of phenylephrine 0.25%, use no more than 1–2 drops and maintain blood pressure at baseline with systemic vasodilation.
9. Nasal ETT should be positioned to avoid pressure-induced ischemia of the nasal ala.

A lubricated (with water-soluble surgical gel, not local anesthetic) *laryngeal mask airway* (LMA), such as either Dr. Brain's LMA Classic™ (best fit) or Dr. Cook's Air-Q™ (wide barrel), can also be used in lieu of mask ventilation and can be removed and replaced repeatedly. New LMA models continue to be developed.

Both the nasal ETT and the LMA, with attached *double swivel connector with port* (DSC), can be used to introduce a small fiber-optic bronchoscope (FOB) without interruption of monitored oxygenation and ventilation.

Using either of these devices for ventilation and intubation allows easy ventilation even with the patient in a more upright position allowing compensation for increased intracranial pressure with the added benefit of allowing the epiglottis to fall forward away from the glottic opening to enhance exposure of the vocal cords during fiber-optic intubation.

Intubation

1. The *correct size of the ETT* is traditionally estimated for patients over 1 year by Cole's formula: internal tube diameter (mm) = (16 + age in years)/4, but age does not always correlate with size, so the correct-sized ETT is usually about the same diameter as the tip of the child's fifth finger.
2. A slightly smaller high-volume low-pressure low-cuffed ETT can be used, inflating the cuff just enough, if at all, to minimize the leak appropriately.

In the normal pediatric airway, the *straight laryngoscope blade* should be inserted midline, approximately perpendicular to the patient, into the vallecula or used directly to lift the epiglottis to expose the vocal cords. Although the straight blade is the traditional blade, the Mac 2 blade, used in the normal manner or used to lift the epiglottis in the same manner as the straight blade, also works very well in many children greater than 1 year.

Grasp the laryngoscope handle close to or even partially on the blade (across the connection between handle and blade) rather than in the middle or toward the end farthest from the blade for better control.

1. If there is a good view of the vocal cords but the approach is difficult and the patient is large enough to accommodate a 3.0 or larger ETT, have an assistant discard the stylet and insert a *Cook Frova® intubating introducer* (bougie) several centimeters past the tip of the ETT.
2. Pinching the ETT tight to the bougie to prevent slippage, introduce the bougie through the vocal cords, and then slide the ETT over it into the trachea, all in one motion.
3. The bougie can alternatively be inserted without the ETT, even down the "barrel" of the blade, without obscuring the view of the vocal cords, but the bougie's adaptor must

first be removed to allow the ETT to be placed over the proximal end of the bougie.

4. Another method of introducing the ETT when the view of the vocal cords is acceptable but the approach is difficult is to have a second operator deliver the ETT via FOB of appropriate size (and there is even a size which will pass through a 2.5 ETT) to and through the vocal cords while the laryngoscopist is exposing the anatomy.

If the vocal cords cannot be seen with a conventional laryngoscope, there are some simple alternative strategies for which equipment is available.

Light-Assisted Blind Intubation

The Trachlight™ stylet and tracheal lightwand come in two sizes, the smaller of which fits through ETT sizes 2.5–4.0 and the larger of which fits through ETT sizes 4.5 and above. The device, a malleable wire in a PVC sheath, attached to a reusable light handle, can aid in blind oral or nasal intubations.

Fiber-Optic Oral Approach Through LMA

1. First, determine whether the appropriate-sized ETT can be inserted through an LMA that fits well and pulled all the way through the distal (cuff) end of the LMA. Cutting off the proximal tip of the ETT will make it pass more easily and will not prevent replacing the ETT connector.
2. Insert LMA, inflate cuff, and demonstrate good $ETCO_2$ waveform.
3. Attach DSC to the LMA and place patient on positive pressure ventilation with low peak inspiratory pressure, monitoring $ETCO_2$ via the normal elbow left connected between the DSC and the circuit.
4. Remove connector from an appropriate-sized ETT and slide the ETT to the top (proximal end) of an appropriate-sized FOB.
5. Introduce the FOB through the open port of the DSC, down the LMA (through the center of the grid if there is a grid), and through the vocal cords to just above the carina.
6. Disconnect the DSC from the LMA and slide it up over the ETT to the top of the FOB. (With the Air-Q™, the LMA connector can also be disconnected, but this must be done before the FOB is introduced, preventing the achievement of a seal between the DSC and the LMA.)
7. Slide the ETT down over the FOB until its top is level with the top of the LMA, at which point the tip will be past the vocal cords.
8. Leaving the FOB in place past the vocal cords, the LMA can now also be slid up over the ETT to the proximal end of the FOB, leaving the FOB and the ETT in place, unencumbered. Leaving the FOB is probably the safest approach, but it delays attaching the ETT connector and delivering a breath, especially if FOB fits snugly into the ETT. This is my preferred approach if it can be done quickly.
9. The ETT can now be positioned optimally and the FOB withdrawn.
10. Alternatively, after the ETT top (proximal end) has been placed level with the top of the LMA, the FOB can be withdrawn. The ETT connector can be temporarily attached, and a breath can be delivered at this point.
11. Grasp the ETT with small tipped long grasping forceps (from pediatric ENT tray or cart) and hold it in place while sliding the LMA up over the forceps, then open the forceps, and remove them with the LMA.
12. If no small tipped long grasping forceps is available, a second ETT of equal size can be inserted into the first ETT after FOB is withdrawn to temporarily create a single long ETT over which the LMA can be withdrawn. The second ETT is removed after the LMA is removed.
13. Attach the ETT connector, attach to the circuit, and confirm that the ETT is appropriately placed in the trachea.
14. Alternatively, the LMA could be left in place during surgery if the risk of removing it (dislocation of ETT) outweighs the benefit.
15. Practice this technique in advance on a manikin. It is helpful to have a second pair of hands.

Fiber-Optic Nasal Approach

1. The nasal approach to the airway is often the more direct approach in a pediatric patient.
2. Once an appropriate-sized ETT is placed nasally just past the nasopharynx, as described above, occlude the other naris and the mouth and attach a DSC to the ETT.
3. Place patient on low positive pressure ventilation or allow patient to breathe spontaneously. Sedation or general anesthesia is possible with sevoflurane and/or intravenous propofol, with $ETCO_2$ monitoring.
4. Introduce the lightly lubricated FOB through the port of the DSC, down the ETT, and through the vocal cords to just above the carina.
5. Slide the ETT down the FOB through the vocal cords, remove the FOB, and confirm that the ETT is appropriately placed in the trachea.

"Fastrach™" Approximation (Blind, $ETCO_2$ Guided)

1. Insert LMA, inflate cuff, attach circuit to LMA, and demonstrate excellent $ETCO_2$ waveform, which suggests good position proximal to vocal cords.
2. Attach circuit to ETT and watch $ETCO_2$ waveform during either spontaneous ventilation or low positive pressure ventilation as ETT is advanced through LMA and then through vocal cords.
3. If no muscle relaxant has been used, whether patient is breathing spontaneously or on low positive pressure ventilation, and $ETCO_2$ waveform disappears, retract ETT slightly.

4. If $ETCO_2$ waveform does not return with retraction, consider laryngospasm, treat, and advance with $ETCO_2$ waveform as it returns.
5. If $ETCO_2$ waveform does return with initial retraction of the ETT, the LMA is probably not directing the ETT toward the vocal cords. Reposition LMA and reattempt or change technique.

Video Laryngoscope and Pediatric GlideScope

1. The Storz® video laryngoscope has a Miller 0 and a Miller 1 blade and can be used to intubate a smaller infant or child. The view in the fairly large screen is from the distal tip of the blade, not the proximal end.
2. Storz has also introduced the C-MAC® which consists of a laryngoscope that attaches directly to a portable LCD screen via a single cable. Everything needed is built directly into these two components, and there are no fragile fiber-optic bundles. It is cheaper and has two associated pediatric blades, but they are bulkier than their video laryngoscope blades.
3. The Verathon® GlideScope's curved disposable blade covers fit over a small pediatric wand which is part of a separate cable, comes in four neonatal/pediatric sizes, and can be used to intubate infants or children. The view in the screen is from the distal tip of the blade, not the proximal end. The GlideScope blade can be partially inserted in order to view the vocal cords of a patient who is smaller or has a more anterior larynx. Pediatric GlideScope handles come in more than one style and can also be reusable (without disposable covers). The pediatric GlideScope stylet, unlike the adult stylet, is too flexible to reliable maintain its shape.
4. All three devices enable the vocal cords to be visualized easily, but the blade must be manipulated to place the vocal cords in the center of the screen so that the ETT, bougie, or ETT-over-bougie (or lightwand) can approach the vocal cords.
5. If the vocal cords appear high or to the left of the screen, the blade should be withdrawn slightly and lifted, dropping the tip, not "cocking" the tip, and enabling the vocal cords to drop lower into view.
6. The blade must be utilized such that the larynx is tilted with the arytenoids and interarytenoid fold more distal to the operator so that the ETT does not slip behind the fold into the esophagus.

Video Laryngoscope or Pediatric GlideScope with FOB

1. If, despite manipulation of the blade, the tube cannot be made to approach the vocal cords, or the stylet shape cannot be maintained, a second operator can introduce the ETT over an FOB, while the first operator is exposing the vocal cords with the video laryngoscope or GlideScope, as described above with the standard laryngoscope.

Implications for the Neurosurgical Patient

When the pediatric patient is a neurosurgical patient, implications include:

1. Urgency (intracranial hemorrhage)
2. Need to avoid stimulation or hemodynamic change during airway management (high ICP)
3. Need to avoid hypoventilation or apnea during airway management (rapid desaturation, high ICP)
4. Positioning issues such as known or possible spinal cord injury, meningomyelocele
5. The presence of a C-collar in a spine at risk of instability.
6. Specific requirement or contraindication for an oral vs. nasal vs. special ETT
   (a) Wire-reinforced tube might be necessary for an operation on the cervical spine when the position of the head may force the ETT to be compressed by the teeth or during a long operation where soft ETT may collapse (cranial synostosis) but would be contraindicated if the patient were anticipated to require an MRI.
   (b) Nasal ETT is less likely to be kinked or compressed during a long operation, thus making a standard ETT less hazardous in a patient who will require an MRI.
7. Possible full stomach and concerns regarding readiness for extubation.
8. Need for postoperative intubation (unstable, requiring another operation, or need to maintain prone position (meningomyelocele, sacrococcygeal teratoma)

In a worst-case scenario, consider a toddler patient with micrognathia who has fallen from a bed just after a meal and has diminished level of consciousness because of an intracranial bleed. The patient is a trauma patient, presumed full stomach, wearing a cervical collar (neck cannot be cleared), and requires an immediate operation. After preoxygenation, perform mask induction (if no IV – can place IV during spontaneous ventilation, although an IV is likely easily placed in a patient with diminished level of consciousness) or IV induction, briefly maintaining, if possible and appropriate, spontaneous ventilation. At this point, an orogastric tube can be placed, exiting at the corner of the mouth, and placed on suction; gentle cricoid pressure can, if desired, be utilized, and ventilation, if necessary, can proceed with mask, LMA, or nasal ETT. Intubation can proceed with or without paralysis. Remember that an LMA can always be replaced and used in lieu of a mask for ventilation, with or without a gastric tube (LMA can be placed alongside a gastric suction tube). The LMA ProSeal™ now comes in the full range of sizes, allowing a small gastric

suction device to be placed through the LMA. One of the techniques described above can enable establishment of a definitive airway. If a videolaryngoscope or GlideScope will be used to visualize the vocal cords, either can be introduced before the administration of muscle relaxant, to preserve spontaneous ventilation. Once a view of the vocal cords has been established, a small dose of succinylcholine will be sufficient to open the vocal cords long enough to allow passage of the ETT.

Another worst-case scenario is the autistic 3-year-old (strong enough to struggle) who was involved in an automobile collision on the way home from a fast-food restaurant. The mechanism placed him at risk for *spinal cord injury* even if plain films have been *without radiological abnormality* (SCIWORA). Although an IV and C-collar were placed initially, he has removed them both and is calm only when seated on his father's lap and not approached by medical professionals. He needs an MRI under anesthesia and arrives in the OR for induction prior to transport to MRI, again with a C-collar but still no IV, lying on top of his mother, who has a pelvic fracture and cannot be moved. Another (aluminum) gurney is obtained quickly. He is soothed by his mother while breathing nitrous oxide and oxygen, sufficient to allow IV placement and transfer to the other gurney, after which mother is wheeled out of the OR. He is then given a dose of propofol sufficient to stun him without at any time causing apnea. Low-dose sevoflurane is started. A small dose of muscle relaxant is given, after which the ETCO2 waveform is observed closely. As the waveform begins to diminish, signaling the onset of paralysis, the patient is quickly intubated with a video laryngoscope or GlideScope, leaving the C-collar in place. No positive pressure ventilation was delivered until after intubation; thus risk of aspiration was minimized, no apnea or desaturation ensued, there was no risk of laryngospasm, and the spine was not placed at risk. The patient was then safely transferred to MRI. He was kept sedated after the MRI until his neck was cleared, after which he was extubated awake.

A third worst-case scenario involves an understandably recalcitrant 13-year-old who was burned at the age of 3 years in another country and adopted by an American couple. She has undergone many, many operations and still refuses IV placement prior to induction. She has severe facial scarring, which limits her ability to open her mouth, and the distance between her upper and lower teeth is less than 1 cm. She is extremely difficult to mask, although it is possible to mask her with vigorous jaw lift and an oral airway. Her neck does not extend because of scarring. She was scheduled for z-plasties of her neck and grafting to relax the tight scars around her mouth. With the presence of her mother but without an anxiolytic (she refuses), an inhalation induction was performed. She was just maskable with the oral airway, as in prior anesthetics. A peripheral IV was placed, and a lubricated size 3 LMA Classic was placed by digitally lifting the jaw from under the lower teeth and alveolar bone. She was started on a propofol infusion to maintain adequate depth of anesthesia while the airway was not a closed system during airway management. A double swivel connector with port (DSC) was connected to the LMA and the normal elbow with $ETCO_2$ sample tube, and the port was opened completely. A 5.0 uncuffed endotracheal tube was loaded onto a FOB, which was inserted through the open port and advanced to the carina. The endotracheal tube was advanced, leaving the upper portion above the open port of the DSC. The DSC was then pulled to the top of the FOB. The LMA was then also pulled to the top of the FOB. The endotracheal tube was adjusted and temporarily secured. An 11 F Cook tube exchanger was then inserted into the 5.0 uncuffed endotracheal tube. The endotracheal tube was removed and replaced with a 5.5 cuffed endotracheal tube. Position of endotracheal tube was then adjusted, confirmed, and secured. The patient was safely intubated, without apnea or desaturation, for a procedure which lasted several hours (Figs. 54.1, 54.2, 54.3, 54.4, 54.5, 54.6, and 54.7).

Fig. 54.1 LMA inserted, cuff inflated, DSC attached to LMA, FOB with uncuffed ETT (connector detached) advanced through LMA past VC

Fig. 54.2 ETT passed down FOB through LMA with proximal end just above DSC

Fig. 54.4 LMA can now also be slid up over the ETT to the proximal end of the FOB, leaving the FOB and the ETT in place, unencumbered.

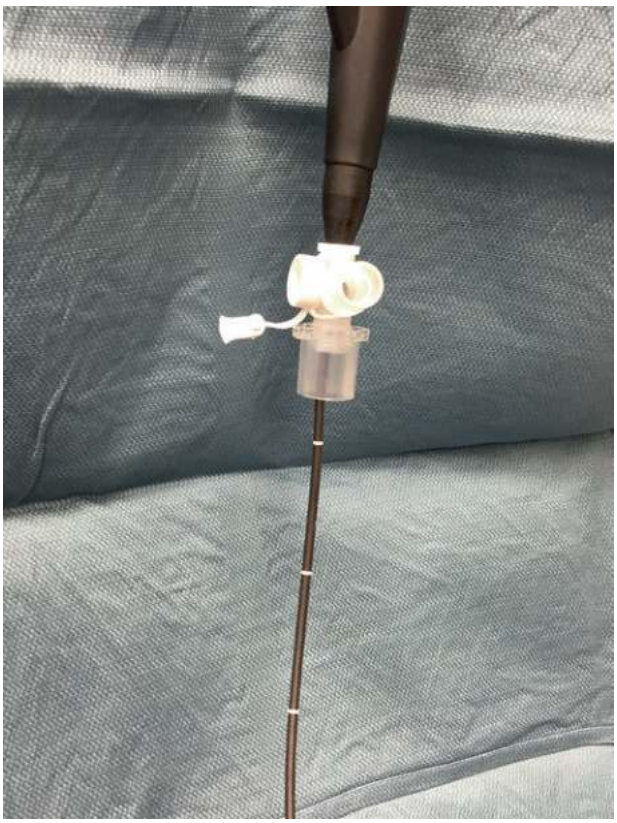

Fig. 54.3 DSC disconnected from the LMA and slid it up over the ETT to the top of the FOB

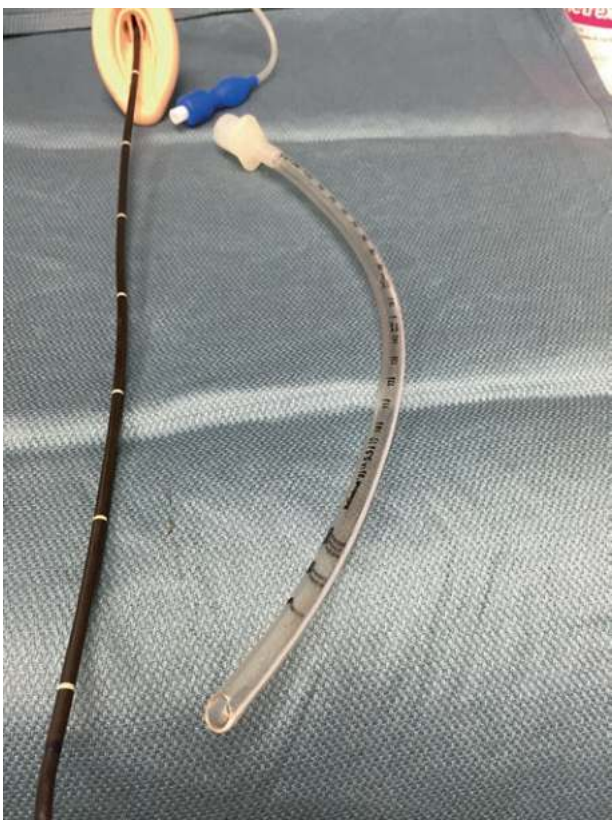

Fig. 54.5 FOB with LMA and DSC removed, leaving uncuffed LMA in place, attach connector and ventilate briefly

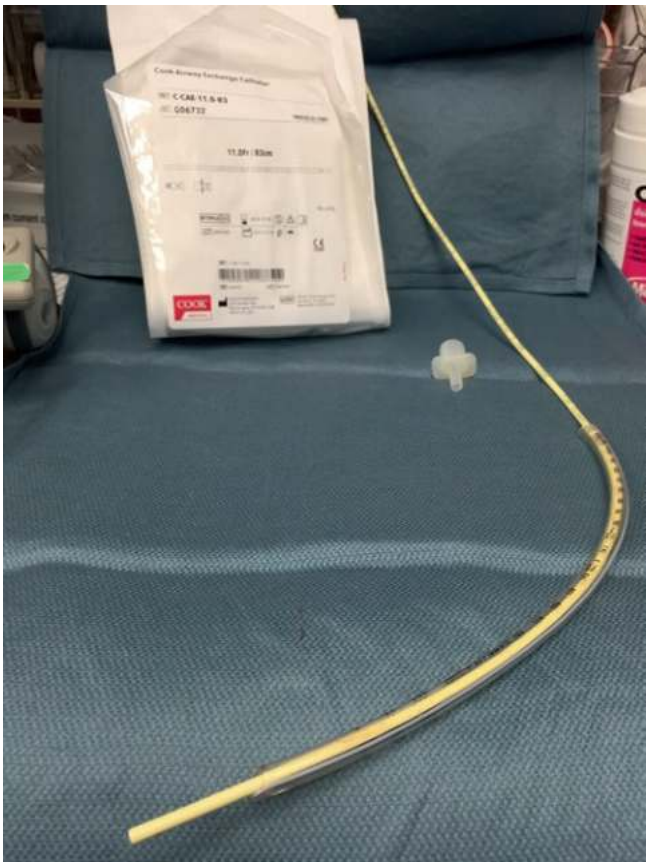

Fig. 54.6 Cook tube exchanger (11 F) passed through uncuffed ETT (connector detached)

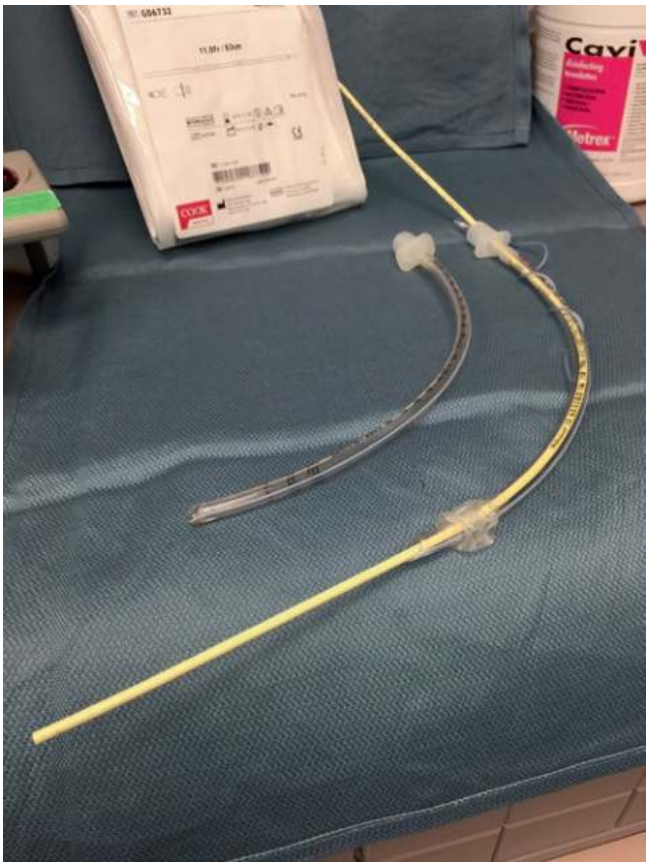

Fig. 54.7 Uncuffed ETT removed and replaced with cuffed ETT (connector detached and replaced after Cook tube exchanger removed)

Concerns and Risks

1. High oxygen flows may dilute $ETCO_2$ during mask ventilation, making it appear that ventilation is inadequate or that patient is being hyperventilated when this is not the case.
2. Low $ETCO_2$ waveform may also be caused by low cardiac output rather than by hyperventilation.
3. Positioning necessary for neurosurgical procedures can result in the ETT advancing to and stimulating the carina, advancing into the right main stem bronchus, withdrawing from the glottis, or being compressed by the teeth or gums. ETT position and patency should always be reconfirmed when the patient is in final position.
4. Insufflating the stomach with mask ventilation can lead to difficulty in ventilation and/or risk of aspiration.
5. An orogastric tube can be inserted and left in place during masking, before an LMA is placed, or through an LMA with a gastric vent.
6. Positioning necessary for neurosurgical procedures can increase the risk of accidental extubation. Prone position plus secretions can loosen tape. The weight of the ventilator tubing can pull out an ETT, especially when the head is resting on a frame instead of the bed (suspend the airway tubing or tie it to the Mayfield frame with umbilical ties to relieve weight/minimize effect of gravity). An ETT secured to the bed instead of to the frame can lead to accidental extubation when the patient is moved.
7. Regarding emergence and extubation, do not rely on a twitch monitor to determine whether or not a pediatric patient is reversible. Assume a patient's muscle relaxant is reversible when the patient is making respiratory efforts. Lifting knees to chest can be considered the equivalent of head lift. Pediatric patients may be at high risk for postoperative apnea; thus a rush to extubate is not always appropriate.

Key Points

- Preparation for neurosurgical anesthesia on a range of pediatric patients includes assembling and handling an array of pediatric airway equipment and supplies (Table 54.1).
- Prepare for the challenging patient by thinking through scenarios while practicing strategies in advance on normal patients (Table 54.2).

Table 54.1 Airway equipment

LMAs: LMA Classic or ProSeal or Air-Q	Masks
Endotracheal tubes: Uncuffed, cuffed, and wire reinforced (know in advance which size tube fits through which LMA) – can make ETT smaller by cutting off proximal tip	Fiber-optic bronchoscopes
	Nasal trumpets
	Suction catheters and gastric tubes
Accordion connectors for patients with tracheostomy who must be positioned prone	Laryngoscopes and blades
	Double swivel connector with port
Long grasping forceps (from pediatric ENT cart)	Cook Frova® intubating introducer
Video laryngoscope/pediatric GlideScope	Surgical lubricant
Nasal vasoconstrictor	1% lidocaine/ MADD adaptor
Trachlight	

Suggested Reading

American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Practice guidelines for management of the difficult airway: an updated report by the American Society of Anesthesiologists Task Force on Management of the Difficult Airway. Anesthesiology. 2003;98:1269–77.

Gregory GA. Classification and assessment of the difficult pediatric airway. Anesthesiol Clin North Am. 1998;16:729–41.

Markakis DA, Sayson SC, Schreiner MS. Insertion of the laryngeal mask airway in awake infants with the Robin sequence. Anesth Analg. 1992;75:822–4.

Seo KS, Kim J-H, Yang SM, Kim HJ, Bahk J-H, Yum KW. A new technique to reduce epistaxis and enhance navigability during nasotracheal intubation. Anesth Analg. 2007;105:1420–4.

Wheeler M. Management strategies for the difficult pediatric airway. Anesthesiol Clin North Am. 1998;16:743–61.

Table 54.2 Syndromes, diagnoses, and scenarios associated with neurosurgical procedures with airway issues

Condition	Potential complications
Myelomeningocele, myelodysplasia, Chiari malformations, sacrococcygeal teratoma	Positioning
	Hydrocephalus
	Difficult intubation
	Latex avoidance
	Risk of postoperative apnea, need for prolonged prone positioning
Craniosynostosis	Difficult intubation
	Long operation/risk of ETT collapse or blockage by secretions
	Airway edema
	Head manipulation leading to right mainstem intubation or unintended extubation
	Need for intermittent suctioning
Intracranial masses	High ICP
	Positioning including sitting with risk of ETT kinking or compression
	Venous air embolism
Intracranial bleed	High ICP
	Emergency
	Positioning
Spine surgery	Positioning
	Risk of venous air embolism
	Difficult intubation
	Risk of unintended extubation
	Airway edema
Vascular anomalies	Avoid stimulation
	Risk of intracranial bleed
Seizure surgery	Ease of emergence for neurological evaluation
	Intraoperative EEG
Encephalocele	Avoidance of nasal intubation
	Difficult intubation
	Positioning
Neuroradiologic procedures	Avoid metal in ETT
	Need to limit equipment or intubate outside MRI suite
	Limited access to patient even during induction
Trauma	Emergency
	Full stomach
	Many of above considerations

Specific Aspects of Positioning, Fluids, Glucose Control, and Temperature Management

55

Gerhard K. Wolf, Sulpicio G. Soriano, and John H. Arnold

Overview

This chapter will discuss the optimal strategies regarding patient positioning as well as intraoperative fluid, glucose, and temperature management as they pertain to children who have to undergo neurosurgical procedures.

Implications for the Neurosurgical Patient

Positioning

Patient positioning requires careful preoperative planning to allow adequate access to the patient for both the neurosurgeon and the anesthesiologist. Table 55.1 describes common surgical positions applied for pediatric neurosurgery and their physiologic sequelae. These issues should be considered because the duration of most neurosurgical procedures can lead to significant physiologic impairment or injury if positioning problems are left undetected. All pressure points should be padded and peripheral pulses checked to prevent compression or pressure injury. In addition to compression and stretch injuries, the prone position can compromise the respiratory and cardiovascular system. It is important to minimize pressure on the abdomen, because increased intra-abdominal pressure can impair ventilation, cause venocaval compression, and increase epidural venous pressure and bleeding during surgical intervention. Soft rolls are used to suspend the chest and abdomen in order to minimize any increase in abdominal and thoracic pressure. During prone procedures the airway *positioning* is often in a dependent position, which may lead to significant airway edema. This can lead to postextubation airway obstruction or croup.

Table 55.1 Physiologic effects of patient positioning

Position	Physiologic effect
Head elevated	Enhanced cerebral venous drainage
	Decreased cerebral blood flow
	Increased venous pooling in lower extremities
	Postural hypotension
Head down	Increased cerebral venous and intracranial pressure
	Decreased functional residual capacity (lung function)
	Decreased lung compliance
Prone	Venous congestion of the face, tongue, and neck
	Decreased lung compliance
	Increased abdominal pressure can lead to venocaval compression
Lateral decubitus	Decreased compliance of downside lung

Neurosurgical procedures are performed with the head slightly elevated to facilitate venous and cerebrospinal fluid drainage from the surgical site. However, superior sagittal sinus venous pressure decreases with greater head elevation, and this increases the likelihood of venous air embolism. Extreme head flexion can cause brainstem compression in patients with pathologic conditions of the posterior fossa, such as mass lesions or Arnold-Chiari malformations. It can also cause endotracheal tube obstruction from kinking or migration into the mainstem bronchus and head and tongue swelling due to impaired venous or lymphatic drainage. Extreme rotation of the head can hinder venous return through the jugular veins and lead to impaired cerebral perfusion, increased intracranial pressure, and cerebral venous bleeding.

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Volume Status

Measurement of urine output as a surrogate for volume status should be interpreted with great caution in neurosurgical patients, as urine output may be profoundly influenced by changes in antidiuretic hormone (ADH) levels rather than by intravascular volume status and renal perfusion alone. Any neurosurgical patient with oliguria could have a component of syndrome of inappropriate vasopressin secretion (SIADH) and be volume overloaded; rather than additional volume boluses, this patient would benefit from fluid restriction until the SIADH resolves. On the other hand, a patient with polyuria could have diabetes insipidus (DI) and be volume depleted after uncontrolled urine losses. This patient would benefit from careful fluid resuscitation and administration of vasopressin. Volume status should be assessed clinically, with emphasis on clinical exam and vital signs. Central venous pressures or echocardiography may provide useful additional information about left atrial pressures and left ventricular preload.

Glucose Control

Normoglycemia should be achieved in all patients. There is sufficient evidence that hyperglycemia contributes to secondary brain injury and is associated with worse outcome in patients with traumatic brain injury. Hyperglycemia may also be associated with an increased risk of wound infection. On the other hand, intensive glycemic control has not been shown to improve mortality in critically ill patients in general and in critically ill patients in the neuro-intensive care setting. Intensive glycemic control may lead to hypoglycemic episodes, which can be detrimental in neurosurgical patients.

Thermal Homeostasis, Fever, and Induced Hypothermia

Infants and children are especially susceptible to hypothermia during any surgical procedure because of their large surface area to weight ratio. Active heating of the patient by increasing the ambient temperature and using radiant light warmers during induction of anesthesia, catheter insertion, and preparation and positioning of the patient are prophylactic measures against hypothermia. Mattress warmers, forced hot air blankets, and humidification of inspired gases can also prevent intraoperative temperature loss and postoperative shivering. Fever has a detrimental effect in patients with traumatic brain injury and stroke. Normothermia should be achieved by antipyretics and active cooling devices. Head cooling and mild hypothermia have been demonstrated to be protective and improve neurological outcome in asphyxiated neonates. Therapeutic hypothermia has been used most frequently in adult patients resuscitated following cardiac arrest, but the benefit is unclear. Induced hypothermia has not been shown to improve outcome following traumatic brain injury or in the intraoperative management of ruptured cerebral aneurysms.

Concerns and Risks

Intraoperative Diabetes Insipidus (DI)

The clinical diagnosis of perioperative DI in pediatric patients is straightforward and is – as in the adult – characterized by the presence of the following:

- Urine output of greater than 4 ml/kg/h.
- Serum Na >145 mEq/L.
- Serum osmolality >300 mosm/kg.
- Urine osmolality <300 mosm/kg.
- Polyuria persisting >30 min.
- Other causes of polyuria must be ruled out (e.g., administration of mannitol, furosemide, osmotic contrast agents, presence of hyperglycemia).

The laboratory diagnosis of DI has been facilitated through the use of copeptin as a marker for ADH secretion. Copeptin (carboxy-terminal pro-arginine vasopressin) is a glycopeptide co-secreted with ADH from a common precursor. While ADH is 90% bound to platelets and ADH levels may be falsely low or elevated, copeptin is not significantly bound to platelets. Copeptin levels of less than 2.6 pmol/l have a 95% sensitivity for central DI, whereas copeptin levels of greater than 20 pmol/l have a 100% sensitivity for renal DI.

Once the diagnosis of DI is established, a vasopressin infusion is commenced at 1 milliunit/kg/h and is increased every 5–10 min to a maximum of 10 milliunits/kg/h aimed at decreasing the urine output to <2 ml/kg/h. Total maintenance fluids (intravenous and oral fluids) should not exceed the insensible losses plus the obligate urinary losses. It is convenient to calculate the total intravenous fluids as 2/3 maintenance. The appropriate intravenous fluid for pediatric patients in the context of neurosurgery is 0–5% dextrose and 0.9% saline with 0–40 mEq of potassium chloride/L. Blood loss should be replaced with normal saline, lactated ringer's solution, or 5% albumin or blood products as appropriate. The antidiuretic effect of vasopressin is commonly viewed as an "all or none" phenomenon. Once the patient's urine output is less than 2 ml/kg/h, the urine output is regarded as "captured."

The following clinical scenarios may occur intraoperatively:

The patient is not responding at all and the urine output remains high:

If the patient is not responding to the vasopressin infusion, the intravenous catheter must be checked for patency, and the infusion preparation and rate should be checked.

The patient stops producing urine:

Even with a maximal dose of vasopressin, the kidneys will produce a minimal urine output if there is adequate intravascular volume status. If a patient stops producing urine entirely, prerenal volume depletion secondary to hypovolemia may be present. In this scenario, patency of the urinary catheter should be confirmed, and a judicious (10–20 ml/kg) fluid bolus of normal saline should be given until urine output resumes. The diagnosis of hypovolemia has to be made using all clinical parameters (clinical exam, vital signs, central venous pressure) except the urine output, and some degree of dehydration is to be expected in most patients after a period of uncontrolled urine output prior to establishing the diagnosis of DI. We do not recommend lowering the vasopressin infusion rate to produce diuresis in this setting. Reducing the vasopressin infusion rate to enhance urine output will result in unnecessary confusion about the patient's volume status.

Post-procedure, the vasopressin infusion should be continued, and the child should be admitted to a pediatric intensive care unit. DI has been reported to occur in 8% of patients preoperatively and 70–90% of all patients presenting postoperatively from craniopharyngioma surgery. Of note, the onset of postoperative DI is usually 1–12 h after surgery. A triphasic response (DI-SIADH-DI) after craniopharyngioma resection has been described. The triphasic response is characterized by initial DI after resection of the pituitary gland, followed by a "honeymoon period" where ADH is thought to be released from necrotic cells in the pituitary stump. This phase of relative SIADH can last 3–6 days and is usually followed by a definitive deficiency in ADH, resulting in permanent DI.

Cerebral salt wasting (CSW) is a disorder of excessive natriuresis in the presence of an intracerebral lesion. The pathophysiology of CSW is poorly understood, and there is no convincing animal model that explains the mechanism by which cerebral disease might lead to renal salt wasting. CSW can easily be confused with SIADH, as hyponatremia, high urine osmolality, and high urine sodium are features of both disorders. It is important to differentiate both diseases as both may occur in brain injury: CSW is associated with volume depletion secondary to natriuresis; SIADH is a situation of volume overload secondary to free water overload. Some authors have speculated that CSW is an overdiagnosed entity; the same group of authors have also pointed out that in most cases where CSW is speculated, natriuresis is secondary to volume expansion and ADH levels are appropriately elevated. It is important to note that it is impossible to make the diagnosis of CSW in the absence of an intracerebral lesion. The therapy of CSW is volume repletion with isotonic saline. In severely hyponatremic patients or in patients with ongoing sodium losses, sodium repletion with 3% NaCl (513 mEq/L) may be required. Symptomatic patients (seizures) may require a 1 ml/kg 3% NaCl bolus over 30 min, which may be given more rapidly if the patient is actively seizing. As a rule of thumb, 1 ml/kg 3% NaCl will elevate the serum sodium by 1 mEq/L.

Hyponatremia is the most common electrolyte disorder in hospitalized patients. Iatrogenic-induced hyponatremia suggests a surplus of water and a deficit of sodium in the extracellular fluid compartment. It is a common but dangerous practice to use hypotonic fluids such as half-normal saline (77 mEq Na/L) or 0.2 normal saline (31 mEq Na/L) as maintenance fluids in children. Pediatric patients who have elevated levels of ADH, such as in children with a diagnosis of pneumonia, sepsis, meningitis, and in postoperative patients, all are at risk for hyponatremia, as their ability to excrete excessive free water is impaired. Bohn and coworkers reported that hyponatremia occurred not uncommonly in the first 48 h of admission to the hospital. Catastrophic neurologic sequelae and death resulting from iatrogenic-induced hyponatremia have been described. Hypotonic fluids must not be used in neurosurgical patients.

Key Points

- In pediatrics, patient positioning for surgery requires careful preoperative planning to allow adequate access to the patient for both the neurosurgeon and the anesthesiologist.
- Infants and children are especially susceptible to hypothermia because of their large surface area to weight ratio.
- Normothermia should be achieved in all pediatric patients, as both fever and hypothermia may produce a worse outcome.
- Neurosurgical patients are at particular risk for electrolyte derangements.
- Normoglycemia should be achieved, but intensive glucose control can lead to potentially detrimental episodes of hypoglycemia.
- Hypotonic fluids must be avoided by all means.
- Volume status should be assessed clinically, as urine output can be influenced by SIADH, DI, and CSW.
- SIADH is characterized by free water retention, and ADH levels are inappropriately elevated.
- Cerebral salt wasting is probably a less common cause of hyponatremia than SIADH in patients with cerebral injury.
- Intraoperative diabetes insipidus is characterized by urine output greater than 4 ml/kg/h, low urine, and high serum osmolality in the absence of other causes of polyuria.

Suggested Reading

Cochran A, Scaife ER, Hansen KW, Downey EC. Hyperglycemia and outcomes from pediatric traumatic brain injury. J Trauma. 2003;55(6):1035–8.

Grady MS, Bedford RF, Park TS. Changes in superior sagittal sinus pressure in children with head elevation, jugular venous compression, and PEEP. J Neurosurg. 1986;65(2):199–202.

Halberthal M, Halperin ML, Bohn D. Lesson of the week: acute hyponatraemia in children admitted to hospital: retrospective analysis of factors contributing to its development and resolution. BMJ. 2001;322(7289):780–2.

Singh S, Bohn D, Carlotti AP, Cusimano M, Rutka JT, Halperin ML. Cerebral salt wasting: truths, fallacies, theories, and challenges. Crit Care Med. 2002;30(11):2575–9.

Van den Berghe G, Wilmer A, Hermans G, Meersseman W, Wouters PJ, Milants I, Van Wijngaerden E, Bobbaers H, Bouillon R. Intensive insulin therapy in the medical ICU. N Engl J Med. 2006;354(5):449–61.

Wise-Faberowski L, Soriano SG, Ferrari L, McManus ML, Wolfsdorf JI, Majzoub J, Scott RM, Truog R, Rockoff MA. Perioperative management of diabetes insipidus in children [corrected]. J Neurosurg Anesthesiol. 2004;16(1):14–9.

Part IX

Critical Situations During Anesthesia for Pediatric Neurosurgery

Challenges During Surgery for Hydrocephalus

56

Inger Aliason and Jeffrey L. Koh

Overview

Hydrocephalus is caused by excessive ventricular cerebrospinal fluid (CSF), usually due to an obstruction (noncommunicating hydrocephalus) or inadequate CSF reabsorption (communicating hydrocephalus). In rare cases, hydrocephalus can result from a choroid plexus papilloma, which causes an overproduction of CSF. The most common causes of pediatric hydrocephalus are myelomeningocele (obstruction) and posthemorrhagic hydrocephalus of prematurity (inadequate reabsorption at the arachnoid granulations).

The prevalence of hydrocephalus is reported to be 0.63–1.2 cases per 1000 children (Garton et al. 2004), making it one of the most common neurosurgical problems encountered in both the adult and pediatric populations. Medical advances in the care of premature infants may be leading to an increased incidence of hydrocephalus due to the survival of infants with intraventricular hemorrhage (Table 56.1).

Symptoms that accompany pediatric hydrocephalus range from mild headache to life-threatening lethargy, bradycardia, and ultimately brain herniation. Key factors that determine how symptomatic the child will be include intracranial compliance and the rate at which the hydrocephalus develops. Neonates have high intracranial compliance, due to open fontanelles and sutures. Therefore development of hydrocephalus is usually accommodated by increasing head circumference and maintenance of near normal intracranial pressure (ICP) (Table 56.2).

Hydrocephalus etiologies

Congenital causes of hydrocephalus	Acquired causes of hydrocephalus
Myelomeningocele	Prematurity (posthemorrhagic hydrocephalus)
Dandy–Walker malformation	
Arnold–Chiari malformation	Subarachnoid hemorrhage (trauma, aneurysm)
Aqueductal stenosis	
Cysts (arachnoid, interhemispheric)	Neoplasm
Neoplasms	Meningitis
Encephalocele	Encephalitis
Vascular malformations	
Mucopolysaccharidoses	
X-linked hydrocephalus	
Maroteaux–Lamy syndrome	
Congenital conditions affecting the skull (Crouzon, Pfeiffer, achondroplasia)	

Hydrocephalus symptoms

Symptoms of *slowly* developing hydrocephalus in neonates	Signs and symptoms of *acutely* increased ICP in patients of all ages
Enlarged head circumference	Headache
Full fontanelle	Lethargy
Separating sutures	Vomiting
Irritability	Cranial nerve dysfunction
Vomiting	Papilledema
	Decorticate or decerebrate posturing
	Hypertension
	Bradycardia
	ECG changes due to brainstem compression
	Irregular respirations
	Eventual brain herniation and death

Hydrocephalus is usually treated with an intraventricular catheter or endoscopic ventriculostomy to relieve the obstruction to CSF flow. Intraventricular catheters shunt CSF to a variety of locations including the peritoneal cavity

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Perioperative concerns

Preoperative	Intraoperative	Ventriculostomy
Further increased ICP	Aspiration	Arrhythmias, asystole
No IV access	Latex allergy	Hemorrhage
External ventricular drain (EVD) dislodgement or acute change in height	Surgical trauma	Hypothalamus or cranial nerve injury
	Subdural hematoma	
	Intrathoracic trauma	
	Venous air embolism	

(most common), pleural cavity, right atrium, or externally (temporary measure). Endoscopic ventriculostomy creates a path between the ventricular system (usually the third ventricle) and another intracranial space.

The remainder of this chapter discusses the preoperative and intraoperative complications that can occur in shunt placement (ventriculoperitoneal (VP), ventriculoatrial (VA), ventriculopleural (V-Pleural)), as well as the complications associated with ventriculostomy (Table 56.3).

Prevention of Preoperative Problems in Children with Increased Intracranial Pressure

The preoperative period can be especially challenging for patients who require surgery for hydrocephalus. Potential preoperative complications include:

- Further increase in ICP
- Problems with external ventricular drains (EVDs)

Premedication is usually avoided due to altered level of consciousness and the elevated risk for respiratory depression. Careful observation should occur during the preoperative period to ensure that a symptomatic increase in ICP can be quickly identified and treated. It is important to secure or evaluate existing IV access as it may be needed for acute intervention or to facilitate a modified rapid sequence induction (RSI) (Table 56.4).

Some children will present to the operating room with EVDs. Prior to transport, it is important to close the EVD to avoid excess CSF drainage. The surgeon can determine how long the EVD can be safely closed; usually, 15 min is not a problem. If the EVD is open and the drainage bag is suddenly lowered, CSF can drain quickly from the patient and lead to collapse of ventricles and rupture of cortical bridging veins causing subdural hematoma (SDH) or even "upward herniation with potentially fatal consequences." During patient transport, the EVD must also be carefully monitored to prevent the catheter from being dislodged from the patient's head (Table 56.5).

Child without IV access and acute hydrocephalus

Crisis	Management
No IV access in a young child with acute symptomatic hydrocephalus for urgent VP shunt placement	Attempt preoperative IV access
	Consider intraosseous (IO) access if pt obtunded
	If IV access cannot be obtained, consider an inhalation induction with cricoid pressure. Take over ventilation as soon as possible and hyperventilate (reduce excess CO2) while IV access is being established

EVD preoperative crises and management

Crisis	Management
External ventricular drain (EVD) dislodgement during transport	Elevate patient head slightly
	Evaluate patient for signs of increased ICP
	Notify surgeon
External ventricular drain (EVD) system falls from IV pole to the floor	Close the EVD if it is not already closed. Return to the proper height
	Evaluate patient's neurologic status for signs of subdural hematoma

Prevention of Intraoperative Problems in Children with Increased Intracranial Pressure

Although shunt placement (VP, VA, V-Pleural) and endoscopic ventriculostomy are common neurosurgical procedures, anesthesia providers must always be vigilant for a few rare but life-threatening complications including aspiration risk, latex allergy, intrathoracic trauma, and venous air embolism (VAE).

Aspiration Risk

Often, these patients either have a full stomach or have been vomiting and are, therefore, at risk for aspiration. A modified RSI should be considered for tracheal intubation. To avoid further increase in ICP, blunting the stimulus of laryngoscopy and intubation will be necessary. Judicious use of opioids, lidocaine, and/or intravenous anesthetics can be considered. However over-administration of these agents can cause a decrease in BP, leading to inadequate cerebral perfusion pressure. Ketamine should be avoided since it can acutely increase ICP. Succinylcholine can slightly increase ICP; however, the ICP increase can usually be offset by an adequate dose of intravenous anesthetics combined with hyperventilation (Table 56.6).

Children with a history of myelomeningocele are at significantly increased risk for latex allergy. Many children with myelomeningocele also have hydrocephalus. The literature

Aspiration

Causes of aspiration	Patient assessment	Treatment/intervention
Full stomach	Gastric contents in the oropharynx or with tracheal suctioning	If aspiration is seen at time of intubation
Increased ICP → vomiting, altered level of consciousness	Hypoxemia	Suction trachea before positive pressure ventilation
Ineffective cricoid pressure	Bronchospasm/increased PIPs	
	CXR can have infiltrates	Ventilate with 100% FIO_2 and use PEEP as needed
		Supportive care
		ICU post-op prn
		Bronchodilators prn
		Steroids and antibiotics have *not* been proven beneficial in the acute situation

Latex allergy

Causes of allergic response	Assessment	Treatment/intervention
Exposure to latex	Hypotension	Remove all latex or other triggering agents
Latex gloves	Tachycardia	
Tape	Bronchospasm	Inform the surgeons
Medication vials	Flushing/ urticaria	Secure the airway, FIO_2 100%
Blood pressure cuffs		
Tourniquets		Epinephrine as needed
Other latex-containing products		Reduce or discontinue volatile or intravenous anesthetics as dictated by hemodynamics
		IV fluid boluses to support blood pressure
		Corticosteroids
		Antihistamines

reports that the prevalence of sensitization to latex may be as high as 64% in children with spina bifida (Rendeli et al. 2006). Allergy to latex is a type 1 IgE-mediated reaction clinically manifested as urticaria, angioedema, bronchospasm, and anaphylactic shock. The best way to prevent latex allergy is to prevent latex exposure (see Table 56.7 for therapeutic interventions).

Surgical Trauma

The other intraoperative problems associated with hydrocephalus surgeries usually involve surgical trauma, either indirectly or directly. It is important to recognize the problem and be ready to manage it in the acute situation.

- *Rapid surgical decompression* of hydrocephalus can lead to rupture of the cortical bridging veins and SDH or upward herniation of the brainstem causing bradycardia, irregular respirations, or ECG changes (Fleisher 2012) (Table 56.8).

Subdural hematoma/upward herniation

Causes	Patient assessment	Treatment/intervention
Rapid surgical decompression	Evaluate vital signs for bradycardia and/or ECG changes (herniation)	Notify surgeon
Rapid lowering of open EVD	Evaluate neurologic status for signs/ symptoms of SDH	Evaluate neurologic status for signs/ symptoms of SDH
		Hemodynamic support as clinical situation dictates

Intrathoracic trauma

Cause	Patient assessment	Treatment/intervention
Shunt passer sheath inadvertently tunneled into chest cavities	Evaluate patient for signs of hemodynamic instability	Depending on which organ has been damaged, the anesthesiologist must be prepared to treat hemorrhage, tamponade, and pneumothorax
Bleeding due to vascular injury	Evaluate ability to oxygenate/ventilate patient	

- *Intrathoracic trauma* (heart, lung, and great vessels) can occur intraoperatively when the VP shunt passer sheath is tunneled across the chest wall and toward the abdomen.
- *Due to the nature of the surgical procedure, VA and V-Pleural shunt placement may carry a somewhat higher risk of intrathoracic trauma such as bleeding (VA) and pneumothorax (V-Pleural)* (Table 56.9)

Venous Air Embolism

VAE can occur at any time, but especially during placement of a ventriculoatrial shunt. To help prevent VAE anesthesia, providers can (1) keep the surgical site lower than the level of the heart (if possible); (2) mechanically ventilate the patient, with careful addition of PEEP; (3) maintain high venous pressure; and (4) remove air from IV tubing and solutions (Table 56.10).

Venous air embolism

Cause	Patient assessment	Treatment/intervention
Surgical site higher than heart	Abrupt decrease in end-tidal CO_2	Notify surgeon who will flood field or pack wound/bone
Air in IV tubing	Hypotension	
	Bradycardia/ arrhythmias	FIO_2 100%
	Hypoxia	Reduce or discontinue volatile or intravenous anesthetics as dictated by hemodynamics
	"Mill wheel" murmur on auscultation	
	Precordial Doppler	Aspirate air if central line is in situ
		IVFs/vasopressors to maintain BP
		Valsalva
		Surgical site below the heart and LLD, if possible
		CPR if cardiac arrest

Complications Associated with Endoscopic Ventriculostomy

Ventriculostomy is performed to relieve noncommunicating hydrocephalus by perforating the septum pellucidum (to allow communication of the lateral ventricles) or the floor of the third ventricle with an endoscope. The benefit of ventriculostomy is that no foreign materials are left in the patient (i.e., VPS). In addition, ventriculostomy is minimally invasive and can be performed via a burr hole. However, endoscopic ventriculostomies carry risks that are mainly related to damage of nearby structures. Endoscopic ventriculostomy can be acutely complicated by arrhythmias, asystole, hypertension, and hemorrhage. Bradycardia can occur in up to 40% of patients during endoscopic ventriculostomy (El-Dawlatly et al. 2000). The hemodynamic instability that often occurs during these procedures is likely due to the local effects on the third ventricle floor (hypothalamus, pons, and medulla) (Baykan et al. 2005). Due to the potential risks, careful consideration should be given to monitoring (arterial line placement) based on the clinical scenario (Table 56.11 and 56.12).

Hemorrhage

Hemorrhage has been reported during third ventriculostomy (Drake 1993). Although it is impossible to predict which patients may suffer this complication, anesthesia providers must always be prepared to respond. Patients undergoing ventriculostomy should have adequate IV access, an arterial line, and blood products readily available in the event of hemorrhage and emergent craniotomy (Table 56.13).

Arrhythmias or bradycardia/asystole during ventriculostomy

Cause	Patient assessment	Treatment/intervention
Stimulation of the floor of the third ventricle by the endoscope	Evaluate cardiac output ($ETCO_2$, BP)	Notify surgeons, ask to stop stimulating floor of third ventricle and to stop irrigation fluid
High-speed irrigation fluid	Evaluate for hypoxia and/or hypercarbia	If arrhythmia does not resolve after stimulation is stopped, then treat supportively according to rhythm disturbance
Rapidly increasing ICP		
Vagal response to surgical or other manipulation (i.e., pressure on eye)		FIO_2 100%
Venous air embolism		Reduce or discontinue volatile or intravenous anesthetics as indicated by hemodynamics

Hypertension during ventriculostomy

Cause	Patient assessment	Treatment/ intervention
Catecholamine release due to surgical stimulation	Evaluate for signs of light anesthesia (tachycardia, sweating, tearing, mydriasis)	Repeat BP measurement to verify accuracy
Local surgical effects on third ventricle floor	Evaluate for hypoxia and/or hypercarbia	Deepen anesthesia if needed
Increased ICP	Evaluate for distended bladder	Notify surgeons, ask to stop stimulating floor of third ventricle and to stop irrigation fluid
		Raised ICP may require mannitol, furosemide, and/or hyperventilation
		Urinary catheter if bladder is distended
		Judiciously consider antihypertensive medication therapies

- Other structures at risk for trauma during endoscopic ventriculostomy include:
  - Hypothalamus; an injury would postoperatively manifest as:
    (a) SIADH or DI (assess sodium levels, fluid status)
    (b) Temperature regulation problems – can be mistaken for malignant hyperthermia
    (c) Post-op "trance-like state" (differential post-op agitation/delirium)
  - Cranial nerves
    (a) Third and sixth nerve palsies have been reported.

Hemorrhage

Cause	Patient assessment	Management
Trauma to the basilar artery or its branches	Visualization of blood via endoscope	Communicate with surgeons
	Hemodynamic instability	Call for help
		FIO_2 100%
		Reduce or discontinue volatile or intravenous anesthetics as indicated by hemodynamics
		IVFs and vasopressors as needed
		Transfusion of blood products as needed
		Manage elevated ICP until craniotomy

Slit ventricle syndrome

Cause	Patient assessment	Management
Overdrainage of CSF	Signs of decreased brain compliance	Avoid excessive and/or hypotonic intravenous fluid administration
	Headache	
	Nausea	
	Lethargy	
	MRI/CT scan	
	Narrow, collapsed, slit-like lateral ventricles	

Slit Ventricle Syndrome

Slit ventricle syndrome occurs when there is overdrainage of CSF and the lateral ventricles become very narrow and small, appearing collapsed on imaging. It is associated with decreased brain compliance and intermittently elevated ICP. Symptoms include headache, nausea/vomiting, and lethargy. Slit ventricle syndrome occurs in 5–10% of children with CSF shunts. The lack of CSF and decreased brain compliance makes patients unable to compensate for alterations in the brain or intracranial blood volume. They are susceptible to cerebral edema if excessive and/or hypotonic intravenous fluids are administered (Eldredge et al. 1997; Dasari et al. 2015; Agarwal et al. 2013). Surgical management of slit ventricle syndrome may include removal of CSF shunt, shunt replacement with a programmable CSF shunt (flow regulated vs. conventionally pressure-regulated), or endoscopic ventriculostomy (Table 56.14).

Programmable VP Shunts and MRI

Although not directly related to the surgical care of children with hydrocephalus, MRI is increasingly being used as part of the evaluation of shunt malfunction (Boyle et al. 2015). In certain circumstances, anesthesiologists may be asked to provide sedation for these patients during their MRI. Along with the anesthetic considerations noted earlier in this chapter, patients with adjustable VP shunts are at risk that the electronic valve programming is accidentally disrupted during the MRI, which could result in symptoms related to either high or low pressure. Risk depends on the type of valve and the strength of the magnetic field (Lavinio et al. 2008). The MRI tech and/or neurosurgery should be consulted prior to the scan to identify risk, and interrogation/reprogramming of the pump should be planned post scan.

Key Points

- Carefully evaluate each patient to determine degree of increased ICP. This is important for making decisions about premedication, type of induction, and urgency of interventions.
- IV access is needed for RSI or rapid intervention for critical increases in ICP.
- If present, close the EVD prior to patient transport.
- Take precautions regarding latex exposure in patients with myelomeningocele or other susceptible patient populations.
- Always be vigilant for surgical trauma and venous air embolus, especially during the tunneling phase of VPS placement.
- Patients undergoing endoscopic ventriculostomy should have adequate IV access and possibly an arterial line in the event of hemorrhage or arrhythmia.
- Avoid excessive and/or hypotonic intravenous fluid administration to patients with slit ventricle syndrome.

References and Suggested Reading

Agarwal N, et al. Slit ventricle syndrome: a case report of intermittent intracranial hypertension. J Child Neurol. 2013;28(6):784.

Baykan N, et al. Ten years experience with pediatric neuroendoscopic third ventriculostomy. J Neurosurg Anesthesiol. 2005;17:33–7.

Boyle TP, et al. Radiographic evaluation of pediatric cerebrospinal fluid shunt malfunction in the emergency setting. Pediatr Emerg Care. 2015;31:435–43.

Dasari R, et al. Unusual vision improvement in a case of slit ventricle syndrome after endoscopic third ventriculostomy. J Evid Based Med Healthc. 2015;13:2134–9.

Drake J. Ventriculostomy for treatment of hydrocephalus. Neurosurg Clin N Am. 1993;4:657–66.

El-Dawlatly A, et al. The incidence of bradycardia during endoscopic third ventriculostomy. Anesth Analg. 2000;91:1142–4.
Eldredge EA, et al. Postoperative cerebral edema occurring in children with slit ventricles. Pediatrics. 1997;99:625–30.
Fleisher LA. Anesthesia and uncommon disease. 6th ed. Philadelphia, PA: Elsevier; 2012.
Gaba DM, et al. Crisis management in anesthesiology, vol. 2e. Philadelphia: Elsevier Saunders; 2015.
Garton H, et al. Hydrocephalus. Pediatr Clin N Am. 2004;51:305–25.
Hamid R, Newfield P. Pediatric neuroanesthesia: hydrocephalus. Anesthesiol Clin N Am. 2001;19(2):207–18.
Lavinio A, et al. Magnetic field interactions in adjustable hydrocephalus shunts. J Neurosurg Pediatr. 2008;2:222–8.
Meier PM, et al. Endoscopic pediatric neurosurgery: implications for anesthesia. Pediatr Anesth. 2014;24:668–77.
Rendeli C, et al. Latex sensitization and allergy in children with myelomeningocele. Childs Nerv Syst. 2006;22:28–32.

Challenges During Surgery for Traumatic Brain Injury in Children and Adults

57

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Overview

For persons under 45 years of age, TBI remains the leading cause of coma and the leading cause of death with a frequency that is twice as high in men when compared to women. In addition to sex bias, the incidence of TBI is greatest at the extremes of age where those most at risk for severe injury are children between the ages of 5 and 9 and adults over 80 years. However, individuals between the ages of 15 and 24 have the greatest number of TBI. Hence, TBI is the leading cause of death in children greater than 1 year of age, and approximately 10–15% of children with TBI suffer from severe TBI.

Since 2008, the National Institute of Neurological Disorders and Stroke (NINDS) has defined TBI as brain damage induced by a sudden trauma, and pediatric TBI is defined as TBI occurring in those less than 18 years of age. TBI can result by one of two mechanisms: (1) closed-head injury (CHI) from a sudden and violent hit with an object or associated with acceleration/deceleration or (2) penetrating head injury when an object pierces the skull and enters brain tissue.

Despite the ability to define TBI, shocking statistics about this major condition remain. While TBI can occur in isolation, 75–85% of all children with multiple traumas will have TBI. This is not insignificant since 80% of all pediatric trauma deaths are associated with TBI. Motor vehicle and vehicle-pedestrian accidents remain the most common causes of TBI (40–50%) in pediatric patients. Falls, which are most common in the very young and the elderly, remain the second most common cause of TBI. In children <4 years old, 30–50% of TBI cases are attributed to falls and abuse. Hence, nonaccidental trauma (NAT) should always be a consideration and is the main cause of death in infants. Assaults, including firearms, are third (5–10%), and recreational accidents, i.e., sports-related injuries, are the fourth most common cause of TBI (10%).

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Clinical Implications/Anticipated Problems

The skull is a rigid structure containing tissue, blood, and CSF. An increase in any of these components increases intracranial pressure. Cerebral swelling can develop within hours of TBI with resultant intracranial hypertension. Intracranial hypertension can significantly decrease cerebral perfusion resulting in ischemia, swelling, possible herniation, and neurological impairment. Moreover, resultant neurological impairment demonstrated by altered arousal, alertness, or responsiveness may impair protective airway reflexes and increase the patient's risk for aspiration of oral secretions or gastric contents.

Young children possess certain anatomical characteristics that predispose them to TBI: (1) a large head-to-body ratio, which alters their center of gravity, (2) thinner cranial bones, and (3) decreased myelination of neural tissue. Some of these individual characteristics or in combination may increase their likelihood of diffuse axonal injury (DAI) and cerebral edema. Moreover, while in infants slow increases in ICP can be accommodated by expansion of cranial suture lines, rapid shifts are less well tolerated due to little time for adaptation.

Prevention

Motor vehicle and vehicle-pedestrian accidents are the most common cause of TBI with alcohol, illicit drugs, and nonprescribed use of prescription medications being the most common contributing factors. Therefore, primary prevention of TBI involves basic safe driving, appropriate utilization of child and infant car seats, in addition to clear legislation to support those practices.

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Crisis Management

Pathophysiology and Clinical Presentation

The pathophysiology of TBI includes both the primary and secondary events. However, there are few randomized controlled trials regarding the pathophysiology of TBI in children. Thus, a large amount of data in the pediatric population is obtained by extrapolation from adult studies:

- *Primary injury* – direct injury to brain parenchyma from tearing, compression, and stretching of tissues and blood vessels. Possible mechanisms include the following:
  - *Compressive stress* – deformation of the brain structure
  - *Tensile stress* – stretching as a result of pulling the axis of the brain in opposite directions
  - *Shear stress* – pushing in opposite directions perpendicular to the axis of the brain that can cause injury to the brain stem
  - *Acceleration/deceleration* – rapid acceleration or deceleration which occurs when the force from the site of impact sends waves through the skull. Since the head-to-torso ratio is large in infants and younger children, acceleration-deceleration injuries are more common in the pediatric population and can lead to diffuse brain and upper spine injuries
  - *Coup and contrecoup* – injury that occurs either in the portion of the brain under the site of impact (coup) or on the side opposite the impact (contrecoup)
- *Secondary injury* – indirect injury to brain parenchyma from hypoxia, hypotension, or biochemical and metabolic events that may occur minutes to days following the initial trauma. Possible mechanisms of secondary injury include the following:
  - Hypoperfusion
  - Increased metabolic demand
  - Damage to the blood-brain barrier
  - Free radical formation
  - Mitochondrial dysfunction
  - Release of neurotransmitters including acetylcholine, glutamate, and aspartate

Pediatric patients with TBI may present with diffuse or focal injuries. Diffuse injury results from microscopic damage throughout many areas of the brain. Types of diffuse injury to brain parenchyma include the following:

- *DAI* – characterized by shearing of large nerve fibers and stretching of blood vessels in the brain. The most common manifestation is impaired cognitive function with resultant impairment in memory, concentration, and organization. Within the pediatric population, DAI is often defined as a loss of consciousness for greater than 6 min without a specific focal lesion on imaging or exam. DAI is most common in the craniocervical junction in children as opposed to the frontotemporal lobes in adults.
- *Hypoxic-ischemic injury* – a consequence of cerebral swelling and resultant restriction in blood flow which limits its delivery oxygen, glucose, and key nutrients to the brain. In infants this is the most common abnormality in NAT.

Focal injury is confined to specific areas of the brain. Types of focal injury include the following (Fig. 57.1):

- *Contusions* – bruises to brain parenchyma that causes swelling, bleeding, and/or damage to brain tissue. These usually occur in frontal and temporal lobes which house the memory and behavior centers. Hence, symptoms of brain contusion may include abnormal sensations, coordination, memory, or behavior.
- *Hemorrhage* – blood escapes damaged blood vessels and enters brain tissue. The magnitude and symptoms depend on the location of the hemorrhage.
- *Stroke* – local blood flow to tissues is compromised by injury to large cerebral arteries or even tissues. Cerebral edema further compromises delivery of oxygen and nutrients. Strokes associated with TBI mostly affect the posterior cerebral artery circulation; however, the symptoms depend upon the vascular distribution. Pediatric strokes typically occur in children with neck injuries.
- *Subdural hematoma* – results from damage to bridging vessels on the surface of the brain. Patients may present with loss of consciousness, confusion, drowsiness, asymmetric pupils, focal deficits, headache, and respiratory changes. In the pediatric population, subdural hematomas >5 mm are often treated with surgical intervention.
- *Epidural hematoma* – results from damage to the middle meningeal artery or epidural veins. Hence, intracranial

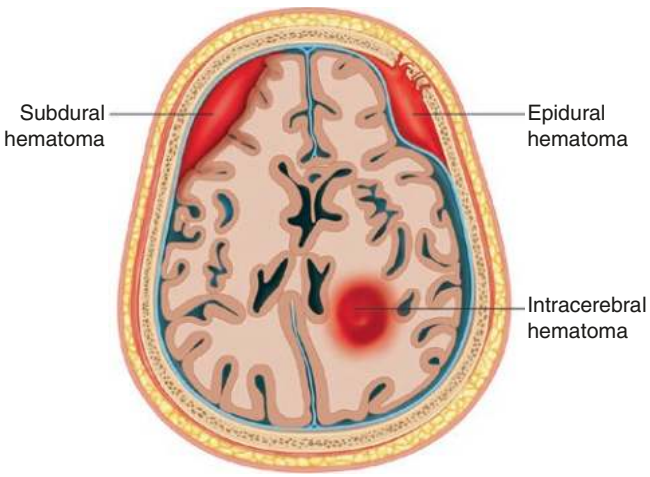

Fig. 57.1 Types of brain injury

pressure can increase within minutes and with symptoms similar to subdural hematoma. When promptly diagnosed and treated, children with epidural hematoma have an excellent prognosis.

- *Subarachnoid hemorrahge* – results from bleeding within the subarachnoid space. Subsequent changes in pupil, neurological and respiratory exam may occur. This injury occurs in children primarily from acceleration/deceleration injury; however, this injury may also occur following NAT. In the pediatric populaiton, SAH carries a high morbidity and mortality even when adequately treated.
- *Skull fracture* – more common within the pediatric population and often does not require surgical intervention except when depressed or open. Depressed, open skull fractures are often treated with immediate surgical debridement and fracture repair to lessen the risk of developing meningitis, CSF leak, and/or seizures. Remember, skull fractures can be associated with underlying brain injury.

The Glasgow Coma Scale (GCS) is often used to help to initially determine the severity of TBI:

- Mild (GCS score 13–15)
- Moderate (GCS score 9–12)
- Severe (GCS score <8)

Mild TBI often has few to no lasting consequences. Severe TBI can cause significant disability and possibly death. Most children with a GCS <5 have a dismal prognosis.

Patient Assessment/Diagnostic Tests

Children with severe TBI should be promptly recognized and stabilized to improve outcomes.

- *Primary survey* – identify and treat potentially life-threatening conditions which include airway compromise and hemorrhagic shock. Always assume cervical spine injury and stabilize the cervical spine using an immobilization collar. Approximately half of the patients with cervical spine injury have concomitant TBI.
- *Secondary survey* – identify secondary life-threatening conditions and perform an in-depth neurological assessment. Children with TBI often have concomitant blunt abdominal trauma and long bone fractures, such as femur fractures, which can serve as a major source of blood loss.
- *Patient history* – obtained from the patient, family members, and/or witnesses should include the mechanism of injury, duration of loss of consciousness, changes in mental status, headache, nausea, vomiting, and progression of symptoms. Past medical history should include birth history and documentation of any congenital abnormalities. Additionally, any history of prior injuries, seizures, learning disabilities, substance abuse, prior psychological or psychiatric problems, as well as medication or food allergies should be ascertained.
- Physical examination of a pediatric patient with TBI includes the following:
  - Assessment of ABCs and prompt management of airway if indicated by exam or if GCS <8. Prompt treatment of hypotension and hypoxia.
  - Vital signs: temperature, blood pressure, heart rate, pulse oximetry, and weight (actual or estimate).
  - Assessment for Cushing triad of hypertension, bradycardia, and irregular respirations may indicate impending herniation. This is a *late sign*.
  - Prompt neck immobilization and cervical spine examination.
  - Focused neurological examination including the following:
    (a) Level of consciousness
    (b) Pupil examination
    (c) Funduscopic examination
    (d) Brainstem reflexes
    (e) Deep tendon reflexes
    (f) Response to pain
  - Pay attention to indicators of increased ICP and impending herniation:
    (a) Cushing's triad *(LATE SIGN)*
    (b) Signs of uncal herniation: third nerve palsy (at rest, the eye tends to look down and to the side; no upward, downward, or inward movement possible; in addition: drooping upper eyelid, i.e., ptosis) followed by hemiplegia
  - GCS score (Table 57.1) – a 15-point scale that assesses the patient's ability to follow directions, move extremities, and speak.

Laboratory Studies

Obtain a hematocrit, electrolyte panel with blood glucose, type and screen, coagulation studies (PT/PTT, INR), and urinalysis, with urine toxicology assessment.

Caveats:

- Hyperglycemia is a poor prognostic indicator for patients with severe TBI.
- Pediatric patients who sustain head injury are at increased risk of coagulopathy because of brain tissue thromboplastin release; therefore, it is imperative to correct any coagulopathy.

Table 57.1 Glasgow Coma Scale (GCS) score

	Infant <1 year	Child 1–4 years	4 years–adult
Eyes			
4	Open	Open	Open
3	To voice	To voice	To voice
2	To pain	To pain	To pain
1	No response	No response	No response
Verbal			
5	Coos, babbles	Oriented speech, interacts	Alert and oriented
4	Irritable but consolable	Confused speech, disoriented but consolable	Disoriented
3	Irritable but inconsolable	Confused speech, inconsolable	Confused speech
2	Moans to pain	Incomprehensible, agitated	Moans, unintelligible speech
1	Nonverbal to pain	Unresponsive	Unresponsive
Motor			
6	Normal spontaneous movements	Normal spontaneous movements	Follows commands
5	Withdraws to touch	Localizes pain	Localizes pain
4	Withdraws to pain	Withdraws to pain	Withdraws to pain
3	Decorticate posturing to pain (flexion)	Decorticate posturing to pain (flexion)	Decorticate posturing to pain (flexion)
2	Decerebrate posturing to pain (extension)	Decerebrate posturing to pain (extension)	Decerebrate posturing to pain (extension)
1	Unresponsive to pain	Unresponsive to pain	Unresponsive to pain

Diagnostic Tests

- *Computed tomography (CT) of the head* – will detect most lesions requiring emergent surgery such as focal brain injuries and skull fractures. Repeat CT scans often show secondary injury as a result of cerebral edema.
- *MRI of the head* – may add information regarding long-term outcome. MRI may not be as useful in an emergency setting.
- *Angiography* – will allow assessment of blood vessels in the brain. CT/MRI angiography as a combined modality often may detect and define blood vessel pathology.
- *Electroencephalography (EEG)* – can be utilized to detect presence of seizure-like activity or absence of cerebral activity.
- *ICP monitor* – can be used to measure intracranial pressure.
- *Single-photon emission computed tomography (SPECT) or positron emission tomography (PET)* – imaging techniques that measure brain cell metabolism and detect changes or injury that cannot be detected by standard imagining modalities.

Surgical Intervention

Management of TBI consists of a variety of medical and surgical modalities. In general, surgical intervention is indicated in any intracranial lesion causing significant or progressive neurological compromise, focal neurologic signs, and/or intracranial hypertension. Since rapid decompression improves the overall outcome in patients with intracranial pathology with significant mass effect, surgical intervention as soon as possible is advisable (Table 57.2).

Table 57.2 Surgical interventions

Injury	Indications for surgery	Surgical technique
Acute epidural hematoma	Volume>30 cc, regardless of GCS score	Craniotomy +/− duroplasty
	Volume <30 cc with GCS<8, >15 mm thickness, or >5 mm midline shift	
Acute subdural hematoma	Thickness>10 mm and/or midline shift >5 mm, regardless of GCS	Craniotomy +/− bone flap removal and duroplasty
	GCS drops 2 or more points, abnormal pupillary function, ICP >20 mm Hg	Burr hole
		Subtemporal decompressive craniectomy
		Decompressive hemicraniectomy +/− duroplasty
Focal traumatic parenchymal lesions	Referable neurologic deterioration	Craniotomy
	Medically refractory intracranial hypertension	
	Signs of mass effect on imaging	
	Any lesion >50 cm^3	
	GCS ≤8, frontal or temporal lesion volume >20 cm^3, midline shift >5 mm, and\or cisternal compression	
Traumatic posterior fossa mass lesions	Mass effect on CT scan, neurological dysfunction, and/or referable neurologic deterioration	Suboccipital craniectomy
Depressed cranial fractures	Open (compound) fractures with depression greater than the thickness of the cranium	Elevation and debridement +\− primary bone fragment replacement
	Dural penetration, significant intracranial hematoma, depression >1 cm, frontal sinus involvement, pneumocephalus	

"Mass effect" on CT scan = distortion of fourth ventricle, compression of basilar cisterns, or obstructive hydrocephalus
Adapted from: Bullock et al. (2006)

Intraoperative Interventions/Treatment

Airway

- Optimize oxygenation and ventilation. Hypoxia and hypercarbia are both potent cerebral vasodilators which increase CBF and ICP. Hypoxemia in pediatric patients is predictive of increased morbidity.
- An oral airway will relieve airway obstruction even in an unconscious child with suspected cervical spine injury.
- Chin lift and jaw thrust maneuvers when performed correctly can relieve airway obstruction with minimal cervical spine motion.
- Endotracheal intubation is commonly required. A rapid sequence technique should be used.
  - Nasotracheal intubation should not be performed in patients with basilar skull or midface fractures.
  - Consider avoiding succinylcholine because of concerns of hyperkalemic cardiac arrests in healthy children with undiagnosed myopathy. For this reason it is recommended that succinylcholine should be reserved only for emergency intubations such as laryngospasm, difficult airway, full stomach, or intramuscular use when IV access is unavailable.
  - Succinylcholine may temporarily increase intracranial pressure; therefore careful consideration should be taken prior to its use.
  - Use positive end expiratory pressure (PEEP) with caution because it may impair cerebral venous return or increase ICP if greater than 10 cm H_2O.

Breathing

- Hyperventilation should be performed if acute signs of increased ICP and impending herniation are present.
  - Hyperventilation in the nonacute setting compromises cerebral perfusion by inducing vasoconstriction at a time when cerebral perfusion is already reduced.
- In the nonacute setting, normoventilation with a goal end-tidal CO_2 of 30 mmHg is utilized.

Circulation

- Fluid resuscitation may occur with isotonic solutions, blood, or blood products if necessary.
- Emergency release blood (O negative) should be immediately available if type and screen or cross-matched blood is not available.
- Systolic blood pressure should be maintained at normal to elevated levels as determined by the age of the patient.
- Utilization of hypertonic saline for fluid resuscitation for up to 72 h has suggested benefits in the pediatric population.
  - Serum sodium must be closely monitored when hypertonic saline is utilized with a goal Na of <155.
- Children <24 months are especially at risk for cerebral hypoperfusion post TBI.
- Arterial and central venous access may be required for close hemodynamic monitoring and to allow for rapid administration of vasoactive substances if needed.

Cervical spine immobilization should be maintained in pediatric trauma patients until cleared by radiological and clinical exam.

Intracranial Dynamics

- Intracranial pressure ranges vary with age. Normal values are less than 10–15 mm Hg for adults.
- ICP values in pediatric patients are not well established. Normal values in older children are 10–15 mm Hg, 3–7 mm Hg in young children, and 1.5–6 mm Hg in infants.
- ICP values greater than 20 mm Hg require treatment.
- Cerebral autoregulation is the mechanism by which the brain is able to maintain cerebral blood flow at an appropriate level during changes in blood pressure. In a healthy brain, normal cerebral blood flow is maintained with a cerebral perfusion pressure that ranges from 50 to 150 mm Hg by inducing vasodilation or vasoconstriction in response to changes in cerebral perfusion pressure. This, in turn, influences ICP.
- After brain injury, cerebral autoregulation may be absent or impaired, and ICP decreases and increases with changes in CPP.

Maintain CPP

- CPP is defined as MAP – ICP or jugular venous pressure, whichever is higher.
- CPP goal of >70 mmHg is often utilized in adults. Given the paucity of data in children, a CPP of greater than 70 mmHg is targeted in children as well.

Minimize ICP

- Elevation of the head to a maximum of 30° promotes venous drainage and potentially decreases ICP.
- Administer hyperosmolar therapy such as mannitol and hypertonic saline to create an osmolar gradient that will assist in normalizing ICP.
  - More specifically, 3% saline may be effective for acute treatment of intracranial hypertension in pediatric patients with TBI.
- Intravenous lidocaine can be utilized to treat acute increases in ICP that occur with suctioning, movement, and laryngoscopy.

- Intravenous sedation-hypnotic agents are potent cerebral vasoconstrictors and decrease CBF and ICP.
  - Ketamine can increase CBF and ICP; therefore, it must be used with caution.
- Consider neuromuscular blockade to control increases in ICP associated with shivering, coughing, or ventilator intolerance.
- In pediatric patients with refractory increases in ICP, barbiturate coma with pentobarbital is often used. Adverse effects of pentobarbital include hypotension.
- A ventriculostomy may also be required to drain the ventricles in the setting of increased ICP.
- Anti-seizure prophylaxis may reduce early posttraumatic seizures. These seizures increase brain metabolic demands and ICP leading to secondary injury.

Avoid Hyperthermia and Hyperglycemia

- Hyperthermia increases cerebral metabolic oxygen demand.
- Hyperglycemia may worsen brain tissue lactic acidosis. Insulin infusions may be required with caution especially for blood glucose levels greater than 200 g/dl.

Electrolyte Disturbances

- Evaluate for electrolyte imbalances caused by diabetes insipidus, syndrome of inappropriate antidiuretic hormone, and cerebral salt wasting syndrome that often occur post TBI.

Key Points

- Eighty percent of all pediatric trauma deaths are associated with TBI.
- Extremes of age (5- to 9-year-olds and >80 years of age) are at increased risk for TBI.
- The most common cause of pediatric TBI is motor vehicle and vehicle-pedestrian accidents. However, NAT is the main cause of TBI in infants.
- Diffuse brain injury includes DAI and hypoxic-ischemic injury. Focal injuries include contusions, hematomas, and hemorrhages.
- The primary survey should identify life-threatening injuries.
- GCS score should be computed and the initial imaging often includes a head CT. If the GCS is <8, urgent endotracheal intubation may be necessary.
- Management of TBI includes close management of ABCs. The head of the bed should be elevated 30°, and neurosurgical consultation should be obtained.
- Hyperosmolar therapy should also be considered.
- Anticonvulsants may help prevent early posttraumatic seizures.
- Patients exhibiting signs of herniation should be emergently managed.

Suggested Reading

Bullock MR, Chesnut R, Ghajar J, Surgical Management of Traumatic Brain Injury Author Group, et al. Guidelines for the surgical management of traumatic brain injury. Neurosurgery. 2006;58(3 Suppl):S2-56–60, S2-47-S2-55, S2-25-S2-46, S2-16-S2-24, S2-7-S2-15.

Comper P, Bisschop SM, Carnide N, et al. A systemic review of treatments for mild traumatic brain injury. Brain Inj. 2005;19(11):863–80.

Ghajar J. Traumatic brain injury. Lancet. 2000;356(9233):923–9.

Graham DI. Paediatric head injury. Brain. 2001;124(7):1261–2.

Langlois JA, Rutland-Brown W, Thomas KE. Traumatic brain injury in the United States: emergency department visits, hospitalizations, and death. Atlanta: Centers for Disease Control and Prevention, National Center for Injury Prevention and Control; 2006.

White JR, Farukhi Z, Bull C, Christensen J, Gordon T, Paidas C, Nichols DG. Predictors of outcome in severely head-injured children. Crit Care Med. 2001;29(3):534–40.

Challenges During Surgery for Myelomeningocele and Encephalocele

58

Brad M. Taicher and Allison Kinder Ross

Myelomeningocele

Damage to Neural Placode

Overview

The first issue that is often confronted in the infant who presents to the operating room for repair of a myelomeningocele is the challenge of positioning for induction and intubation prior to surgery. An infant with myelomeningocele is at risk of damage to the exposed neural placode if any pressure or weight is placed on the unprotected neural elements.

Prevention

To protect the neural placode after birth, infants are typically kept in the prone position with a light sterile wrap over the affected area. Because the prone position is not conducive to smooth airway management for induction and intubation prior to surgical repair, steps need to be taken to protect the neural placode during that critical time. To put the infant into the supine position, a platform needs to be built that elevates the infant above the height of the bed so that the defect is suspended without any pressure or weight on the neural elements. Several methods have been described that aim to not only keep the neural tube defect protected from pressure but to also keep it sterile. The presence of hydrocephalus with relative increased head size may add to the difficulty of positioning the patient for optimal airway management.

A small defect may simply require that a sterile towel be unwrapped and then twisted to form a circle that will perfectly surround the defect and allow the skin around it to rest upon the towel itself, while the defect falls into the hole in the middle. For stability, the head and legs will also need to be supported with either towels or foam padding.

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A larger defect will require a higher platform. A foam head ring can support the defect by allowing the skin to sit upon the foam while the defect falls to the center hole. Another head ring may be turned in its opposite direction to hold the head and upper body in place. If one is unable to support a particularly large neural tube defect in a supine infant, intubation should occur in the left lateral decubitus position.

Similar to induction and intubation, upon emergence, if it is determined that the infant is to be extubated following repair, this may be done in the prone or lateral position as long as there is a backup elevated platform available if the infant needs to be put urgently into the supine position for airway issues.

Extra help should be utilized throughout induction, intubation, and emergence to ensure that proper positioning is maintained.

Key Points

- Risk can be completely avoided with proper positioning.
- Infant should remain in prone or lateral position even after repair.

Hydrocephalus

Overview

Hydrocephalus occurs from either overproduction of CSF, inability to absorb CSF effectively, or, most commonly, obstruction to CSF flow. While 15–25% of patients with myelomeningocele may initially present with hydrocephalus, up to 90% will eventually develop it. The cause of hydrocephalus in an infant with myelomeningocele is the presence of a Chiari II malformation. A Chiari II results in the partial or full obstruction of the flow of CSF from herniation of the cerebellar vermis, brainstem, and fourth ventricle into the

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upper cervical region of the spinal canal. In fact, complications from Chiari II malformation are the leading cause of death in individuals with myelomeningocele who are less than 2 years, and many of these are due to the resulting hydrocephalus.

Prevention

There is no clear way to prevent hydrocephalus in an infant with myelomeningocele; however, it is possible to prevent the complications of hydrocephalus by shunting the CSF, most commonly using a ventriculoperitoneal shunt. Not every infant with myelomeningocele defects will require a CSF shunt, particularly those who have more caudal defects. Application of stringent guidelines for shunt placement may reduce the number of shunts that needs to be inserted down to 51% but does not reduce the actual risk of hydrocephalus. A promising practice may be the in utero closure of the myelomeningocele, which has shown to decrease the incidence of hydrocephalus at 12 months of age. Although fetal surgery may result in a reduced incidence of shunt-dependent hydrocephalus, maternal and fetal risks remain, and long-term improved outcomes have not yet been proven.

Crisis Management

Pathology and Clinical Presentation

It is not the hydrocephalus itself that is the complication leading to crisis. In fact, slowly developing hydrocephalus often does not require immediate attention. It is the increasing intracranial pressure with a defined brain mass in a limited, restricted skull that creates the crisis (Monro-Kellie hypothesis). Potential complications of hydrocephalus include oculomotor palsy, dysphagia, protracted vomiting, and failure of closure of cranial sutures. When the sutures have closed and the intracranial space is restrictive, increased intracranial pressure is a risk. Twenty percent of infants with myelomeningocele may present with stridor due to hydrocephalus from Chiari malformation. Infants may also develop nerve dysfunction with life-threatening hypoventilation or apnea, even in cases where pressure on the brainstem is relieved with appropriate shunting.

Children with myelomeningocele have sleep-disordered breathing at an incidence as high as 20%. In children with obstructive sleep apnea, nasal CPAP is more effective than adenotonsillectomy. Central apnea may be treated with methylxanthines and supplemental oxygen, but these are not 100% effective, and the children may ultimately require positive-pressure ventilation.

Patient Assessment

Although most children will receive a CT scan for monitoring of hydrocephalus, symptoms and physical findings are more commonly used for diagnosing the degree of insult from the enlarging ventricles (Table 58.1). In an infant with open sutures, a large head with massive open fontanels may be present. Signs of increased ICP may occur late in the process as the head expands slowly with the increasing volume of CSF. A child with sutures that are beginning to fuse or are closed will present with signs of increasing ICP such as headache, vomiting, lethargy, ataxia, visual disturbances, and in extreme cases, bradycardia or cardiorespiratory arrest. Patient assessment should primarily determine the degree of compromise from the increased intracranial pressure that is present with the hydrocephalus so that appropriate steps may occur in a timely fashion.

Table 58.1 Hydrocephalus signs and treatment

	Signs/symptoms	Treatment
Increased ICP – mild or chronic	Nausea/vomiting	Shunt placement
	Headache	Mild hyperventilation
	Lethargy	
Increased ICP – severe or acute	As above, plus	Emergent shunt or ventricular decompression
	Bradycardia and/or irregular respirations	Mannitol 0.25–0.5 g/kg (max of 30 g)
		Furosemide 0.5–1 mg/kg (max of 10 mg)
		Moderate hyperventilation
Respiratory irregularity	Tachypnea	Secure airway or CPAP depending on severity/ timing
	Apnea	
	Stridor	
Aspiration	Vomiting	Rapid sequence induction (modified)
	Preinduction	Cricoid pressure

Intervention and Treatment

Treatment for symptomatic hydrocephalus is placement of a shunt or ventriculostomy; however, these procedures are not without risk (see Table 58.1). Firstly, in a child with increased ICP, the anesthetic plan should take into consideration the desire to avoid any further increase in the ICP. Barbiturates for induction with little to no apneic period (thus avoiding a rising PCO_2) and rapid tracheal intubation are necessary. The infant or child who has recurrent vomiting is at risk for aspiration during anesthetic induction. One must weigh the risk of aspiration and need for rapid sequence induction against the risk of herniation and desire for a controlled, hemodynamically stable induction for neuroprotection. A modified rapid sequence induction may be a fair compromise in this circumstance. A combination of agents that allows for cardiovascular stability and, therefore, reduces the risk of increasing intracranial pressure should be used during induction. Cricoid pressure should be applied and relatively small positive pressure breaths utilized prior to intubation. Agents that are suitable in this circumstance are lidocaine 1 mg/kg and a narcotic to blunt the response to laryngoscopy, either propofol or thiopental as the induction agent, and a nondepolarizing muscle relaxant. Intubation should be gentle, and moderate hyperventilation to an end-tidal

CO_2 in the mid to low 30s is acceptable while the patient is prepped waiting for shunting. Avoid extreme head flexion, as it may result in brainstem compression in the presence of a Chiari malformation. Intraoperatively during the shunting procedure, the basilar artery or its branches may be violated – this can result in severe intracranial bleeding and emergency craniotomy.

Of note, in an infant or child with hydrocephalus who has had a ventriculostomy tube inserted and connected to a drainage bag, it is important to keep the bag at the height of the head (ideally tragus level) so that sudden changes in CSF flow and pressure do not occur. The tubing should be clamped or closed during transport and transfer of the child to their bed.

Key Points

- Hydrocephalus in an infant with myelomeningocele is a result of a Chiari II malformation.
- Acute hydrocephalus that results in increased intracranial pressure requires rapid treatment.
- Anesthetic technique in an infant or child with symptomatic acute hydrocephalus should aim at reducing the effects of the increased ICP while protecting the lungs from potential aspiration events.

CSF Leak

Overview

Following repair of a myelomeningocele, there is risk of continued CSF leak, particularly in those infants who have ongoing hydrocephalus or increased pressures. In these infants, the path of least resistance for the "pop off" of fluid pressure is at the fresh suture line after repair.

Prevention

Prevention of a CSF leak is primarily through surgical intervention at the time of repair and avoidance of hydrocephalus or increased pressures that result in leakage. Simultaneous insertion of a ventriculoperitoneal shunt during neural tube repair may reduce the chance of CSF leak by avoiding progressive ventricular dilation and increased CSF pressure at the fresh operative site. From an anesthetic standpoint, it is conceivable that other maneuvers that may increase cerebral or spinal pressures should be avoided such as sustained high airway pressures, coughing, or straining on emergence.

Crisis Intervention

Typically, the infant or child with CSF leak will present with a history of fluid or soft, fluctuant bulge at the site of repair. The child may or may not have other signs or symptoms of complications from the leaking CSF; however, leakage of cerebral spinal fluid may present with findings of hypotension and/or electrolyte imbalance from the loss of fluid. Appropriate volume resuscitation must occur prior to bringing these infants back to the OR for repair of their leak only after a recent electrolyte panel has been drawn and attempts made to correct any abnormalities. Because of potential electrolyte abnormalities, risk of postoperative apnea may be increased, and the infant may need to remain intubated postoperatively depending on the preoperative condition.

An additional risk in these infants with CSF leak is CSF infection and, ultimately, life-threatening sepsis. Antibiotic administration should be ongoing throughout the perioperative period to avoid meningitis or ventriculitis from infected CSF. Perioperative myelomeningocele repair infections are often polymicrobial with gram negatives and *Staphylococcus aureus*. A protective covering or flap firmly affixed caudal to the myelomeningocele repair site helps to prevent fecal contamination of the wound.

Latex Allergy

Overview

Infants who are to undergo the repair of a myelomeningocele are not necessarily at risk for latex allergy at the time of surgery. However, as they age, children with spina bifida, even in the absence of multiple surgical procedures, are at risk for developing latex sensitization. Children with myelomeningocele who require many urologic and orthopedic procedures have a higher association with the development of latex sensitization than those who do not. True latex allergy is a Type I IgE-mediated hypersensitivity reaction that may present as local urticaria or may lead to life-threatening anaphylaxis.

Prevention

The best way to avoid latex allergy is to manage children who have myelodysplasia in a latex-free environment. This not only includes the perioperative area but also all urinary catheters, syringes, Band-Aids, tourniquets, and any gloves that are used for other procedures in children at risk. As of 1998, the FDA mandated that products that contain latex have a warning label. In addition, some antibiotics and certain foods (bananas, avocados, and kiwi are only a few examples) should be avoided because of cross-reactivity in children with true latex allergy. The ASA recommends that patients who have latex allergy be posted as first case in the morning when latex allergens are at their lowest level. In addition, the room should be labeled as being a latex-free environment, and a resuscitation cart should be immediately available. If possible, medications should be drawn from glass vials into syringes that are either glass or have latex-free

plungers. Stopcocks may be used for intravenous injections rather than injection ports that may be made of latex.

The prophylactic administration of antihistamines, steroids, or H-2 blockers is not recommended as they may blunt the early signs of anaphylaxis such as urticaria or mild bronchospasm, thus leaving cardiovascular collapse as the first sign of anaphylaxis.

Crisis and Intervention

Pathology and Clinical Presentation

In a child with myelodysplasia, if there is evidence of anaphylaxis during a surgical procedure despite all precautions taken, latex allergy should immediately be suspected and treated. The pathology of latex allergy is the sensitization and production of IgE antibodies. The IgE binds to mast cells and blood basophils, and, upon reexposure, degranulation of the sensitized mast cells and basophils occurs and the patient suffers a reaction. Under anesthesia, the most common manifestations detected intraoperatively are bronchospasm and cardiovascular instability. It may be difficult to detect cutaneous signs of allergy or anaphylaxis in a child who is under surgical drapes.

Patient Assessment

A rapid survey of the skin for urticaria (if possible), vital signs for hypotension and tachycardia, and auscultation of the lung fields for signs of bronchoconstriction should occur immediately upon suspicion. Serum tryptase levels should be sent once the patient is stabilized. Skin tests to confirm the diagnosis are performed at least 4–6 weeks after the event, and caution should be used, as the test itself may induce anaphylaxis.

Intervention and Treatment

When latex reaction is suspected, all latex-containing items should be removed immediately and any areas of exposure washed. A sign should be posted on the operating room door noting latex allergy so that other providers do not enter and risk spreading airborne latex from glove powder or other venues. Although anaphylaxis may occur from other agents intraoperatively, the treatment is essentially the same and should be initiated when signs are present (see Table 58.2). One hundred percent oxygen and fluid boluses should be delivered. Epinephrine may be required and is advantageous in children with anaphylactic reactions because of its alpha and beta effects.

Secondary therapy includes the addition of intravenous antihistamines, H-2 blockers, and steroids. Dosing is as follows:

Diphenhydramine 1 mg/kg (max of 50 mg)
Ranitidine 1 mg/kg (max of 50 mg)

Table 58.2 Intraoperative latex allergy signs and treatments

Reaction	Treatment	Potential side effect
Bronchospasm	100% oxygen	
	Epinephrine 0.1–10 mcg/kg	Dysrhythmias
	Albuterol or levalbuterol neb via anesthetic circuit	Tachycardia (with albuterol)
Hypotension – mild	Epinephrine 0.1–1 mcg/kg	Dysrhythmias
	Saline or Ringer's lactate solution 10–20 ml/kg	Pulmonary edema
Hypotension – severe	Epinephrine 10 mcg/kg	Dysrhythmias
	Epinephrine infusion 0.01–0.1 mcg/kg/min if needed	
	Saline or Ringer's lactate 20–50 ml/kg	Pulmonary edema
Tachycardia	Saline or Ringer's lactate 10 ml/kg up to 50 ml/kg	Pulmonary edema

Hydrocortisone 5 mg/kg and then 2.5 mg/kg q 4–6 h
Methylprednisolone 1 mg/kg and then 0.8 mg/kg q 4–6 h

Key Points

- Manage children at risk in a latex-free environment.
- Have a high index of suspicion of latex reaction intraoperatively if signs/symptoms of allergy or anaphylaxis are present.
- Rapid treatment with epinephrine, fluid, and second-line agents should occur in the presence of an anaphylactic event.

Miscellaneous Complications

Blood Loss

Blood loss is typically not a major risk in the simple repair of a myelomeningocele but is more of an issue when an extensive flap or undermining of the skin is required for closure. A hemoglobin and hematocrit should be drawn, and a type and screen for blood products should be available preoperatively in case products are required.

Hypothermia

Neonates have poor ability to maintain body temperature due to their large body surface area and inability to create thermogenesis under normal circumstances. In infants and children with myelomeningoceles, there is also the potential of having poor autonomic control below the level of the defect, thus putting them at greater risk of hypothermia in the operating room. Therefore, it is important to warm the operating room prior to entering with the patient; to use radiant warmers during line placement, intubation, and positioning; and to provide forced air warmers around the patient during the procedure.

Urinary Retention

Urinary retention may be thought of as a late complication in children with myelodysplasia; however, only 12% of neonates actually have normal bladder emptying after closure of myelomeningocele. The remaining 88% have urinary retention with a mean volume of 20 ml due to a clinical pattern that is similar to spinal shock. Although most infants will have resumption of near-complete emptying within 2 weeks after closure, many will require catheterization for up to 6 weeks after repair.

Long-term myelomeningocele is the most common cause of neurogenic bladder in children. Routine catheterization is typically required, and these children often require a significant number of urologic procedures. Renal insufficiency or renal failure occurs in up to 30–40% due to vesicoureteral reflux despite routine clean intermittent catheterizations. In addition, ventriculoperitoneal shunt infection occurs more commonly in children who have undergone an intraperitoneal urologic procedure.

Other Considerations

Spina bifida occulta may exist with normal-appearing overlying skin. A sacral dimple that suggests a dermal sinus, a patch of hair, or a fatty swelling should alert the practitioner to the presence of possible abnormal underlying neural structures. In these patients, caudal anesthetic techniques should be avoided until workup has occurred to avoid accidental neural trauma.

Additional complications secondary to myelomeningocele that often lead to further operative intervention include the following:

- Tethered cord
- Poor to no ambulation
- Decubitus ulcers
- Scoliosis

Encephalocele

An encephalocele is a protrusion of cranial contents through a defect in the skull that may occur either posteriorly at the occiput or can also be found in the frontal area. Although the overall incidence is about 1 case per 5000 births, occipital encephaloceles present most commonly. Occipital, or basal, encephaloceles are typically managed by neurosurgeons in the neonatal period. An encephalocele, although similar in embryologic origins to the myelomeningocele, has unique characteristics that present additional challenges not only upon presentation but also in the intraoperative period. Complications that are similar to the myelomeningocele include the following:

- Risk of damage to neural placode
  - Lateral position is preferred due to difficulty in safely securing the airway while protecting a large defect in the occipital region.
- CSF leak
  - Risk of CSF leak is significant due to the lack of normal tissue and disrupted fascial planes from the encephalocele itself.
- Blood loss
- Increased ICP

The two latter problems tend to be more severe in the infant with encephalocele compared with the infant with myelomeningocele.

Blood Loss

Overview

An encephalocele may present in many locations, but an occipital encephalocele presents the practitioner with the risk of significant blood loss intraoperatively because of its proximity with the transverse sinus.

Prevention/Treatment

Blood loss can only be prevented if there is no entry into the larger venous sinuses during encephalocele repair. An MRI is typically performed preoperatively so that the location of blood vessels in relation to the encephalocele helps guide the surgeon with their dissection. Prevention of significant hemodynamic instability from blood loss can occur if blood is available in the room, appropriate vascular access is obtained, and the anesthesia team is aware of the risk of bleeding in this type of procedure. If blood loss is ongoing or significant, FFP and platelets should also be made available and delivered depending on laboratory or clinical evidence of clotting abnormalities from massive transfusion. DIC is a risk in these infants when this occurs.

Increased ICP

Overview

With manipulations of the encephalocele, surgically increased intracranial pressure may occur and needs to be treated (see above treatment under section "Hydrocephalus"). To close an encephalocele, good brain relaxation must be present, and ICP must be maintained within the normal range. Unfortunately, as ICP increases, blood loss also increases and requires additional volume resuscitation requiring a delicate balance between decreasing ICP and increasing intravascular volume.

Suggested Reading

Adzick NS, Walsh DS. Myelomeningocele: prenatal diagnosis, pathophysiology and management. Semin Pediatr Surg. 2003;12:168–74.

Chakraborty A, Crimmins D, Hayward R, Thompson D. Toward reducing shunt placement rates in patients with myelomeningocele. J Neurosurg. 2008;1:361–5.

Fichter MA, et al. Fetal spina bifida repair-current trends and prospects of intrauterine neurosurgery. Fetal Diagn Ther. 2008;23:271–86.

Hamid RK, Newfield P. Pediatric neuroanesthesia. Hydrocephalus. Anesthesiol Clin N Am. 2001;19:207–18.

Hepner DL, Castells MC. Latex allergy: an update. Anesth Analg. 2003;96:1219–29. http://www.asahq.org/publicationsAndServices/latexallergy.pdf.

Hunt JA, Hobar PC. Common craniofacial anomalies: facial clefts and encephaloceles. Plast Reconstr Surg. 2003;112:606–16.

Kaufman BA. Neural tube defects. Pediatr Clin N Am. 2004;51:389–419.

Muller T, Arbeiter K, Aufricht C. Renal function in myelomeningocele: risk factors, chronic renal failure, renal replacement therapy and transplantation. Curr Opin Urol. 2002;12:479–84.

Shaer CM, Chescheir N, Schulkin J. Myelomeningocele: a review of the epidemiology, genetics, risk factors for conception, prenatal diagnosis, and prognosis for affected individuals. Obstet Gynecol Surv. 2007;62:471–9.

Challenges During Cranial Decompression

59

Benjamin B. Bruins and Todd J. Kilbaugh

Overview

Decompressive craniectomy involves the removal of sections of the calvaria and, depending on the indication, dural resection and duraplasty. Although first described over a century ago in the early 1900s by Drs Kocher and Cushing, decompressive craniectomy has survived as an operative approach to increased ICP but with continued controversies on indication, approach, and timing. In this chapter, we focus on the anesthetic approach to patients undergoing a decompressive craniectomy for refractory intracranial hypertension, resulting from traumatic brain injury (TBI) and non-TBI, and Chiari malformations.

Posterior Fossa Decompressive Craniectomy for Chiari Malformations

Chiari malformations are a group of disorders characterized by the caudal prolapse of the medulla, cerebellum, and fourth ventricle through the foramen magnum into the cervical canal. This caudal prolapse is secondary to abnormalities of the brain and a small, malformed skull base. There are four classifications of Chiari malformations (CM), Types I–IV, depending on anatomic compression. Symptoms can vary dramatically: headache, neck pain, myelopathy (neurologic deficit related to spinal cord), and brainstem compromise (Cushing triad: bradycardia, hypertension, and abnormalities in breathing), all resulting from anatomic compression/crowding of the brain stem, cerebellum, lower cranial nerves, and spinal cord. The two most common types of CM are Type I and Type II. Chiari malformation Type I (Chiari I) is the caudal displacement of the cerebellar tonsils less than 6 mm below the foramen magnum into the cervical canal. This displacement is often associated with the disruption of CSF flow, causing CSF to enter the spinal cord and create a fluid-filled cavity called a syrinx. The chronic expansion of a syrinx can cause compression of the surrounding spinal cord nerve fibers and lead to a constellation of symptoms, collectively referred to as syringomyelia. Syringomyelia can occur at any portion of the spinal cord, but, in association with Chiari I and other posterior fossa abnormalities, it is often communicating from the cervical region to the fourth ventricle. In combination with syringomyelia or in isolation, Chiari malformations may also be associated with obstructive hydrocephalus due to fourth ventricular outflow obstruction or aqueductal stenosis, necessitating CSF diversion. Traditionally, CSF diversion has been accomplished with the placement of a ventriculoperitoneal shunt; however, endoscopic third ventriculostomy has also been described with good results. Chiari malformation Type II (Chiari II) is associated with myelomeningocele and often with cerebellar herniation and a malformed brain stem. Chiari malformations Types III and IV are rare and usually present with gross herniation of the cerebellum and severely malformed brain stem. Due to the complexity of the many forms of Chiari malformations and inter-patient variability, surgical approach varies, but the basic tenets address decompression and stabilization of the craniocervical junction, restoration of CSF flow, and ablation of syringomyelia when applicable. A common approach is suboccipital decompression of the posterior fossa, with or without duraplasty, with occipitocervical fusion with autogenous bone graft or posterior stabilization via screw fixation with bone fragments.

Decompressive Craniectomy for Refractory Intracranial Hypertension

Intracranial hypertension (ICH) is a pathologic increased pressure within the calvarium due to a multitude of etiologic processes. Clinical entities such as isolated extra-axial bleeds, mass lesions with surrounding vasogenic edema,

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and obstructive hydrocephalus are often more appropriately treated with addressing the underlying condition. Decompressive craniectomies are most commonly employed in patients with cytosolic edema associated with traumatic brain injury (TBI), cerebrovascular accidents (CVA), and meningoencephalitis. While there are case series reporting good neurologic outcomes after decompressive craniectomies for ICH with viral and bacterial meningoencephalitis, randomized trials are lacking. Additionally timing and surgical approach are topics of contention in the discussion of surgical decompression of patients with ICH associated with meningoencephalitis. In young adults (less than 60 years old), decompressive hemicraniectomy for ischemic stroke is known to have a mortality benefit. Pediatric case series are limited, but these studies also support the use of surgical decompression for patients with ischemic strokes, with improved mortality and functional outcomes. Therefore, we feel decompressive craniectomy should be strongly considered for the pediatric patient with clinical evidence of sustained, intracranial hypertension due to ischemic stroke.

TBI is the leading cause of death and disability in children and adolescents in the USA. In 2012, "Guidelines for the acute management of severe TBI in infants, children, and adolescents," the primary focus is on controlling ICP and minimizing secondary insults to brain parenchyma. *Sustained* elevations of ICP greater than 20 mmHg have been associated with increased morbidity and mortality in the pediatric patient. When first-line therapies (Table 59.1) fail to control ICP, decompressive craniectomy can decrease ICP, maintain cerebral perfusion pressure (CPP), and prevent herniation. There are two current approaches: hemicraniectomy or bifrontal craniectomy. A hemicraniectomy is usually performed when there is a focal or unilateral insult and bifrontal craniectomy with diffuse swelling. A section of the calvaria is removed, the dura is resected, and a duraplasty is performed to relieve ICP and allow cerebral expansion. The section of bone that is removed is usually stored in a bone freezer or can be surgically placed in the subcutaneous tissue of the abdomen until ICP issues have resolved. Decompressive craniectomy reduces ICP and, in some reports, can increase cerebral oxygenation. In contrast to adult studies, Taylor et al. describe a randomized trial suggesting that decompressive bitemporal craniectomy with maximal medical therapy within 24 h of elevated ICP has better outcome scores than medical therapy alone. However, ongoing trials may provide some answers concerning optimal timing, type of decompression, and patient selection for future clinical decisions (Fig. 59.1) (Table 59.1).

Table 59.1 Therapeutic interventions to control intracranial pressure (ICP)

Cerebral blood volume (CBV) reduction	Sedation (decreased cerebral metabolic rate)
	Hypothermia
	Hyperventilation
	Midline head position at 30°
	Diuretics
	Seizure control
Cerebral spinal fluid (CSF) reduction	CSF drainage (ventriculostomy, lumbar drain)
Brain parenchyma volume reduction	Excision dead/injured brain tissue
	Excision tumor or foreign body
	Drainage of epidural/subdural hematoma
	Hypertonic saline administration
	Mannitol administration
Decompressive craniectomy	Hemicraniectomy
	Bifrontal craniectomy
	Posterior fossa craniectomy

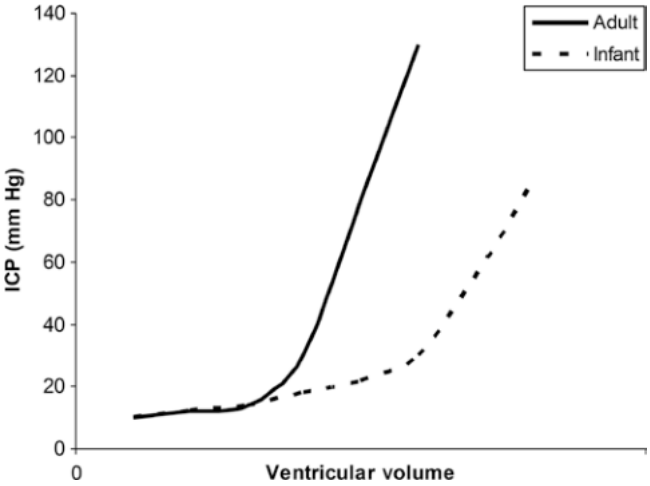

Fig. 59.1 Incremental increases in intracranial volume result in exponential increases in intracranial pressure (ICP)

Perioperative Management for Chiari Malformations

Chiari Malformation Patient Assessment

Patients require a detailed preoperative assessment, focusing on history and physical and diagnostic studies to detect craniocervical anomalies, autonomic instability, atlanto-occipital instability, and cerebellar/lower cranial nerve involvement. Chiari I may be associated with central sleep apnea syndrome, and there are case reports describing sleep apnea as the presenting symptom for Chiari I confirmed by polysomnography. Chiari I is also frequently associated with tethered cord and Klippel–Feil syndrome. Klippel–Feil is a rare disorder associated with fusion of any of the cervical vertebral, as well as a low posterior hairline and short neck. Other associated anomalies with Klippel–Feil are rib and vertebral anomalies, cardiac and renal defects, cleft palate, scoliosis, torticollis, deafness, and atlanto-occipital instability.

An anesthetic plan for a patient with Chiari and associated Klippel–Feil syndrome must anticipate difficult mask ventilation and intubation secondary to limited neck movement due to cervical fusion, atlanto-occipital instability, scoliosis, and palate abnormalities. During intubation and positioning, particular attention should be paid to in-line stabilization of the cervical spine, if there is a suspicion or diagnosis of atlanto-occipital instability. Finally, prior to suboccipital decompression, the anesthetic plan must avoid further elevations in ICP that may precipitate herniation and further decompensation.

Chiari Malformation Intervention and Treatment

In the event of life-threatening intracranial hypertension, acute management should include acute hyperventilation, hyperosmolar therapy with either mannitol (0.25 g/kg, may be repeated and titrated to effect) or hypertonic saline (3%: 5 ml/kg, may be repeated and titrated to effect), and discussion with neurosurgery about emergent placement of ventriculostomy. While this scenario may be a rare occurrence in patients with a thorough preoperative evaluation, many children with Chiari malformations undergoing surgical procedures other than a decompressive craniectomy are at increased risk for intracranial hypertension during the perioperative period, especially patients undergoing neurosurgical or craniofacial surgery, and require close monitoring in the perioperative period.

Perioperative Management for Refractory Intracranial Hypertension

TBI with Refractory Intracranial Hypertension Patient Assessment

Patients with refractory ICP require a detailed perioperative assessment, focusing on mechanism of neurologic injury and severity of extracranial injuries. Often this includes detailed discussions with neurosurgeons, trauma surgeons, and critical care physicians to delineate current CPP targets and required therapies. Additionally, a detailed understanding of intrathoracic, intraabdominal, and other injuries must be elicited prior to the induction of anesthesia. Physical exam should focus on findings of impending herniation syndromes: pupil exam, cranial nerve abnormalities, posturing, and Cushing's reflex (hypothalamic response to ischemia secondary to poor cerebral blood flow, with resulting sympathetic discharge attempting to raise arterial blood pressure, with accompanied bradycardia). In the setting of tissue factor release associated with neurologic injury, coagulopathy is common and should be aggressively treated throughout the perioperative course. Screening for preoperative anemia is important as this can predispose vulnerable neuronal tissue to injury from decreased oxygen delivery.

Decompressive Craniectomy for TBI with Refractory Intracranial Hypertension

Continual reassessment of an unstable multi-trauma patient during the intraoperative period is critical. Ideally monitors should include: arterial access for blood pressure management and CPP optimization, central venous access for central venous pressure, and vasoactive and hyperosmolar delivery. However, placement of these monitors should not delay access by the neurosurgeons to the patient for definitive treatment: emergency decompressive craniectomy. In addition, discussions should take place with neurosurgery for insertion of multi-modal intracranial monitoring including ICP (pressure monitoring or ventriculostomy for pressure monitoring and CSF drainage.) Other multi-modal intracranial monitoring may also include brain tissue oxygen monitoring ($PbtO_2$) and cerebral microdialysis. There is limited data on the impact of anesthetic management on patient outcomes with intracranial hypertension. All volatile anesthetics can increase cerebral vasodilation and CBF especially above one minimal alveolar concentration. In uninjured patients this can be offset via cerebral vasoconstriction with mild hyperventilation. However, the traumatically brain injured patient may have impaired cerebral vasoreactivity and response to vasodilatory and vasoconstrictive stimulus can be less predictable. In addition, there continues to be much debate on anesthetics as neuroprotectants, and their potential for neuronal damage via apoptosis. In animal models, nitrous oxide increases neurotoxic/neuroexcitation mediators, ICP, and CBF and should be avoided in this patient population. Other anesthetic medications (barbiturates, propofol, benzodiazepines, and etomidate) decrease cerebral metabolic rate coupled with CBF and decrease ICP. Opioids should be administered for anti-nociception to prevent ICP spikes from noxious stimuli. Intraoperative goal-directed therapy for pediatric intracranial hypertension should include ICP <20 mmHg, PbtO2 >10–15 mmHg, and age-directed CPP of greater than 40–50 mmHg as minimums. The adult guidelines concur with goals of ICP <20 mmHg, PbtO2 >15 mmHg, and CPP 50–70 mmHg. First tiered therapies for the reduction of ICP and improvement of $PbtO_2$ include brief periods of hyperventilation, drainage of CSF via a ventriculostomy, sedation and paralysis, and hyperosmolar therapy. The optimal intraoperative approach to hyperosmolar therapy has yet to be determined; however, hyperosmolar therapy with hypertonic saline (HTS) may have some theoretical advantage over

mannitol. Mannitol (0.25 g/kg, may be repeated, up to 1 g/kg, and titrated to effect) causes a significant osmotic diuresis, resulting in a loss of preload and a potential rise in hematocrit (decreasing rheology) and ultimately hypotension (decreasing CPP). Mannitol may also result in rebound ICP. Serum osmolarity should be monitored with a target less than 320 mmol. There are two potential mechanisms both resulting in an increased parenchymal reflection coefficient and subsequent cerebral edema with mannitol administration. One, mannitol moves across a disrupted blood brain barrier, and, two, mannitol administration triggers the production of idiogenic osmoles within the brain parenchyma. HTS administration is very effective in lowering ICP (3%: 5 ml/kg, may be repeated and titrated to effect), avoiding the side effects of mannitol discussed above, as well as supporting preload by acting as an excellent peripheral volume expander which, in turn, may support CPP. HTS is more expensive than mannitol, and is not universally available. Additionally, volume expansion with HTS can be associated with increases in central venous pressure, potentially to the point of preventing venous drainage of the cerebral circulation, decreasing CPP. Due to the hypertonicity of HTS, doses should be administered into a central venous line whenever possible. Again, serum osmolarity should be monitored with repeated doses of HTS with goal serum osmolarity less than 360 mmol. Especially in the setting of pretreatment hyponatremia, it is important to closely monitor serum sodium, as rapid changes in serum sodium can lead to central pontine myelinolysis. Additionally, acid-base status must be monitored, as the chloride load is associated with a hyperchloremic metabolic acidosis.

With any disruption of the blood brain barrier such as occurs with decompressive craniotomies, disseminated intravascular contamination can occur. Vigilance in monitoring and correcting PT, PTT, fibrinogen and platelets can prevent bleeding in the perioperative period.

Non-TBI with Refractory Intracranial Hypertension Patient Assessment

Patients with cerebral edema or ICH without traumatic injury require a general assessment of clinical status, focusing primarily on medical comorbidities. Discussions with primary medical teams, neurointensivists, and neurosurgeons will typically revolve around current therapies for seizures, infectious issues, hematologic derangements, as well as blood pressure goals. Many patients with CVA and meningoencephilits will not have intracranial pressure monitors, but instead will have clinical manifestations of refractory hypertension such as Cushing's reflex and/or pupillary abnormalities. If available, preoperative physical exam should be documented to compare to the postoperative neurologic exam. Additionally cardiac exam should be assessed for signs of cardiogenic shock such as gallops and poor peripheral perfusion. Irregular heartbeats and murmurs maybe associated with thromboembolic conditions and should prompt echocardiographic evaluation if time permits.

Decompressive Craniectomy for Non-TBI with Refractory Intracranial Hypertension

The operative course is incredibly dependent upon the underlying etiology of the intracranial hypertension. Regardless of underlying pathology, exquisite attention must be paid to avoidance of hyperthermia, hypoglycemia, hypoxia, and hypotension. The anesthesiologist should have vasoactive medications available, as septic shock is frequently associated with meningoencephalitis and other infections. Vasodilation with volatile agents may exacerbate hypotension, risking additional neuronal injury. Similarly, patients with ischemic strokes are at risk for worsening neuronal injury with hypotension and may require inotropes and/or vasopressors to maintain normotension. Many patients with ischemic strokes will be exposed to anticoagulant and/or thrombolytic medications. The risks and benefits of surgical timing should be clearly discussed with all team members. If patients must have a surgical procedure with residual hematologic derangements, care must be taken to avoid excessive intraoperative bleeding and hypovolemia which can be associated with hypotension and potential neurologic injury.

Key Points

- Decompressive craniectomy involves the removal of sections of the calvaria and, depending on the indication, dural resection and duraplasty.
- Chiari malformations may also be associated with obstructive hydrocephalus due to fourth ventricular outflow obstruction or aqueductal stenosis necessitating diversion of CSF.
- Intraoperative goal-directed therapy for pediatric intracranial hypertension should include ICP <20 mmHg, PbO_2 >10–15, and age-directed CPPs. Infants likely require a CPP greater than 40 mmHg, while adult targets at 50–70 mmHg.
- Maintenance of physiologic parameters, including coagulation, is paramount to successful management in the perioperative period.
- Early decompressive craniectomy (within 24 h) should be considered in the treatment of severe TBI and refractory intracranial hypertension in infants and children.

Suggested Reading

Cakmakkaya OS, Kaya G, Altintas F, Bakan M, Yildirim A. Anesthetic management of a child with Arnold-Chiari malformation and Klippel-Feil syndrome. Paediatr Anaesth. 2006;16(3):355–6.

Cruz-Flores S, Berge E, Whittle IR. Surgical decompression for cerebral oedema in acute ischaemic stroke. Cochrane Database Syst Rev. 2012;1:CD003435.

Friess SH, Helfaer MH, Raghupathi R, Huh JH. An evidence-based approach to severe traumatic brain injury in children. Pediatr Emerg Med Pract. 2007;4(12):1–27.

Kochanek PM, et al. Guidelines for the acute medical management of severe traumatic brain injury in infants, children, and adolescents—second edition. Pediatr Crit Care Med. 2012;13(Suppl 1):S1–82.

Kofke W, Stiefel M. Monitoring and intraoperative management of elevated intracranial pressure and decompressive craniectomy. Anesthesiol Clin. 2007;25(3):579–603.

Pompucci A, De Bonis P, Pettorini B, Petrella G, Di Chirico A, Anile C. Decompressive craniectomy for traumatic brain injury: patient age and outcome. J Neurotrauma. 2007;24(7):1182–8.

Sahuquillo J, Arikan F. Decompressive craniectomy for the treatment of refractory high intracranial pressure in traumatic brain injury. Cochrane Database Syst Rev. 2006;1:CD003983.

Soriano SG, Eldredge EA, Rockoff MA. Pediatric neuroanesthesia. Anesthesiol Clin N Am. 2002;20(2):389–404.

Taylor A, Butt W, Rosenfeld J, Shann F, Ditchfield M, Lewis E, Klug G, Wallace D, Henning R, Tibballs J. A randomized trial of very early decompressive craniectomy in children with traumatic brain injury and sustained intracranial hypertension. Childs Nerv Syst. 2001;17(3):154–62.

Challenges During Surgery for Craniosynostosis and Craniofacial Surgery

60

Heike Gries and Jeffrey L. Koh

Difficult Airway

Overview

Approximately 20% of craniosynostosis patients are in the category of syndromic craniosynostosis. The most common syndromes that present with craniosynostosis are Apert's syndrome and Crouzon's syndrome. In these patients, craniosynostosis repair often involves difficult airway management. Craniofacial surgeries, such as mandibular osteotomies and genioplasties, are often performed on patients with facial disproportion and other congenital anomalies (e.g., Crouzon, Pierre Robin, and Treacher Collins syndromes) and may lead to difficulties in airway management.

Prevention

Identifying patients at risk for airway problems is the first step to successful airway management. Take a careful history (including any prior history of surgery or intubation), perform a thorough physical examination, and tailor the anesthetic plan to include appropriate backup strategies. This will minimize the risk of being caught by surprise. When a potentially difficult airway is identified, appropriate preparation is the next step. All airway equipment should be available, checked, and ready prior to the induction of anesthesia. In addition to the usual intubation equipment, the difficult airway equipment should include at least a fiberoptic bronchoscope as well as appropriately sized laryngeal masks, a rigid bronchoscope, and equipment for tracheostomy and resuscitation.

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Premedication may be varied to suit the patient's needs. Preoperative IV placement (consider topical anesthesia) is usually indicated when a difficult airway is anticipated. Intravenous glycopyrrolate (0.005–0.01 mg/kg) or intravenous atropine (0.01–0.02 mg/kg) is administered to block excessive secretions and to prevent unwanted autonomic vagal reflexes. An intravenous dose of corticosteroid (dexamethasone 0.4 mg/kg) can be given as prophylaxis against airway edema. Finally, topical decongestant such as 0.05% oxymetazoline intranasally should be considered prior to the induction to prevent nasal bleeding if one considers nasal intubation. The decision regarding the use of anxiolysis either orally or intravenously should be balanced with the anticipated degree of airway compromise.

After communicating with the surgeon about the plan(s) and when the surgeon is in the operating room, inhalational or intravenous induction can be initiated. If a difficult airway situation is anticipated and an ENT surgeon is not already involved in the patient's care, consideration should be given to preoperative consultation and presence during induction in case emergency airway assistance is needed. If the ENT surgeon is not available, it is suggested to ask a second anesthesiologist to be available.

Inhalational induction with 100% oxygen and sevoflurane can be used safely with the goal of maintaining spontaneous ventilation. It is often necessary to use jaw thrust and place an oral/nasopharyngeal airway as the upper airway muscles start to relax. Alternatively, intravenous induction with careful titration of propofol, dexmedetomidine, or ketamine can be used (Table 60.1). As with an inhalational induction, the initial titration goal should be to maintain spontaneous ventilation, at least until the provider can confirm the ability to mask ventilate. Muscle relaxants should be held at least until bag-mask ventilation for the patient is established.

In a patient with a potentially difficult airway, it might be reasonable to try a direct laryngoscopy while the patient is breathing spontaneously; however, each attempt for direct

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Table 60.1 Intravenous induction

	Bolus	Continuous infusion
Propofol	1–2 mg/kg	150–200 μg/kg/min
Dexmedetomidine	0.5–1 μg/kg	0.5–1 μg/kg/h
Ketamine	0.5–1 mg/kg	

intubation may cause trauma and will make a potential fiber-optic intubation more difficult.

If it is difficult to manage spontaneous breathing under anesthesia, a laryngeal mask airway (LMA) is often very useful. Although, in most cases, the LMA must be replaced with an endotracheal tube before surgery, it can be helpful to place an endotracheal tube exchanger (Cook Airway Exchange Catheter, Cook Critical Care, Bloomington, IN) before removing the LMA and use it to place the endotracheal tube. Alternatively, fiber-optic intubation can be performed through the LMA. If one choses the latter option, it can be challenging to withdraw the LMA without removing the ETT as well. One option is to telescope two nearly identical ETTs over the fiber-optic scope. The most distal ETT will be left in the trachea, while the proximal ETT is used to maintain the lower tube in position while withdrawing the LMA. The proximal ETT is then removed and replaced with the appropriate ETT adapter. One should always test the ETT setup prior starting the intubation to make sure the ETT combination will fit through the LMA, especially when a cuffed ETT is used. Lubrication of the ETT will also help with passage through the LMA.

Crisis Management

Figure 60.1 shows an algorithm for the unexpected difficult airway in pediatric patients.

Key Points

- Thorough evaluation of the patient to identify a potentially abnormal airway is the first step in preventing difficult airway situations.
- Designing a tailored anesthesia plan with appropriate backup strategies and preparation with attention to details followed by clear communication with the surgical team are essential for a safe and successful procedure.
- Call for help early in an emergency and use algorithms thoughtfully to manage the situation.

Blood Loss and Blood Transfusion

Overview

Blood loss during craniosynostosis repair is very common. This blood loss combined with the small blood volume of the young patients that typically undergo craniosynostosis repair makes transfusion of red blood cells often unavoidable. The need for additional blood products such as platelets and fresh frozen plasma (FFP) is much less common in sagittal and unicoronal suture repair where a blood loss of approximately 25% of the estimated blood volume has been described. However, FFP and platelets are sometimes needed in bicoronal suture repair where blood loss of up to 65% of estimated blood volume has been described.

Accurate assessment and replacement of blood loss in cranial vault repair are difficult, but most blood loss will occur during elevation of the vascular periosteum and then continue slowly throughout the procedure after the osteotomy has been performed. Blood loss will depend not only on the type of craniosynostosis but also on the surgical technique, with procedures requiring more bony dissections, such as cranial vault remodeling, often resulting in higher blood loss. To minimize the risk of transfusion-related morbidity (posttransfusion hepatitis, acquired immunodeficiency, hemolytic transfusion reactions and allergic reactions, transfusion-related lung injury, and leukocyte-platelet allogenic immunization), use all appropriate strategies to decrease the need for homologous transfusion, including utilization of antifibrinolytics.

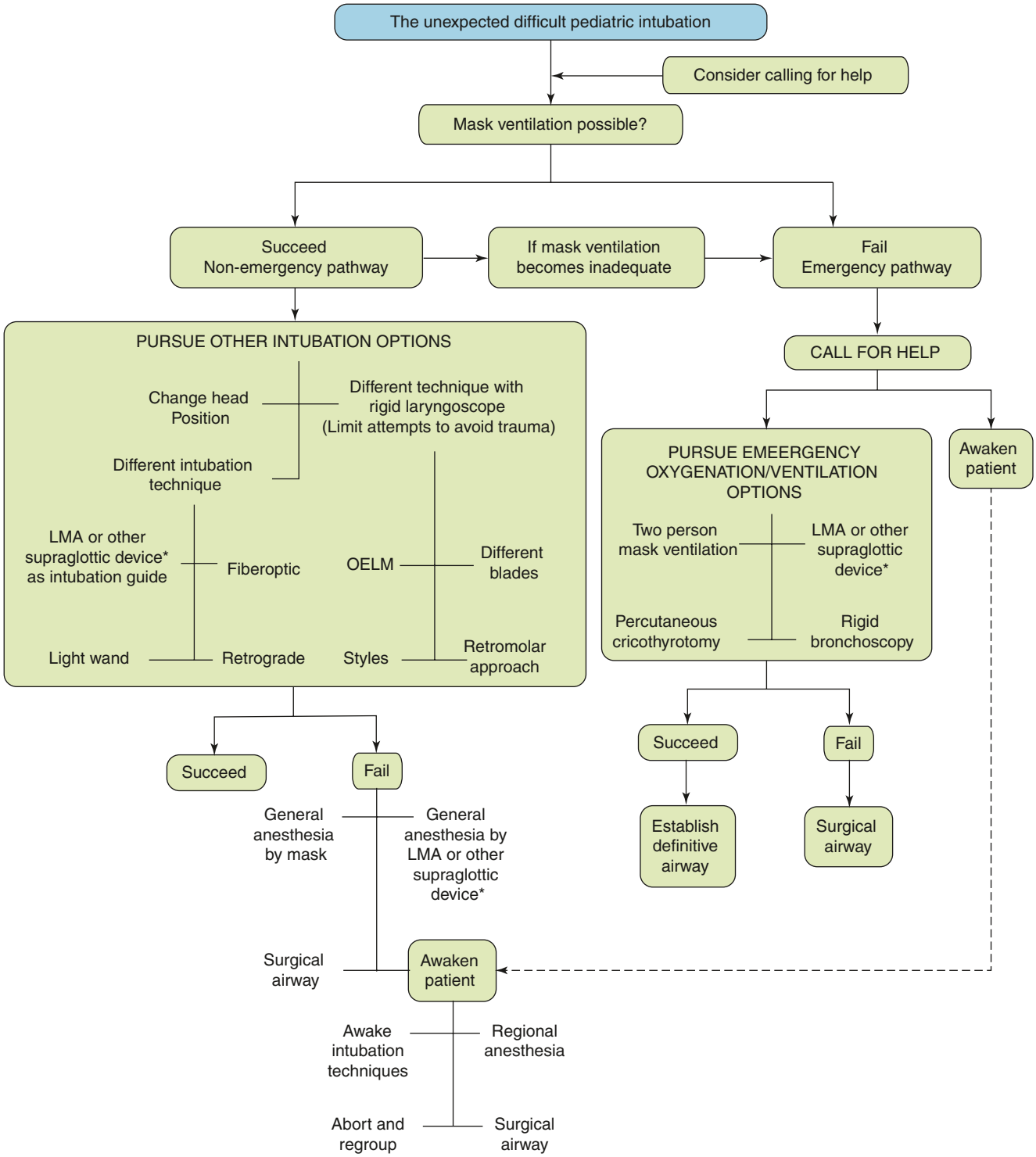
Prevention

The surgical technique will define the range of expected blood loss. The anesthesiologist must prepare before surgery to manage blood loss:

- Evaluate preoperative hematocrit, platelet count, and coagulation studies.
- Type and cross for packed red blood cells and use:
  - Leukocyte-depleted components
  - Cytomegalovirus seronegative products for children younger than 1 year
  - Red blood cells stored < 3 weeks
- Insert two large-bore intravenous catheters (22–20 gauge catheters for infants less than 6 months are adequate).
- Place an arterial line.
- Consider monitoring central venous pressure, especially if large blood loss is anticipated.
- Estimate the maximal allowable blood loss (MABL) before surgery (Fig. 60.2).

The following techniques may help to prevent blood transfusion:

- Antifibrinolytics (e.g., tranexamic acid: Loading dose not clearly established but clinical reports suggest a loading dose between 10 and 50 mg/kg IV over 20 min with a maintenance dose of 5–10 mg/kg/h)



*Consider using PLMA if the child is at risk for aspiration or if high inflation pressures are needed

Fig. 60.1 A proposed algorithm for the management of the unexpected difficult pediatric airway. *LMA* laryngeal mask airway, *OELM* optimal external laryngeal manipulation, *PLMA* ProSeal LMA. (With permission from Elsevier, from Wheeler, M, Cote CJ, Todres ID. The pediatric airway. In: Cote CJ, Lerman J, editors. A practice of anesthesia for infants and children. 5th ed. Saunders Elsevier; 2013. p. 263)

$$MABL = EBV \frac{(Ho - HI)}{Ho}$$

EBV = Estimated blood volume
Ho = Baseline (preoperative) Hematocrit (%)
HI = Lowest acceptable Hematocrit (%)

Fig. 60.2 Maximal allowable blood loss (MABL)

- Preoperative treatment with recombinant human erythropoietin (300 U/kg erythropoietin every other day subcutaneously for 3 weeks with additional elemental iron (2 mg/kg TID) orally)
- Perioperative blood salvage (cell saver)
- Acute normovolemic hemodilution, especially in older children

Crisis Management

Signs of significant blood loss include:

- Tachycardia.
- Low blood pressure.
- Low CO_2 can be an indicator for diminished cardiac output.
- Respiratory variation in arterial line pressure wave.

Transfusion guidelines:

- As a rule of thumb: *Red blood cell transfusion* is rarely indicated when the hemoglobin concentration is >10 g/dL and is almost always indicated when the hemoglobin concentration is <6 g/dL. Sometimes, red blood cells must be given before the MABL is reached, e.g., with rapid blood loss or when hemodynamic instability occurs despite adequate volume replacement. Be aware that rapid blood transfusion in an infant can cause hyperkalemia and cardiac arrest, primarily because of the high concentration of potassium in stored blood.
- *Platelet transfusion* is usually required if the platelet count is $<50 \times 10^9$/L. The therapeutic dose is one platelet concentrate per 10 kg body weight or 5–10 mL/kg body weight.
- *FFP* is indicated to correct microvascular bleeding when prothrombin and partial thromboplastin times are >1.5 times normal or in the setting of massive transfusion when coagulation tests cannot be obtained in a timely manner. To achieve an increase in plasma factor concentration of 30%, 10–15 mL/kg FFP should be given.
- *Cryoprecipitate* must be considered when microvascular bleeding is present and fibrinogen levels are <80–100 mg/dL. One unit of cryoprecipitate per 10 kg body weight will normally raise the plasma fibrinogen concentration by approximately 50 mg/dL.
- *Calcium gluconate* (30–45 mg/kg) or calcium chloride (10–20 mg/kg via central venous line) may be indicated to stabilize myocardial function and to treat hypocalcemia, which occurs in cases requiring larger volumes of citrate-containing blood products.

Key Points

- Blood loss during craniosynostosis repair is very common, and blood transfusion is often necessary.
- Preparing for anticipated blood loss and using strategies to decrease homologous transfusion will contribute to an excellent patient outcome.

Venous Air Embolism

Overview

Venous air embolism has been reported in up to 83% of craniosynostosis repairs, most of them without hemodynamic consequences. Positioning the head above the heart and exposing open noncollapsible veins to air after opening the skull together with a decreased central venous pressure during rapid blood loss can result in a pressure gradient that favors venous air entry. Furthermore, the persistence of a patent foramen ovale in 50% of children younger than 5 years increases the potential for a paradoxical air embolism and may result in a coronary or cerebral embolism.

Prevention

- Avoid positioning the head above the heart as surgical indications allow.
- Avoid nitrous oxide due to its low blood/gas partition coefficient and its ability to increase the size of any air embolus that occurs.
- Use a precordial Doppler ultrasonic probe to detect venous air embolism early.
- Maintain adequate intravascular volume status, and avoid a sudden decrease in the central venous pressure.
- Control ventilation and prevent negative intrathoracic pressure.

Crisis Management

- Ventilate patient with 100% oxygen.
- Communicate with the surgeon immediately to treat early (flood the surgical field) and minimize further air entrainment.

- If central venous access is in place, try to aspirate air from the central venous pressure line.
- Consider compressing the jugular veins until the surgeon has occluded air entry.
- In the case of severe venous air embolism, consider lowering the head to decrease the rate of air entrainment.
- Do not use PEEP. This may cause a paradoxical air embolism by increasing right atrial pressures and opening a patent foramen ovale.

Key Points

- Venous air embolism is common in craniosynostosis repair but usually asymptomatic.
- A precordial Doppler ultrasonic probe will detect venous air embolism immediately and, therefore, will allow early treatment.
- Communication with the surgeon is a key to early treatment.

Increased Intracranial Pressure

Overview

Approximately 30–40% of patients with syndromes and complex craniosynostosis have intracranial hypertension, while 15–20% of patients with single suture craniosynostosis have increased ICP. Restricted skull volumes are responsible for this increase in pressure as well as anomalous intracranial venous drainage, hydrocephalus, and upper airway obstruction, especially in patients with craniofacial syndromes.

Prevention

Each patient should be assessed preoperatively for any signs or symptoms of increased ICP. In addition, preoperative studies such as CT scans or MRIs should be reviewed for signs of increased ICP. To prevent further increases in ICP:

- Establish and secure the airway meticulously, and control ventilation to minimize the risk of hypoxia and hypercapnia.
- Avoid arterial hypertension.
- Position the head carefully, and avoid Trendelenburg position if possible.

Crisis Management

- Check oxygenation and ventilation of the patient.
- Assess level of sedation, and increase anesthesia, if appropriate.
- Check head positioning to rule out venous outflow obstruction.
- Consider moderate hyperventilation and maintain a normal arterial pressure.
- Consider mannitol and/or furosemide.

Key Points

- A significant number of patients for craniosynostosis repair may present with increased ICP.
- An established well-secured airway is the key to avoid hypoxia and hypercapnia and, therefore, to prevent a further increase in ICP.
- Moderate hyperventilation, mannitol, and furosemide as well as positioning are important treatment options.

Suggested Reading

Difficult Airway

Butler MG, Hayes BG, Hathaway MM, et al. Specific genetic diseases at risk for sedation/anesthesia complications. Anesth Analg. 2000;91:837–55.

Sunder RA, Haile DT, Farrell PT, et al. Pediatric airway management: current practices and future directions. Pediatr Anesth. 2012;22:1008–15.

Blood Loss and Blood Transfusion

British Committee for Standards in Hematology Transfusion. Transfusion guidelines for neonates and older children. Br J Haematol. 2004;124:433–53.

Goobie SM, Haas T. Bleeding management for pediatric craniotomies and craniofacial surgery. Pediatr Anesth. 2014;24:678–89.

Koh JL, Gries H. Perioperative management of pediatric patients with craniosynostosis. Anesthesiol Clin. 2007;25:465–81.

Venous Air Embolism

Faberowski LW, Black S, Mickle JP. Incidence of venous air embolism during craniectomy for craniosynostosis repair. Anesthesiology. 2000;92:20–3.

Increased Intracranial Pressure

Tamburrini G, Caldarelli M, Massimi L, et al. Intracranial pressure monitoring in children with single suture and complex craniosynostosis: a review. Childs Nerv Syst. 2005;21:913–21.

Challenges During Tumor Surgery in Children and Infants

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Jonida Zeqo, Gregory W. Albert, and Jayant Deshpande

Neuromonitoring Failure

Overview

Evoked potentials increasingly are used in neurosurgery to monitor the integrity of specific sensory or motor pathways. Specific pathways that are monitored depend on the location of the tumor. Sensory evoked potentials (SEPs) can monitor somatosensory (SSEPs), brain stem auditory (BAEP), or visual (VEP) pathways. Motor evoked potentials (MEPs) can monitor the dorsolateral and ventral spinal cord as well as some cranial nerve functions. Other cranial nerves can be monitored with triggered and free-running electromyography (EMG).

For evoked potentials (SSEP, BAEP, VEP, MEP), an electrical stimulus is applied, and appropriately placed electrodes detect the transient potential differences along the neural pathway. Latency and amplitude of the potential differences are compared to values at baseline obtained before the initial incision is made. Significant increases in latency and/or decreases in amplitude may indicate compromise of the monitored neural pathway. EMG detects target muscle activity induced by electrical (triggered EMG) or mechanical (free-running EMG) stimulation of the nerve.

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Prevention

Anesthetic, physiologic, and environmental factors are all capable of producing changes in evoked potentials that mimic pathway compromise. Communicating changes in both anesthetic dosing and monitored vital signs with the neuromonitoring team are crucial to avoid inadvertently assuming that changes in monitored variable are necessarily secondary to a surgical or pathologic intervention.

All anesthetics that have been studied influence evoked potentials to some extent. Volatile agents have the most profound effect and, therefore, are often avoided all together in favor of a total intravenous anesthesia (TIVA) technique. A significant change in dosing regimen of an IV agent (e.g., boluses) will affect the neuromonitoring. Thus, any changes to anesthetic dosing must be communicated to the monitoring team. In addition, pharmacologic paralysis should be avoided when MEPs or EMGs are used as detection of muscle activity is crucial for these techniques.

Significant changes in most physiologic factors, such as temperature, blood pressure, PaO_2, and $PaCO_2$, can also alter signals from baseline. Much like anesthetic use, maintaining steady levels of these parameters is imperative to avoiding large changes in signal latency and amplitude.

Crisis Management

Significant changes in monitored evoked potentials should be immediately communicated by the neuromonitoring team to the surgeon and anesthesiologist. Concurrently, the anesthesia team should evaluate possible contributing factors, including (a) anesthetic changes (i.e., volatiles turned on, bolus agents given, paralytic agents given, etc.) or (b) significant decrease in cerebral/spinal cord oxygen delivery (e.g., hypotension, hypoxia). If using deliberate hypotension, discuss with the surgeon the possibility of

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returning blood pressure to baseline. The surgeon should evaluate any recent surgical maneuvers (retraction, implant placement, irrigation, tumor resection, etc.) that may have caused damage or irritation of a neural structure.

Key Points

- Evoked potential monitoring can guide the neurosurgeon and help to maintain cortical and spinal pathway integrity.
- The latency and amplitude of potentials are recorded to monitor any pathway compromise. Muscle activity can be used to monitor the integrity of certain cranial nerves (e.g., cranial nerve VII).
- Changes in anesthetics and physiological parameters can cause evoked potential changes that mimic pathway compromise.
- Maintaining systemic perfusion and oxygen delivery during any episode of possible pathway compromise is essential.

Massive Hemorrhage

Overview

The child has a smaller total circulating blood volume compared with an adult (Table 61.1). Blood loss that is inconsequential to adults may lead to circulatory collapse in children.

Close monitoring of blood loss is important and consists of evaluating not only blood in the suction canister but also that in the drapes and on surgical sponges. Large amount of blood loss may go undetected or may be difficult to control because of the constraints of the operative field or the inaccessibility of the offending vessels. In addition, some pediatric brain tumors (e.g., medulloblastoma) can be very vascular with many abnormal, thin-walled blood vessels. This abnormal nature of these vessels can make bleeding difficult to control until the tumor is completely resected.

Table 61.1 Total circulating blood volume (child)

Age	Total blood volume (mL/kg)
Newborn	80–85
6 weeks to 2 years	75
2 years to puberty	72

Prevention

The first step to prevention is good preoperative planning. The anesthesiologist and neurosurgeon should discuss the patient beforehand. The surgeon should give an indication of the expected nature of the tumor (vascular versus not vascular) and other sources of blood loss that may be encountered (e.g., nearby arteries, veins, or venous sinuses). The team should also consider whether it is prudent to have a type and screen performed or blood products immediately available (in the room/OR refrigerator). The patient should have had recent CBC and coagulation studies checked. Consideration should be given to any medications the patient is on that may affect clotting status, including certain anticonvulsants which may inhibit platelet function. All involved in the operation must also understand that unexpected occurrences do happen and need to be prepared for these events.

Adequate surgical access with appropriate positioning and surgical exposure are also critical for prevention and control of blood loss. The better the visualization, the easier it may be to avoid vessels and, if necessary, to respond to any hemorrhaging that does occur. Maintaining a low-normal $PaCO_2$ (35–40 mmHg) decreases cerebral blood volume and provides better surgical access. Deliberate hypotension may also be requested to reduce surgical bleeding.

Adequate IV access is important. At a minimum, the patient for intracranial tumor resection should have two large-bore IVs that allow for rapid administration of fluids and resuscitation drugs. Placement of an arterial line is also important for monitoring of blood pressure and laboratory values during surgery. The anesthesiologist also must have a plan to address loss of IV access or placement of additional IV lines during surgery if needed.

Crisis Management

Large amounts of blood loss will result in hypovolemia as well as cerebral and systemic hypoperfusion. Acutely, blood pressure may decrease and heart rate may increase, but infants often compensate very well and may not exhibit hypotension or tachycardia until late. Rapid blood loss may quickly precipitate to acute hypotension and bradycardia. If evoked potentials are being monitored, they will show increased latency and decreased amplitude as cerebral or spinal perfusion decreases. Maintaining oxygen delivery to vital organ systems is the goal of therapy.

- Oxygen delivery may be improved by increasing FiO_2 to 100%.

- Isotonic crystalloids (0.9% normal saline) or colloids can be given as a bolus (10–20 mL/kg).
- Warmed packed red blood cells (PRBCs) should be transfused if the patient becomes hemodynamically compromised (start with 10 mL/kg). Institution of a massive transfusion protocol with transfusion of PRBCs, platelets, and clotting factors may become necessary.
- Coagulation studies and hematocrit levels should be obtained to help guide the use of PRBCs and other blood components (e.g., FFP or platelets); consider checking serum calcium levels after the use of blood products.

Key Points

- Massive hemorrhage may occur at any point during tumor resection.
- Adequate IV access and blood product availability are essential to treatment.
- In the unstable patient, blood loss should be replaced with a blood transfusion.
- Serial lab studies will help to guide further treatment after the acute hemorrhage has resolved.

SIADH

Overview

Antidiuretic hormone (ADH) is produced by the posterior pituitary gland. It promotes the resorption of free water in the collecting tubules of the kidneys. This causes a decrease in serum osmolality and subsequent increase in circulating blood volume. ADH release is regulated by numerous stimuli. The two main stimuli are changes in osmolality sensed in the hypothalamus and activation of stretch receptors located in the left atrium.

SIADH occurs when there is excessive ADH present. SIADH results in an abnormal decrease in serum osmolality (<280 mOsm/kg), hypervolemia, and urine output that is low volume and highly concentrated (>300–400 mOsm/kg and urine sodium >30 mEq/L). SIADH appears to be more common in children with tumors in the cerebral hemispheres or posterior fossa.

Prevention

While prevention might not be possible, early recognition is key in avoiding the complications secondary to the hyponatremia associated with SIADH. Hyponatremia can cause altered levels of consciousness, cerebral edema, coma, and seizures. Electrolytes should be checked before surgery. It is important to monitor urine output during surgery and recheck electrolytes if necessary. Hypotonic IV solutions must be avoided to minimize the incidence of these symptoms.

Crisis Management

Hyponatremia is treated according to etiology, the rapidity of onset, level of serum osmolality, and estimation of total body sodium (TBS). Since TBS is typically normal in SIADH, excess total body water should be calculated:

$$\mathrm{TBW}\left(\mathrm{liters}\right) = 0.611\left(\mathrm{weight\,kg}\right) + 0.251$$

$$\mathrm{Normal\,TBW} = \mathrm{TBW} \times \left(\mathrm{serum\ sodium} / 140\right)$$

$$\mathrm{Excess\,TBW} = \mathrm{TBW} - \mathrm{normal\,TBW}.$$

Severity of symptoms of hyponatremia relate to the rapidity of the drop in serum sodium levels. Symptoms usually begin to manifest postoperatively as serum sodium levels decrease. In the OR, symptoms may be masked by the anesthetic agents used. Treatment is guided by sodium levels and serum osmolality. Discontinuing hypotonic IV solutions in mild cases of hyponatremia may be all that is needed. Serum sodium levels <115–120 mEq/L require more aggressive therapy:

- Mild postoperative hyponatremia may be treated with free water restriction.
- Hypertonic 3% saline may be administered at a rate of 1–2 mL/kg/h to raise plasma sodium levels by 1–2 mEq/L/h but not >10 mEq/L/day.
- Normal 0.9% saline along with 0.5–1 mg/kg of IV furosemide may be used as an alternative.
- For persistent SIADH in children >8 years old, postoperative treatment with demeclocycline 6–12 mg/kg/day PO divided into two to four doses may be necessary.

Rapid correction may cause permanent neurologic sequelae secondary to osmotic demyelination syndrome. This condition classically occurs in the pons (central pontine myelinolysis) but can occur in other central nervous system structures as well. Risk factors for osmotic demyelination syndrome include rapidity of correction and also duration of hyponatremia, the patient's nutritional status, and other underlying pathologies.

Key Points
- SIADH results in hypervolemic hyponatremia.
- SIADH is a diagnosis of exclusion that presents with decreased urine output, urine sodium >30 mEq/L, urine osmolality >300–400 mOsm/kg, and serum osmolality <285 mOsm/kg.
- Symptoms are related to the rapidity of onset and chronicity of the hyponatremia.
- Mild hyponatremia treatment consists of avoidance of free water and hypotonic fluids and fluid restriction.
- Severe hyponatremia should be corrected cautiously with frequent evaluation to avoid osmotic demyelination.

Central Diabetes Insipidus

Overview

Diabetes insipidus (DI) results from inadequate secretion of ADH or the inability of ADH to act on the kidneys. This results in polydipsia, hypernatremia, and large amounts of very dilute urine. Hypernatremia produces worsening neurological symptoms (mental status changes, coma, and seizures) and can cause renal insufficiency which may progress to renal failure. Reduction in brain volume may damage delicate vessels leading to subdural, subarachnoid, or even subcortical hemorrhage.

Patients with sellar and suprasellar tumors (e.g., craniopharyngioma, pituitary adenoma) are most likely to develop DI from tumor resection. Intracranial neurosurgical procedures, alone, may also cause DI. The clinical course varies and depends on the location and type of tumor and the amount of cerebral manipulation. Polyuria may be present for only a few days after surgery, may be permanent, or may present in a triphasic sequence with return of function followed by recurrent DI.

Prevention

Similar to SIADH, prevention of DI may not be possible. However, the consequences of electrolyte derangement can be prevented. The most feared complication of acute hypernatremia is central pontine myelinolysis (CPM). CPM is nerve damage caused by the destruction of the myelin sheath covering nerve cells in the brain stem. Urine output should be monitored during and after surgery. In a patient with polyuria undergoing neurosurgical intervention, frequent urine and serum electrolyte monitoring is needed to detect episodes of hypernatremia.

Patients already diagnosed with DI are often on DDAVP (desmopressin). It is a synthetic analog of ADH that can be given by a variety of routes. When given intranasally, it has prolonged antidiuretic activity (12–24 h) and is associated with a low incidence of pressor effects.

Crisis Management

The clinical signs of severe hypernatremia and hypovolemia associated with DI are largely masked by general anesthesia. However, polyuria in the face of rising serum sodium should raise suspicion. Typically, urine sodium is <10–15 mEq/L and urine osmolality is <400 mOsm/kg. Decreased blood pressure and tachycardia due to hypovolemia can also be seen, if DI has been allowed to progress. Total body water deficit (TBWD) can be calculated to help aide in fluid management: $TBWD = TBW \times [([Na] - 140)/140]$.

- Fluid replacement with isotonic IV solutions.
- DDAVP 0.3 mcg/kg IV as a slow push is useful as replacement therapy. Postoperatively, DDAVP can be administered IV, orally, or intranasally.
- If the patient is on an intranasal dose of DDAVP, 1/10 of the nasal dose may be given IV.
- Serum electrolytes should be checked frequently to ensure that the decrease in plasma sodium is no faster than 1–2 mEq/L/h.

Hypotonic solutions are rarely needed perioperatively. However, if the patient is actively seizing or is having severe neurologic symptoms, hypotonic solutions can be used with very great caution. Overly aggressive correction may result in acute brain swelling.

Key Points
- Central DI results in the underproduction of ADH by the posterior pituitary.
- Diagnosis is made in the presence of polyuria with urine sodium <10–15 mEq/L, urine osmolality <400 mOsm/kg, and serum sodium >150 mEq/L.
- Symptoms are related to hypernatremia (changes in mental status, coma, and seizures) and hypovolemia (low blood pressure, tachycardia, and organ underperfusion).
- Treatment involves correction of hypovolemia (with isotonic IV solutions) and correction of hypernatremia (with DDAVP).
- Frequent electrolyte monitoring is recommended to avoid a too rapid correction of hypernatremia.

Suggested Reading

Barash PF, Cullen BF, Stoelting RK. Clinical anesthesia. 5th ed. Philadelphia: Lippincott Williams & Wilkins; 2006. p. 760–3, 1149–50.

Cote CJ, Lerman J, Todres ID. A practice of anesthesia for infants and children. 4th ed. Philadelphia: Saunders Elsevier; 2008.

Jaffe RA, Samuels SI. Anesthesiologist's manual of surgical procedures. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2004.

Matta BF, Menon DK, Turner JM. Textbook of neuroanesthesia and critical care. 1st ed. London: Greenwich Medical Media; 2000.

Steward DJ, Lerman J. Manual of pediatric anesthesia. 5th ed. Philadelphia: Churchill Livingstone; 2001. p. 29–30, 207.

Challenges During Surgery for Vascular Anomalies in Pediatrics

62

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Overview

Cerebrovascular disease (CVD) is rare in pediatric patients and commonly manifests its presence as hemorrhagic or ischemic stroke. Underlying vascular anomalies that can result in stroke can be categorized as follows:

1. Structural changes in preexisting blood vessels (aneurysms or arterial dissections)
2. Pathologic vascular structures [arteriovenous malformations (AVMs), vein of Galen malformations (VOGMs), arteriovenous fistulas (AVFs), and cavernous malformations (CMs)]
3. Progressive arteriopathies (moyamoya syndrome or heritable arteriopathies)

Prevention

The perioperative management of pediatric patients with vascular anomalies should focus on optimizing cerebral perfusion. Operative management may be associated with massive blood loss, and these patients require reliable, large-bore IV access and invasive hemodynamic monitoring. Hemodynamic stability during intracranial surgery requires careful maintenance of intravascular volume. Massive blood loss should be anticipated and treated with blood replacement therapy. Hypotension can transiently be treated with vasopressor bolus or infusion (e.g., dopamine, epinephrine, norepinephrine) to temporize during fluid resuscitation. Ischemia can result from blood loss or inadvertent occlusion of parent arteries by the surgeon. In both cases, avoidance of hypotension is critical to maintain collateral perfusion to compromised neural tissue. Table 62.1 lists management techniques for specific lesions.

Table 62.1 Vascular anomalies in children

Aneurysms	Prevent hypertension preclip with vasodilators (labetalol and nitroprusside)
	Anticipate temporary clipping events with planned relative hypertension after clip
AVM/ VOGM	Preoperative staggered embolization (interventional radiology)
	Post-resection hypertension may result in hyperemic cerebral edema (consider antihypertensives)
Moyamoya	Maintain normocapnia, normotension, and normovolemia

Crisis Management

Pathophysiology and Clinical Presentation

Aneurysms

The pathogenesis of pediatric aneurysms includes trauma, infection, and predisposing genetic disorders. These manifest clinically as a subarachnoid hemorrhage (SAH), rapidly increasing intracranial pressure (ICP), and/or direct mass effect. Both microsurgical and endovascular approaches have been described as effective techniques in children. However, the aneurysms in children have distinct pathologic differences with those in the adult population.

Postoperative Complications

- Hydrocephalus – can result from subarachnoid blood and be treated initially with external drain to lower CSF volume and monitor ICP. Approximately one-third of all SAH patients will ultimately require ventricular shunt.
- Vasospasm – extremely rare in children but has been reported. It occurs usually post-hemorrhage day 4–14. It can be identified with transcranial Doppler (TCD) and angiography. It needs to be treated to prevent stroke. Treatment includes nimodipine (controversial in children), induced hypertension, maintenance of euvolemia, and angioplasty/intra-arterial vasodilators (suggestions are extrapolated from evidence in the adult; however, no clinical studies have proven these treatment options effective in children).

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- Hyponatremia – can result from cerebral salt wasting (hypovolemic hyponatremia – treated with replacement) or SIADH (hypervolemic hyponatremia – treated with water restriction); accurate differential diagnosis based on laboratory results is of high importance to avoid further deterioration, particularly in the context of cerebral vasospasm.
- Rehemorrhage or stroke – can occur from faulty clip placement (very rare). Treat with evacuation of clot (if needed) and/or repositioning of clip.

AVM

AVMs consist of direct arterial-to-venous connections without intervening capillaries. They can occur in the cerebral hemispheres, brainstem, and spinal cord. Functional neural tissue does not reside within the lesion. Pathologically 80–85% of all pediatric AVMs present with hemorrhage. Clinically AVMs may present as seizures, headache, or focal neurologic deficits. Hemorrhagic AVMs have been associated with a 25% mortality rate. Rebleeding rates are approximately 6% for the first 6 months, and then 3% per year afterward. This lesion produces neurological deficits through mass effect or from cerebral ischemia that is due to diversion of blood to the AVM from the normal cerebral circulation ("steal"). Recently, an approach consisting of a combination of preoperative embolization (if appropriate) followed by microsurgical excision and followed by confirmatory angiography has been demonstrated to achieve outstanding results (obliteration rate of 100%).

Perioperative Complications

- Hydrocephalus (see above).
- Rehemorrhage or stroke – can occur from faulty clip placement or residual AVM. Evaluate for residual lesion immediately following resection with vascular imaging if possible. Treat as above.
- Normal perfusion pressure breakthrough (NPPB) – a small number of patients with high-flow AVMs will experience postoperative parenchymal hemorrhage and cerebral edema resulting from markedly increased blood flow in cerebral vessels after in toto embolization or surgical resection of the AVM. This NPPB phenomenon should be anticipated after treatment of high-flow lesions and can sometimes be avoided through staged embolization prior to surgical resection and maintenance of normal to slightly low blood pressure postoperatively.

Arteriovenous Fistulas/Vein of Galen Malformations

AVFs and VOGMs are direct connections between cerebral arteries and existing veins. Unlike AVMs, they do not usually have a nidus and, in some cases of AVFs, may exist as a single pathologic connection between an artery and vein. In VOGMs, single or multiple small arterial vessels directly drain into the vein of Galen. The result of this type of direct connection is markedly increased cerebral venous pressure, leading to an increased ICP and potential hemorrhage or even venous stroke. In some VOGMs, the connections have such rapid flow rates that children develop high-output cardiac failure. Carotid cavernous fistulas (CCFs), a subtype of AVF, manifest as a pathologic connection between the carotid artery and cavernous sinus. They can result from trauma, infection, or iatrogenic misadventure. Patients may present with any or all of proptosis, chemosis, pain, and visual problems (loss of acuity and ophthalmoplegia). In general, AVFs are either congenital or they are acquired: they may occur after trauma or in settings of venous stasis as is seen in transverse sinus thrombosis after severe mastoiditis, presumably by the connection of dural arteries in the wall of the sinus into the partially recanalized lumen of the dural sinus.

Perioperative complications: same as AVM. Additionally, patients with large VOGMs may have concomitant high-output heart failure. This may require the use of inotropic cardiac support. Pharmacologic support may be weaned as tolerated immediately following embolization. In large VOGMs, treatment may need to occur over several sessions of embolization and several anesthetics. Practitioners should be prepared to rapidly increase or decrease inotropic support in such situations.

Moyamoya

Moyamoya is an arteriopathy characterized by chronic progressive stenosis to occlusion at the apices of the intracranial internal carotid arteries including the proximal anterior cerebral arteries and middle cerebral arteries resulting in ischemic stroke. Moyamoya *disease* is the idiopathic form of moyamoya, while moyamoya *syndrome* is defined as the arteriopathy found in association with another condition, such as prior radiotherapy to the head or neck for optic gliomas, craniopharyngiomas, and pituitary tumors; genetic disorders such as Down syndrome, neurofibromatosis type I (NF1) (with or without hypothalamic-optic pathway tumors), large facial hemangiomas, sickle cell anemia, and other hemoglobinopathies; and autoimmune disorders such as Graves' disease, congenital cardiac disease, or renal artery stenosis.

Perioperative Complications

- Stroke and transient ischemic attacks (TIAs).
- Maintenance of cerebral perfusion is paramount. Caregivers must be vigilant to maintain normotension, normocapnia, and normovolemia. These patients appear

Table 62.2 "Red flags" on examination or history

Bradycardia, hypertension, decreased respirations (Cushing response)
Dilated pupil, hemiparesis (uncal herniation)
Fixed downward gaze (Parinaud's syndrome)
Lethargy, tense open anterior fontanel in infants
Ataxia with nausea and vomiting
Sudden onset of a third nerve palsy, including involvement of the pupil, would appear dilated
Sudden onset of severe headache
Regression or missing of milestones

to possess some degree of autoregulation, but the absolute limits are unknown (may vary by patient), and the range is likely more narrow. This may result in falling off the curve if even slight hyperventilation or hypotension occurs.

Patient Assessment

Many patients with intracranial vascular anomalies will have no antecedent history or findings on exam. However, clinicians should be attentive to specific "red flags" in the history or exam that may herald an emergency related to CVD (Table 62.2).

Review of Systems

Look for:

- Headaches, seizures, focal neurological deficits – motor (weakness, numbness, visual field problems) or cognitive
- Previous TIAs or strokes
- Systemic illnesses such as lupus erythematosus (SLE), congenital cardiac disease, or high-output cardiac failure and illicit drug use, such as cocaine

Examination

- Typical patient may not have any obvious findings on general physical exam.
- Focal weakness or numbness in a cortical distribution and visual field deficits.
- Presence of a systolic bruit over the eye, head, or neck; present in 15–40% of patients with AVMs or carotid dissections.
- Intracranial arteriovenous shunts may be associated with tachycardia, cardiomegaly, and cardiac failure; especially in infants, consider VOGM.

Radiographic Evaluation

- *Intracranial ultrasonography. Indications:* Infants with open fontanel as initial, nonurgent screening test; can detect hemorrhage, hydrocephalus, large infarcts, or lesions (AVM, VOGM).
- *Duplex ultrasonography* may be useful in children of any age if the diagnosis of an extracranial carotid dissection is being considered.
- *Computerized tomography (CT)/computerized tomography angiography (CTA). Indications:* CT is often the initial study for hemorrhage, delayed stroke, or larger vascular lesions. CTA is excellent for emergent evaluation of AVM and aneurysm and may help with identifying a dissection.
- *Magnetic resonance imaging (MRI) and magnetic resonance angiography (MRA). Indications:* Evaluation of urgent stroke with diffusion-weighted images – DWI, CMs (susceptibility imaging), and nearly all vascular lesions. Consider obtaining frameless stereotaxic sequences if desired in surgery.
- *Digital subtraction catheter angiography (DSA). Indications:* Gold standard for all vascular lesions *except* CMs.

Intervention/Treatment

The surgical treatment for aneurysms, AVMs, and AVF aims toward eliminating the malformation from the cerebral circulation in order to prevent intracranial hemorrhage. This requires clipping or coiling (aneurysm) or embolization and/or resection (AVM/AVF). Alternatively, AVM/AVFs are treated by Gamma Knife over several months if the location precludes an operative approach.

Aneurysms

- *Diagnosis (CT/CTA)* – angiogram after patient stabilized. Lumbar puncture should be considered only if question of diagnosis from history with negative CT; remember to use small-gauge needle and limit CSF removal; xanthochromia is useful in positive diagnosis for SAH.
- Blood pressure control (labetalol, nicardipine, or nitroprusside) – (nimodipine to prevent vasospasm is controversial in children).
- ICP control – external ventricular drain (EVD) if hydrocephalus (avoid overdrainage of CSF to prevent rerupture; often no more than 5 ml at a time). Elevate the head of the bed.
- Consider antiepileptic medication (phenytoin, levetiracetam).

AVM/VOGM

- Most VOGMs and AVFs are treated endovascularly. Post-occlusion hypertension and cerebral hyperemia should be treated aggressively with antihypertensives, e.g., vasodilators. Most high-flow lesions can be treated with staged embolization, reducing the risk of this complication.
- Hydrocephalus – high venous pressures from the fistula can impair CSF drainage, resulting in hydrocephalus. This hydrocephalus usually resolves following treatment of the lesion and often will not require shunting. There is a risk of hemorrhage from passing a ventricular catheter through a swollen brain with high venous pressures. As such, temporizing measures (such as head elevation and medical management) are useful while treating the primary cause of the problem – the fistula.

Moyamoya

The surgical treatment in patients with symptomatic moyamoya disease or syndrome aims at improving cerebral perfusion distal to the lesions in order to prevent cerebral infarction. This requires the creation of one or more cerebrovascular bypass.

Preoperative

- As discussed in the preoperative section, careful management of moyamoya patients before they arrive in the OR can have a significant influence on complication avoidance; patients ideally should be neurologically stable prior to surgery and at least 1 month should have passed after the last significant ischemic stroke. Patients must be medically optimized for surgery, including intravenous prehydration the night prior to surgery. Preoperative imaging is critical to planning vessel selection (the parietal branch of the superficial temporal artery (STA) may be small or absent, necessitating utilization of a frontal or retroauricular branch for the bypass). Preservation of spontaneous collateral vessels (as identified by the preoperative angiogram) from the external carotid system should be maintained during the craniotomy.

Intraoperative

- Maintenance of cerebral perfusion is paramount. Avoid hyperventilation and hypotension at all times. Tight control of blood pressure and ventilatory parameters is crucial. The goal should be normotension and normocapnia based on preoperative values. These patients appear to possess some degree of autoregulation, but the limits are unknown and likely more narrow than unaffected people.
- Meticulous hemostasis.
- EEG is employed during surgery to identify slowing, indicative of inadequate cerebral blood flow, so that the anesthesia team can institute immediate compensatory measures. EEG technicians are part of the OR team and must communicate changes in the tracing to allow the anesthesia providers to respond immediately, with appropriate changes in blood pressure, pCO2, and anesthetic agents.

Postoperative

- Continued IV fluids at 1.5× maintenance for 48–72 h until taking oral liquids.
- Frequent and detailed neurologic examinations to identify ischemia early.
- Aggressive pain control to minimize BP fluctuations and hyperventilation.
- Aggressive prophylaxis and treatment of postoperative nausea and vomiting for the same reasons as above.

Key Points

- Intracranial vascular anomalies may be clinically silent prior to a catastrophic presentation – clinicians should be attuned to "red flags" on evaluation (Table 62.2).
- Preoperative imaging is critical to proper diagnosis, operative planning, and safe treatment.
- Key aspects of anesthetic management center on an understanding of cerebral hemodynamics relevant to each lesion type both pre- and postoperatively, meticulous monitoring of hemodynamic and respiratory parameters, and anticipation of blood loss. The primary goal of perioperative management is maintenance of cerebral perfusion pressure.

Suggested Reading

Awad IA, Robinson JR Jr, et al. Mixed vascular malformations of the brain: clinical and pathogenetic considerations. Neurosurgery. 1993;33(2):179–88. discussion 188

Friedlander RM. Clinical practice. Arteriovenous malformations of the brain. N Engl J Med. 2007;356(26):2704–12.

Gross BA, Storey A, Orbach DA, Scott RM, Smith ER. Microsurgical treatment of arteriovenous malformations in pediatric patients: the Boston Children's Hospital experience. J Neurosurg Pediatr. 2015a;15:71–7.

Gross BA, Smith ER, Scott RM, Orbach DA. Intracranial aneurysms in the youngest patients: characteristics and treatment challenges. Pediatr Neurosurg. 2015b;50:18–25.

Millar C, Bissonnette B, et al. Cerebral arteriovenous malformations in children. Can J Anesth. 1994;41(4):321–31.

Sato K, Shirane R, et al. Effect of inhalational anesthesia on cerebral circulation in Moyamoya disease. J Neurosurg Anesthesiol. 1999;11(1):25–30.

Smith ER, Scott RM. Surgical management of moyamoya syndrome. Skull Base. 2005;15(1):15–26.

Soriano SG, Sethna NF, Scott RM. Anesthetic management of children with moyamoya syndrome. Anesth Analg. 1993;77(5):1066–70.

Challenges During Epilepsy Surgery in Pediatric Patients

63

R. Ryan Field, Abraham Rosenbaum, and Zeev N. Kain

Overview

At least 2.2 million people in the USA have epilepsy – 0.7% of the population by the 2014 US Census. Most often epilepsy presents during the first decade of life, with up to 50% of the cases occurring before the age of 5 years. Of these, 60% have focal epilepsy, and approximately 20% become drug resistant or refractory. Early onset of intractable seizures, particularly in children less than 3 years old, has a very poor prognosis. Epilepsy is considered refractory if seizures continue after 2 years of pharmacological treatment with 2–3 appropriately selected drugs with good patient compliance. Typically, the frequency or severity of seizures in this situation prevents normal function and/or development. Moreover, patients with refractory epilepsy commonly suffer from the side effects and complications of high-dose anti-epileptic drugs. Indeed, even in the therapeutic range, anti-epileptic medications can significantly influence the developing brain.

In addition to the risk of cognitive dysfunction, physical issues are also associated with medically intractable seizures. These patients have higher rates of accidental death or sudden death, ranging from 2% to 18%, as compared to cause of death in all people with epilepsy. Only half of the patients with medically intractable seizures or refractory epilepsy are able to become self-supporting on reaching adulthood. Therefore, early surgical intervention increases the chances of significantly reducing or eliminating seizures, improving quality of life; reducing the risk of cognitive, behavioral, and motor developmental damage; and decreasing the risk for permanent brain injury in infants and young children.

Common causes of pediatric refractory epilepsy that are amenable to surgery include tumors, cortical malformations, vascular abnormalities, and certain epileptic syndromes. Consequently, approximately one-third of children with refractory epilepsy are candidates for surgery. Of those, children with refractory *unifocal* epilepsy are the best candidates for surgical interventions. Although freedom from seizures is important in defining surgical success in the pediatric population, preventing cognitive and developmental decline or stagnation may be an equally, if not more, important measure.

Implications for the Neurosurgical Patient

Surgical therapy for medically intractable epilepsy has traditionally been viewed as an extreme measure, reserved as a last resort when the disease becomes a life-threatening condition or a progressive neurologic disorder. However, recent publications have shown a favorable outcome following surgery in young children with catastrophic epilepsy. For these patients, *when* to have surgery is a critical factor in the decision to have any surgery. Some argue that the young brain demonstrates high neuroplasticity, allowing for better behavioral and cognitive development following trauma or surgery.

In order to determine who will benefit most from surgery, four questions need to be answered: (1) Are the seizures truly epileptic in origin? (2) Is there a consistent anatomical focal origin? (3) Is there more than one seizure focus? (4) Is the lesion excisable? General contraindications including acute psychiatric disorder, neurodegenerative disorder, and medical contraindication need to be ruled out prior to surgical intervention.

Initial epilepsy evaluations should include characterization of the seizures and optimization of medical therapy. A detailed history should identify previous central nervous sys-

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tem infection, trauma, family history, range of previous drugs used, and patient compliance. Neuropsychological assessment is necessary to lateralize brain dominance and speech and memory areas for future follow-up. Further evaluation should include localization of the seizure focus zone.

During the last decade, multiple diagnostic modalities, such as multichannel electroencephalogram (EEG) and video monitoring, high-resolution magnetic resonance imaging (MRI), positron emission tomography (PET), and single-photon emission computed tomography (SPECT), allow noninvasive initial evaluation of patients. Certain invasive techniques, such as depth and surface electrodes, grids, strips, and stereoelectroencephalography (SEEG), have also been shown to be safe and, indeed, more efficacious under certain circumstances.

Radiological evaluation is classically defined as structural and functional; for example, MRI supplemented by CT or cerebral angiography can detect structural pathologies. On the other hand, functional MRI (fMRI) can elucidate active areas of the functioning cortex during simple tasks. PET can show a focal interictal reduction in metabolism, and SPECT can show a focal increase in blood flow. Scalp EEG can identify a focal locus or demonstrate multifocal seizure activity. Many cases begin with noninvasive techniques as a screening tool, followed by either immediate resection or further invasive techniques for final foci identification through seizure mapping. Patients may additionally undergo a WADA test, in which half of the brain is "anesthetized" by injecting sedative/hypnotic through one of the internal carotid arteries. While the brain is partially anesthetized, speech and memory are tested to verify that these critical cognitive functions will be maintained after surgery. fMRI results may eliminate the need for WADA.

When seizure foci are generalized, neurosurgeons most commonly recommend vagal nerve stimulator (VNS) implantation. When multifocal, but confined to one hemisphere, corpus callosotomy or functional or true hemispherectomy may be chosen. Temporal lobectomy frequently improves temporal focus seizures. Occasionally, the surgeon and patient may elect to not proceed with any surgical intervention.

Surgical Techniques (Fig. 63.1)

Temporal Lobectomy

Temporal lobe epilepsy is not the most common etiology of childhood seizures. Nonetheless, this syndrome is usually focal and accessible, making it the most common surgically treated type of epilepsy. Indeed, 56% of all pediatric epilepsy surgeries are temporal lobe resections.

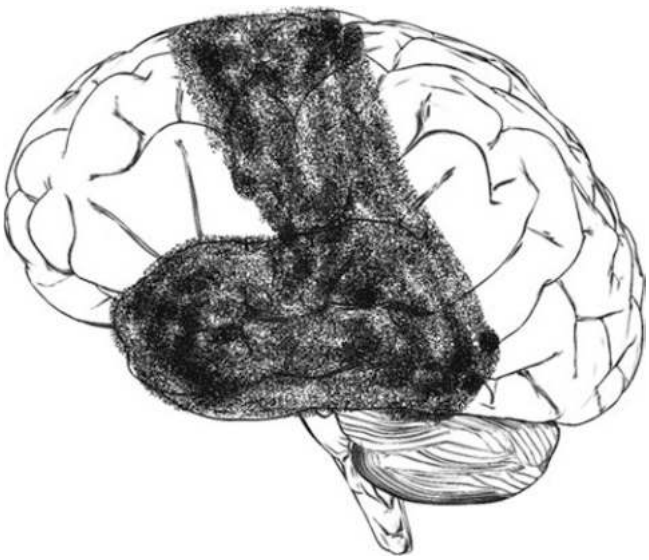


Fig. 63.1 Summary of the most common surgical interventions for intractable seizure disorder. (Partially adopted from Elger and Schmidt (2008))

Hemispherectomy

The most invasive and radical surgical technique for intractable epilepsy is true hemispherectomy. Typically, children with extensive hemispheric damage, as seen in Sturge-Weber syndrome, present for hemispherectomy. Functional hemispherectomy may find preferential use when possible. Disconnection of the epileptogenic hemisphere from the subcortical centers and other hemisphere generally results in fewer complications as compared to true hemispherectomy and may yield equivalent results. Approximately 80% of children who undergo this surgery become seizure free, while another 15% show improvement.

Corpus callosotomy patients most often present without identifiable epileptogenic foci, although many intractable epilepsy cases may find improvement with this surgery. The surgery mainly disrupts the propagation of seizure discharge from one hemisphere to the other. Reduction of generalized seizures with this type of surgery ranges from 56% to 100%. Thirty percent of patients become seizure free after this operation.

Other Interventions

Multiple subpial transections (MSTs) describe a surgical technique where a well-identified epileptogenic locus exists in a cortical area that controls vital function. After identifying the epileptogenic locus, multiple cuts are made in the carefully marked cortex zone. This procedure isolates small cor-

tical sections from each other while still allowing other useful outflow to persist. This technique is very time consuming.

Gamma knife surgery (stereotactic radiosurgery) is a technique that uses a high-energy photon beam directed at a single point in the brain. The tissue in the epileptogenic area becomes necrotic or neurologically altered without harming the surrounding tissue. Generally, there is a lag time of 12–36 months between the treatment and a seizure-free state.

VNS is the least invasive technique for the control of intractable epilepsy. Neurosurgeons most commonly insert vagal nerve stimulators under general anesthesia although some centers use local anesthesia. The VNS mechanism of action needs further clarification; however, pathways through the nucleus of the solitary tract appear at least partially responsible. Interventions with VNS less commonly involve children compared to adults; however, two studies demonstrated a reduction in seizure activity of 60% in 80% of the cases and 50% in 38% of the children, respectively. The patient receives a magnet to take home, which increases stimulation during pre-seizure aura and actual seizure by passing the magnet over the generator for 1–2 s. The magnet can also inhibit stimulation by keeping it over the generator. Currently FDA indication for VNS covers patients 18 years and older. Off-label usage in children 12 years and older frequently occurs, with studies showing clinical efficacy in even younger pediatric patients as well.

Concerns and Risks

Surgical risk must be taken into consideration during preoperative patient counseling, given that, in at least two studies, the overall complication rate was around 3%. Surgical risk can be further divided into transient (infection, hematoma, DVT, hydrocephalus, CSF leakage) and permanent complications (hemiparesis, hemianopia, cranial nerve injury, and dysphasia).

Temporal Lobectomy

This procedure has an infrequent morbidity with an almost 1 in 600 person-years mortality rate. The risk of temporal lobe resection relates to the proximity of the Sylvian vessels as well as to the vessels and optical tract in the ambient cistern. The most common neurological side effect produces homonymous superior quadrantanopsia resulting from interruption of the optic tract. Language and verbal deficits can occur in dominant hemisphere resection, although they usually resolve quickly and often do not occur in children younger than 9 years. Other neurological deficits may occur as a result of Sylvian vessel vasospasm, bone flap infection, wound infection, transient cranial nerve palsy, postoperative psychosis, and postoperative depression. One study found a 5.1% mortality rate, attributable primarily to continuation of seizures after the surgery. Accidents and suicide were also among the causes of mortality.

Hemispherectomy

High-volume blood loss with a need for blood component transfusion can occur during and following this surgery, most commonly in patients with malformation of cortical development, Rasmussen's encephalitis, and Sturge-Weber syndrome. Consequently, strategies such as autologous blood transfusion and staging of the hemispheric surgery in very young patients may improve outcomes. Other reported complications include hydrocephalus, recurrent seizures that require reoperation (usually because of incomplete disconnection), and syndrome of inappropriate ADH secretion (SIADH). There is an expected motor impairment and worsening of preoperative hemiplegia. Homonomous hemianopia is another expected complication, as is loss of useful hand function. Postoperative severe headache and chronic intracranial hypertension have been reported along with new onset of migraine headache.

Poor postoperative cognitive and maladaptive function directly relates to the duration of seizure activity, possibly by affecting the non-operated hemisphere. Thus, as suggested by some authors, early surgical intervention should be a high priority, and patient age at surgery is an important factor for favorable outcome. Postsurgical linguistic outcome is related to the side of the damage and resection, age at the time of surgery, seizure control, and etiology. Most patients show only moderate change in cognitive performance, with variable changes in intelligence quotient.

Corpus Callosotomy

Reported acute complications were wound infection and CSF leak, hydrocephalus requiring shunt, and chemical meningitis/ventriculitis. Hemispheric edema may occur due to prolonged and vigorous retraction of the hemisphere. Corpus callosotomy is known for *acute postoperative neurological syndrome* that includes mutism,

non-dominant arm and leg apraxia, bilateral Babinski signs, and urinary incontinence. These complications are almost always transient, with mutism usually resolving within several weeks. More long-term complications are corpus callosotomy with forniceal injury, possibly resulting in memory disturbances. Damage to the corona radiata may lead to motor weakness. Injury to the pericallosal arteries may result in vasospasm from excessive manipulation and can result in lower-extremity weakness secondary to ischemia. Permanent side effects of callosotomy are relatively uncommon, with weakness or apraxia and language/behavior impairment occurring in 8–12% of cases. Dysphasia and dysgraphia were observed in patients with mixed or crossed cerebral dominance. Some patients have difficulty learning new bimanual tasks, but previously acquired bimanual tasks remain intact. Most of the persisting deficits following corpus callosotomy involve the incomplete integration of information processing across the hemispheres, often referred to as *disconnection syndrome*. These changes are subtle and require neuropsychological testing to be detected.

Vagus Nerve Stimulator

VNS is a relatively safe, well-tolerated procedure with low rates of complication. The most common side effects are noted during stimulation of the vagus nerve consisting of hoarseness, voice alteration, coughing, discomfort, dyspnea, vomiting, and local neck/throat paresthesias, all of which subside in time. Surgical complications include device failure, left vocal cord paralysis, lower facial muscle paresis, and fluid accumulation around the generator and infection around the device. Erosion of the generator through the chest wall is a rare complication and of more concern in small children with little subcutaneous fat. Occasionally patients exhibit transient bradycardia and asystole during intraoperative testing of the device, most commonly treated by cessation of testing. No long-term cardiovascular effects were reported.

Intracranial Electrodes

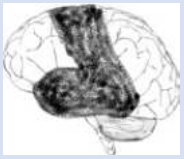
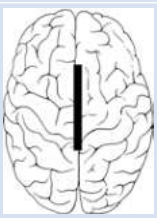
Complication rate of intracranial electrode placement as part of intractable epilepsy workup and diagnosis is as low as 3%, and these mainly include intracranial hemorrhage, infection (meningitis), status epilepticus, aseptic meningitis, and transient neurological deficit. Age, gender, number of electrodes, and number of days with the electrodes do not influence the complication rate.

Key Points

- Up to one-third of children with epilepsy are refractory to medical therapy.
- Far beyond mere seizure control, enhancing development and cognitive potential, treating psychological and behavior problems, and avoidance/reduction of brain damage are goals for treatment in children with intractable seizure disorders.
- Additional complicating factors must be considered, such as the cause of epilepsy and the effect of drugs on the developing brain and brain plasticity when determining the course of treatment.
- Epilepsy surgery is now widely accepted and has a high success rate, even when success is not measured by complete resolution of epileptic episodes.
- Temporal lobectomy is the most common epilepsy procedure in children, followed by extratemporal lesion resection, callosotomy, multiple lobar transections, hemispherectomy/hemispherotomy, and MSTs.
- Complication rates of epilepsy surgery are low and can be divided into transient (infection, hematoma, DVT, hydrocephalus, CSF leakage) and permanent complications (hemiparesis, hemianopia, cranial nerve injury, and dysphasia).
- Vagus nerve stimulators have proven to be an efficient, minimally invasive modality of seizure suppression and control, both in adults and children.

Appendix Summary of the Most Common Surgical Interventions for Intractable Seizure Disorder

Procedure		Clinical use	Percent[a]	Complications[b]
Temporal lobectomy		Temporal lobe isolated lesion	55%	Visual field defects
				Hemiparesis
				Psychotic symptoms
				Homonymous superior quadrantanopsia
				Language/verbal deficit
				Stroke/ischemia of the internal capsule or corticospinal tract

Procedure		Clinical use	Percent[a]	Complications[b]
Topectomy		Extra-temporal lesions	26%	Hemiparesis (transient/permanent) Visual field defect Transient dysphasia Epidural hygroma
Hemispherectomy/ hemispherotomy		Hemispheric lesions Encephalitis Cortical dysplasia Sturge-Weber syndrome	2.8%	Major blood loss Hydrocephalus Early postoperative seizures Incomplete disconnection SIADH Motor impairment Severe headache Transient aggravated hemiparesis Transient dysphasia
Multiple subpial transections (MST)		Lesions in eloquent brain areas Landau-Kleffner syndrome	0.2%	Transient hemiparesis Long-term seizure recurrence Neurological deficit depends of the transected area
Multiple lobar resections		Extended lesions Sturge-Weber syndrome	4.6%	Neurologic outcome depends on location and extent of the resection Seizure-free outcome is poorer compared to unilobar resection
Partial/complete callosotomy		Atonic/drop attack seizures	14.6%	Postoperative disconnection syndrome Lower extremity weakness Personality and memory changes Hemispheric edema CSG leak/hydrocephalus/chemical meningitis

[a]The percent of each procedure out of all the surgical treatments for epilepsy
[b]Most common side effects reported in the literature, not including general complications shared by all procedures which include wound infection, meningitis, or residual hematoma/hematoma creation

Suggested Reading

Albright AL, Pollack IF, Adelson PD. Principles and practice of pediatric neurosurgery. New York: Thieme; 2008. p. 1056–68, 1078–86, 1115–8.

Basheer SN, et al. Hemispheric surgery in children with refractory epilepsy: seizure outcome, complications, and adaptive function. Epilepsia. 2007;1:133–40.

Boon P, et al. Vagus nerve stimulation for refractory epilepsy. Seizure. 2001;10:448–55.

Elger CE, Schmidt D. Modern management of epilepsy: a practical approach. Epilepsy Behav. 2008;12:501–39.

Gonzalez-Martinez JA, et al. Hemispherectomy for catastrophic epilepsy in infants. Epilepsia. 2005;9:1518–25.

Jea A, et al. Corpus callosotomy in children with intractable epilepsy using frameless stereotactic neuronavigation: 12-year experience at the Hospital for Sick Children in Totronto. Neurosurg Focus. 2008;3:E7.

Kemeny AA. Surgery for epilepsy. Seizure. 2001;10:461–5.

Rydenhag B, Silander HC. Complications of epilepsy surgery after 654 procedures in Swede, September 1990–1995: a multicenter study based on the Swedish national epilepsy surgery register. Neurosurgery. 2001;49:51–7.

Challenges During Pediatric Endoscopic Neurosurgery

64

Nina Deutsch

Overview

Endoscopic neurosurgery increasingly has become an important modality in the treatment of several pediatric neurologic conditions. With improvements in imaging, fiberoptic technology, and equipment, minimally invasive techniques have allowed for safe visualization and manipulation of areas that were previously difficult to access through conventional neurosurgical procedures. Table 64.1 summarizes some of the more common pediatric conditions treated with endoscopic neurosurgery and the preferred noninvasive interventions.

The most common pediatric intraventricular endoscopic procedure is the third ventriculostomy. The endoscope is introduced through a burr hole and placed through the frontal cortex into the lateral ventricle. It is then directed through the foramen of Monro and into the third ventricle, where the anterior floor is opened to the infundibular recess to allow for drainage of cerebrospinal fluid (CSF). To visualize the structures, the surgeon uses continuous irrigation with warmed saline or lactated Ringers solution through the scope, with drainage of cerebrospinal fluid through the scope or burr hole.

Table 64.1 Pediatric indications for endoscopic neurosurgery

Diagnosis	Intervention
Hydrocephalus	Third ventriculostomy for aqueductal stenosis, for fourth ventricular outlet obstruction, for septostomy
Arachnoid cysts	Fenestration
Colloid cysts	Endoscopic removal
Periventricular tumor	Biopsy
Pituitary tumor	Endoscopic transnasal hypophysectomy
Cranial synostosis	Endoscopic strip craniectomy
Hematoma or brain abscess	Endoscopic drainage

Extraventricular endoscopic procedures include endoscope-assisted strip craniectomy for treatment of craniosynostosis. This modality has continued to gain in prevalence with efficacy similar to the more invasive open procedures but with the added benefit of a decreased incidence of blood loss and lower transfusion rates. For best results, it is performed in younger children (within the first 3–4 months of life) who are greater than 5 kg. The patient is in the prone position, and the surgeon inserts the endoscope through a midline burr hole in order to better visualize emissary veins and dural attachments during dissection and cutting of the bone along the fused sutures.

Significant complications in endoscopic neurosurgery occur very rarely, with varying incidence depending on the procedure performed and the patient's condition and anatomy. An endoscopic approach has been shown to improve patient safety and allow for shorter hospital stays with virtually no mortality (0–1%) when compared to conventional open procedures. The incidence of intraoperative and postoperative complications varies widely from 5% to 30% based on published patient series from several centers. In noncommunicating hydrocephalus, endoscopic third ventriculostomy has become the standard surgical treatment (success rate of 60–95%) and has allowed patients to live without indwelling shunts in the majority of cases, thereby reducing overall morbidity (endoscopic surgical risk of 5%) in this patient population. The more commonly associated complications of endoscopic neurosurgery are summarized in Table 64.2.

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Table 64.2 Complications of endoscopic neurosurgery

Complications
Cardiovascular
Arrhythmia
Hypertension
Neurologic
Increased intracranial pressure
Delayed emergence
Seizures
Nerve palsy
Venous/arterial hemorrhage
CSF leakage
Meningitis
Diabetes insipidus or SIADH
Disturbances in temperature regulation
Electrolyte disturbances

Prevention

The likelihood of successful outcomes increases greatly with appropriate patient selection (anatomy conducive to the procedure) combined with a neurosurgeon experienced with these techniques. By tailoring the anesthetic to the anticipated procedure, the anesthesiologist can also help to decrease the probability of complications. The following points need to be considered.

Anesthetic Technique

- Despite the less-invasive aspect of endoscopic neurosurgery, anesthetic considerations do not differ greatly from conventional neurosurgical procedures.
- Preoperatively, patients may present with symptoms of increased intracranial pressure (ICP) such as vomiting, headache, confusion, or altered mental status. A full neurologic exam should be documented. Preoperative anxiolytics may need to be used sparingly, if at all, due to both the preoperative neurologic status and the desire to prevent delayed emergence after the procedure.
- Intraoperatively, general anesthesia is the preferred method to ensure immobility throughout the procedure. Arrhythmias or hemodynamic instability can occur without warning, necessitating constant vigilance on the part of the anesthesiologist who should intervene when appropriate and modulate systemic hemodynamics to allow for optimal surgical conditions. ICP can also rise during the procedure, often necessitating treatment, including hyperventilation and blood pressure management to maintain cerebral perfusion pressure. Drainage of CSF may also be performed by the surgeons. Nitrous oxide should be avoided as it can cause expansion of ventricular air bubbles that are introduced by the endoscope. The use of shorter-acting opioids will allow for rapid emergence and early neurologic examination.
- Invasive arterial blood pressure monitoring is rarely needed unless the patient has serious comorbidities that warrant it (i.e., cuff pressures are adequate in most cases). However, adequate large bore intravenous access is important for both venous blood sampling and administration of fluids and blood, especially in endoscopic strip craniectomy, during which there is a higher likelihood of bleeding.
- Placement of a Foley catheter is often not performed due to the shorter duration of these procedures and decreased anticipated blood loss compared to open procedures. However, a catheter should be placed to better monitor urine output in the following scenarios: diuretic therapy is anticipated, and diabetes insipidus and SIADH are suspected.
- Postoperatively, continued neurologic examination and monitoring of serum electrolytes is important for early detection of postoperative bleeding, increased ICP, diabetes insipidus, or hypothalamic dysfunction.

Communication

- The importance of communication between the anesthesiologist and the surgical team cannot be underestimated and should be ongoing. Some examples specific to endoscopic procedures are:
  - The incidence of cardiovascular instability is more likely to occur during third ventriculostomy when the surgeon is stimulating the floor of the third ventricle with the tip of the endoscope. Notifying the anesthesiologist of this event helps him/her to prepare for and more quickly treat such an occurrence. Likewise, communication to the surgeon of arrhythmias can allow for him/her to pull back the endoscope, which is often the only treatment necessary.
  - The occurrence of bleeding should always be communicated to allow for blood pressure control and transfusion when appropriate.
  - The need to convert to an open procedure or to abort the current procedure should be part of the ongoing dialogue between teams.

Crisis Management

Cardiovascular Instability

Cardiovascular instability (reported in 28–32% of patients) most often manifests as arrhythmias (bradycardia most commonly) and hypertension. Ventricular irritability and sudden cardiac arrest, though rare, have also been reported. Table 64.3 summarizes the more common cardiovascular findings.

Table 64.3 Cardiovascular instability

Pathophysiology and presentation	Patient assessment	Treatment/intervention
Arrhythmias secondary to increased pressure in the ventricular system (related to increased irrigation and CSF drainage) and direct stimulation of the floor of the third ventricle with the endoscope Most commonly seen bradycardia Hypertension secondary to increased ICP	Is there evidence of raised ICP? Is it associated with painful stimuli? Is there adequate analgesia? What are the pulse, rhythm, and BP? Is there hypoxia?	Have the surgeon pull the scope away from floor of third ventricle Check that there is appropriate drainage of fluid through the endoscope May need pharmacologic treatment (atropine for unresolving bradycardia, antihypertensives, or analgesics) Treat ICP

Venous/Arterial Hemorrhage

Several neurologic complications can develop during and after endoscopic neurosurgery, including increased intracranial pressure, delayed emergence, seizures, nerve palsy, and CSF leakage. Part of the management of these patients is to be aware of these complications and tailor the anesthetic to allow for rapid emergence and full neurologic examination as soon as possible. One of the most severe complications, however, is the development of hemorrhage, which is summarized in Table 64.4.

Table 64.4 Venous/arterial hemorrhage

Pathophysiology and presentation	Patient assessment	Treatment/intervention
Basilar artery disruption is most significant but rare Venous bleeding from disruption of subependymal vessels or the choroid plexus by the endoscope Hemorrhage at the insertion site or the burr hole Bleeding can prevent further visualization through the scope, and the surgeon may need to abandon endoscopic procedure and convert to open procedure	Is bleeding visualized in the scope's field of vision? What are the pulse, rhythm, and BP (signs of increased ICP)? Is there delayed emergence? Is there a progressive change in the neurologic exam postoperatively?	Supportive care in arterial bleeding including transfusion and control of BP Continuous irrigation of venous bleeding by surgeon can be enough to stop it Be prepared to rapidly convert to open procedure for uncontrolled bleeds Treat ICP Postoperative EVD may be necessary

Diabetes Insipidus or SIADH

Diabetes insipidus (DI) or syndrome of inappropriate secretion of ADH (SIADH) can develop either intraoperatively or postoperatively. Each is thought to be due to hypothalamic dysfunction from injury caused by the endoscope or higher pressures generated by the irrigation fluid. Diabetes insipidus is typically self-limited. The presentation, patient assessment, and treatment of each are summarized in Table 64.5.

Table 64.5 Diabetes insipidus and SIADH

Pathophysiology and presentation	Patient assessment	Treatment/intervention
Diabetes insipidus: Increased dilute urine output developing either during or after the procedure associated with hypernatremia Can lead to dehydration and hypotension if not recognized and treated SIADH: See hyponatremia, concentrated urine, and water retention without hypertension Can develop postoperative headache, nausea, vomiting, confusion, or seizures	What are the serum electrolytes? What is the concentration of the urine? What are the pulse and BP? Is there delayed emergence? Is there a progressive change in the neurologic exam?	Diabetes insipidus: Continued hydration with balanced electrolyte solution and continued monitoring of electrolytes Often self-limited; may need short course of desmopressin SIADH: Follow serum sodium levels; replace as needed; fluid restriction Monitor for seizures

Electrolyte Disturbances

Postoperative electrolyte imbalances often occur in patients undergoing endoscopic neurosurgery. While disturbances in sodium can be attributed to DI or SIADH with hypothalamic injury, one often sees hyperkalemia in the postoperative period. Table 64.6 summarizes the findings with electrolyte disturbances.

Table 64.6 Electrolyte disturbances

Pathophysiology and presentation	Patient assessment	Treatment/intervention
Hyperkalemia appears to increase with the use of lactated Ringer's solution for irrigation of surgical field Normal saline irrigation produces a relative hypokalemia, though not usually clinically significant Disturbances in sodium discussed above	What are the pulse and rhythm? What are the postoperative serum electrolytes? Is there delayed emergence? Is there a progressive change in the neurologic exam?	Close monitoring of serum electrolytes Treat potassium if cardiac rhythm disturbances appear Lactated Ringer's irrigation closer physiologically to CSF but can increase potassium levels Normal saline may have less effect on potassium

Delayed Emergence

Delayed emergence can be related to the surgical procedure or the anesthetic management of the patient and warrants immediate investigation into the cause to allow for timely management. Table 64.7 summarizes the salient features of delayed emergence.

Table 64.7 Delayed emergence

Pathophysiology and presentation	Patient assessment	Treatment/intervention
Residual anesthetic, including inhalational agents, opioids, paralytic agent, or premedication Neurologic causes, including intraventricular bleed, edema, increased ICP, structural damage to the brain, and ischemia Electrolyte abnormalities Hypoglycemia Hypoxia Hypotension/arrhythmia Can see focal deficits or generalized obtundation	What are the SpO_2 and $EtCO_2$? What are the pulse, rhythm, and BP? What are the serum electrolytes/glucose? Were there signs of bleeding during the procedure or high irrigation pressures? Is there a focal neurologic deficit on the exam or signs of high ICP? Have paralytics been reversed? Is there residual inhalation agent present? Could this be residual opioid or premed?	Close monitoring of vital signs and treatment of hypotension, hypertension, and hypoxia Correct electrolyte abnormalities and glucose Reversal of all anesthetic agents Imaging studies to evaluate neurologic causes (bleeding, ischemia) ICP monitoring?

Key Points

- Endoscopic neurosurgery allows for less invasive and safe treatment of several neurologic conditions in the pediatric population.
- Complete preoperative assessment, including full history, physical and neurologic exam, and laboratory evaluation, should be well documented and help guide the anesthetic management of the patient.
- Good communication with the surgeon and constant vigilance on the part of the anesthesiologist are invaluable to help ensure the safety of the patient.
- Know what the most common complications of endoscopic neurosurgery are and how to treat them.
- Always be prepared to convert to an open procedure in case of emergency.
- Continued evaluation of the patient in the postoperative period can help to prevent catastrophic complications from going unnoticed.

Suggested Reading

Baykan N, Isbir O, Gercek A, et al. Ten years experience with pediatric neuroendoscopic third ventriculostomy. J Neurosurg Anesthesiol. 2005;17:33–7.

Chowdhry SA, Cohen AR. Intraventricular neuroendoscopy: complication avoidance and management. World Neurosurg. 2013;79(2 Suppl):S15.e1–10.

El-Dawlatly AA. Endoscopic third ventriculostomy: anesthetic implications. Minim Invasive Neurosurg. 2004;47:151–3.

Johnson JO. Anesthesia for minimally invasive neurosurgery. Anesthesiol Clin N Am. 2002;20:361–75.

Meier PM, Guzman R, Erb TO. Endoscopic pediatric neurosurgery: implications for anesthesia. Pediatr Anesth. 2014;24:668–77.

Schubert A, Deogaonkar A, Lotto M, et al. Anesthesia for minimally invasive cranial and spinal surgery. J Neurosurg Anesthesiol. 2006;18:47–56.

Challenges During Diagnostic and Perioperative Imaging in Children with Brain Pathology

65

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Introduction

As the fidelity of a variety of neuroimaging modalities has advanced, neurosurgeons and neurologists become increasingly reliant on information obtained from these procedures to diagnose as well as plan and guide treatment of a myriad of disease of the central nervous system. Technologies such as magnetic resonance imaging (MRI), computerized tomography (CT), positron emission tomography (PET), single-photon emission tomography (SPECT), angiography, MRI-guided surgery, and others have allowed surgeons' and neurointerventionalists' ever-increasing ability to diagnose and treat disease of the CNS. It is beyond the scope of this chapter to go into an in-depth discussion of the intricacies of the many imaging modalities. However, we will attempt to focus our discussion on some common, relevant aspects of both diagnostic and therapeutic neuroimagings that are common to the care of adults and children with central nervous system pathology. This chapter will highlight some of the anesthetic concerns inherent to care of patients in these unique environments.

Diagnostic Neuroradiology

The most common modalities used to image the brain are CT and MRI. In the adult population, it is much less common to need to perform general anesthesia or even deep sedation to facilitate imaging in patients. However, in the pediatric population, it is quite common, especially in younger children, to need to induce general anesthesia or deep sedation to facilitate these diagnostic procedures. CT scans involve exposure to ionizing radiation but can be performed rapidly and often without the need for sedation or anesthesia, even in young children because the images can be captured in fractions of a second using modern scanners with modern software packages. Much has been made in recent years of the elevated risk of various types of cancers in patients with frequent exposure to medical ionizing radiation (such as CT scans). In many situations where CT was previously the imaging modality of choice, MRI has supplanted CT due to this concern.

MRI scans do not expose the patient to ionizing radiation but take significantly longer (often they may take >1 h depending on the imaging sequences and protocols) and require patients to be motionless during image acquisition. Many children cannot remain still enough to allow adequate image capture and, thus, will often require sedation or general anesthesia to achieve this. The choice of imaging modality will depend upon the suspected pathology and information desired by the referring team and radiologist. However, it is important to note that when making the decision regarding imaging modality, the risks posed to the patient (including the risks of anesthesia/sedation) must be balanced against the benefit to the patient of having the scan. It is also important to note that CT and MRI are each useful for different types of imaging and are not simply substitutable in many situations.

Magnetic resonance imaging (MRI) provides a unique set of challenges for anesthesia providers. These challenges can be broadly divided into different two main groups, environmental and medical:

Environmental

- Powerful magnetic fields restrict equipment that can be used inside the scanner area.

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- The high strength magnetic fields can induce ferromagnetic objects to fly through the air and pose a risk of significant injury or death to patients and caregivers.
- There is significant noise in the scanning room while scanning that can ultimately result in hearing damage to both patients and care providers.
- In order to maintain the high strength magnetic field, the magnet is supercooled, and the ambient temperature in the room must remain low. This can create problems for patients who are quite small (babies) or who require long scans under anesthesia.
- The care providers are distant from the patient as, most commonly, they are outside of the scanner room during scanning.
- Radiofrequency interference from the rapidly oscillating magnetic fields may cause problems with electronic equipment such as physiologic monitors and anesthesia delivery systems (machines and infusion pumps). Thus, there are special versions of physiologic monitors, infusion pumps, and anesthesia machines specifically designed for use and safety in these environments.
- Likewise, electronic interference from the anesthesia equipment may cause artifact on the images unless such special equipment is utilized and manufacturer recommendations are followed regarding safe proximity to the bore of the magnet. These safe distances may be different for different strength magnets.

Medical

- The inherent risks of sedation/general anesthesia
- The additional risks posed by the underlying pathophysiology of the patient

Risks of Sedation/Anesthesia

Most adult patients will not likely need the help of an anesthesiologist to get through routine CT or MRI procedures. Often, these patients can either have these images obtained wide awake or with minimal sedation provided by other services. However, there may be a number of instances where deep sedation or general anesthesia is required. Caregivers must not lose sight of basic neuroanesthesia principles while focusing on the unique challenges of off-site anesthesia. For urgent or emergent neuroimaging, the patients may have a variety of comorbidities and not be as well prepared for an anesthetic as we would like. For example, patients may not be appropriately starved while simultaneously having significant intracranial pathology (such as hydrocephalus, subarachnoid hemorrhage, etc.)

Some pediatric patients such as older children may simply require mild anxiolysis and distraction therapy (such as watching a movie or listening to music) during the scan. Others, such as younger children, and those who cannot lie still, usually require more significant pharmacologic interventions to facilitate the scan. There is often confusion over the continuum of sedation and anesthesia, particularly relating to the use of terms such as "moderate and deep sedation," "monitored anesthesia care," and "anesthesia." The American Society of Anesthesia's 2013 statement on Monitored Anesthesia Care addresses this clearly:

> *If the patient loses consciousness and the ability to respond purposefully, the anesthesia care is a general anesthetic, irrespective of whether airway instrumentation is* required. (ASA position on monitored anesthesia care 2013)

From a safety perspective, this is important to emphasize. Children who cannot cooperate and lie still invariably need to be rendered unconscious and have their ability to respond purposefully removed in order to obtain optimal images. Because the scan is painless, it is often possible (and perhaps desirable) to maintain spontaneous respiration without the use of airway adjuncts; many texts and papers describe this as "sedation" or "monitored anesthesia care." It would be more accurate to use a term such as "general anesthesia with a natural airway," but given the vagaries of the language used in the body of literature examining this topic, this review will use the terms sedation, MAC, and anesthesia interchangeably. Certainly, the choice of approach to any individual patient may vary tremendously depending upon the context of situation where anesthesia is needed.

Patients with complicated comorbidities, such as difficult airways, may be best served by having sedation or general anesthesia induced outside of the imaging room itself. With this approach, optimal equipment, personnel, and monitoring can be utilized to safely help achieve the desired level of sedation or general anesthesia and allow the patient to be stabilized and then subsequently transported into the imaging room. This approach is particularly useful for patients needing anesthetics for MRI procedures. Care must be exercised to ensure all MRI unsafe objects are removed from the patient, bed, and caregivers prior to entering the scanning room. Patients can then be returned to such an "induction room" after imaging to be safely emerged if necessary. One rule of thumb is to never bring an unstable patient into a CT or MRI scanner. Resuscitative efforts in these environments are profoundly complicated by space and positioning issues as well as ferromagnetic safety concerns in the case of MRI. If a patient under anesthesia becomes unstable or arrests during an MRI procedure, the correct approach is to

Table 65.1 Adverse events and rates are expressed as number of events per 10,000 sedations

Adverse events	Incidence per 10,000	*N*	95% CI
Death	0.0	0	(0.0–0.0)
Cardiac arrest	0.3	1	(0.0–1.9)
Aspiration	0.3	1	(0.0–1.9)
Hypothermia	1.3	4	(0.4–3.4)
Seizure (unanticipated) during sedation	2.7	8	(1.1–5.2)
Stridor	4.3	11	(1.8–6.6)
Laryngospasm	4.3	13	(2.3–7.4)
Wheeze (new onset during sedation)	4.7	14	(2.5–7.8)
Allergic Reaction (rash)	5.7	17	(3.3–9.1)
Intravenous related problems/ complication	11.0	33	(7.6–15.4)
Prolonged sedation	13.6	41	(9.8–18.5)
Prolonged recovery	22.3	67	(17.3–28.3)
Apnea (unexpected)	24.3	73	(19.1–30.5)
Secretions (requiring suction)	41.6	125	(34.7–49.6)
Vomiting during procedure (non-GI)	47.2	142	(39.8–55.7)
Desaturation – below 90%	156.5	470	(142.7–171.2)
Total adverse events unplanned treatments	339.6 (1 per 29)	1020	(308.1–371.5)
Reversal agent required – unanticipated	1.7	5	(0.6–3.9)
Emergency anesthesia consult for airway	2.0	6	(0.7–4.3)
Admission to hospital – unanticipated (sedation related)	7.0	21	(4.3–10.7)
Intubation required – unanticipated	9.7	29	(6.5–13.9)
Airway (oral) (unexpected requirement)	27.6	83	(22.0–34.2)
Bag-mask ventilation (unanticipated)	63.9	192	(55.2–73.6)
Total unplanned treatments conditions present during procedure	111.9 (1 per 89)	336	(85.3–130.2)
Inadequate sedation, could not complete	88.9 (1 per 338)	267	(78.6–100.2)

Table 65.2 Airway interventions for propofol-sedated patients

Unplanned airway intervention	N	Rate	95% CI
Intubation	53	11.4	(8.6, 15.0)
Jaw thrust	525	113.2	(103.8, 123.3)
LMA placement	50	10.8	(8.0, 14.2)
Nasopharyngeal airway placement	211	45.5	(39.6, 52.1)
Blow-by O_2 required	1899	409.6	(391.7, 428.0)
Oral airway insertion required	300	64.7	(57.6, 72.4)
Bag-mask ventilation required	531	110.6	(101.3, 120.6)
Repositioning of head	721	155.5	(144.4, 167.2)
Suctioning required	341	73.6	(66.0, 81.8)
No data	17	3.7	(2.1, 5.9)

remove the patient from the scanning room as the very first step before resuscitative efforts are undertaken. This will ensure the safety of not only the patient but also of care providers who are responding to assist.

When we look at the safety of caring for patients outside of traditional OR environments, some of the best information we have comes from the use of pooled data from multiple institutions. One of the best examples of this is the Pediatric Sedation Research Consortium (PSRC). This group is made up of 30 institutions in the United States and Canada. Information for each sedation/anesthesia from selected sites at each participating institution is collected. This includes demographic data, procedure, coexisting illness, provider of sedation, drugs used, monitors used, outcomes of the sedation, etc. There are over 300,000 records in the database.

The first paper from the PRSC was published in pediatrics in September 2006 (see "Suggested readings"). This described the adverse events encountered in the first 30,000 cases in the database. These are summarized in Table 65.1.

It is clear from the rates of airway-related complications that recognition of apnea, airway insertion, and the provision of positive pressure ventilation are critical competencies that must be present for those caring for these children. This skill set is part and parcel to anesthesiology providers, but many patients in these situations may not have an anesthesiologist caring for them.

Subsequently, in 2009, a second paper from the PRSC was published that looked specifically at adverse events associated with the use of propofol outside the OR environment. This publication reports data from 49,836 encounters utilizing primarily propofol, with the original intention for the patients to breathe spontaneously with a natural airway. Adverse events associated with the airway are summarized in Table 65.2.

It is clear that airway compromise is an important adverse event that needs to be rapidly addressed, but in children with neuropathology, there are other potential risks that must be considered.

Risks Posed by the Underlying Neuropathology

These are generally related to the control of cerebral blood flow (CBF) and cerebral metabolic rate (CMR).

It should be remembered that "cerebral perfusion pressure (CPP) = mean arterial pressure (MAP) – intracranial pressure (ICP)," so any factor affecting these variables can be problematic. CMR describes cerebral oxygen consumption and is increased in the presence of acute illness, trauma, and seizure activity:

- Raised intracranial pressure may be worsened in the presence of hypercapnia in a patient under anesthesia, particularly if they are breathing spontaneously and are not receiving controlled ventilation.
- Anesthetic agents can have significant hemodynamic effects, causing a drop in cardiac output and MAP. Cerebral perfusion pressure should be maintained throughout the anesthetic and IV fluids, and vasopressor/inotropic support may be needed to achieve this. Occasionally beat-to-beat blood pressure monitoring may be required necessitating the use of intra-arterial catheters.
- Hyperthermia increases cerebral oxygen consumption. General anesthesia abolishes the body's ability to actively control temperature. Thus, during prolonged imaging the temperature should be assessed and measures taken to maintain normothermia. This can be profoundly difficult in MRI environments as skin temperature stickers and core temperature probes may be contraindicated. Efforts to prevent heat loss such as keeping the patient wrapped in a warm blanket can be useful when employed preemptively.
- Hypotonic IV fluids should be avoided due to the possibility of causing significant hyponatremia and subsequent cerebral edema. Problems such as cerebral salt wasting, the syndrome of inappropriate antidiuretic hormone secretion, or diabetes insipidus may all cause significant electrolyte disturbances. These disturbances are more common in neurosurgical patients.

Interventional Radiology

Care for patients in an interventional radiology (IR) suite presents several challenges to the anesthesiologist. Anesthetizing patients outside the main operating room environment potentially increases the risk of patient harm, due to a combination of factors including working in an unfamiliar environment, increased patient acuity (patients may be too ill to go to the OR), and decreased access to help from other anesthesiologists. These issues can be mitigated in part by standardizing patient evaluation, defining rescue protocols, and establishing a team-based culture of safe practice, which includes anesthesiologists comfortable in this environment. In addition to the systems-based issues of patient safety, physical safety is threatened in the IR suite in the form of radiation. Neuroimaging cases in IR utilize significant radiation doses, and both patients and staff must be protected from this invisible hazard.

Broadly speaking, procedures for patients with central nervous system pathology can be grouped in to diagnostic imaging and therapeutic procedures. Examples of diagnostic imaging include angiography, most commonly cerebral angiography. There is also an ever-expanding use of the neurointerventional suite to perform therapeutic procedures. Examples of these include catheter-guided coiling of intracranial aneurysms and embolization of intracranial vascular malformations.

Diagnostic Procedures in IR

The mainstay of neurodiagnostic procedures in IR is cerebral angiography. It remains the gold standard for characterization of neurovascular pathology, despite the recent gains in sophistication of CT and MRI angiography. Adults and mature teenagers often tolerate an angiogram without sedation or with only mild anxiolysis. However, deeper levels of sedation run the risk of a disinhibited patient or a patient too sleepy to cooperate for intermittent apnea. Therefore, younger patients may require general anesthesia with an endotracheal tube. Endotracheal anesthesia may also be preferable based on a patient's comorbid conditions.

While simple cerebral angiography, which usually takes an hour or less, itself does not warrant anything more than a day surgical visit, careful consideration must be given to patient comorbidities that would increase patient risk with anesthesia and perhaps warrant pre- or post-procedure admission. Consistent standards for chart review and the need for communication with consulting services will ensure that patients receive appropriate assessment and optimization before they arrive in radiology for their procedure.

When anesthetizing any patient with potential cerebrovascular disease, careful consideration must be given to blood pressure and fluid management. Especially on induction of anesthesia, one must avoid hypotension that can cause patients with a vasculopathy, such as moyamoya disease, increased risk of cerebral hypoperfusion. Minimizing fasting time can be helpful for these patients. Conversely, acute hypertension that could precipitate catastrophic bleeding in an unstable aneurysm or arteriovenous malformation (AVM) must also be avoided. Arterial lines for this short procedure are generally unnecessary if reliable readings can be obtained from a noninvasive blood pressure cuff. Normocapnia is usually desirable, and any proposed acute hypocapnia should be discussed with the neuroradiologist. While the risk of significant bleeding is extremely low, intravenous access sufficient for adequate hydration is necessary. The patient will receive significant amounts of IV contrast through the sheaths on the field. Thus, the anesthesiologist must be cognizant of the risk of contrast-induced nephropathy. Normovolemia to slight hypervolemia will offset the diuretic effect of nonionic contrast medium and reduce the slight chance of any contrast-induced nephropathy.

The major post-procedure concern after diagnostic cerebral angiography is hemostasis at the site of femoral puncture. Patients must lie flat for several hours, which particularly in the younger pediatric patients can be challenging. Distraction and pharmacologic assistance with benzodiazepines, opiates, or a-2 agonists can make this experience more tolerable.

Therapeutic Procedures in IR

It is increasingly common for patients with a variety of differing central nervous system pathologies to undergo treatment or palliation in the neurointerventional suite. Where open clipping of intracranial aneurysms was once the treatment of choice, coiling or embolization in the neurointerventional suite has become much more common and is rapidly supplanting open surgical procedures as the preferred route of treatment for a large number of patients. Likewise, embolization of central nervous system vascular malformations, as either the prime therapeutic approach or as part of a staged combined approach with open surgical resection, has become more prevalent. Whereas diagnostic cases can be reliably shorter with fewer incidences of significant physiologic changes, therapeutic cases often take significantly longer. Thus, many of the patients that would tolerate shorter diagnostic cases, with no sedation/anesthesia or only mild anxiolysis, may not be candidates for the same sedation/anesthetic regimen when undergoing a therapeutic neurointerventional case. Even patients who may have been fine with a shorter diagnostic procedure, with nothing but a single dose of midazolam, may not tolerate lying supine and be still for the often hours of a therapeutic case. The implications for pediatric patients are even more profound with virtually all children requiring general, endotracheal anesthesia for therapeutic neurointerventional procedures.

As with diagnostic cases, therapeutic cases may often require breath holding, where respirations are suspended during angiographic runs. There may be greater chance of intra-procedure disaster (such as rupture of the aneurysm) as well as increased bleeding. Bleeding may be difficult to assess, as essentially all blood will be lost through the sheath. These cases tend not to have acute, large volume blood loss. Rather, the loss can be insidious, occurring over time with frequent changes of catheters, drawbacks, and flushes. Patients may also be exposed to larger volume of contrast dye and therefore be at higher risk for contrast-induced nephropathy. In smaller patients and children, care must be taken to account, in detail, for the volume of contrast utilized, and the anesthesiologist must be ready to step up and say that the patient has reached their limit. Aggressive hydration is prudent in this situation, and a urinary catheter should be placed to accurately monitor urine output.

In children, it is becoming more common to have either staged or combined procedures to treat intracranial vascular malformations, such as arteriovenous malformations (AVMs). The neurointerventional component consists of embolization in an effort to decrease the chance of catastrophic bleeding during the open surgical resection. These procedures may be done in a staged fashion with the embolization occurring in the first day and then the open resection on the next or in a single combined anesthetic. The same considerations regarding concern for post-arterial puncture remain for therapeutic procedures, and patient will need to be still, flat, and supine for several hours after the sheath is pulled at the end of the case. Thus, it is often useful to have pharmacologic help to facilitate, especially in younger children.

Image-Guided Neurosurgery

The worlds of traditional operating rooms and neuroimaging suites are rapidly merging. The idea of image-guided neurosurgery has been popular for a couple of decades now. Various imaging modalities have been employed to assist neurosurgeons in complicated procedures including CT, ultrasound, and PET scanning. While those modalities offer additional tools to the neurosurgeon, the conduct of these anesthetics in these particular environments doesn't radically change how the anesthesiologist approaches the case. Other than concerns over positioning and possible movement and transport of patients, the anesthesiologist can continue to use the same equipment to care for the patient. However, an even more popular variant on image-guided neurosurgery combines the power of images obtained from MRI with the operating room.

Intraoperative MRI (iMRI) is a quantum leap forward in image-guided surgery and intraoperative navigation. For a more detailed discussion of the anesthetic considerations of iMRI, the reader should refer to one of several review articles readily available in the published literature. Briefly, delivering an anesthetic for a patient in an iMRI suite can be fraught with challenges. Among them are the issues of equipment, the type of iMRI suite (movable magnet-stationary patient or movable patient-stationary magnet), maintenance of sterility during open intraoperative scanning, and maintenance of general MRI safety standards during a combined imaging and surgical procedure. These are not the kind of issues to be dealt with lightly or on the spot. Rather, careful planning and design of safety systems are required. Given that multiple services (surgery, anesthesiology, nursing, and radiology) will all be working together in this suite, each service should have a seat at the table during initial planning and design of such seats. It is useful to have several different "stops" or time-outs throughout the case at defined points to ensure the necessary safety considerations at that point of the procedure have been addressed before moving on to the next steps. For example, after mass resection but prior to placing the patient in the bore of the magnet, it is useful to ensure all non-MRI safe equipment has been accounted for and removed from the patient's bed and from the area that will become Zone 4 during iMRI. All such equipment must remain safely outside of the 5 gauss lines in such a suite. Various strategies have been devised for facilitating these processes. The details of these approaches will vary depending on the nature of the suite and the patients cared for within the suite. The bottom line is that, as these facilities become ever more common, anesthesiologists involved in neurosurgical care must be familiar with the intricacies of performing anesthetics in this unique environment.

Key Points

1. Neuroimaging includes diagnostic imaging and therapeutic procedures. Safety of the patient and the provider is threatened by increased doses of radiation, particularly in interventional neuroimaging. Both patients and staff must be protected from this invisible hazard
2. The most common modalities used to image the brain are CT and MRI. In the adult population, it is much less common to need to perform general anesthesia or even deep sedation to facilitate imaging in patients.
3. Risks include those posed by the imaging environment, by the medical conditions of the individual patient, and by the underlying neuropathologic process.
4. Anesthetizing patients to obtain neuroimaging typically occurs outside of the main operating room and is associated with an elevated risk secondary to the unfamiliar work environment, likelihood for higher patient acuity, and more distant access for help. Protocols and guidelines are needed to reduce the likelihood of complications and limit patient harm.
5. Intraoperative neuroimaging including CT, ultrasound, and PET scanning typically do not change anesthesiology management in principle. In contrast, intraoperative MRI (iMRI) can be challenging, and careful planning and design of safety systems are required in a multidisciplinary approach.

Suggested Reading

ASA position on monitored anesthesia care. 2013. https://www.google.com/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&ved=2ahUKEwjduJflt6DiAhWBtVkKHf8XAiIQFjAAegQIARAC&url=https%3A%2F%2Fwww.asahq.org%2F-%2Fmedia%2Fsites%2Fasahq%2Ffiles%2Fpublic%2Fresources%2Fstandards-guidelines%2Fposition-on-monitored-anesthesiacare.pdf%3Fla%3Den%26hash%3D65679C53CDDE5ACD2C7448B52C2D9D0340F8F78E&usg=AOvVaw31wa8H5XAE3x79Oj6PRtjy.

Bergese SD, Puente EG. Anesthesia in the intraoperative MRI environment. Neurosurg Clin N Am. 2009;20(2):155–62.

Chang B, Kaye AD, Diaz JH, Westlake B, Dutton RP, Urman RD. Interventional Procedures Outside of the Operating Room: Results From the National Anesthesia Clinical Outcomes Registry. J Patient Saf. 2018;14(1):9–16.

Cravero JP, Blike GT. Pediatric anesthesia in the nonoperating room setting. Curr Opin Anaesthesiol. 2006;19(4):443–9.

Cravero JP, Blike GT, Beach M, Gallagher SM, Hertzog JH, Havidich JE, et al. Incidence and nature of adverse events during pediatric sedation/anesthesia for procedures outside the operating room: report from the Pediatric Sedation Research Consortium. Pediatrics. 2006;118(3):1087–96.

Cravero JP, Beach ML, Blike GT, Gallagher SM, Hertzog JH, Pediatric Sedation Research C. The incidence and nature of adverse events during pediatric sedation/anesthesia with propofol for procedures outside the operating room: a report from the Pediatric Sedation Research Consortium. Anesth Analg. 2009;108(3):795–804.

Dagal A. Radiation safety for anesthesiologists. Curr Opin Anaesthesiol. 2011;24(4):445–50.

Landrigan-Ossar M, McClain CD. Anesthesia for interventional radiology. Paediatr Anaesth. 2014;24(7):698–702.

McClain CD, Rockoff MA, Soriano SG. Anesthetic concerns for pediatric patients in an intraoperative MRI suite. Curr Opin Anaesthesiol. 2011;24(5):480–6.

Orbach DB, Stamoulis C, Strauss KJ, Manchester J, Smith ER, Scott RM, et al. Neurointerventions in children: radiation exposure and its import. AJNR. 2014;35(4):650–6.

Practice Advisory for Anesthetic Care for Magnetic Resonance Imaging: an updated report by the American Society of Anesthesiologists task force on anesthetic care for magnetic resonance imaging. Anesthesiology. 2015;122(3):495–520.

Smith ER. Structural causes of ischemic and hemorrhagic stroke in children: moyamoya and arteriovenous malformations. Curr Opin Pediatr. 2015;27(6):706–11.

Part X

Postoperative Concerns in Pediatric Neuroanesthesia

Emergence from Anesthesia Following Pediatric Neurosurgery

66

Kirk Lalwani

Overview

Emergence from general anesthesia and tracheal extubation may be associated with tremendous physiologic and metabolic stress in patients. These stress-induced alterations in physiologic parameters may be harmful to patients as they can exacerbate preexisting disease or produce medical or surgical complications in the recovery period. It is important therefore to implement measures that minimize these stress-induced changes during emergence from anesthesia, particularly in patients at higher risk or after procedures where complications may result in significant morbidity or even mortality.

Implications for the Neurosurgical Patient

Pediatric Considerations

Neonatal blood pressure range for cerebral autoregulation has been estimated to be similar to that in adults, with no age-related differences in autoregulatory capacity. The steep slopes at either end of this range predispose the neonate to cerebral ischemia or intraventricular hemorrhage in the event of hypotension or hypertension, respectively. Intracranial compliance in infants is generally higher in the presence of gradually increasing ICP as a result of open fontanelles and cranial sutures. Older children, on the other hand, have decreased intracranial compliance compared to adults as a result of higher brain water content, less CSF volume, and a higher ratio of brain content to intracranial capacity. Therefore, as fontanelles and sutures close, children may be at higher risk for ischemia and herniation in the event of similar relative increases in ICP when compared to adults as a result of lower intracranial compliance. Much of the literature on emergence from anesthesia following craniotomy has not been performed in children; therefore, studies on adults will also be discussed in this chapter in the interest of understanding concepts and applying techniques that in all probability fulfill the same goals in both children and adults.

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Metabolic Changes

Recovery from general anesthesia is associated with sympathetic stimulation, increased catecholamine secretion, increased oxygen consumption (VO_2), tachycardia, and systemic hypertension, which in turn may lead to intracranial hypertension. It has been demonstrated that independent of whether propofol or isoflurane is used, cerebral blood flow velocity increases by 60% above the awake value at extubation and is significantly increased for at least 30 min following extubation. Interestingly, this increase did not correlate with MAP or $PaCO_2$ at any time, likely as a result of central adrenergic stimulation during emergence from anesthesia. Multiple additional sources of stress such as stimulation by the endotracheal tube, coughing, suctioning of the oropharynx or trachea, awareness of surroundings, auditory stimulation, shivering, emergence agitation, and pain related to surgery may greatly magnify the hemodynamic response to emergence (Fig. 66.1).

Early Versus Delayed Emergence

Early Emergence

Patients undergoing neurosurgical procedures that involve intracranial structures are particularly prone to the devastating effects of surgical hemorrhage or brain edema postoperatively, mostly as a result of pressure effects on the brain within the confines of the rigid cranium. Early detection is therefore critical in order to avoid permanent morbidity or death. This is typically accomplished by early and frequent

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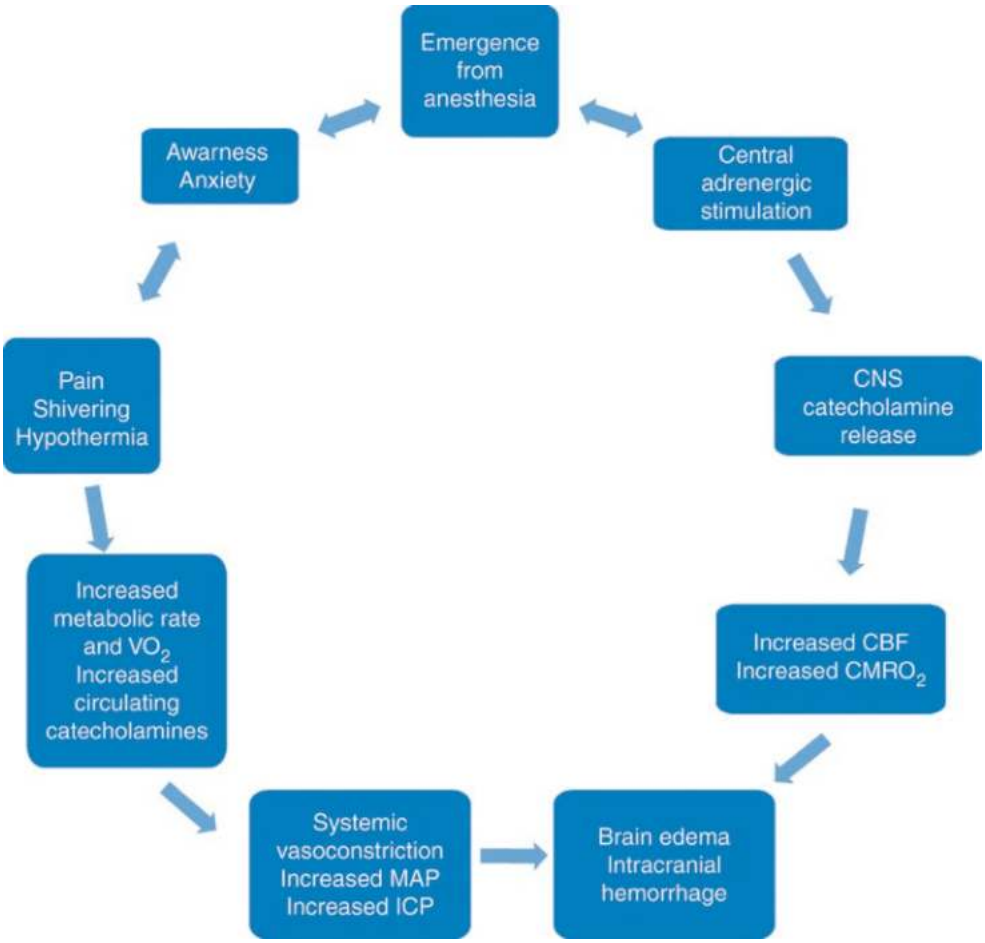

Fig. 66.1 Stress-induced changes during emergence from anesthesia

neurological examination following surgery to determine the presence of any neurologic deficits. In high-risk cases, this may be supplemented by early CT imaging of the brain, often prior to or immediately after emergence from anesthesia and tracheal extubation.

It seems intuitive, therefore, that rapid emergence and early awakening following craniotomy is a prerequisite for early neurological examination. In practice, however, achieving rapid emergence and awakening is often accompanied by profound alterations in physiologic parameters related to the stress of emergence and extubation, unless the anesthetic technique is tailored to specifically prevent these changes. Paradoxically, the techniques that attenuate these hemodynamic changes may adversely affect early awakening and return to consciousness. Therefore, careful planning is required to balance the dual requirements of early awakening versus meticulous hemodynamic control following craniotomy.

Delayed Emergence

There exists a subgroup of patients in whom early awakening and emergence entail significant risk, and postoperative mechanical ventilation is desirable. These high-risk patients must be identified as early as possible in the perioperative period in order to optimize intraoperative anesthetic care as well as postoperative requirements for imaging, continued ventilation, sedation, correction of acid-base, electrolyte, temperature, and coagulation parameters prior to extubation on the ICU.

It is important to realize that the effect of delayed extubation (2 h of propofol sedation after surgery) exacerbates the production of markers of stress when compared to early (immediate) extubation following surgery and therefore cannot be recommended for this purpose alone. However, likely candidates for delayed extubation are patients with altered consciousness preoperatively, lengthy surgery (>6 h), large tumor resection with preoperative midline shift, injury to cranial nerves (especially IX, X, XI), complications during surgery, intraoperative brain swelling, hypothermia, coagulopathy, and significant acid-base or electrolyte abnormalities. To facilitate early diagnosis of intracranial complications in patients for whom delayed extubation is planned, many surgeons routinely request a CT scan en route from the operating room to the ICU or soon after arrival on the ICU as a substitute for early awakening and neurological examination. In a recent prospec-

tive randomized study of pediatric patients undergoing resection of supratentorial tumors, maintenance of anesthesia with desflurane or sevoflurane resulted in shorter emergence times when compared to isoflurane with a similar incidence of intraoperative and postoperative adverse effects. In this study, the shorter time to extubation was clinically significant as well, particularly in the desflurane group, but the difference in time to reach a predetermined Aldrete score was less obvious clinically, even though statistically significant.

Concerns and Risks

Neurological Complications

In a prospective study of 162 adult patients, the incidence of complications following craniotomy in the first 6 h postoperatively was reported to be as high as 57%, of which 3% were neurological complications such as seizures, neurologic deficits, and delayed awakening. Other complications included respiratory events like hypoxia and hypercarbia, hypotension, hypertension, pain, shivering, nausea, and vomiting. Of the patients who experienced complications, 45% had more than one complication. In a retrospective study of perioperative complications after pediatric craniotomies, von Lehe et al. noted that the incidence of new neurologic deficits was higher in posterior fossa craniotomies when compared to supratentorial (23.6% vs. 6.7%, respectively); the incidence of postoperative bleeding requiring reoperation was 1.7%, and the incidence of other severe systemic complications (sepsis, pneumonia, etc.) was 3.8%.

Intracranial hemorrhage has been linked to intraoperative hypertension; patients with postoperative intracranial hypertension were 3.6 times more likely to be hypertensive than matched controls. There was also a strong association between intracranial hemorrhage and patients who were normotensive during surgery, but hypertensive in the postoperative period, presumably as a result of inadequate hemostasis at a lower range of blood pressures. Intracranial hypertension is common after craniotomy (12–18%) and was associated with clinical deterioration in 52% of adult patients and CT findings of cerebral edema and cerebral hemorrhage. Arterial hypertension in premature infants or newborns can result in intraventricular hemorrhage as a result of impaired autoregulatory ability coupled with rapid alterations in cerebral blood flow and pressure. In addition, children may be at increased risk of herniation compared with adults as a result of low intracranial compliance. Neonates and infants, on the other hand, are able to tolerate fluctuations in intracranial pressure and volume better than older children as a result of open fontanelles and sutures.

Anesthetic technique may also affect the incidence of intraoperative and postoperative complications. A recent systematic review analyzed 14 clinical trials that compared maintenance of anesthesia with propofol to volatile agents, with outcomes ranging from brain relaxation scores, cerebral hemodynamics, recovery profiles, postoperative complications, and clinical outcomes. The conclusion was that ICP was lower and CPP higher with propofol anesthesia, as was postoperative nausea and vomiting, but there was no difference in any other outcomes; there was also insufficient data to compare significant neurological outcomes.

Shivering

Hypothermia after surgery is more common in infants and children as a result of several factors. Neonates have a skin surface area to body mass ratio of ~1, whereas in adults this ratio is about 0.4. Neonates also lose heat easily via thermal conduction as a result of a thin layer of subcutaneous fat; in addition, the ambient temperature limit of thermoregulation for neonates is 22 °C compared to 0 °C in adults. This propensity to lose heat more rapidly coupled with the decreased ability to regulate body temperature requires careful attention during surgery in order to prevent hypothermia. Shivering related to hypothermia or volatile anesthetic agents can increase VO_2 by 200–400% and MAP by approximately 35% or more. Patients who develop mild hypothermia during surgery experience a much greater increase in norepinephrine concentration, more significant vasoconstriction, and increased systemic blood pressure in the early postoperative period compared to normothermic patients. Even in the presence of mild hypothermia, forced air warming decreases the incidence and intensity of shivering. It is useful to remember that though shivering may occur in neonates following emergence from anesthesia, it is unimportant as a method of thermogenesis in this age group and tends to occur more commonly in children over 6 years of age.

Pain

Pain is a significant stress factor that increases VO_2 and induces catecholamine release in the postoperative period, and the use of intraoperative analgesia attenuates these metabolic changes in the postoperative period. One study demonstrated that the use of morphine analgesia reduced VO_2 in critically ill patients by 20%, but the effect of analgesics on VO_2 in restless patients may be even greater as a result of the additional sedative benefits conferred by opioid analgesics. Peripheral nerve blocks of the scalp are effective in decreasing postoperative pain following craniotomy, and the effect may persist for as long as 48 h after

surgery, even if the block is performed at the end of surgery. Scalp nerve blocks may also decrease postoperative opioid consumption and reduce postoperative nausea and vomiting (PONV). Wound infiltration with local anesthetic has also been shown to result in decreased pain scores for up to an hour after arrival in the PACU. Because of the dense vascularity of the human scalp, providers must take great care when employing scalp blocks or wound infiltration to avoid hematomas, and they should calculate the total maximum allowable dose of local anesthetic carefully so as to avoid systemic toxicity, especially in children.

In children, pain must be distinguished from separation anxiety, hunger, disorientation to surroundings, a full bladder, and emergence delirium. Simple comfort measures are often all that is required to placate a child following surgery; if pain is the likely diagnosis, opioids should be titrated to effect. Acetaminophen is useful rectally or orally, but ketorolac is usually avoided in the immediate postoperative period for fear of altered platelet function that could exacerbate bleeding. In a recent multicenter prospective study of pediatric pain after major neurosurgery, there were no differences in average pain score, length of stay, or parental satisfaction with care despite considerable variation in modality and route of analgesic administration; overall, pain scores were low, side effects were minimal, and parental satisfaction was high.

Emergence Agitation

Agitation on emergence may occur in children or adults as a result of pain, bladder distention, hypoxia, airway obstruction, unfamiliar surroundings, disorientation, hunger, electrolyte imbalance, and paradoxical reactions to drugs such as midazolam or diphenhydramine or true emergence delirium that occurs more often in children following the use of volatile anesthetic agents, particularly sevoflurane. Recent data suggests that maintaining children on a lighter plane of anesthesia (as assessed by BIS) is associated with a lower frequency of emergence agitation. It is important to exclude and treat remediable causes of agitation such as pain, avoid agents that may precipitate the condition in patients with the history of a previous episode following anesthesia, and employ strategies to decrease the incidence in susceptible patients by the use of prophylactic opioids, propofol, clonidine, or dexmedetomidine. If suspected, propofol in a dose of 0.5–1 mg/kg terminates the episode rapidly without the potential hazard of excessive opioid use and may decrease the likelihood of morbidity related to intracranial complications, loss of surgical drains, surgical site bleeding, and injury to patients and providers.

Anesthetic Techniques and Drugs

Stress Response

Techniques

A prospective randomized trial by Bhagat et al. of three different anesthetic techniques for reduction of stress related to early emergence from anesthesia and for up to 1 h following extubation concluded that a low-dose fentanyl infusion (1.5 mcg/kg/h) was superior to a propofol infusion (3 mg/kg/h) or to low-dose isoflurane inhalation (end-tidal concentration of 0.2%) in allowing early awakening and limiting emergence hypertension when each regimen was administered from the start of dural closure until the start of skin closure. In addition, patients in the propofol group had a significantly higher incidence of hypotension at the time of dural closure; there were no statistically significant differences in the incidence of PONV, return to full Glasgow Coma Scale, postoperative complications, or length of stay in the ICU. One significant predictor of emergence hypertension in this study was a preoperative midline shift of >5 mm on cerebral imaging scans. In children, titration of intravenous fentanyl is usually adequate to ensure smooth extubation with minimal coughing following emergence. This can be supplemented with intravenous lidocaine (1 mg/kg) if necessary. Following neurovascular surgery, "deep" extubation may be the best way to avoid coughing; however, if there is any suspicion of respiratory or airway compromise, the patient should be left intubated and transferred to ICU with additional sedation to minimize intracranial hypertension.

Drugs

Beta blockers such as labetalol and esmolol can be effective in preventing the stress response to emergence and extubation in neurosurgical patients, though their effect may be unpredictable or associated with bradycardia and conduction delays, respectively. Calcium channel antagonists such as nicardipine, while effective, cause dose-dependent cerebral vasodilatation, inhibition of autoregulation, and frequent hypotension. Dexmedetomidine, an alpha-2 agonist, is gaining popularity in this area as a result of its sedative, sympatholytic, and analgesic effects. In a double-blind, prospective, randomized, placebo-controlled trial comparing a supplemental dexmedetomidine infusion to placebo for adult craniotomy patients undergoing anesthesia with sevoflurane, opioids, and antihypertensive medications at the discretion of the blinded neuroanesthesiologists, patients in the dexmedetomidine group had improved hemodynamic stability without episodes of hypotension or bradycardia despite the best efforts of the anesthesiologists. Fewer patients in the treatment group required antihypertensive medications (42% vs. 86%), and patients in this group were discharged from the PACU earlier (91 min vs. 130 min). Despite numerous

reports of the widespread use of dexmedetomidine in children, it has not been approved for use in this age group, and no data exists for its use in this scenario in children.

Respiratory Complications

Techniques to minimize coughing and tracheal stimulation can effectively blunt the large increases in ICP that may result during emergence and extubation. Intravenous or intratracheal lidocaine with or without short-acting opioids such as alfentanil or remifentanil decreases coughing, agitation, cardiovascular stimulation, and emergence hypertension. In addition, care should be taken to ensure adequate preoxygenation prior to extubation, full reversal of neuromuscular block, and a patent, unobstructed airway following extubation to minimize hypoxia and/or hypercarbia. Specifically, measures to prevent and treat airway or soft tissue edema, laryngospasm, stridor, postobstructive pulmonary edema, pulmonary aspiration, and bronchospasm are fundamental in this regard. Clinical evaluation should always precede extubation to ensure optimal conditions for safe extubation. It is imperative to monitor children for respiratory obstruction following extubation, particularly in infants and younger children, or in the presence of significant facial edema. Vocal cord paralysis as a result of cranial nerve dysfunction following removal of posterior fossa tumors is an important cause of postoperative respiratory obstruction that usually requires immediate reintubation.

Postoperative Nausea and Vomiting

The incidence of PONV in children and adults following craniotomy is reported to be as high as 50–60%. PONV is unpleasant, can raise blood pressure and intracranial pressure, and may cause dehydration and alkalosis, all of which may lead to morbidity following intracranial surgery. Prevention of PONV following craniotomy with the use of one or more prophylactic antiemetic drugs should be a part of routine management of these patients. In particular, craniotomy for resection of lesions in the posterior fossa may be accompanied by severe nausea. A meta-analysis looking at the use of 5-HT_3 receptor antagonists in 448 patients showed a significant reduction in the risk of emesis at 24 (relative risk = 0.50, 95% C.I. 0.38–0.66) and 48 h (relative risk = 0.52, 95% C.I. 0.36–0.75) following craniotomy, but had no effect on nausea. Interestingly, the use of prophylactic ondansetron alone has not been shown to be effective in preventing postoperative vomiting in children following craniotomy when compared to placebo. School-age children (4–12 years of age) are more likely to vomit in the first 24 h following surgery compared to adolescents. There is some evidence that the use of other agents such as dexamethasone, low-dose droperidol, preoperative gabapentin, and propofol can lower the incidence of PONV following craniotomy.

Key Points

- Emergence from anesthesia and tracheal extubation may be associated with physiological stress that results in hypertension, increased oxygen consumption, and central and peripheral adrenergic stimulation.
- The metabolic stress response may cause devastating complications such as intracranial bleeding and/or dangerously elevated intracranial pressure. Premature infants have a high risk of intraventricular hemorrhage as a result of impaired autoregulatory capacity.
- The anesthesiologist should decide early on whether the child is suitable for early emergence and extubation or would benefit from a period of postoperative ventilation; anesthetic management should be tailored to best achieve this outcome while taking steps to minimize the metabolic stress response during emergence and following extubation.
- In children, prevention or attenuation of hypothermia, shivering, anxiety, pain, coughing, airway obstruction, emergence agitation, and PONV will reduce but not eliminate the stress response to emergence and extubation.
- Peripheral nerve blocks of the scalp, intravenous lidocaine at extubation, and low-dose fentanyl during wound closure are useful in attenuating the stress response to emergence and extubation in children.
- Prophylaxis of PONV with 5-HT_3 receptor antagonists is ineffective in children; therefore alternative agents such as dexamethasone, gabapentin, and propofol should be considered for prophylaxis of PONV.

Suggested Reading

Basali A, Mascha EJ, Kalfas I, Schubert A. Relation between perioperative hypertension and intracranial hemorrhage after craniotomy. Anesthesiology. 2000;93(1):48–54.

Bekker A, Sturaitis M, Bloom M, et al. The effect of dexmedetomidine on perioperative hemodynamics in patients undergoing craniotomy. Anesth Analg. 2008;107(4):1340–7.

Bhagat H, Dash HH, Bithal PK, Chouhan RS, Pandia MP. Planning for early emergence in neurosurgical patients: a randomized prospective trial of low-dose anesthetics. Anesth Analg. 2008;107(4):1348–55.

Bruder NJ. Awakening management after neurosurgery for intracranial tumours. Curr Opin Anaesthesiol. 2002;15(5):477–82.

Bruder N, Ravussin P. Recovery from anesthesia and postoperative extubation of neurosurgical patients: a review. J Neurosurg Anesthesiol. 1999;11(4):282–93.

Chui J, Mariappan R, Mehta J, Manninen P, Venkatraghavan L. Comparison of propofol and volatile agents for maintenance of anesthesia during elective craniotomy procedures: systematic review and meta-analysis. Can J Anaesth. 2014;61(4):347–56. https://doi.org/10.1007/s12630-014-0118-9. Epub 2014 Jan 31.

Eldredge EA, Soriano SG, Rockoff MA. Pediatric neurosurgical anesthesia. In: Cote CJ, Todres DI, Ryan JF, Goudsouzian NG, editors. A practice of anesthesia for infants and children. 3rd ed. Philadelphia: W. B. Saunders; 2001. p. 493–521.

Ghoneim AA, Azer MS, Ghobrial HZ, El Beltagy MA. Awakening properties of isoflurane, sevoflurane, and desflurane in pediatric patients after craniotomy for supratentorial tumours. J Neurosurg Anesthesiol. 2015;27(1):1–6. https://doi.org/10.1097/ANA.0000000000000058.

Magni G, La Rosa I, Gimignani S, Melillo G, Imperiale C, Rosa G. Early postoperative complications after intracranial surgery: comparison between total intravenous and balanced anesthesia. J Neurosurg Anesthesiol. 2007;19(4):229–34.

Maxwell LG, Buckley GM, Kudchadkar SR, Ely E, Stebbins EL, Dube C, Morad A, Jastaniah EA, Sethna NF, Yaster M. Pain management following major intracranial surgery in pediatric patients: a prospective cohort study in three academic children's hospitals. Paediatr Anaesth. 2014;24(11):1132–40. https://doi.org/10.1111/pan.12489. Epub 2014 Jul 29.

Udomphorn Y, Armstead WM, Vavilala MS. Cerebral blood flow and autoregulation after pediatric traumatic brain injury. Pediatr Neurol. 2008;38(4):225–34.

Vlajkovic GP, Sindjelic RP. Emergence delirium in children: many questions, few answers. Anesth Analg. 2007;104(1):84–91.

Postanesthesia Care Unit Risks Following Pediatric Neurosurgery

67

Balvindar Kaur and Andrew Davidson

Overview

In this chapter, we will review the issues that are of importance in the initial postoperative recovery of the pediatric neurosurgical patient. The pediatric anesthesiologist is able to control many factors that influence cerebral blood flow (CBF), cerebral metabolic rate for oxygen ($CMRO_2$), and intracranial pressure (ICP). When there are immediate postsurgical concerns, failure to awaken, or new neurological signs, the actions of the anesthesiologist may be instrumental in determining the outcome. The advantages and disadvantages of obtaining a CT or MRI scan prior to emergence from anesthesia versus a delayed or "as-needed" scan will be discussed. The goal of the pediatric neuroanesthesiologist is to provide stability of hemodynamics, respiratory parameters, and temperature control and of metabolic and endocrine factors. This stability must continue into the postoperative period to ensure an optimal neurological outcome.

Implications for the Neurosurgical Patient

Blood Pressure Control

A normal newborn autoregulates intracerebral blood flow at mean blood pressures between 20 and 60 mmHg, with a steep rise and fall at either end of the autoregulatory curve. The brain of an infant or child receives a relatively larger percentage of the cardiac output as compared to adults. After traumatic brain injury, young age (less than 4 years) has been shown to be an independent risk factor for impaired cerebral autoregulation. These factors place pediatric neurosurgical patients at particular risk for ischemia at low blood pressures and for hemorrhage at high blood pressures. Short-acting vasoactive agents such as intravenous esmolol or labetalol may be needed in PACU for acute control of hypertension, and adequate fluid and blood replacement must be given to avoid hypotension.

Pain Management

Adequate analgesia is essential, so that the hyperventilation that may occur with crying can be avoided. A balance of adequate analgesia without oversedation (which may mask a change in neurological status) can be challenging. Short-acting intravenous opioids such as fentanyl or remifentanil are commonly used, but there is then a need to titrate longer-acting intravenous agent during emergence. If remifentanil has been used, there is the possibility of acute tolerance with an unexpectedly high opioid requirement in PACU, although studies have not universally confirmed this finding. An age-appropriate pain scale must be used accurately to determine the level of pain, so that it may be adequately controlled. Some scales to consider include the modified infant pain scale (MIPS), the FLACC behavioral scale, the Wong–Baker FACES pain rating scale, and the Oucher. Older children may be asked to report using the familiar 0–10 visual analogue scale (VAS). If opioids are needed, a patient-controlled analgesia (PCA) system may be a good option for delivery, so that the older child can titrate to an adequate level of analgesia but can also avoid sedation that may occur if opioids are given by continuous infusion or by nurse-administered bolus doses. Excessive treatment of pain may result in sedation of the patient, making neurological assessment difficult. In addition, there may be respiratory depression leading to elevated arterial levels of carbon dioxide (CO_2) which may in turn cause somnolence. Patients who have had surgery close to the brain stem, such as a Chiari decompression, may be especially sensitive to even a mildly elevated level of CO_2. Hence there is a need to balance treatment of pain versus the risk of somnolence and impaired neurological assessment. Administration of intravenous naloxone to relieve narcotic-induced somnolence or respiratory depression can cause significant hypertension, so opioids must be titrated with care to avoid the need for reversal of their effects.

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COX-2 inhibitors do not have antiplatelet properties compared to NSAIDs and can reduce opioid requirements without increasing bleeding risks. Adult studies have demonstrated a 6–12 h post-op pain reduction in patients undergoing craniotomy who received a single dose of parecoxib but no significant effect on overall analgesia post-op. There are concerns of possible cardiovascular effects due to thrombotic events. Therefore, COX-2 use in the pediatric population is still unknown – the decision to use it needs to be discussed with the surgical team to weigh the risk benefits.

Temperature Management

Shivering significantly raises oxygen consumption and metabolism, and so efforts should be made to maintain normothermia and to treat shivering promptly with warming blankets or pharmacological treatments such as ketamine or low-dose meperidine if it occurs. Hyperthermia may occur with either an infectious or noninfectious etiology and should be treated, no matter what the cause. Combination therapy (acetaminophen, ibuprofen, and physical cooling) may be needed effectively to maintain normothermia.

Postoperative Nausea and Vomiting

Postoperative nausea and vomiting (PONV) should be treated to avoid the potentially deleterious effects of a Valsalva maneuver during vomiting which may transiently raise ICP or increase the risk for intracranial hemorrhage. A combination of 5-HT3 inhibitors along with dexamethasone is commonly used. Dexamethasone has additional anti-inflammatory effects via modulation of peripheral nociceptors and reduces vasogenic edema. It also reduces pain when used in combination with other analgesics in a multimodal approach.

Endocrine Issues

A few patients who have had surgery in or close to the pituitary fossa will need close monitoring for early signs of the development of diabetes insipidus, manifested by abnormally high volumes of dilute urine and plasma hypernatremia. Judicious fluid therapy is essential – these patients often need hypertonic fluids and frequent monitoring of electrolytes. Other endocrine derangements such as hyperglycemia or hypoglycemia are also possible. One study demonstrated a poor outcome following brain injuries in children when blood glucose levels were elevated (above 250 mg/100 ml).

Respiratory Management

Neurogenic pulmonary edema (NPE) is a complication unique to neurosurgical patients who have had intracranial surgery or injury. It can be life-threatening, and the exact etiology and pathophysiology are incompletely understood. The neuroanesthesiologist must be ready to provide respiratory support, including reintubation and ventilation, if this complication develops in order to maintain oxygenation and normocarbia.

Concerns and Risks

Elevated ICP

Neurosurgical patients experience cerebral hyperemia during emergence from general anesthesia, independent of the anesthesia technique used. Delay of extubation does not attenuate the increase in heart rate, mean arterial pressure and oxygen consumption, and catecholamine surge that occur at extubation. For patients whose raised ICP has not been alleviated by surgery, who had surgery of long duration, had major blood loss, or may have cranial nerve damage that impairs airway protective reflexes, controlled ventilation with adequate sedation may be necessary after surgery. When the time comes to extubate such patients, one should remember that raised ICP has an association with delayed gastric emptying, so suction must be available, and the patient should be fully awake and optimally positioned to reduce the possibility of aspiration.

Seizures

Seizures significantly raise the cerebral metabolic rate for oxygen. Early postoperative seizures are defined as those occurring within the first week after surgery. They occur in 15–20% of patients who have had a supratentorial tumor resection. Close monitoring for postoperative seizures is necessary. Prophylaxis for seizures is generally left to the neurosurgeon's preference as prospective trials are lacking. Phenytoin is commonly given in the perioperative period. A seizure postoperatively must be treated promptly with basic airway and respiratory support, with concurrent communication with the neurosurgical team.

Postoperative Neuroimaging

Timing of postoperative CT or MRI scans is controversial. This practice is not universal; some institutions scan on an as-needed basis only (change in neurological status or seizures being indications to scan), while other institutions scan routinely on postoperative day 1. There is a strong argument for rapid awakening of these patients to allow early neurological assessment and early diagnosis of adverse postoperative neurological outcomes. The anesthesiologist in PACU must be able to respond in a timely manner to adverse hemodynamic and respiratory events. Delayed response to these hemodynamic and respiratory changes can theoretically result in cerebral ischemia, raised ICP, altered consciousness level, and long-term adverse outcomes.

Failure to Awaken

The following goals are desirable clinical targets in the pediatric neurosurgical patient. One or more of these factors may need to be corrected for the patient who fails to awaken at the end of surgery (Table 67.1).

Table 67.1 Failure to awaken

Metabolic:
Temperature – >36°, avoid hyperthermia
Blood glucose – >60 mg/100 ml and <200 mg/100 ml
Osmolality – >275 mOsm/kg, <300 mOsm/kg
Respiratory:
Spontaneous ventilation – CO2 <50 mmHg, Sp02% >94%
Circulation:
Euvolemia, normal BP
Coagulation and hematocrit within normal limits
Neurological:
Intact cranial nerves
Near normal or baseline neurological state
No significant brain edema
No further seizure activity
Pharmacology:
Adequate reversal of muscle relaxants

If all of the above parameters have been considered and corrected if necessary, emergent imaging and neurosurgical consultation may be needed to rule out postoperative hemorrhage or edema for any patient who fails to awaken.

New Neurological Signs

A concerning development in PACU is the occurrence of new neurological signs and symptoms. These must be assessed promptly by both neurosurgeon and anesthesiologist (Fig. 67.1).

Key Points

- The major concern when caring for a pediatric neurosurgical patient in the PACU is finding the balance between adequate analgesia while providing an alert, interactive patient for confirmation that no new neurological deficits have occurred.
- The effect of any intervention (or lack of intervention) on ICP, the threshold for seizure activity, or altering level of consciousness must always be

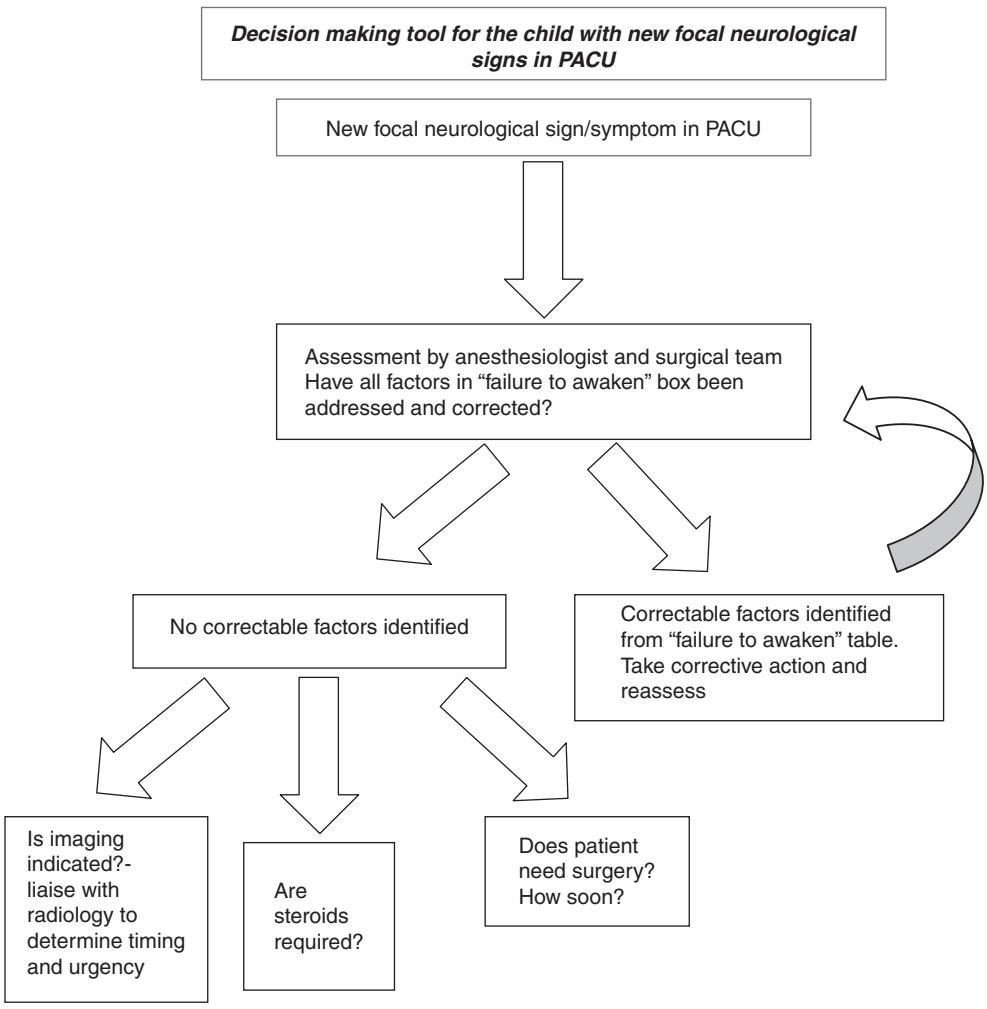

Fig. 67.1 Decision-making tool for the child with new focal neurological signs in PACU

considered as etiologies for postoperative neurologic dysfunction.

- Meticulous attention to pain control, control of PONV, careful management of fluid status to achieve euvolemia, and maintenance of normothermia, normal osmolality, and normoglycemia are essential.
- In pediatric neurosurgical patients, it is particularly important to avoid hypoxemia, hypercarbia, and hyper-/hypotension, since derangements in arterial blood gases or in blood pressure can have profound effects on the cerebral vasculature, resulting in intracranial hemorrhage, raised ICP, or vasospasm, causing new neurological deficits.

Suggested Reading

Brown JM, Udomphorn Y, Suz P, Vavilala M. Antipyretic treatment of noninfectious fever in children with severe traumatic brain injury. Childs Nerv Syst. 2008;24:477–83.

Bruder N, Stordeur J-M, Ravussin P, et al. Metabolic and hemodynamic changes during recovery and tracheal extubation in neurosurgical patients: immediate versus delayed recovery. Anesth Analg. 1999;89:674–8.

Bruder N, Pellissier D, Grillot P, Gouin F. Cerebral hyperemia during recovery from general anesthesia in neurosurgical patients. Anesth Analg. 2002;94:650–4.

Fàbregas N, Bruder N. Recovery and neurological evaluation. Best Pract Res Clin Anaesthesiol. 2007;21(4):431–47.

Freeman SS, Udomphorn Y, Armstead WM, et al. Young age as a risk factor for impaired cerebral autoregulation after moderate to severe pediatric traumatic brain injury. Anesthesiology. 2008;108(4):588–95.

Michaud LJ, Rivara FP, Longstreth WT Jr, et al. Elevated initial blood glucose levels and poor outcome following brain injuries in children. J Trauma. 1999;31:1356–62.

Pryds O. Control of cerebral circulation in the high-risk neonate. Ann Neurol. 1991;30:321–9.

Šedý J, Zicha J, Kunes J, et al. Mechanisms of neurogenic pulmonary edema development. Physiol Res. 2008;57:499–506.

Sulpicio GS, Eldredge EA, Rockoff MA. Pediatric neuroanesthesia. Anesthesiol Clin North Am. 2002;20:389–404.

Vadivelu N, Kai AM, et al. Options for perioperative pain management in neurosurgery. J Pain Res. 2016;9:37–47.

Intensive Care Risks of Pediatric Neurosurgery

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Craig D. McClain and Michael L. McManus

Introduction

Pediatric patients who have undergone intracranial neurosurgical procedures are generally best managed in a critical care setting. These patients may experience hemodynamic, respiratory, and neurologic fluctuations postoperatively and will therefore need frequent assessment to ensure a stable recovery. In centers with high-volume, specialized neurocritical care teams have been demonstrated to improve patient outcomes for both adult and pediatric populations. The transition from operating suite to ICU should begin with clear communication of the patient's history, intraoperative course (including relevant events such as airway issues, bleeding, and brain edema), and anticipated postoperative course including potential concerning focal neurologic deficits.

All new admission to the ICU will require an immediate, thorough physiologic and neurologic assessment. These thorough assessments should then be repeated frequently, as changes in the neurologic exam will be sensitive indicators of potential postoperative complications.

Respiratory Support

- While it is desirable, not all patients who have undergone neurosurgical procedures meet extubation criteria prior to admission to the ICU.
- Postoperative mechanical ventilation aims to support gas exchange while permitting ongoing neurological assessment.
- Triggered modes (i.e., pressure support) offer a method for providing support without losing respiratory drive as a marker of neurologic function and minimize respiratory muscle deconditioning.
- PEEP should be used with caution, especially in smaller children. Even small amounts may impair venous return, compromise cardiac output, and ultimately impair cerebral perfusion. Ultimately, a balance between cardiac output and oxygenation must be struck that still allows for adequate cerebral perfusion. PEEP does not seem to increase ICP unless fairly high levels of PEEP are employed.
- In infants with open fontanelles, there is no association between mean airway and intracranial pressures (ICPs).

Hemodynamic Support

Overview

- Goals – avoid hypotension and maintain adequate cerebral perfusion pressure (CPP).
- In sick neonates, intermittent pressure passivity of the cerebral circulation is present and can predispose to intracranial hemorrhage.
- Even in very low-birth-weight infants, both dopamine and epinephrine are effective in supporting systemic pressure and restoring cerebral blood flow.
- Concepts surrounding factors that regulate cerebral perfusion are changing somewhat from classical teaching. It is becoming more understood that values of blood gas tensions and arterial blood pressure are not where the concept of autoregulation stops. Rather, there is synergism and interdependence between these systems as well as neurogenic mechanisms. Further, it is understood now that cerebral autoregulation does not maintain a constant perfusion over a range of pressures and

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that this autoregulation is not controlled solely through the muscles in the pial arterioles. Finally, the autonomic nervous system plays a vital role in modulating cerebral autoregulation and acts as a buffer in surges to perfusion pressure. In fact, recent evidence would suggest that at lower levels of mean arterial pressure, cerebral autoregulation behaves in a much more pressure passive manner, whereas at higher levels of blood pressure, autoregulatory mechanisms maintain much tighter control over cerebral blood flow.

Implications for the Neurosurgical Patient

- When increased ICP is present, it is generally agreed upon that critical CPP for preschool children (2–6 years) is approximately 50 mmHg, rising to 55–60 mmHg in older children.
- The lower limit of pressure autoregulation in infants and prematures is approximately 30–35 mmHg, depending on the adjusted post-gestational age of the infant. There are some recent data that would support this idea of much lower needed mean arterial pressures to provide adequate cerebral blood flow in infants, at least under sevoflurane anesthesia. It must be mentioned that sevoflurane decrease CMRO2. Therefore, these measured limits may not necessarily apply to patients not under sevoflurane anesthesia.

Fluid Management

Overview

Meticulous fluid management is critical in the care of neurosurgical patients. Small size, immature renal function, and variable intake make fluid and electrolyte imbalances common in pediatrics. These dispositions are further magnified in neurosurgical patients by the disruption of normal homeostatic controls.

- Overall, more than 10% of all children experience postoperative hyponatremia, and this percentage is likely higher after neurosurgery.
- Elevated ADH levels can result from a variety of stimuli ranging from surgical manipulation, to postoperative pain and nausea to fluid shifts and intravascular hypovolemia.
- Since sudden, unrecognized falls in serum sodium can provoke seizures, it is prudent to follow electrolytes closely throughout the perioperative period.

Concerns and Risks

- Nonosmotic secretion of ADH makes hyponatremia common after neurosurgery, despite intraoperative fluids that are high in sodium and isotonic – or slightly hypertonic – to plasma (lactated Ringer's, 272 mOsm/L; Plasma-Lyte, 295 mOsm/L; normal saline, 308 mOsm/L).
- When significant hyponatremia occurs, treatment may include hypertonic saline with free water excesses addressed through fluid restriction and administration of diuretics.
- Small premature infants, with limited reserves of glycogen and limited gluconeogenesis; require continuous infusions of glucose at 5–6 mg/kg/min in order to maintain serum levels.
- The stress of critical illness and resulting insulin resistance can produce hyperglycemia that, in turn, is associated with neurologic injury, infection, and poor outcomes in adults.
  - Previously, tight glycemic control has been widely recommended in adults, but recent evidence paints a controversy over tight or standard glucose control. Hyperglycemia in patients with brain injury has been associated with increased rates of infection, longer ICU stays, and poorer neurologic outcomes.
  - However, the effects of hypoglycemia can be deleterious to patients with brain injury as well.
  - In pediatrics, hyperglycemia has been linked to poor outcome, but it remains unclear that tight glycemic control offers significant benefits to children.
  - Limited evidence now suggests that tight control may carry undue risk of hypoglycemia.
  - A conservative approach that maintains random serum glucose levels below 180 mg/dL may be utilized.

Key Points

- Avoid hypotonic solutions altogether in the perioperative period.
- Infants are at particular risk for hypoglycemia. Monitoring of serum glucose is crucial during the perioperative period in these patients.

Fluid and Electrolyte Abnormalities in the ICU

Syndrome of Cerebral Salt Wasting (CSW)

- Common in children, can be seen following head trauma and many neurosurgical procedures.
- Has been diagnosed with increasing frequency and reported in association with:
  - Meningitis
  - Calvarial remodeling
  - Tumor resection
  - Hydrocephalus
- Incidence is approximately 11.3/1000 procedures with mean duration of symptoms of 6 days, with a range of 1–5.
- Marked by polyuria and natriuresis leading to hyponatremia and hypovolemia.
- Result of excessively high atrial or brain natriuretic peptide levels, which also block steroidogenesis – CSW is typically accompanied by mineralocorticoid deficiency.
- Classic treatment involves saline administration; more rapid resolution has been achieved with fludrocortisone.

Diabetes Insipidus

- Complication of procedures involving the pituitary and hypothalamus.
- Most frequently seen in association with craniopharyngioma, where it can be a presenting symptom in 40% of the cases.
- Noted by an elevated serum sodium (>150 mg/dL) and polyuria (>4 mL/kg/h).
- Severe dehydration and hypovolemia may result.
- A standardized protocol is helpful when postoperative care is multidisciplinary.
  - Unconscious patients, those unable to take oral fluids, or those in whom normal thirst mechanisms are impaired, are best managed using a continuous infusion of vasopressin titrated to minimize urine output (1–0.5 mL/kg/min) – other clinical markers of volume status must be followed.
  - Awake and thirsty patients may be transitioned to oral fluids and DDAVP.

Sedation

Overview

Pain control and sedation present unique challenges in the pediatric intensive care unit. Ideally, postoperative neurosurgical patients are comfortable, awake, and cooperative with their care. In pediatrics, some level of sedation is often necessary to insure a safe recovery. While the ideal sedation regime would include short-acting or reversible agents that can be withdrawn intermittently to permit neurologic assessment, a single agent suitable for children has yet to be developed.

Implications for the Neurosurgical Patient

Propofol

- Propofol is a potent, ultra-short-acting, sedative-hypnotic that is extremely useful in adult neurocritical care with limited utility in the pediatric ICU because of its association with a fatal syndrome of bradycardia, rhabdomyolysis, metabolic acidosis, and multiple organ failure when used over extended periods in small children.
- The mechanism of this remains unclear; it appears related to both the duration of therapy and the cumulative dose. These difficulties are much less common in adults.
- If propofol is utilized, continuous infusions of limited duration are recommended.

Opioids/Benzodiazepines

- The mainstay of sedation in the pediatric intensive care unit remains a combination of narcotic and benzodiazepine administered via continuous infusion.
- Titration to a validated sedation score is advised, and regular "drug holidays" help insure that excessive sedation is avoided.
- Infants and children receiving opioid and/or benzodiazepine infusions for more than 3–5 days are subject to tolerance and experience symptoms of withdrawal when infusions are discontinued.

Dexmedetomidine

- A short-acting single-agent sedative may be used in the postoperative period. Apnea is not a problem with spontaneous breathing easily maintained.

- Pediatric studies are limited, but the drug appears to be safe and effective when used for periods of 24 h or less.
- Pharmacokinetics of dexmedetomidine in pediatric patients is similar to published adult values.
- Opioid cross-tolerance makes it a useful agent for treatment of fentanyl or morphine withdrawal.
- Transient increases in blood pressure can be seen with boluses followed by hypotension and bradycardia as sedation deepens. In our experience, both hypo- and hypertension can occasionally be observed with long-term infusions, and a withdrawal syndrome results when extended infusions are discontinued.

Seizures

Overview

Seizures are a common manifestation of neurological illness in pediatrics. In the child with unexplained, altered mental status, nonconvulsive status epilepticus is also an important consideration. Prophylaxis in the perioperative period and aggressive treatment of new seizure activity are well-recognized mainstays of care.

Agents

- While phenytoin is the agent used most commonly for prophylaxis, maintaining therapeutic serum levels can be a challenge.
- Alternative agents include phenobarbital, carbamazepine, and valproic acid.
- Though potentially compounding respiratory depression, phenobarbital 20 mg/kg is also an effective first-line antiepileptic drug.
- For status epilepticus, lorazepam 0.1 mg/kg IV or diazepam 0.5 mg/kg PR are effective.
- Lorazepam may be repeated after 10 min and accompanied by fosphenytoin 20 mg/kg IV or IM if initial doses are ineffective.
- Increasingly, levetiracetam is being used for seizure prophylaxis and treatment. Purported benefits over phenytoin include the following:
  - No need to follow drug levels
  - Lack of significant drug interactions
  - Similar bioavailability between oral and intravenous forms
  - Broad spectrum of antiepileptic activity

Status Epilepticus

- Refractory status epilepticus continues to present a significant challenge.
- Chemically induced coma remains the mainstay of care with AEDs titrated to EEG burst suppression.
- Pentobarbital, midazolam, or phenobarbital may be employed in bolus-infusion regimes with adjustments directed by continuous EEG.
- Mechanical ventilation and invasive monitoring are necessary since therapy often results in hypotension and myocardial depression. In addition, barbiturates have been associated with depression of immune function and increased rate of nosocomial infection.
- Propofol is also effective in quenching seizures and inducing coma, but the propofol infusion syndrome limits its use in pediatrics.
- Patients may require hemodynamic support from pressors and/or inotropes when being placed in an induced coma.

Seizure Prophylaxis for Head Trauma

- The utility of seizure prophylaxis after pediatric head trauma continues to be controversial.
- Although some data suggest that children may benefit more than adults from routine prophylaxis, the overall risk of seizures is low after blunt injury.

Intracranial Pressure

Overview

- ICP monitoring is desirable in trauma and in neurosurgical patients at risk for brain swelling or sudden expansion of a mass lesion.
- Symptoms are nonspecific in children, and intermittent apnea may be its first sign in infancy.
- Low thresholds are kept for invasive monitoring of unconscious patients since physiologic parameters are less sensitive than mental status changes.
- In babies, split sutures and bulging fontanelles provide clinical evidence of increasing ICP, but noninvasive quantitative measures are not reliable.
- The treatment of increased ICP in infants and children is still largely informed by adult data.

  - A notable exception to this, as discussed above, is that target thresholds for mean arterial pressure and CPP vary with age.
- Osmotherapy with 3% (hypertonic) saline is widely used in boluses or infusion to control ICP; it may more rapidly lead to severe hypernatremia in small children than in adults.
- Other elements of management extrapolated from adult data include avoidance of steroids, the preference of crystalloid over colloid resuscitation fluids, and the reluctance to employ hyperventilation.
  - Regarding the latter, it is particularly important to recognize that small children are subject to inadvertent overventilation and that hyperventilation-associated cerebral ischemia can occur. Careful monitoring of blood gasses, minute ventilation, and end-tidal carbon dioxide tensions are therefore recommended.
- When CPP is low and ICP remains high despite medical management, early decompressive craniectomy may have a better outcome in children than adults.

Brain Death

Overview

- Determination of brain death in older children is similar to adults, but the diagnosis is difficult in infancy.
- The Uniform Determination of Death Act defines death as "irreversible cessation of circulatory and respiratory function or irreversible cessation of all functions of the entire brain, including the brainstem."
- Diagnosis requires
  - Normothermia
  - Normotension
  - Normal systemic oxygenation
  - Absence of confounding toxins or medications
- An apnea test (documenting the absence of respiratory effort despite $pCO_2 > 60$ torr) is conducted last since elevated pCO_2 may exacerbate neurologic injury.
- To establish irreversibility, age-related observation periods are necessary:
  - For premature newborns and infants under 7 days of age, no such period has been established.
  - For infants 1–8 weeks of age, our institution utilizes two exams and two isoelectric electroencephalograms 48 h apart.
  - Infants 2–12 months of age require two clinical exams separated by 24 h.
  - Patients older than 1 year require exams 6–12 h apart, or 24 h if the proximate cause of death is hypoxia-ischemia.
- The exam seeks to establish the complete absence of cortical and brainstem function.
- Cerebral ^{99}Tc-ECD single-photon emission computed tomography (SPECT) scanning is used to document the absence of cerebral perfusion when confounders complicate the clinical diagnosis.

Key Points

- Extubation and initial neurological assessment are ideally accomplished in the operating room.
- Postoperative mechanical ventilation aims to support gas exchange while permitting ongoing neurological assessment.
- Hemodynamic goals are to avoid hypotension and maintain adequate CPP.
- Sudden, unrecognized falls in serum sodium can provoke seizures and can be life-threatening.
- Avoid hypotonic solutions altogether in the perioperative period.
- Ideally, postoperative neurosurgical patients are comfortable, awake, and cooperative with their care.
- Seizure prophylaxis in the perioperative period and aggressive treatment are well-recognized mainstays of care.
- ICP monitoring is desirable in trauma and in neurosurgical patients at risk for brain swelling or sudden expansion of a mass lesion.
- In babies, split sutures and bulging fontanelles provide clinical evidence of increasing ICP, but noninvasive quantitative measures are not reliable.
- The Uniform Determination of Death Act defines death as "irreversible cessation of circulatory and respiratory function or irreversible cessation of all functions of the entire brain, including the brainstem."

Suggested Reading

Abend NS, Dlugos DJ. Nonconvulsive status epilepticus in a pediatric intensive care unit. Pediatr Neurol. 2007;37:165–70.

Bell MJ, Carpenter J, Au AK, et al. Development of a pediatric neurocritical care service. Neurocrit Care. 2009;10(1):4–10.

Caricato A, Conti G, Della Corte F, et al. Effects of PEEP on the intracranial system of patients with head injury and subarachnoid hemorrhage: the role of respiratory system compliance. J Trauma. 2005;58:571–6.

Huang SJ, Hong WC, Han YY, et al. Clinical outcome of severe head injury using three different ICP and CPP protocol-driven therapies. J Clin Neurosci. 2006;13:818–22.

Jauch-Chara K, Oltmanns KM. Glycemic control after brain injury: boon and bane for the brain. Neuroscience. 2014;283:202–9.

Liu J, Zhu YS, Hill C, Armstrong K, Tarumi T, Hodics T, et al. Cerebral autoregulation of blood velocity and volumetric flow during steady-state changes in arterial pressure. Hypertension. 2013;62:973–9.

Mathur M, Petersen L, Stadtler M, Rose C, et al. Variability in pediatric brain death determination and documentation in southern California. Pediatrics. 2008;121(5):988–93.

Nemer SN, Caldeira JB, Santos RG, Guimaraes BL, Garcia JM, Prado D, et al. Effects of positive end-expiratory pressure on brain tissue oxygen pressure of severe traumatic brain injury patients with acute respiratory distress syndrome: a pilot study. J Crit Care. 2015;30:1263–6.

Rhondali O, Pouyau A, Mahr A, et al. Sevoflurane anesthesia and brain perfusion. Pediatr Anesth. 2015;25:180–5.

Skippen P, Seear M, Poskitt K, et al. Effect of hyperventilation on regional cerebral blood flow in head-injured children. Crit Care Med. 1997;25:1402–9.

Willie CK, Tzeng YC, Fisher JA, Ainslie PN. Integrative regulation of human brain blood flow. J Physiol. 2014;592(5):841–59.

Wise-Faberowski L, Soriano SG, Ferrari L, et al. Perioperative management of diabetes insipidus in children [corrected]. J Neurosurg Anesthesiol. 2004;16:14–9.

Part XI

Fundamentals of Interventional Neuroradiology

Radiation Safety in Interventional Neuroradiology

69

Justin P. Dodge, Neil E. Roundy, and Kenneth C. Liu

Overview

Information obtained using radiation is clinically valuable and often could not be obtained by any other reasonable means. Thus the radiation exposure of the patient is warranted as the clinical benefit typically exceeds the potential risk. In contrast, the healthcare provider receives no benefit from the radiation; therefore, their radiation exposure should be kept as low as possible. The most common exposure of healthcare personnel to medical X-rays comes from the use of fluoroscopy units. It should be noted that there are many other sources of naturally occurring and other man-made sources of radiation (including other sources of medical radiation). *The essence of radiation safety in relation to medical X-rays involves three basic principles – time, distance, and shielding*. There are also several functions of modern fluoroscopy equipment that are designed to reduce patient and fluoroscopist dose. The information within this chapter should be regarded as a minimalist approach in understanding the basics of limiting radiation exposure. A good radiation safety program will utilize a Health Physics office or equivalent. The Health Physics office has many important roles, including safety information and training, equipment inspections, and the management of the radiation exposure monitoring (dosimetry).

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Background

Many scientific units are used to measure radiation. The units that are most important to the healthcare worker are the rad (*r*adiation *a*bsorbed *d*ose) and the rem (*r*adiation *e*quivalent [dose in] *m*an). System International (SI) unit conversions are 100 rad = 1 Gray (Gy) and 100 rem = 1 Sievert (Sv). These units and conversions are provided for familiarity purposes.

Fluoroscopy

A fluoroscopy unit or C-arm is the most commonly encountered X-ray-generating device in the operating room or angiographic suite. Several specific concepts are imported when using or being exposed to the X-rays produced by a fluoroscopy unit. The radiation effect most important in increasing the healthcare worker's exposure is through scattered radiation which is ideally approximately 0.1% of the radiation exposure of the patient at 1 m. A key element in reducing scatter includes keeping the image intensifier (X-ray detector) as close to the patient as possible.

Several design elements are available to aid the fluoroscopist in reducing radiation exposure, and learning to effectively utilize them is critically important for the fluoroscopist. Many of these elements are equipment specific, and it is advisable to request training on each fluoroscopic unit. Pulsed-fluoro activates the X-ray tube intermittently and can greatly reduce dose. The lower the pulse rate (pulses per second), the less the radiation exposure. For most procedures that do not have a critical time sensitive component, the lowest pulsed setting can be used, thus significantly reducing the time factor. An additional feature to reduce the time factor would be using "last image hold." This allows an image to be displayed that can be used to plan the next portion of the procedure. Collimating the X-ray beam to the smallest size possible for the particular procedure is beneficial in both

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reducing the radiation exposure and improving the image quality. Grids will filter out internally scattered radiation which can be helpful in improving image quality especially in large patients; however, their use always increases dose. Magnification can be helpful in imaging a particularly small anatomy, but whether geometric or electronic, magnification will increase dose.

Time

Time is the easiest principle to understand. *The actual time the fluoroscopy unit is generating X-rays is directly related to exposure*. That is to say if the X-ray generator is active for twice as long, radiation exposure cumulatively increases by twice as much. Keeping this principle in mind during a procedure means being aware of the amount of time the X-ray unit is on, limiting the time the unit is on to the minimum amount to effectively care for the patient, and learning to be as efficient with radiation utilization as possible.

Distance

Distance from the radiation source is an important principle and most important for the personnel not actively involved in patient care. *The distance from the radiation source correlates to exposure by the inverse square law*. This means that doubling the distance from the X-ray source, radiation exposure is reduced by a factor of four. Furthermore, tripling (or quadrupling) the distance from the X-ray source, radiation exposure is reduced by a factor of 9 (or 16). Keeping this principle in mind during a procedure simply means spending most of your time as far from the X-ray source as possible while still being able to effectively care for the patient. Particularly critical is keeping your body outside of the direct beam unless absolutely necessary.

Shielding

Shielding personnel from radiation exposure is the principle that the healthcare provider has the most direct control over. Shielding is a material that effectively "absorbs" the energy of the radiation and thus protects the healthcare worker. The effectiveness of shielding is a much more complex calculation and not practical for the scope of this chapter.

Shielding is present in many forms from the design of the room and equipment to barrier devices. Most of the personnel reading this chapter will not have control over the design of the room or equipment. *The critical portion of this principle is that the safety devices that are not used will offer no protection*. Commonly used safety equipment utilized includes lead aprons, thyroid shields, and lead glasses. These devices effectively absorb between 90% and 99.5% of the radiation depending on several variables such as the thickness and design of the shielding device and the energy of the X-ray being generated. Lead aprons can be obtained that offer only frontal coverage or "wrap-around" 360-degree coverage. The wearer of an apron that offers only frontal coverage must remain conscientious in keeping themselves facing the X-ray source at all times. "Leaded glass," commonly made of special plastic, is also available and can be placed between the healthcare worker and the X-ray source in addition to worn safety devices.

As the radiation exposure of a healthcare worker is significantly increased (1000-fold) when they place their body directly in the fluoroscopy beam, this situation requires particular concern. The best choice would be to use a tool or device to do the same procedure without placing their body into the beam. If this is not possible or practical, using specialized shielding such as a leaded glove is advisable.

Implications for the Patient

During fluoroscopy, the patient is directly in the X-ray beam. In other words, the patient is receiving approximately 1000 times or more the radiation exposure as the healthcare worker. Due to the nature of the procedure and the design of the equipment, several items should be reviewed in regard to patient safety.

In regard to time, the longer the fluoroscopy unit is on, the more radiation exposure the patient receives. Using effective collimation (narrowing of the X-ray beam), keeping the tube current as low as possible to obtain a diagnostic image, and effectively utilizing the previously described fluoroscopy unit design features will all combine to decrease the patient's dose.

Distance from the X-ray generator to the patient (source object distance) is fixed in many systems, but again, the furthest distance from the patient decreases the radiation exposure. When using a C-arm, this concept becomes particularly important as the distance from the X-ray generator to the image intensifier is fixed. *It is desirable to keep the image detector as close to the patient as possible, therefore making the X-ray generator as far as possible from the patient* (Fig. 69.1). This is a win–win scenario where the patient radiation exposure is decreased (the distance component), the fluoroscopic image is improved, and the healthcare radiation exposure is decreased (the scatter effect).

The last of the principles is again shielding. Shielding the patient can usually be done only for body parts outside the region of treatment interest. Commonly used patient shield devices include breast, gonad, and thyroid shields which are designed to protect the most radiosensitive organs.

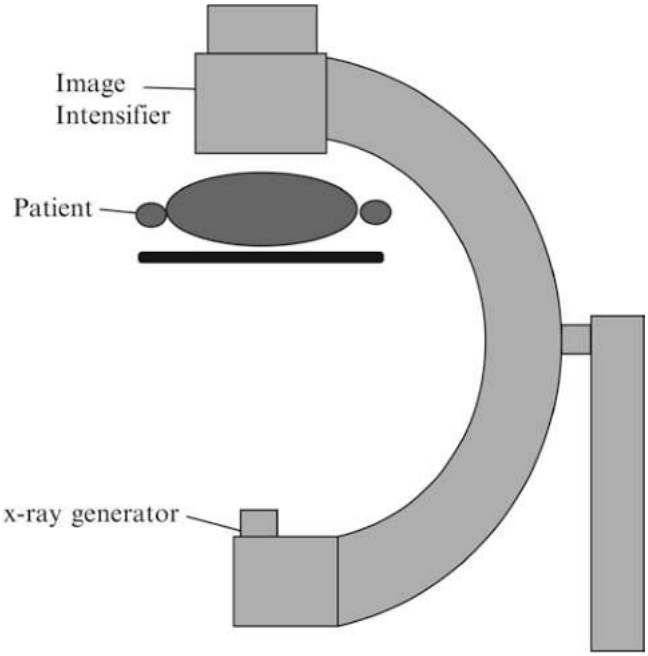

Fig. 69.1 Illustration demonstrating the ideal configuration of the C-arm with the image intensifier placed close to the patient and the X-ray generator far from the patient

Concerns and Risks

The radiation used in medical imaging is ionizing radiation. This means that the radiation can cause biological damage on the molecular level. There are four main negative effects (risks) of radiation exposure, including tissue damage, radiation-induced cancers, genetic effects, and fetal exposure. As a general rule, a rapidly dividing cell type is more sensitive to the effects of radiation.

In the practical use of medical X-rays, hair loss, skin erythema, and desquamation are the most commonly encountered tissue damage and typically occur on the order of 3 weeks after the exposure. These effects occur in a threshold or deterministic model. This means that a certain level of radiation exposure must be reached before the effect occurs. These levels are possible if misusing fluoroscopy equipment. As a side note, several states have been adopting training requirements for healthcare workers that use fluoroscopy.

The carcinogenic effects of radiation are not completely understood, but several general statements can be made. The higher the radiation exposure(s) are, the higher the risk becomes. There is typically a one-to-several decade delay between the radiation exposure and the development of cancer. Children are at the highest risk of radiation-induced cancer. The most common radiation-induced cancers are breast, thyroid, lung, leukemia, and GI cancers. Genetic effects of radiation are not typically encountered at the doses used in medical imaging and are felt to occur at a much lower rate than the carcinogenic effects.

The rapidly growing fetus is extremely sensitive to radiation exposure; therefore, limiting exposure to pregnant patients or healthcare workers is highly desirable. Fetal gestation is divided into three major components: preimplantation, organogenesis, and fetal growth. During the preimplantation stage, the fetus is particularly sensitive, and excessive radiation exposure typically results in fetal demise. Radiation exposure during organogenesis has a higher likelihood of causing organ malformations. The fetal growth phase radiation exposure most commonly results in neurologic and sensory organ anomalies and childhood cancers.

Dosimetry

Monitoring the exposure of radiation healthcare workers is important for safety and in many places for legal purposes. A Health Physics office typically monitors this program and assesses the individuals' appropriate monitoring requirements based on their exposure to medical radiation. Special requirements are utilized for pregnant personnel. Monitoring devices most commonly used are film badges and less commonly dosimeters. These devices allow the healthcare worker to monitor their radiation exposure and to compare their exposure rates to established limits. *The most important principle in dosimetry is that the required monitoring devices are worn appropriately*. Single dosimeters are typically worn *outside* of lead shielding on the front of the body. Two dosimeter systems are also common and have one dosimeter outside and one dosimeter inside the lead shielding. For specifics, please consult your Health Physics office. Special care should be taken to store the dosimetry units in a location that is reasonably excluded from radiation exposure.

Key Points

While using or being exposed to medical radiation, the healthcare worker should understand the basic principles of radiation safety. Most healthcare workers should also be familiar with the *ALARA* concept which means keeping the radiation exposure *a*s *l*ow *a*s *r*easonably *a*chievable.

- Keep the time of the procedure and the radiation exposure as short as reasonably possible from the X-ray source.
- Increase the distance of the healthcare worker as far as reasonably possible from the X-ray source.
- Utilize safety devices and shielding whenever possible.
- Be familiar with the appropriate use of fluoroscopy and the specific techniques to reduce radiation exposure for both the healthcare workers and the patient.

Suggested Reading

Bushberg JT, et al. The essential physics of medical imaging. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2011.

Dagal A. Radiation safety for anesthesiologists. Curr Opin Anesthesiol. 2011;24:445–50.

Understanding Basic Techniques and Procedures in Interventional Neuroradiology

70

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The Neuroangiography Suite

The neuroangiography suite is based around the biplane angiography unit, which uses two C-arm X-ray tubes to capture simultaneous orthogonal images. These tubes are mobile and allow 360° rotation, which is used in capturing 3-D images, for example, during intracranial aneurysm embolization. The neuroangiography suite further consists of an angiography table; a rack of monitors; and a mobile table for equipment, along with anesthesiology monitors, and storage areas for the angiographic equipment. Due to all of these, the suite may easily become cluttered and equipment such as IV tubing, IV poles, patient warming devices, or drug carts can interfere with the function of the fluoroscopy unit. To avoid inadvertent collision of equipment and traction on tubing, careful planning by both anesthesia, surgical, and radiology technician staff is required to arrange the equipment in a manner that allows for both the anesthesiologist and surgeon to work unencumbered. Careful spacing of IV poles and incorporation of tubing extensions for the endotracheal and IV tubes are usually necessary.

Fluoroscopy and Radiation Safety

Fluoroscopy is a dynamic process, by which the flow of contrast through the circulation is recorded. Modern digital image intensifiers allow increased signal-to-noise while maintaining lower levels of radiation than were previously required. Even so, anesthesia providers are typically located near the patient's airway and need to be cognizant of their proximity to the X-ray tubes.

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Radiation exposure depends on the amount of radiation emitted, intensity of the source, nature/energy of the source, and the area exposed to radiation. Effective dose (HE) is a standardized unit and is used to compare radiation doses across procedures and exposure types. Radiation exposure can lead to skin erythema, necrosis, cataracts, sterility, and cancer, among other effects. However, these are very rare at doses <2 Gray (Gy) of radiation. Fluoroscopy generally generates a skin dose from 10 to 100 mGy/min. Smaller doses may affect cellular function by causing genetic damage, which disproportionately affects rapidly dividing tissues, such as the bone marrow, lung, stomach, colon, and lymphatics, and may lead to subsequent solid tumor formation.

Limiting radiation exposure is an important consideration for any provider working regularly in the neuroangiography suite. Principles of reducing exposure include increased distance, reduced exposure time, and shielding. Practically, this may be done in a variety of ways. The use of thermoluminescent dosimeter (TLD) badges, monitored by institutional radiation safety officer, is encouraged. Providers should make use of lead suits, lead lined glasses, and radiation shields. The operator can also limit radiation by using colimiters, high frame rates, and filters and placing the source as close to the patient as possible.

Basic Neurointerventional Procedures

Patient Positioning

The patient is generally positioned supine (with some exceptions, as with vertebroplasty or kyphoplasty procedures). The head should be in neutral position and may be strapped in place. For certain aneurysms in which it is anticipated that the image intensifier may need to be positioned in an extreme submento-vertex position, the operator may request that the patient's head be extended. Other head positions may be requested in a dynamic manner to assist with catheterization of difficult anatomic variants in some circumstances.

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Vascular Access

Any neurointerventional procedure begins with vascular access, which is usually achieved by right femoral arterial puncture, but may be accessed via the left common femoral artery or left or right radial arteries. For venous procedures, usually the right or left common femoral vein is cannulated. Ultrasound may be used to assist vascular access, and anatomic markers are used to minimize the risk of a high stick that may put the patient at risk for retroperitoneal hematoma. The artery is cannulated using a Seldinger technique, and a sheath is typically placed which remains in place for the duration of the procedure. The sheath is attached to a drip, which provides a continuous flow of heparinized saline to prevent clot formation at any point in the arterial system. Any catheter, wire, or device that is introduced into the patient must be flushed and checked to ensure no air bubbles are present, as even a small air bubble in the arterial system may embolize to the cranial circulation and cause a stroke. Occasionally, the brachial artery or carotid artery may be accessed by a cut-down procedure, or the superior ophthalmic vein may be accessed via a transorbital route.

Arteriotomies may be closed by manual compression or by a variety of arterial closure devices. The advantage of these devices is that typically they do not require the patient to lie flat longer than 2 h (compared with 6 h for manual compression). However, all patients should have as smooth a recovery from sedative or anesthesia as possible to prevent vigorous coughing or straining that may dislodge clot from the arterial wall or cause device failure. Some oozing from the groin site is relatively common, but should quickly disappear, and any hematoma that is observed to form after a neurointerventional procedure must be carefully outlined and observed. A femoral artery Doppler ultrasound will delineate any pseuroaneurysm, if it has formed.

The sheath is a short catheter that provides access for the devices and equipment used in most neurointerventional procedures. While it is preferable to select the smallest size sheath that will fit the catheters and equipment necessary for a procedure, it is sometimes useful to insert a larger sheath in order to provide the anesthesia team with an arterial line, instead of placing a dedicated radial arterial line and saving the patient an additional stick.

Monitoring in the Anesthetized Neurointerventional Patient

The majority of neurointerventional procedures are directed toward intracranial vascular pathology, including acute stroke, cerebral aneurysms, arterial-venous malformations (AVMs), fistulae, and diseases of the dural sinuses. Specific considerations associated with individual pathologies will be discussed below. However, a number of general considerations should be emphasized.

The principles of neuroanesthesia should be followed in these cases just as in patients undergoing intracranial surgical procedures in the operating room. However, the monitoring of the anesthetized neurointerventional patient requires particular vigilance. The procedures often involve the manipulation of micro-guidewires and the navigation of microcatheters through the intracranial circulation. This presents risk to the patient of guidewire perforation or vessel rupture. Unlike open procedures where the vessel is directly visualized, periprocedural hemorrhage or other untoward events can occasionally go unnoticed and may be manifested only by changes in the patient's vital signs. Following an intracranial bleed, these can be as subtle as a very transient bradycardic episode or as evident as a brisk Cushing's response.

An arterial line may or may not be necessary depending on the procedure, but is generally desired for intracranial aneurysm embolization, AVM embolization, carotid stenting, and acute stroke intervention. Depending on the procedure, the interventionalist may be able to provide an intra-arterial line or an intravenous line from the groin access by upsizing the sheath.

The monitoring of intravascular volume and volume status may be complicated by the use of continuous flush of heparinized saline, which is usually attached to most sheaths, guide catheters, and microcatheters. Although the rate of flush is usually about one drop per second, it can be variable and, over the course of a complex case, may accumulate to a significant volume.

Because the procedures are image-based, live image processing by workstations occurs. This often consists of overlaying digitally processed images over live images. The use of roadmap technology, which involves acquisition of images in a particular viewing angle, reversing the image, and overlaying it on an active image, requires the patient to be fully immobilized, as any small movement disrupts the accuracy of the roadmap overlay. Digital subtraction angiography allows non-opacified structures such as bone or other artifacts to be subtracted from the image so that greater detail and accuracy can be obtained. Re-masking or "pixel shifting" can correct for small movements, but the technique is very sensitive to small patient movements. For this reason the use of neuromuscular blockade is usually recommended among patients undergoing general anesthesia for intracranial endovascular procedures. This should be specifically discussed with the interventionalist prior to anesthesia induction. In addition, suspension of respirations for temporary apnea may be used so that ventilator chest motion does not degrade the study quality.

Even though most of these intracranial interventional procedures are performed with the patient under general anesthesia, the movement of guidewires, catheters, and balloons in the intracranial vessels is very stimulating, as these arteries are highly innervated. Changes in the blood pressure and heart rate are often seen and can be variable from patient to

patient. Traction on intracranial arteries may induce a transient bradycardia.

Ruptured and Unruptured Intracranial Aneurysms

All ruptured and most unruptured intracranial aneurysm interventions are performed under general anesthesia. The patient should be immobilized with neuromuscular blockade, and an arterial line should be placed most of the time. The anesthetic team should ensure that protamine is drawn up prior to the start of the procedure and have an intravenous line available for the immediate infusion of nicardipine if it needed. Treatment of intracranial aneurysms may involve coiling alone, or it may involve the placement of adjunctive devices such as intracranial stents or balloons. The insertion of multiple catheters or devices involves an increased risk of thrombus formation, which may embolize and may require acute intervention either with a glycoprotein (GP) IIb/IIIa inhibitor (a class of antiplatelet agents) or with mechanical thrombectomy. A newer treatment for an increasing variety of aneurysms is flow diversion, which involves placement of a specialized stent that channels blood flow away from the aneurysm dome.

If, during treatment, the aneurysm is ruptured by require a microwire or coil, the operator will ask for immediate administration of protamine. Heparinization for these procedures is usually performed after placement of the arterial sheath at the beginning of the procedure, typically with intravenous dosages of 3000–6000 or 70 U heparin per kilogram of body weight. The dosage of protamine for heparin reversal is 1.0–1.5 mg per 100 IU heparin, injected intravenously, with a maximum dosage of 50 mg. The blood pressure should be immediately lowered to a systolic blood pressure of <140. Sometimes, balloons are used to occlude the point of hemorrhage. Acute ruptures are also managed by placing an external ventricular drain at the bedside to relieve intracranial pressures.

Arteriovenous Malformations and Fistulae

Embolization of arteriovenous malformations (AVMs) and fistulae often entails injection of glue or Onyx embolization liquid through a microcatheter in small, distal intracranial vessels. This is done under general anesthesia. Due to the fragility of the vessels that need to be catheterized for AVM or fistula embolization, the risk of rupture is a real concern. Additionally, the use of liquid embolic agents brings with it the risk of embolization to the intracranial venous sinuses, potentially causing sinus thrombosis, intracranial hypertension, and venous hemorrhage (although not usually an acute problem during the case itself).

For any AVM that has been completely embolized, the institution of strict blood pressure control, usually with a beta blocker such as metoprolol, is necessary to prevent normal perfusion pressure breakthrough. This strict control continues in the 24–48 h following embolization, while the patient is observed in the neurointensive care unit.

Carotid Stenosis

Percutaneous balloon angioplasty and stenting for carotid stenosis may be done under general anesthesia, depending on operator preference, but is most commonly performed under conscious sedation. Among these patients, a small amount of movement is acceptable given the advantages of continuous neurological assessment. However, balloon angioplasty for carotid stenting places pressure on the carotid bulb disrupting vagal tone to the cardiovascular system. The surgeon will often ask for the anesthesiologist to administer an anticholinergic agent (e.g., atropine) prior to dilating the carotid bulb. Even so, carotid angioplasty can cause a severe enough hypotensive state that vasopressor support is needed. These patients may also have atherosclerotic disease in their coronary circulation and need pressor support to avoid cardiac ischemia.

High-risk patients for carotid artery stenting have age >80 years old, renal failure, long duration of embolic protection device placement, and tortuosity or calcification of aortic arch and great vessels. Typically, a stent is placed across the area of stenosis, which most often spans the carotid bifurcation. A distal protection device, consisting of a basket which catches embolized clot or plaque, is used throughout the case. Pre- and/or post-stent angioplasty may also be performed using a balloon. Adrenergic inhibition, related to baroreceptor firing after carotid angioplasty, may require prolonged pressor support. This normally resolves within 24 h but may persist, especially in older patients with heavily calcified carotid bifurcations.

Acute Ischemic Stroke

Recent Grade I evidence has supported the efficacy of acute endovascular intervention for ischemic stroke affecting the large intracranial vessels (ICA and first segments of the MCA and ACA). Randomized trials have supported the utility of neurointervention for up to 8 h from the onset of symptoms, although thrombectomy has been performed at much later time points in certain instances in which perfusion imaging or the presence of robust collateralization indicates a potential for salvageable neurologic tissue. Given this emerging consensus, stroke centers and other institutions offering these procedures have established institutional protocols for the emergent evaluation and intervention for patients with treatable lesions. This may include CTA, CT

perfusion, or MR perfusion studies, but the cornerstone is rapid evaluation and triage to neurointervention.

Patients with acute ischemic stroke undergoing thrombectomy usually require an anesthetic team to manage the patient's airway and monitor vitals and hemodynamic parameters. Evidence supports the performance of these procedures under conscious sedation where possible, although agitated patients or those unable to cooperate with the examination may require intubation.

Administration of tissue plasminogen activator (tPA) does not preclude angiography, and if a patient is receiving IV tPA, this should be continued throughout the periprocedural period. A variety of procedures are currently used for acute thrombectomy, including suction (either manually or via a suction device) and mechanical thrombectomy. This involves placement and subsequent removal of a stent (called a "stentriever"), which over the course of 5 min incorporates itself into the clot allowing it to be pulled out along with the device, while the guide catheter is maintained on suction. The manipulation of intracranial vessels during this process can result in significant vasospasm, and intra-arterial infusion of verapamil is often used to treat this.

Blood pressure management after intervention for acute stroke can be complex and is best guided by a multidisciplinary collaboration between the neurointerventional team and the neurology/stroke team. A dedicated arterial line should be placed at the beginning of the procedure as it will be used to monitor blood pressure over the following 24 h. Prevention of reperfusion injury usually requires blood pressure control, although mild permissive hypertension may also be helpful in maintaining perfusion for overall neurologic function. Sudden spikes in blood pressure must be avoided, as they are correlated with hemorrhagic conversion.

Vascular Injuries of the Head and Neck

The most common vascular injury of the head and neck requiring emergent neurointervention is epistaxis, but a wide variety of other injuries may be sustained requiring embolization or parent vessel sacrifice. These procedures typically require general anesthesia. Of course, the main area of concern is acute blood loss, so close monitoring of the patient's volume status and hemoglobin is essential. Pulmonary aspiration of clotted blood can cause acute lung collapse or respiratory arrest. Typically treatment involves coil or glue embolization of the affected vessel, possibly with the deployment of a vascular plug or Gelfoam pledget. Depending on the institutional preference or individual patient situation, the ENT physician may prefer to take the nasal packing down with the patient still anesthetized, which may necessitate a transfer to the operating room.

Vertebroplasty and Kyphoplasty

The most common nonvascular procedures performed in the neurointerventional suite are vertebroplasty, kyphoplasty, and vertebral bone biopsies. All of these procedures are performed with the patient lying prone, and due to the often painful nature of the pathologies treated – compression fracture, pathologic fracture, or vertebral body metastatic disease – anesthesia is often required to provide sedation and pain relief. Under fluoroscopic guidance, a needle is introduced percutaneously from a posterior approach, through the pedicle into the vertebral body where cement is then injected. This stabilizes the fracture and typically brings significant pain relief to the patient. Kyphoplasty involves using a balloon to create a cavity prior to cement injection. Because a foreign material is injected, perioperative antibiotics are administered.

Other Procedures

A wide variety of other procedures are performed in the neurointerventional suite and may require a range of neuroanesthetic care. Spinal angiography; venography, venous manometry, and venous stenting; embolization of pediatric vascular malformations; embolization of carotid-cavernous fistulae; and preoperative tumor embolization are among many others. Although individual patient factors and specific situations vary, the basic techniques and procedures in the neurointerventional suite remain the same. Close collaboration with the neurointerventional team, including the radiation technicians and the nursing staff, is essential to the smooth and efficient running of the suite and for the safety of the patients.

Key Points

- Patient motion can severely degrade imaging quality and compromise the surgeons' ability to deliver optimal care; the use of neuromuscular blockade should be discussed with the surgeons preoperatively.
- Neurovascular structures are exquisitely sensitive to the intraluminal movement of wires and catheters as well as extraluminal traction; unexpected changes in heart rate and blood pressure can occur during manipulation and should be anticipated.
- Subtle changes in the patient's vital signs can signify the presence of a significant wire perforation or hemorrhage.
- Maintain adequate lead shielding and follow radiation safety guidelines at all times.

Suggested Reading

Deshaies EM, Eddleman CS, Boulos AS, editors. Handbook of neuroendovascular surgery. New York: Thieme; 2012.

Hurst RW, Rosenwasser RH, editors. Interventional neuroradiology. New York: Informa Healthcare; 2008.

Morris P. Practical neuroangiography. Philadelphia: Lippincott Williams & Wilkins; 2007.

Osborn AG, editor. Diagnostic cerebral angiography. 2nd ed. Philadelphia: Lippincott Williams & Wilkins; 1999.

Basics of Image Interpretation in Interventional Neuroradiology

71

Wibke S. Müller-Forell

Overview

The majority of patients with cerebral vascular diseases, demanding neuroradiological interventions, are those who present with potential life-threatening spontaneous intracranial/intracerebral haemorrhages due to cerebral aneurysms and/or arteriovenous malformations (AVMs) or with cerebral infarction due to intraarterial thrombi in cerebral arteries. Neuroradiological procedures (interventional neuroradiology) (IN) mainly performed in general anaesthesia can be divided into occluding and opening interventions.

Examples of occluding interventions include endovascular occlusion of cerebral aneurysms (with platin-coils, sometimes in a combination with endovascular stent application), AVMs, and dural fistula (often performed with a combination of coils and glue administration). The most frequently used glues are *N*-butyl cyanoacrylate (Histoacryl®) or ethylene vinyl alcohol combined with dimethyl sulfoxide (DMSO) and tantalum (Onyx®). These procedures should be performed only by experienced neuroradiologists, as they carry the risk for severe complications as, for instance, intracerebral haemorrhage or ischaemic stroke (Table 71.1).

Examples of opening interventions include revascularization by local medical lysis/direct, mechanical (stent-assisted/aspiration) removal of embolic thrombi from main cerebral vessels (i.e. endovascular treatment of ischaemic stroke) or arterial application of vasodilators in cerebral vessels affected by vasospasm following aneurysmal subarachnoid haemorrhage (SAH).

Table 71.1 Overview of diagnostic procedures, therapy (alternative therapy), and complication of neuroradiological interventions (1–3 demand occluding, 4 and 5 opening procedures)

Disease	Diagnostic imaging	Therapy	Complications of NR interventions
1. Cerebral aneurysm	1. CT/CTA	Interventional:	*Acute*: arterial rupture
	2. DSA	1. Coiling	*Follow-up*: vasospasm → interventional procedure (see below)
		2. Coiling + stent	
		Neurosurgical: clipping	
Iatrogenic aneurysm		Interventional: stent	Vessel occlusion
2. AVM	1. MRI/MRA	Interventional: glue/(coils)	Rupture with intracerebral haemorrhage and/or CSF disturbance
	2. DSA	Neurosurgical: extirpation	
	3. (CT/CTA)	(Radiation)	
3. Dural fistula	1. CT/CTA	Interventional: glue/coils (venous > arterial approach)	Rupture
	2. MRI/MRA		Intracerebral haemorrhage
	3. *DSA*		CSF disturbance
4. Arterial thrombi/stenosis	1. CT/CTA	Interventional: local lysis, aspiration of the thrombus, stent (balloon dilatation)	Failure of recanalization, arterial emboli in distant territory, arterial rupture
	2. DSA	(Conservative: systemic lysis)	
5. Vasospasm	CT/CTA, perfusion map	Local lysis (papaverine, nimodipine)	Arterial rupture
		Balloon dilatation	

Implications for Neurosurgical Patients

The imaging method of choice in emergency cases is computed tomography (CT). In combination with CT angiography (CTA; CT plus iodinated contrast injection followed by 3D reconstruction to identify vascular pathology or cerebral tumours), computed tomography today allows a quick and exact structural overview and also helps to diagnose site and

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size of an aneurysm, presence of space-occupying intracerebral haemorrhage, acute CSF disturbance, and existence/extend of perfusion deficits.

The main diagnostic tool for interventional neuroradiological procedures, and still the gold standard in patients with cerebrovascular vascular diseases, is the digital subtraction angiography (DSA). In combination with 3D angiography, DSA allows to determine the exact size, width, and configuration of the neck and dome of cerebral aneurysms.

Magnetic resonance imaging (MRI)/MR angiography is less important in the early phase of emergency care for these patients but plays an important role in pre-therapeutic imaging of AVMs or in the follow-up of coiled aneurysms.

Independent of the imaging technique used, timely image interpretation by a specialized neuroradiologist is essential to assure the best possible and most immediate therapeutic intervention.

Cerebral Aneurysms

The underlying pathology of spontaneous, non-traumatic SAH is the rupture of a cerebral artery aneurysm. The most common location for a cerebral aneurysm (due to hemodynamic factors) is at the level of Willis. Therefore, with aneurysm rupture, blood commonly collects in basal cisterns. Neuroradiological intervention with the application of multiple individual platinum coils inside the aneurysm is an alternative therapy to neurosurgical clipping (Table 71.2).

On CT acute haemorrhage presents with hyperdensity, in case of SAH in the basal cisterns. Distribution and amount of the SAH may suggest approximate location of the aneurysm, while CTA and DSA (including 3D rotational angiography) confirm the exact size, width, and configuration of the aneurysm neck and dome. This information is critical to allow the clinician to make therapeutic decisions regarding the best approach (i.e. surgery or IN). In the event that the treatment team recommends IN, CTA and DSA are also critical in helping the team determine if a stent should be placed to guarantee the stable delivery and safe placement of the coils inside the aneurysm (Fig. 71.1).

In case of iatrogenic aneurysms that, although rare, occur as a complication of neurosurgical or ENT operations, occlusion of the leak is usually achieved with covered stents (Fig. 71.2).

Cerebrovascular Vasospasm

Vasospasm, associated with delayed cerebral ischaemia, represents a severe (but common) complication in the early (first 2 weeks) postoperative course after aneuriysmal SAH and remains a major cause of morbidity and mortality in this patient population. Repeated neurologic examination and monitoring with transcranial Doppler ultrasound, CT perfusion measurements, and CTA are helpful in these patients to guide the need for DSA and intervention. The focus for IN treatment is improvement in cerebral perfusion (as evidenced by vasodilation on angiography, reduction of Doppler blood flow velocities, and improved clinical exam) either by intraarterial drug administration (e.g. papaverine, verapamil, and nimodipine) or local vessel (balloon) dilatation (Fig. 71.3).

Arteriovenous Malformation

The majority of cerebral AVM are believed to be a congenital disorder; they mainly present with haemorrhage, seizure, chronic headache, or focal neurological deficits. The pathological substrate is the lack of capillaries, leading to a compact or diffuse network of channels interposed between feeding arteries and draining veins, the so-called nidus, the target of the occlusion with glue, which is frequently followed by surgical resection. On MRI, the nidus presents as an area of intraparenchymal pathological vessels and on

Table 71.2 Characteristic findings of CT/CTA

	Native CT	CTA	Additional findings
SAH	Hyperdensity of the basal cisterns	Site/width/configuration of the aneurysm	Hydrocephalus caused by CSF disturbance
AVM	Intracerebral haemorrhage	Width of the nidus	Hydrocephalus due to intraventricular haemorrhage
	Density disturbances (caused by combination of enlarged vessels, parenchymal defects)	Enlarged feeding arteries	
		Enlarged draining veins	
Dural fistula	Intracerebral haemorrhage	Uncommon, enlarged (mainly) extracerebral vessels	Hydrocephalus due to venous congestion
	General brain oedema		
	Uncommon vessels		
Arterial thrombi	Hyperdense vessel sign (basilar, middle cerebral artery)	Vessel occlusion at the site of the thrombus	Malignant brain oedema
Vasospasm	Hypodense territories (infarction)	Narrowed vessels	Perfusion deficit

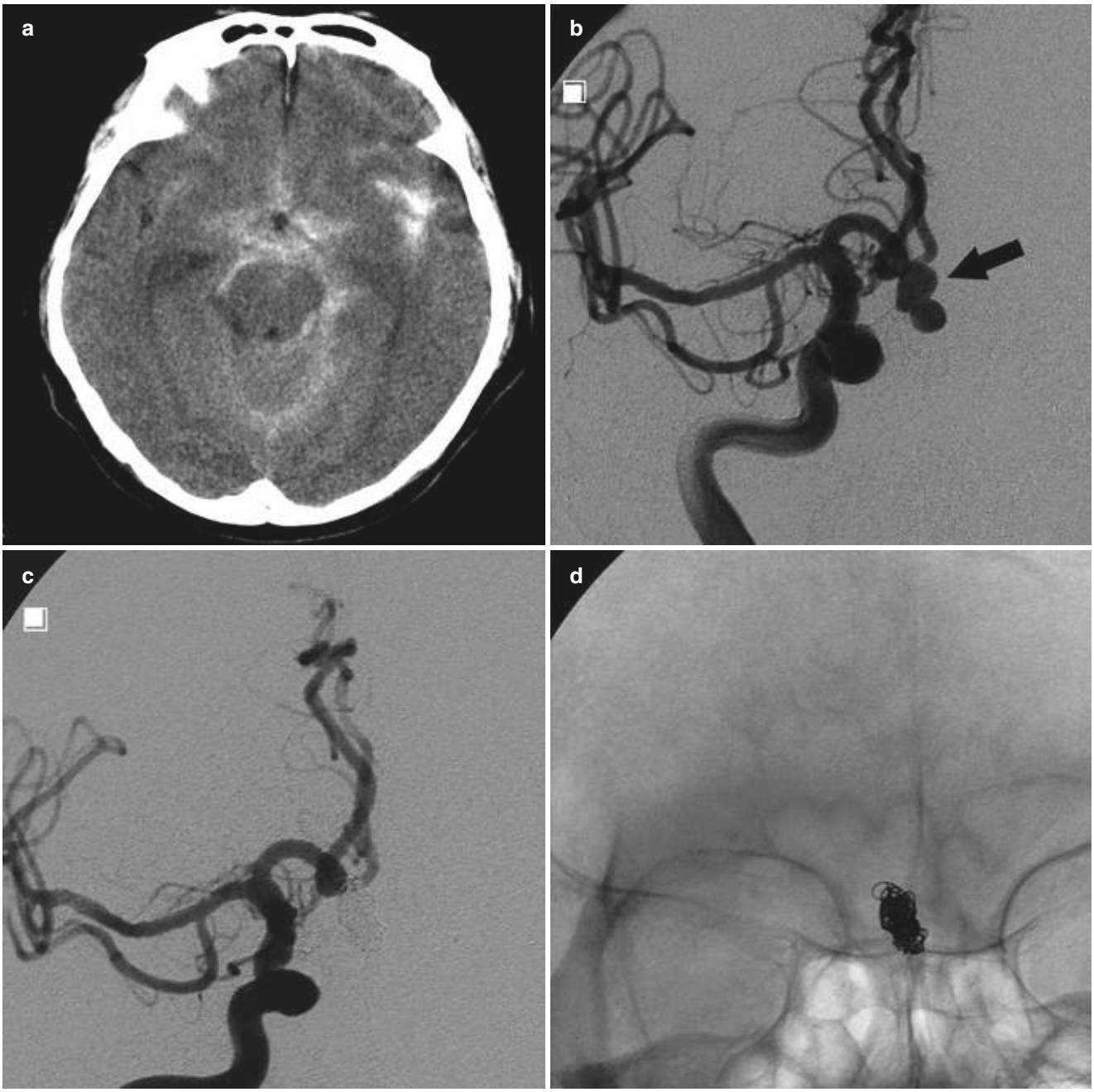

Fig. 71.1 Subarachnoid haemorrhage (SAH). A 43-year-old man with acute headache, meningism, and progressing vigilance deficits. (**a**) Native CT, demonstrating the hyperdensity of the basal cistern, due to acute subarachnoid haemorrhage. (**b**) DSA of the right internal carotid artery in frontal view, demonstrating an aneurysm of the anterior communicating artery (*arrow*). (**c**) Corresponding view after coiling of the aneurysm. (**d**) Corresponding unsubtracted view, showing the coil package

DSA as a convolution of enlarged arteries and draining veins (Fig. 71.4). Especially in complex AVMs, neuroradiological interventions mainly are preoperative procedures to minimize the size of the AVM nidus by intraarterial embolization with glue.

Dural arteriovenous fistulas (DAVF) (syn. dural arteriovenous malformations [DAVM]), mainly located in the skull base, are rare lesions and are characterized by abnormal connections (shunts) between arterial and venous intradural vessels. Their clinical presentation depends on the venous

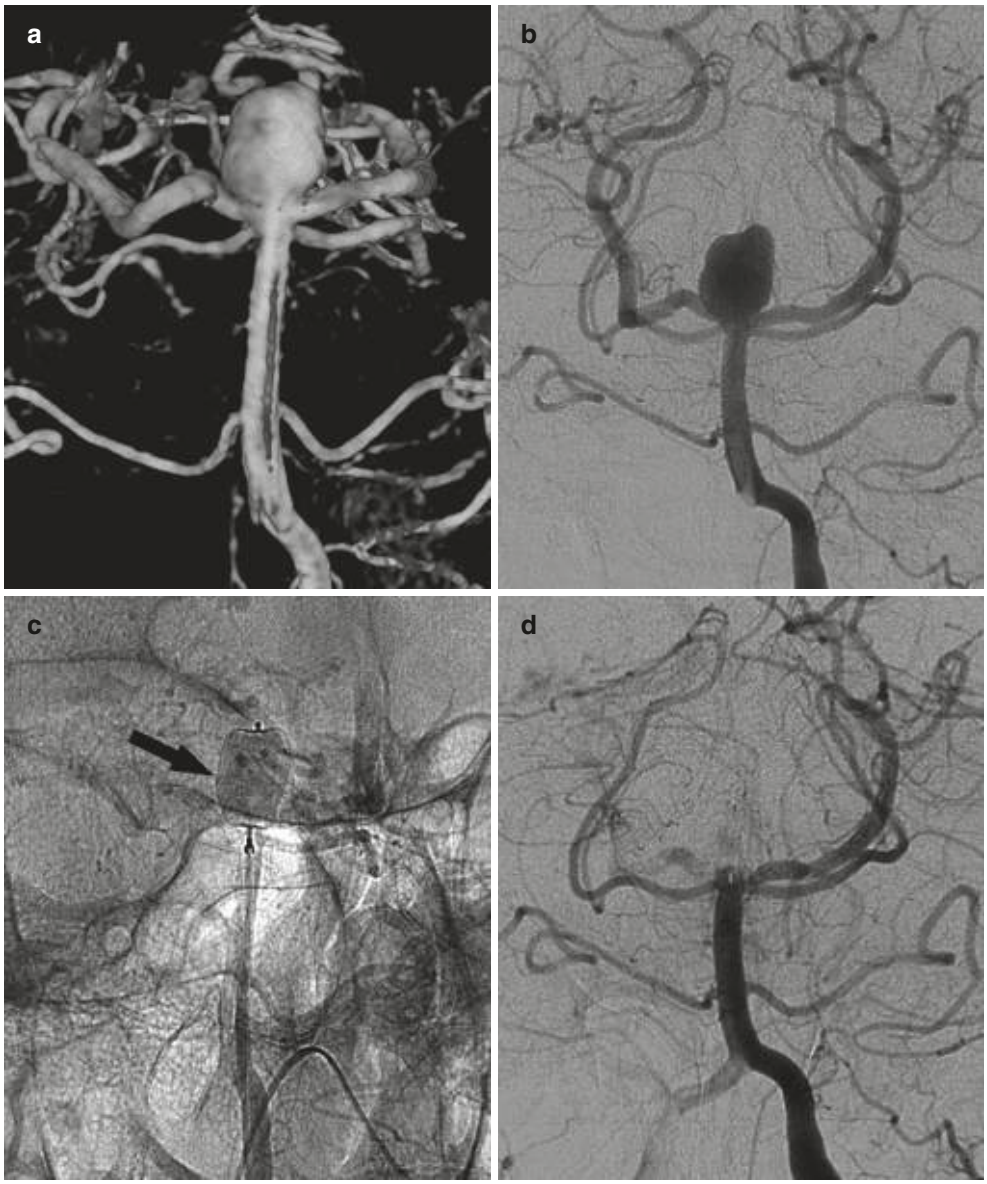

Fig. 71.2 Giant basilar tip aneurysm. A 50-year-old woman with SAH, due to a wide-neck aneurysm of the basilar tip. **(a)** 3D angiography, demonstrating the wide neck with inclusion of both P1 segments. **(b)** Corresponding DSA before placement of the intra-aneurysmal stent. (**c**) WEB device (*arrow*) seen in the unsubtracted view covers the complete aneurysm. (**d**) Post-interventional view with occlusion of the entire aneurysm. Reduced flow in the right posterior cerebral artery (PCA), due to flow changes. A DSA-control half a year later showed complete reopening of the PCA

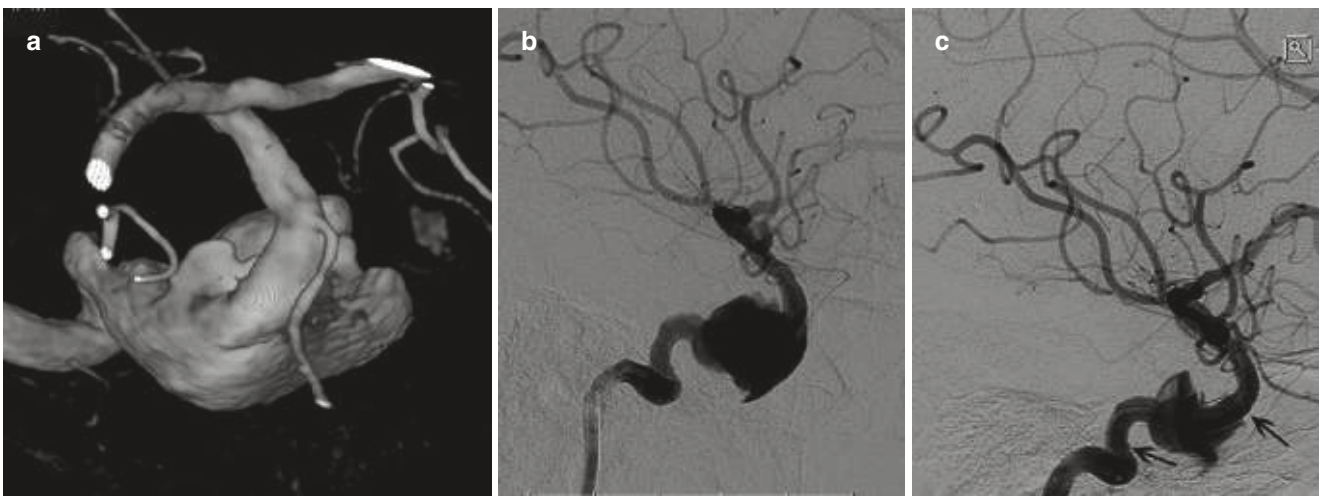

Fig. 71.3 Giant aneurysm of the cavernous segment of the ACI. (**a**) 3D angiography, demonstrating the complex configuration of the extradural ACI. (**b**) Corresponding DSA, lateral view of the right ACI. (**c**) A relevant flow reduction into the aneurysm is demonstrated after placement of the flow diverter (*arrows*)

drainage pattern. Especially in the more benign types of DAVM, where non-invasive imaging (CT, MRI, and MRA) may not have adequate diagnostic sensitivity, the gold standard of identification, analysis, and classification of the lesion is DSA. Indication for IN treatment (Fig. 71.5), with the target of occlusion of the shunt area(s), performed either by transvenous application of coils into the affected sinus or transarterial application of glue, depends on the prognosis of the disease. The main indication for interventional therapy is a venous drainage into superficial cerebral veins, as this finding harbours the risk of intracerebral haemorrhage, due to venous congestion.

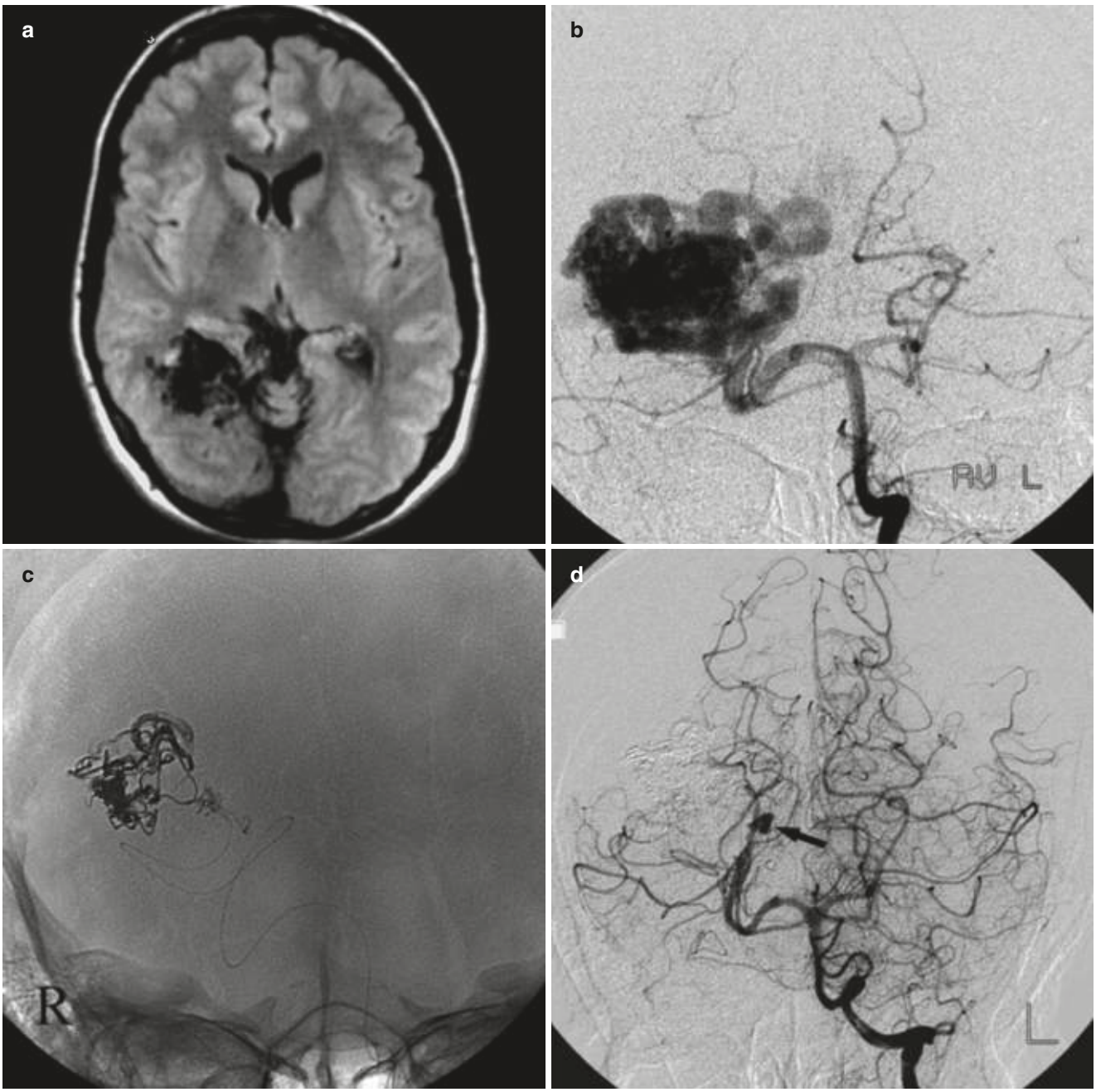

Fig. 71.4 Arteriovenous malformation (AVM). A 30-year-old woman with acute homonymous hemianopia to the left. (**a**) T2-weighted (T2w) axial MRI showing the nidus of the AVM in the right occipital lobe. (**b**) DSA of the left vertebral artery in frontal view. Note the enlarged diameter of the right posterior cerebral artery in comparison to the left, due to high arteriovenous shunt volume. (**c**) Corresponding unsubtracted view, where the way of the microcatheter to the nidus is apparent. Note the (radiologically marked) glue in the nidus. (**d**) Corresponding frontal view after neurointervention (transarterial glue application) demonstrating a small, flow-related aneurysm (*arrow*) of the distal perimesencephalic segment (P3) of the posterior cerebral artery (PCA), as the only pathological remnant

Arterial Thrombosis (Ischaemic Stroke)

Depending on the size of intraarterial thrombi, a main trunk of cerebral vessels may be occluded, leading to an infarction of the cerebral territory. On CT, the thrombus may be apparent due to its hyperdensity (positive vessel sign) (Fig. 71.6), sometimes with additional slight hypodensity of the affected vessel territory. The consequence of untreated basilar thrombosis is severe morbidity or even death of the patient. This is known too in the course of a thrombotic occlusion of the main trunk of the middle cerebral artery (MCA), as the natural history of brain swelling leads to brain herniation and death (so-called malignant infarc-

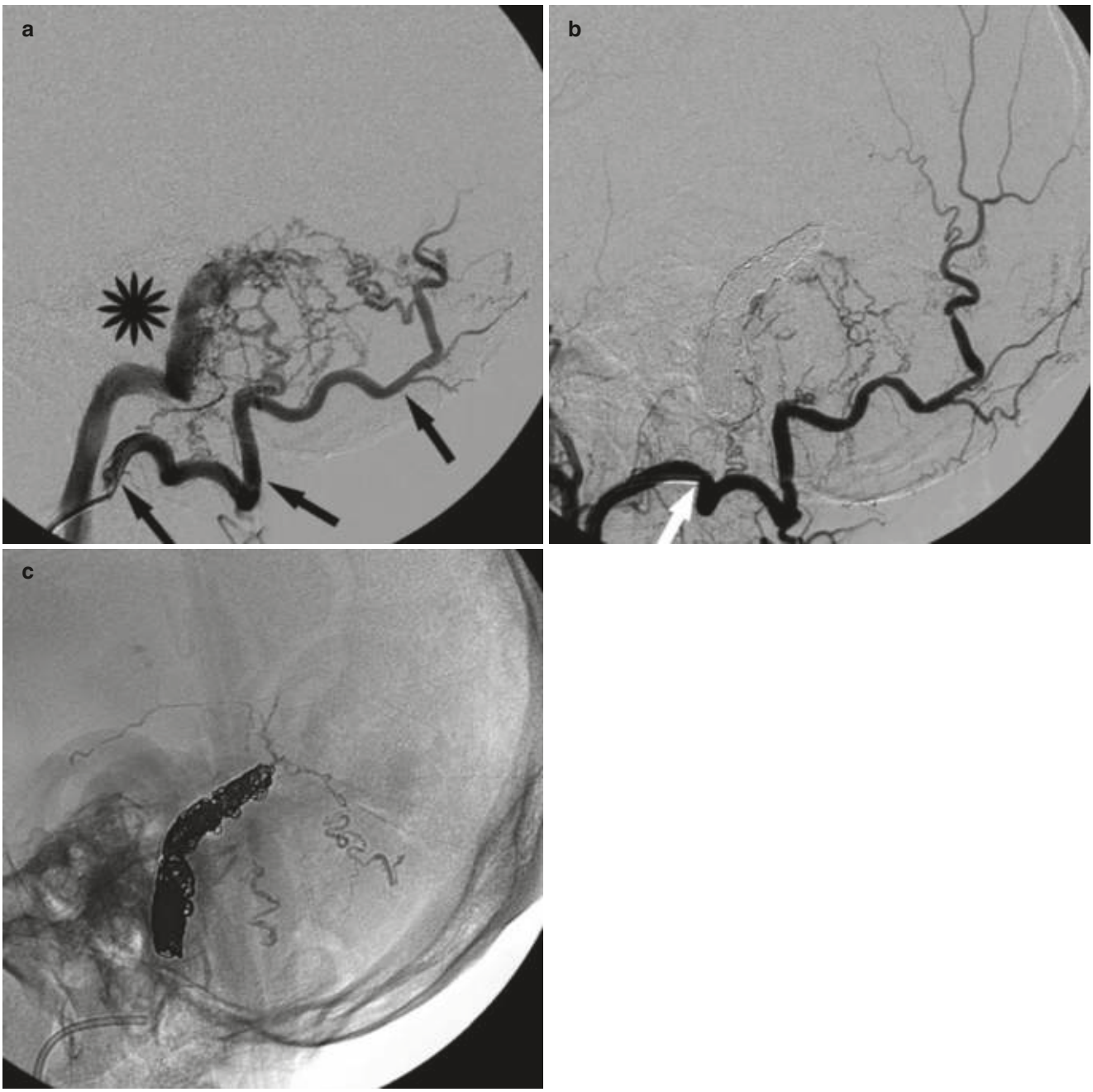

Fig. 71.5 Dural fistula. DSA of a 64-year-old man with pulsatile tinnitus of the left side. (**a**) Lateral view of the left occipital artery (*arrows*), showing the extent of the involved part of the sigmoid sinus with intradural arteries, shunting the ipsilateral sigmoid sinus (*star*), and the jugular bulb. (**b**) Post-interventional corresponding view (transvenous coiling of the sigmoid sinus plus intraarterial glue). No AV shunts are seen, although some enlarged collaterals are still apparent (the *white arrow* marks the end of the catheter in the occipital artery). (**c**) Corresponding unsubtracted view, demonstrating the coils in the entire sigmoid sinus and glue in some feeding arteries

tion). The target of IN intervention is the recanalization performed with stent-assisted clot removal or direct aspiration of the thrombus (Fig. 71.7), more and more performed not with general anesthesia but with conscious sedation.

An increasing indication for IN intervention is stenting of intracerebral stenosis mainly of the basilar or middle cerebral artery (Fig. 71.8), to avoid total occlusion with subsequent fatal course of territorial infarction.

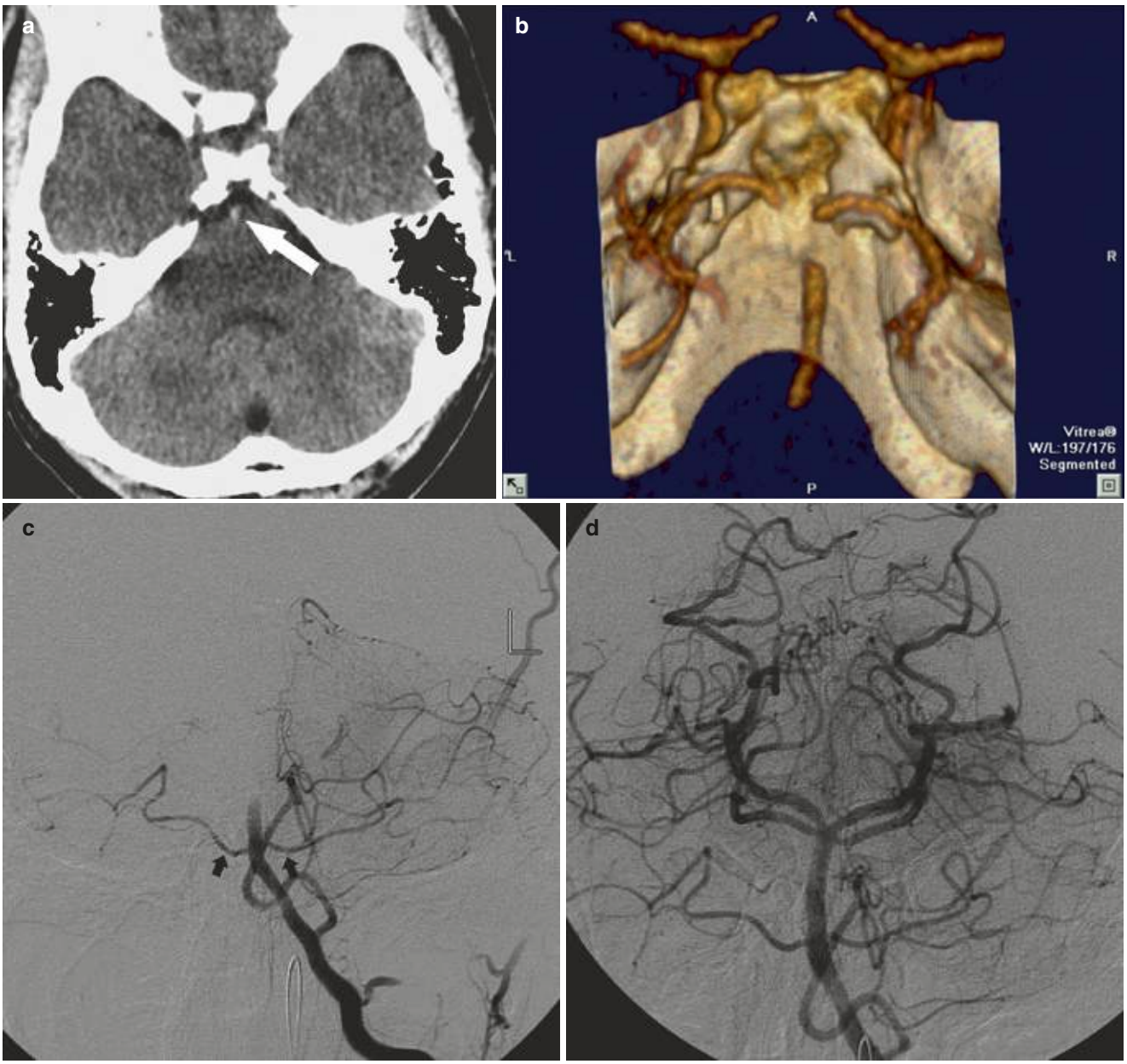

Fig. 71.6 Thrombosis of the basilar artery. A 36-year-old man with acute vigilance deficit and horizontal nystagmus. (**a**) Native axial CT. The hyperdensity (*arrow*) is due to the thrombus in the basilar artery (*positive vessel sign*). (**b**) 3D-CTA (pa view) demonstrating the closed distal part of the basilar artery. (**c**) DSA of the left vertebral artery with KM-stop of the basilar artery distal to the branching of both inferior cerebellar arteries (AICA) (*small arrows*). (**d**) Corresponding post-interventional view (aspiration of the thrombus) with complete filling of the arteries of the basilar territory (both superior cerebellar and posterior cerebral arteries)

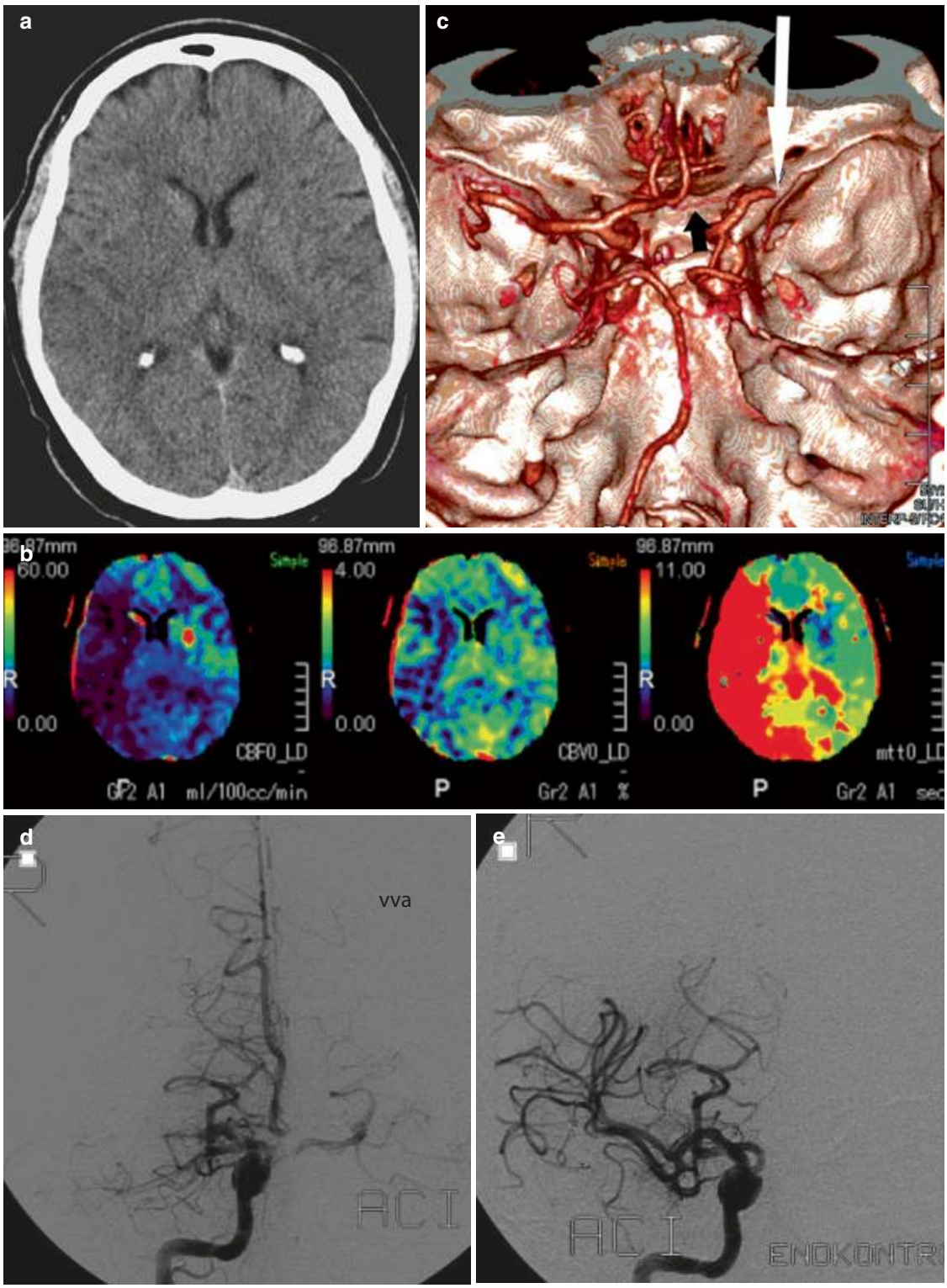

Fig. 71.7 Thrombosis of the MCA. A 60-year-old man with acute hemiplegia of the left side (time window: 1.5 h). (**a**) Native CT with slight hypodensity of the right territory of the middle cerebral artery (MCA). Note the effacement of the grey and white matter distinction of the insular, basal ganglia, and fronto-temporal region with slight narrowing of the cortical sulci, compared with the left hemisphere, as early signs of infarction. (**b**) CT perfusion map, demonstrating the different areas of perfusion parameters with a related mismatch: elongated mean transit time (MTT) (*right*), reduced cerebral blood flow (CBF) (*left*), but relatively small reduction of cerebral blood volume (CBV) (*middle*). (**c**) 3D-CTA with complete occlusion of the left (MCA) (*white arrow*). Note the hypoplasia of the left anterior cerebral artery (ACA) (*small black arrow*). (**d**) DSA of the right ICA (ap view) with complete loss of vascularization of the media territory but filling of the small, hypoplastic ACA and ipsilateral posterior cerebral artery (PCA) via posterior communicating artery (Pcom). (**e**) Corresponding post-interventional DSA (intraarterial application of r-tPA and aspiration of the thrombus) with recanalization of the media territory but (due to normalization of the intravascular pressure) lack of contrast in the ACA, which was seen in the filling of the contralateral ICA (not shown)

Concerns and Risks

As a substantial part of neuroradiological interventions timely IN is mandatory in every case, as we deal with lif-threatening diseases with the demand of emergency procedures (especially in patients with cerebral artery thrombosis or symptomatic vasospasm), which need immediate therapy. Although IN may provide life-saving treatment, many of these procedures are associated with significant risk of complications, including rupture of a main artery and embolism from glue, particles, and coils.

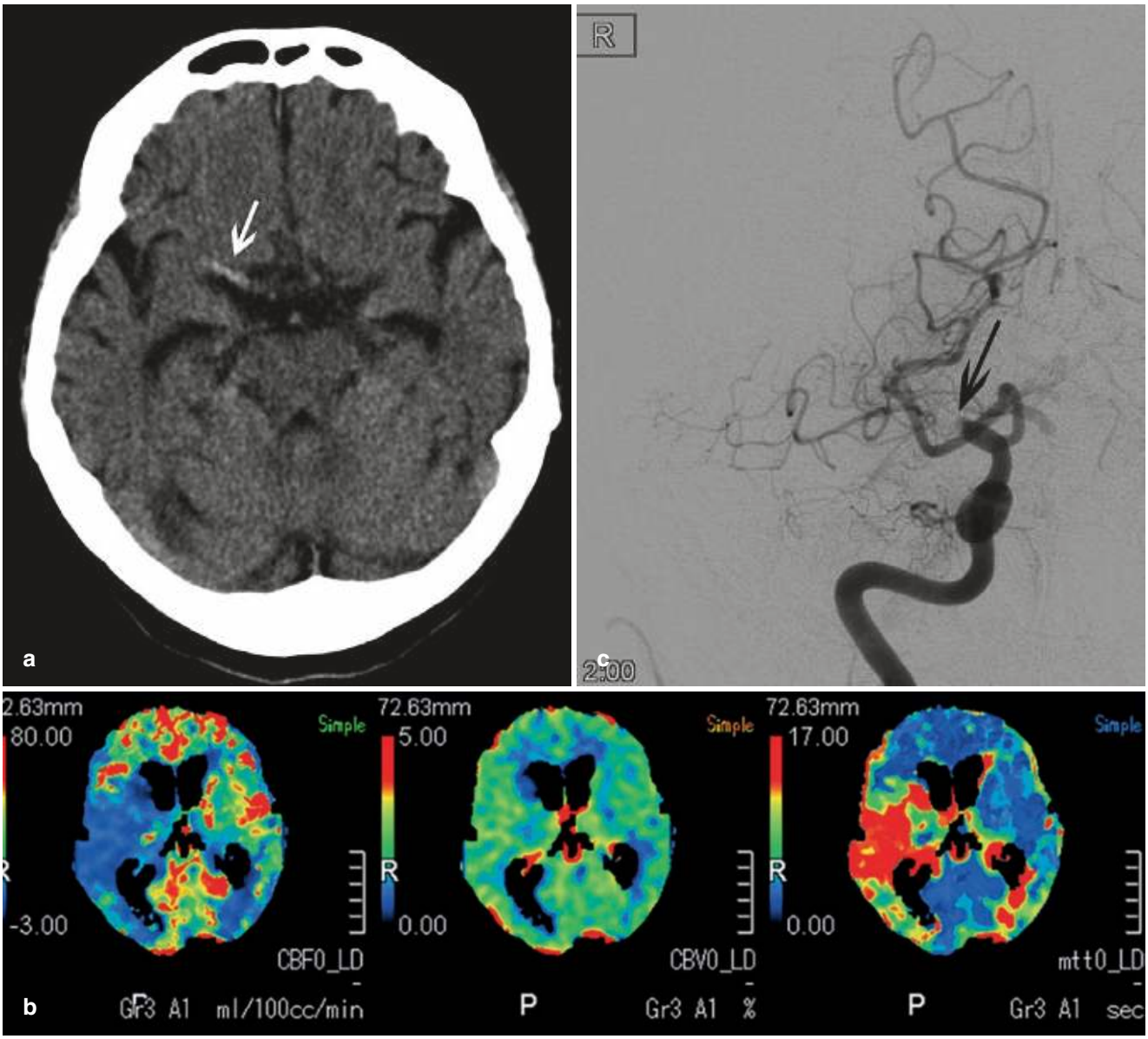

Fig. 71.8 Acute occlusion of ACI T-bifurcation. A 78-year-old lady with acute, complete left hemiparesis. (**a**) Native CT 1.5 h after stroke onset, demonstrating the hyperdense thrombus in the M1 segment (hyperdense media sign). (**b**) Corresponding CT perfusion map. Different areas of perfusion parameters with great mismatch: elongated mean transit time (MTT) (*right*) and reduced cerebral blood flow (CBF) (*left*), but no reduction of cerebral blood volume (CBV) (*middle*). (**c**) DSA of the right ICA (ap view) with occlusion of the distal part of the ACI (*arrow*). Missing of the anterior cerebral artery (ACA) as well as the middle cerebral artery (ACM); only the ipsilateral posterior communicating artery (Pcom) and posterior cerebral artery (PCA) are contrasted. (**d**) Unsubtracted view, showing the placement of the stent retriever (arrows). (**e**) Post-interventional DSA of the right ACI, demonstrating the complete recanalization of the entire ACM and ACA. Duration of the procedure: 30 min

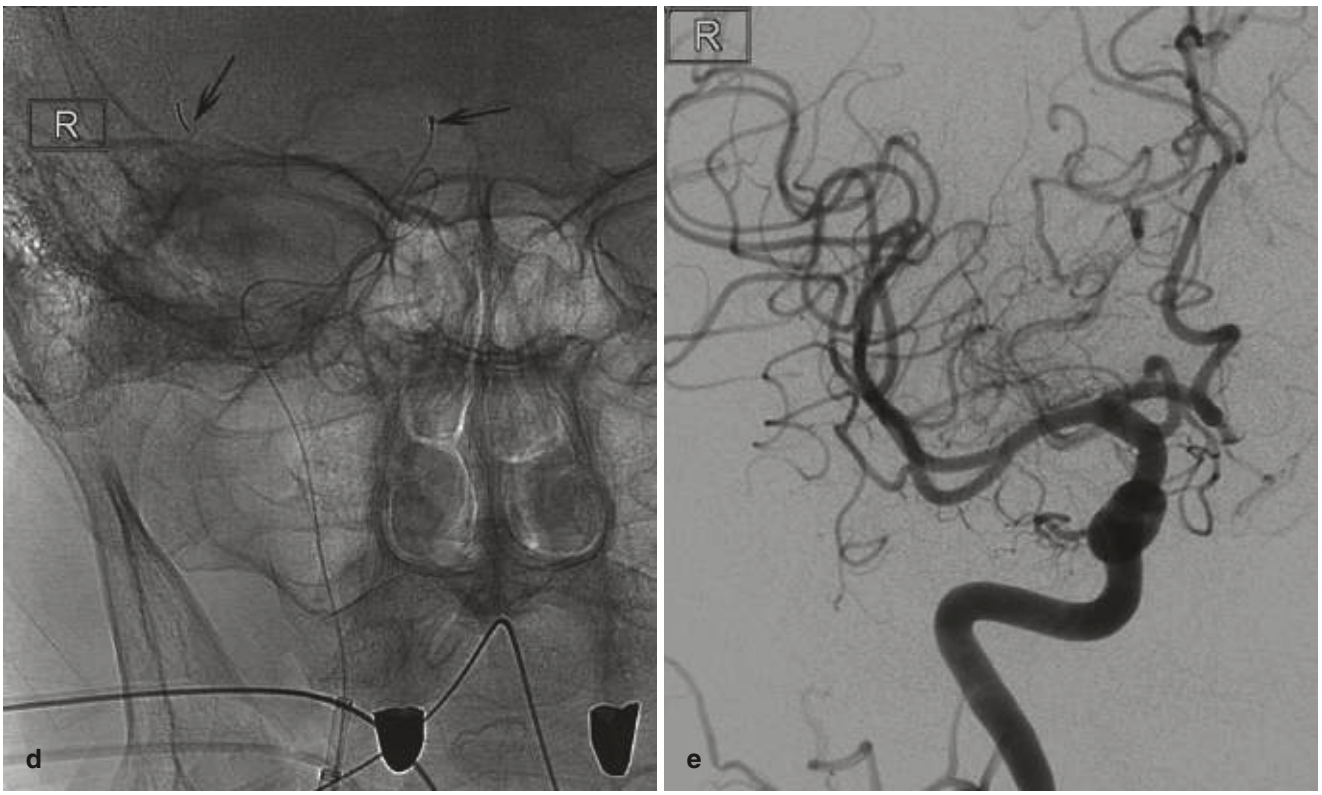

Fig. 71.8 (continued)

Key Points

- Neuroradiological interventions concern life-threatening diseases and are frequently emergency procedures.
- Amendable to neuroradiologic intervention are patients with cerebrovascular aneurysms (coiling/stenting), arteriovenous malformations (gluing/coiling), cerebral artery thrombosis (clot removal), vascular stenosis (angioplasty, stenting), and cerebral vasospasm (intraarterial vasodilators).
- While often life-saving, many procedures are associated with significant risk of complications, including intracranial haemorrhage due to vascular injury and ischaemic stroke secondary to embolism from dislodged coils or glue.
- Neurointerventional procedures basically can be divided into occluding (coiling and glue) and opening interventions (thrombus aspiration, intraarterial vasodilators).
- Although CT/CTA and MRI/MRA plus computerized 3D reconstruction are emerging techniques, DSA remains the main diagnostic tool and gold standard in cerebrovascular diseases.
- Timely image interpretation by a specialized neuroradiologist is essential to assure the best possible and most immediate therapeutic intervention.

Suggested Reading

Cognard C, Spelle L, Pierot L. Pial arteriovenous malformations. In: Forsting M, editor. Intracranial malformations and aneurysms. From diagnostic work-up to endovascular therapy. New York: Springer; 2004. p. 39–100.

Gnanalingham KK, Apostolopoulos V, Barazi S, O'Neill K. The impact of the international subarachnoid aneurysm trial (ISAT) on the management of aneurismal subarachnoid hemorrhage in a neurosurgical unit in the UK. Clin Neurol Neurosurg. 2006;108:117–23.

Molyneux A, Kerr R, Stratton I, Sandercock P, Clarke M, Shrimpton J, et al. International Subarachnoid Aneurysm Trial (ISAT) of neurosurgical clipping versus endovascular coiling of 2143 patients with ruptured intracranial aneurysms: a randomised trial. Lancet. 2002;360:1267–74.

Müller Forell W, Engelhard K. Neuroimaging for the anaesthesiologist. Anesthesiol Clin. 2007;25:413–39.

Sayama CM, Liu JK, Couldwell WT. Update on endovascular therapy for cerebral vasospasm induced by aneurismal subarachnoid hemorrhage. Neurosurg Focus. 2006;21:E12.

Szikora I. Dural arteriovenous malformations. In: Forsting M, editor. Intracranial malformations and aneurysms. From diagnostic work-up to endovascular therapy. New York: Springer; 2004. p. 101–42.

Wanke I, Dörfler A, Forsting M. Intracranial aneurysms. In: Forsting M, editor. Intracranial malformations and aneurysms. From diagnostic work-up to endovascular therapy. New York: Springer; 2004. p. 143–247.

Pan X, Liu G, Wu B, Liu X, Fang Y. Comparative efficacy and safety of bridging strategies with direct mechanical thrombectomy in large vessel occlusion. Medicine. 98(14):e14956.

Nordmeyer H, Chapot R, Haage P. Endovascular treatment of intracranial atherosclerotic stenosis. RöFo - Fortschritte auf dem Gebiet der Röntgenstrahlen und der bildgebenden Verfahren.

Powers CJ, Dornbos D, Mlynash M, Gulati D, Torbey M, Nimjee SM, Lansberg MG, Albers GW, Marks MP. Thrombectomy with Conscious Sedation Compared with General Anesthesia: A DEFUSE 3 Analysis. Am J Neuroradiol.

Part XII

Specific Concerns Regarding Anesthesia for Interventional Neuroradiology

Procedural Challenges in Interventional Neuroradiology

72

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Overview

Interventional neuroradiology, or endovascular neurosurgery, has blossomed in recent years as engineering advances have enabled physicians to treat neurovascular disorders in new and exciting ways. As a result, interventional neuroradiology has become an integral part of modern neuroanesthetic practice. Elective procedures include diagnostic angiography as well as therapeutic interventions for aneurysms, arteriovenous malformations, fistulae, and occlusive cerebrovascular diseases. Emergent procedures include acute ischemic stroke interventions, securing aneurysms in the setting of subarachnoid hemorrhage, endovascular vasospasm therapy, and treatment for medically refractory cerebral sinus thrombosis. The anesthetic care of these patients can be quite complex, requiring tight hemodynamic control to avoid injury to the central nervous system from hypo- or hyperperfusion, quick and smooth emergence to facilitate neurologic assessment, and extreme time sensitivity in emergent cases. The use of GA or varying degrees of sedation carries risks and benefits that must be considered in optimizing the care of an individual patient.

Physical Environment

Interventional neuroradiology suites use biplanar fluoroscopy, typically with one C-arm in an anterior-posterior plane and another C-arm positioned laterally (Fig. 72.1). This poses significant ergonomic challenges to the anesthesiologist as imaging devices, display monitors, and ultrasound devices surround the patient bed, which is in a fixed position. Access to the airway is invariably restricted, as the biplanar equipment must rotate freely around the patient's head. Anesthetic equipment must be positioned out of the way, usually at the level of the patient's hip or feet, and a relatively long distance from the patient's head. Extensions to breathing circuits and intravenous tubing require careful planning and experience, particularly during anticipated or emergent administration of critical anesthetic, vasoactive, and/or anticoagulant agents. The essential aspect of providing quality anesthetic care in the neurointerventional suite is the presence of experienced team members 24/7. This requires careful planning that is somewhat unique to and must be optimized at each institution.

Radiation Safety

Radiation is a significant occupational hazard in the neurointerventional suite. The two primary methods of protection from radiation are distance and shielding. Radiation intensity is inversely proportional to the square of the distance from the

Fig. 72.1 Interventional neuroradiology suite

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https://doi.org/10.1007/978-3-030-17410-1_72

source (https://en.wikipedia.org/wiki/Radiation_protection). Protective equipment should include a wraparound lead apron covering the thorax/abdomen/pelvis, thyroid shield, and eye protection. Leaded plexiglass shields (Fig. 72.2) should be available and positioned to reduce direct exposure to the fluoroscopy equipment. One study concluded that, when radiation dose was measured at the forehead, the anesthesiologist was actually exposed to more radiation than the interventionalist (https://www.ncbi.nlm.nih.gov/pubmed/21285864). In addition, the number of medication interventions performed by the anesthesiologist was directly correlated to his or her exposure. Embolizations of cerebral aneurysms and arteriovenous malformations are considered high-dose radiation procedures, as digital subtraction angiography (DSA) entails significantly more ionizing radiation than standard fluoroscopy. Vigilance regarding cumulative radiation exposure is of great importance. Dosimeters should be utilized, and exposure to the anesthesiologist should be kept lower than the annual limit for healthcare workers (https://www.osha.gov/dte/library/radiation/ion_rad_20021007/index.html; https://www.osha.gov/SLTC/etools/hospital/clinical/radiology/radiology.html).

Fig. 72.2 Metal and plexiglass shield

Anesthetic Goals

Overall anesthetic goals for the patient undergoing any neuroradiologic intervention include anxiolysis, analgesia, immobility, hemodynamic control, and rapid emergence.

Patient Comfort

Factors associated with patient discomfort include groin cannulation, contrast injection which may produce a burning sensation in the area of the arterial distribution, angioplasty, intravascular thrombus removal, and relatively long periods of motionless supine positioning on the angiography table with minimal padding for comfort. Therefore, for complex procedures or those of prolonged duration, deep sedation or general anesthesia is routinely used to ensure optimal patient comfort with prevention of patient movement. Important consideration when deciding between CS and GA is surgeon preference and experience/proficiency with a given procedure, baseline neurologic deficits (ability of patient to cooperate with instructions and communicate with the team members), and patient comorbidities.

Immobility

Motion artifact is a significant problem for image quality. During digital subtraction angiography (DSA) "road mapping," the contrast-enhanced vascular anatomy is inverted to appear white (Fig. 72.3) and serves as an accurate guide for endovascular wires and catheters in small cerebral vessels – as long as the patient has not moved. The need for precise imaging, coupled with the risk of vessel injury, makes GA preferable in many procedures. The use of a low-dose inhaled anesthetic with intravenous opioid (e.g., remifentanil or sufentanil) infusion usually makes re-dosing of neuromuscular blockade unnecessary to ensure immobility. Note that a pressor infusion is frequently necessary to offset the hypotensive effects of the anesthetic drugs.

Hemodynamic Control

Hemodynamic goals are chosen based on the individual patient's susceptibility to injury from hypo- or hypertension. This is subjective, so it is imperative that the neuroanesthesiologist, neurologist (if involved), and interventional neurora-

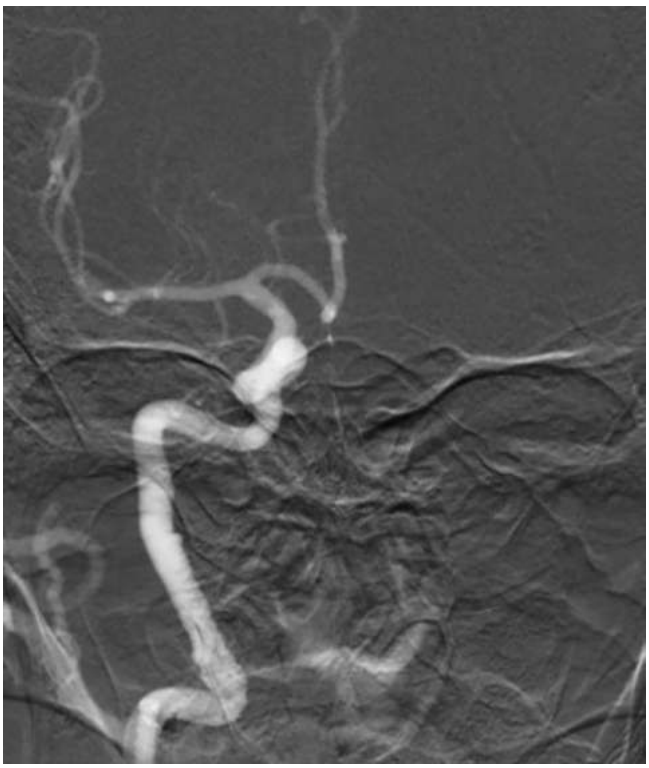

Fig. 72.3 White "road map" obtained by inverting the contrasted angiographic image

diologist communicate/agree regarding the targeted hemodynamic parameters. Assessment of the baseline blood pressure is critical, along with assessment of the potential to cause injury from hypo- or hypertension. For example, hypertension could have fatal consequences in the patient with acute aneurysmal rupture and subarachnoid hemorrhage undergoing coil embolization. One week later, that same patient with severe vasospasm coming for endovascular vasodilators or angioplasty could, on the other hand, suffer ischemic strokes with any fall in blood pressure.

Beat-to-beat monitoring of arterial blood pressure is often critical for early recognition of complications, as well as for careful titration of vasoactive agents to a narrow target blood pressure range. In general, an arterial cannula should be placed for procedures in which intervention to the cerebral or spinal vasculature is anticipated. If time pressure does not allow arterial catheterization by the anesthesiology team, such as in acute stroke cases, the femoral sheath placed by the neurointerventionalist may be used to transduce arterial pressures until a radial arterial line can be placed.

Choosing the Ideal Anesthetic Regimen

An obvious benefit of mild to moderate sedation is the ability to monitor neurologic function at various stages of the procedure. In fact, some studies (discussed below) suggest that sedation may be preferable to GA for acute stroke interventions. Due to the physical environment in the neurointerventional suite, access to the airway is significantly impeded. Therefore, patients with difficulty maintaining their airways (due to obesity, posterior circulation stroke, cranial nerve dysfunction, etc.) are unlikely to tolerate a procedure without GA. Aspiration risk is another consideration in emergent cases in non-fasted patients. Anesthetic agents for non-GA conscious sedation must be chosen to avoid significant respiratory depression with subsequent hypoxemia and hypercapnia. Although a nasopharyngeal airway is often used in sedated patients in the operating room, most neurointerventional procedures require significant levels of anticoagulation, making bleeding into the airway a concern. Laryngeal mask airways can be used effectively in select GA cases (Table 72.1).

Special Considerations in Interventional Neuroradiology: Emergency Cases

Ruptured Cerebral Aneurysms (i.e., Aneurysmal Subarachnoid Hemorrhage)

Aneurysmal rupture with subarachnoid hemorrhage has a high mortality rate. Even among survivors, only ~1/3 are able to live independently after the event. Thus, the primary goal in the early management of patients with known intracerebral aneurysms is the prevention of rupture – either via elective open cranial surgery or endovascular intervention. Endovascular interventions such as standard coil embolization and flow-diverting stent devices are increasingly being used in lieu of surgery, in appropriate candidates. The choice of procedure is largely determined by the location and morphology of the aneurysm. While these endovascular procedures can be done under CS, GA allows for more precise blood pressure control and immobility and is preferred.

For the patient with spontaneous aneurysmal rupture and subarachnoid hemorrhage, hypertensive surges must be avoided to avoid recurrent bleeding. The most vulnerable time is usually during endotracheal intubation. Arterial line placement is therefore desired prior to induction. However, in some patients, arterial line placement may be difficult, and the danger of hypertension during line placement (and potential aneurysm rupture) must be balanced against the advantages of tight blood pressure control during endotracheal intubation. An effective approach in appropriate patients is to induce anesthesia, mask ventilate, and place the arterial line prior to endotracheal intubation. As with other endovascular cases, hemodynamic goals should be agreed upon preoperatively. Target systolic blood pressure <140 mmHg is typically chosen. An antihypertensive agent

Table 72.1 Commonly used anesthetic and hemodynamic drugs for interventional neuroradiology. A list of "clinical pearls" is included

Anesthetic drug	**Use**	**Advantage**	**Disadvantage**
Midazolam	Anxiolysis (premedication) or procedural sedation	Amnestic, anxiolytic	May contribute to post-op confusion/delirium
Propofol	Induction agent, procedural sedation; sedation/amnesia as part of the maintenance general anesthetic	No cerebral vasodilatation; suppresses cerebral metabolism without increasing cerebral blood flow/volume	Hypotension, use with phenylephrine; difficult to determine drug accumulation (unless using target-controlled infusers)
Nitrous oxide	*Avoid*		Exacerbation of injury from intra-arterial air emboli
Halogenated inhalational anesthetics	Sedation/amnesia as part of the maintenance general anesthetic (typically ~0.6 MAC)	Ease of use, ability to monitor end-tidal concentrations	Cerebral vasodilators, emergence issues (coughing/bucking/etc.)
Remifentanil	Potent analgesic (typically 0.1–0.3 mcg/kg/min as part of a maintenance general anesthetic)	Facilitates smooth emergence (i.e., "remi wake-up"); no context sensitivity	Remifentanil-induced rigidity/respiratory arrest; no post-procedural analgesia, expense
Sufentanil	Potent analgesic (typically 0.1–0.3 mcg/kg/h as part of a maintenance general anesthetic)	Lower cost than remifentanil	Context-sensitive sedative properties
Dexmedetomidine	Adjunct to sedation or GA	Facilitates hemodynamic control; reduces emergence hypertension and agitation	Bradycardia (can be remedied with glycopyrrolate), hypotension
Hemodynamic drug	**Use**	**Advantage**	**Disadvantage**
Clevidipine	Antihypertensive (dihydropyridine CCB)	Titratable; ultrashort-acting selective arterial vasodilator (no venodilatation-minimal ICP effect)	Similar appearance to propofol (white liquid); more expensive than labetalol
Nicardipine	Antihypertensive (dihydropyridine CCB)	Titratable; selective arterial vasodilator (no venodilatation- minimal ICP effect)	More expensive than labetalol
Labetalol	Antihypertensive (alpha and beta blocker)	Ease of use, familiarity	Often not sufficient to provide necessary hemodynamic control
Phenylephrine	Pressor (alpha-agonist) bolus and/or infusion to offset anesthetic effects	Ease of use, familiarity	No inotropy
Norepinephrine	Pressor (alpha-agonist) bolus and/or infusion to offset anesthetic effects	Ease of use, familiarity	Minimal inotropic effects
"Pearls"	**Use**	**Dose**	
Remifentanil bolus	Ablate the response to endotracheal intubation	1–2 mcg/kg IV bolus	
Lidocaine paste	Coat the endotracheal tube	2–5% paste applied liberally to ETT	
Laryngotracheal analgesia ("LTA")	Ablate the response to endotracheal intubation	4 ml topical (4% lidocaine)	
Propofol + ketamine	Non-GA sedation	Ketamine (1–2 mg/ml) mixed with propofol, for example, 50 mg ketamine in 50 ml (500 mg) propofol	
Remifentanil wake-up	Smooth emergence/extubation from GA; the idea is to avoid coughing and agitation during emergence by turning off the inhalational anesthetic prior to the remifentanil	Increase the remifentanil infusion dose and turn off inhalational anesthetic; turn off the remifentanil when the end-tidal inhalational anesthetic is sufficiently low (and be sure to flush the IV line of any residual remifentanil prior to extubation)	
Choosing anesthetic depth	Surgical stimulation is episodic, such as with cerebral vessel manipulation. Light anesthesia is sufficient for most of the interventional neuroradiology procedure; however, certain points in the procedure require deep anesthesia/analgesia	It is generally safer to administer higher dose remifentanil infusion along with a pressor infusion, rather than administering low-dose remifentanil (i.e., close to the lower edge of the therapeutic window) without pressors	

such as labetalol or nicardipine should be available during induction, as should a pressor, as intraoperative hypotension is a relatively common occurrence. Bolus remifentanil or sufentanil is very effective for ablating the response to noxious stimuli. Laryngotracheal analgesia with topical lidocaine is also very effective.

Finally, hydrocephalus is common following subarachnoid hemorrhage and necessitates external ventricular cerebrospinal fluid drainage (i.e., ventriculostomy). For patients with a ventriculostomy, intracranial pressure should be monitored *throughout* the procedure, with intermittent cerebrospinal fluid drainage for intracranial pressure elevations (typically >20 mmHg). Overdrainage can place the patient at risk re-rupturing an unsecured aneurysm, while underdrainage can place the patient at risk for injury from high intracranial pressure.

Cerebral Vasospasm Refractory to Medical Therapy

Cerebral vasospasm is a commonly encountered complication of subarachnoid hemorrhage and can have devastating consequences. Vasospasm onset is ~5 days (but can be earlier or later) after the initial hemorrhage and can cause ischemic strokes (Fig. 72.4). Screening is with serial transcranial Doppler sonographic and clinical neurologic examinations. Continuous EEG can also be used to detect early hemispheric ischemia as a result of vasospasm. Treatment for symptomatic vasospasm (e.g., causing hemiparesis or aphasia) is with induced hypertension (i.e., hypertensive euvolemia). "HHH therapy" is no longer used as detailed in a separate chapter. When symptoms do not resolve with hypertension (e.g., norepinephrine titrated to systolic blood pressure >160 mmHg), emergent endovascular intervention can be effective and even life-saving. Options for endovascular treatment include intra-arterial vasodilators and/or mechanical intervention with transluminal balloon angioplasty. The primary goal is to increase regional cerebral blood flow to prevent cerebral infarction.

GA is typically used, although not exclusively. *The neuroanesthesiologist must maintain cerebral perfusion throughout the case.* Most patients will have a preexisting arterial line and central line, to facilitate the hypertensive therapy. The choice of balloon angioplasty or intra-arterial vasodilators depends on the location of the vasospasm as determined by cerebral angiography, with transluminal balloon angioplasty possible in the proximal large vessels. In these cases, the anesthesiologist should monitor closely for intracranial bleeding from vessel rupture – manifesting as a rise in intracranial pressure (if an ICP monitor is present), sudden hypertensive episode (i.e., Cushing response; typically with bradycardia), and/or decline in level of consciousness/neurologic exam.

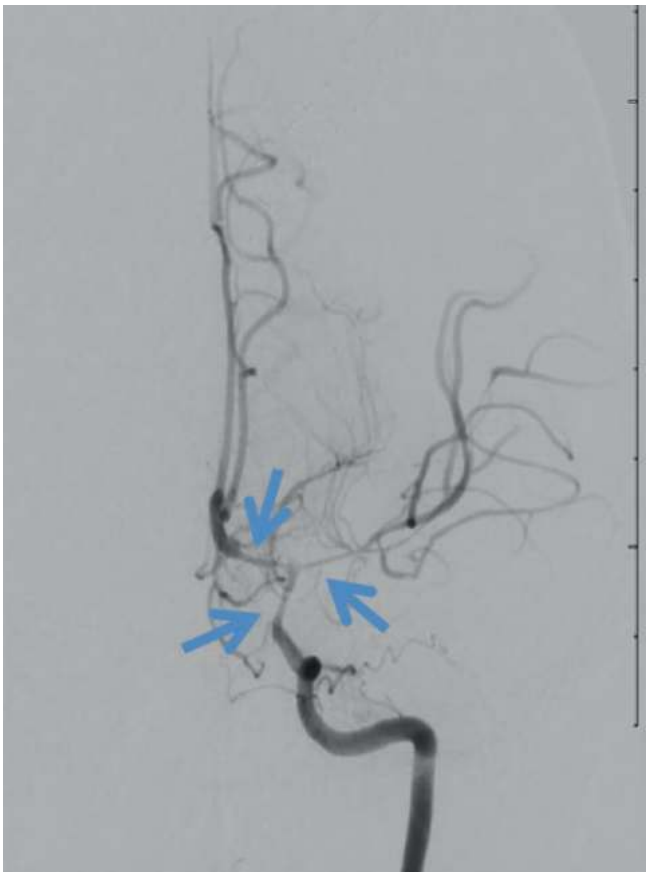

Fig. 72.4 Severe vasospasm involving the distal internal carotid artery, proximal middle cerebral artery, and proximal anterior cerebral artery

Smaller vessels are less amenable to angioplasty and can only be treated with intra-arterial vasodilators. In these situations, a catheter is placed in the vascular territory of vasospasm, and the vasodilator is administered. The most commonly used vasodilators are verapamil, papaverine, nicardipine, and milrinone, administered either in small bolus doses or as infusions. Hypotension during these procedures is common, and infusion of a pressor or several pressors may be necessary to maintain blood pressure parameters defined with the neurointerventionalist prior to treatment (generally in the systolic range 150–200mmHg). It is prudent to have bolus pressor syringes readily available (phenylephrine, vasopressin, dilute epinephrine). The largest blood pressure drops may be seen with the use of with use of intra-arterial nicardipine. The effects of intra-arterial vasodilators are temporary, and repeated treatments are frequently necessary over a number of days.

Acute Ischemic Stroke

Stroke is the third leading cause of death in the United States, with acute ischemic stroke accounting for ~4/5 of these cases. Prior to 2015, there was no high-level evidence to support the use of endovascular thrombectomy over intravenous thrombolysis in acute stroke cases. In 2015, five prospective randomized trials were published, all demonstrating the superior efficacy of endovascular thrombectomy over intravenous alteplase (i.e., tissue plasminogen activator or TPA) in patients with acute anterior circulation large vessel occlusion (LVO) strokes. Current standard of care is intravenous alteplase (within 4.5 h of stroke onset; with some exceptions) followed by emergent endovascular thrombectomy in patients with large cerebral vessel occlusion. For patients outside this treatment window, or in whom intravenous thrombolysis is contraindicated (such as after cardiac surgery), endovascular thrombectomy remains an option up to ~6 h after stroke onset. Two recent trials, DAWN and DEFUSE-3, demonstrated that this treatment window can be extended using CT or MR perfusion imaging to distinguish core infarct from ischemic penumbral regions Some patients can now be treated up to 24h after stroke onset. Nonetheless, 'time is brain' and the data is clear that each minute of delay between stroke onset and reperfusion correlates with increased long term neurologic disability. In other words, the patient who is successfully treated at 16h after stroke onset would have been better off if treated at 10 h.).

Options for endovascular revascularization include thrombolysis, suction thrombectomy, angioplasty and stent revascularization, and mechanical revascularization with thromboembolectomy. At present, the stent-like clot retrievers (Fig. 72.5) are preferred and are credited with the success of the five interventional stroke trials. New suction devices have shown similar success in recent trials.

Time from stroke onset to reperfusion is the critical issue (Fig. 72.6). It is estimated that patients lose 1.9 million *neurons per minute* during a large vessel stroke (https://www.ncbi.nlm.nih.gov/pubmed/16339467). "Door to groin time" (i.e., the time from hospital arrival to groin puncture) should

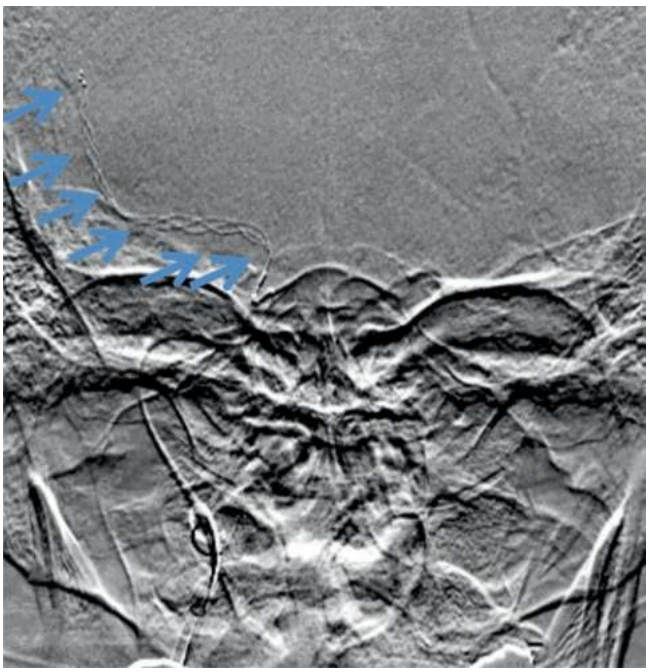

Fig. 72.5 Stent retriever deployed in the middle cerebral artery of an acute stroke patient

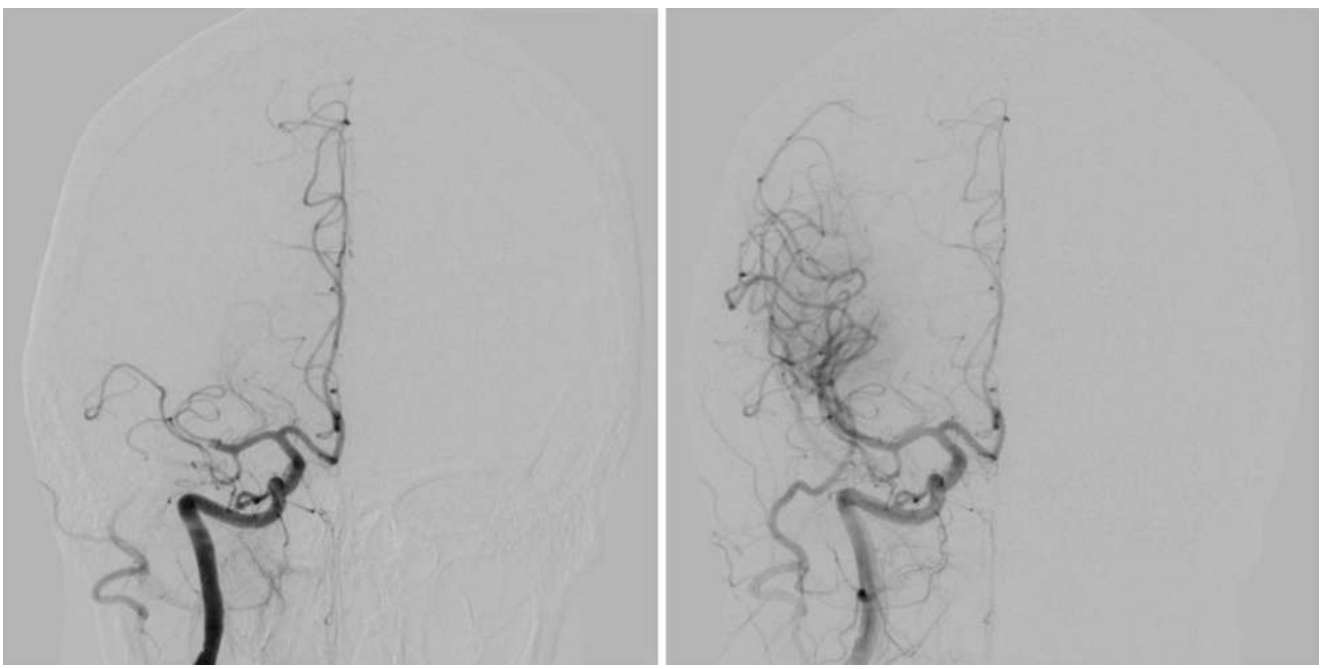

Fig. 72.6 Acute middle cerebral artery (distal M1 segment occlusion) before and after endovascular thrombectomy

typically be *90 min or less*. To facilitate these goals, the anesthesiologist must obtain as much clinical history as possible prior to patient arrival in the interventional suite and ideally decide on the preferred choice of anesthetic in conjunction with the neurointerventionalist in advance. Monitored anesthesia care (i.e., "MAC") using minimal sedation offers the benefit of allowing ongoing assessment of neurologic status and reduces the risk of hypotension with induction. Retrospective data suggest better clinical outcomes with sedation than with GA; however, three prospective randomized trials have been conducted in Europe to address this issue (ANSTROKE, GOLIATH, and SIESTA; www.clinicaltrials.gov). The German SIESTA trial was published in October 2016 (JAMA; PMID 27785516). One hundred fifty patients with anterior circulation acute ischemic stroke were randomized to GA or CS. Intravenous anesthetic agents were used. Careful attention was paid to maintenance of cerebral perfusion pressure (average SBP ~145 mmHg in both groups). There was no difference in neurologic outcome at 24 h (primary endpoint) or 3 months post stroke. The Swedish ANSTROKE trial was published in May 2017 (Stroke; PMID 28522637). Ninety patients with anterior circulation acute ischemic stroke were randomized to GA or CS. Inhalational anesthetic agent plus remifentanil was used in the GA group and remifentanil alone in the CS group. Again, careful attention was paid to maintenance of cerebral perfusion pressure (average MAP ~91 mmHg in both groups). There was no difference in neurologic outcome at 24 h or 3 months (primary endpoint) post stroke. Interestingly, in both trials there was a delay associated with induction of general anesthesia but a shorter procedural time in the GA group resulting in no overall time delay. Finally, the 128 patient GOLIATH trial was published in April 2018 (JAMA Neurol; PMID 29340574). Similar to SIESTA, propofol and remifentanil/fentanyl were used in both groups. There was no difference in the GA and CS groups in regards to the primary outcome, change in median acute infarct size. Neurologic outcome at 3 months was actually better in the GA group. At present, anesthesiologists should be reassured that GA is safe for acute stroke intervention/thrombectomy provided that attention is paid to avoiding time delay and maintaining cerebral perfusion pressure (target SBP 140–180 mmHg).

Permissive or induced hypertension is appropriate until the clot is evacuated (i.e., recanalization), at which point blood pressure should be reduced to a target agreed upon with the neurointerventionalist. In general, systolic blood pressures between 140 and 185 mmHg prior to clot evacuation and 130–150 mmHg afterwards are acceptable. Pressors are generally required to maintain these hemodynamic goals, and while arterial line placement is preferable, it should *not* delay the procedure. Induction and maintenance of GA (if chosen) should be accomplished with drugs best suited to the hemodynamic goals and least likely to interfere with the immediate postoperative neurologic examination. Normocapnia should be the goal in order to avoid any cerebral oligemia from hyperventilation.

Currently the American Heart Association (https://www.ahajournals.org/doi/full/10.1161/STR.0000000000000158) recommends an individualized approach to the choice of anesthetic type while avoiding time delay (each 30 min delay worsens a 3-month outcome by ~10%; http://journals.lww.com/jnsa/Fulltext/2014/04000/Society_for_Neuroscience_in_Anesthesiology_and.1.aspx), and hypotension/hypoperfusion. Normocapnia, normothermia, and normoglycemia should be maintained. If GA is chosen, extubation as soon as possible after the procedure is optimal. Finally, keep in mind that posterior circulation stroke patients frequently have cranial nerve dysfunction, obtundation, and difficulty maintaining their airways and hence typically require GA. (Table 72.2).

Table 72.2 Antithrombotic therapy in interventional neuroradiology

Antiplatelet agents	**Purpose**	**Monitoring**	**Reversal**
Aspirin	Used preoperatively to avoid thrombotic complications	Antiplatelet effect monitored with platelet function assays	Platelet transfusion
Thienopyridine class P2Y12 inhibitors (clopidogrel, ticlopidine, ticagrelor)	Used in combination with aspirin to avoid thrombotic complications in patients undergoing intra-arterial stent placement	Antiplatelet effect monitored with platelet function assays	Platelet transfusion
Glycoprotein IIB/IIIA inhibitors (tirofiban, abciximab, eptifibatide)	Used intraoperatively if dual-antiplatelet therapy is not initiated preoperatively; also used to treat intraoperative iatrogenic thrombi	Antiplatelet effect monitored with platelet function assays	Stop infusion; consider platelet transfusion
Anticoagulant agents	**Purpose**	**Monitoring**	**Reversal**
Heparin	Used intraoperatively to avoid catheter-induced microthrombi (used in most procedures)	Activated clotting time; intraoperative goal approximately 2–3 times baseline; follow ACT and re-dose heparin ~hourly	Protamine
Direct thrombin inhibitors (bivalirudin, lepirudin, argatroban)	Anticoagulation in patients with contraindications to heparin (such as heparin-induced thrombocytopenia)	ACT	Stop infusion; recombinant factor VIIa, 4 factor prothrombin complex concentrate

Conclusion

Interventional neuroradiology is an essential component of neuroanesthesia practice. Systems for providing both emergent and non-emergent anesthetic care should be optimized at each hospital. Familiarity with the interventional suite is essential, as is the understanding of the critical urgency (i.e., delay = injury) in acute stroke and other emergent endovascular cases. Choices regarding anesthetic type and hemodynamic goals should be determined in collaboration with the neurointerventionalist prior to the case. Further trials regarding the comparative efficacy of CS vs. GA in acute stroke interventions, along with new technologies for treating cerebrovascular disease, promise to make interventional neuroradiology an ever-evolving landscape for the neuroanesthesiologist. At present, anesthesiologists should be reassured that GA is acceptable for acute stroke interventions provided that time delay is minimized and blood pressure is maintained (140–180 mmHg systolic).

Suggested Readings

English JD, Yavapai DR, Gupta R, Janardhan V, Zaidat OO, Xavier AR, Nogueira RG, Kirmani JF, Jovin TG. Mechanical Thrombectomy-Ready Comprehensive Stroke Center requirements and endovascular stroke systems of care: recommendations from the endovascular stroke standards Committee of the Society of Vascular and Interventional Neurology (SVIN). Interv Neurol. 2016;4(3–4):138–50. https://doi.org/10.1159/000442715. Epub 2016 Feb 19

Goyal M, Menon BK, van Zwam WH, Dippel DW, Mitchell PJ, Demchuk AM, Dávalos A, Majoie CB, van der Lugt A, de Miquel MA, Donnan GA, Roos YB, Bonafe A, Jahan R, Diener HC, van den Berg LA, Levy EI, Berkhemer OA, Pereira VM, Rempel J, Millán M, Davis SM, Roy D, Thornton J, Román LS, Ribó M, Beumer D, Stouch B, Brown S, Campbell BC, van Oostenbrugge RJ, Saver JL, Hill MD, Jovin TG, HERMES collaborators. Endovascular thrombectomy after large-vessel ischaemic stroke: a meta-analysis of individual patient data from five randomised trials. Lancet. 2016;387(10029):1723–31. https://doi.org/10.1016/S0140-6736(16)00163-X. Epub 2016 Feb 18

Löwhagen Hendén P, Rentzos A, Karlsson JE, Rosengren L, Leiram B, Sundeman H, Dunker D, Schnabel K, Wikholm G, Hellström M, Ricksten SE. General anesthesia versus conscious sedation for endovascular treatment of acute ischemic stroke: the AnStroke Trial (anesthesia during stroke). Stroke. 2017;48(6):1601–7. https://doi.org/10.1161/STROKEAHA.117.016554.

Saver JL, Jahan R, Levy EI, Jovin TG, Baxter B, Nogueira RG, Clark W, Budzik R, Zaidat OO, SWIFT Trialists. Solitaire flow restoration device versus the Merci Retriever in patients with acute ischaemic stroke (SWIFT): a randomised, parallel-group, non-inferiority trial. Lancet. 2012;380(9849):1241–9. https://doi.org/10.1016/S0140-6736(12)61384-1. Epub 2012 Aug 26

Sayama CM, Liu J, Couldwell W. Update on endovascular therapies for cerebral vasospasm induced by aneurysmal subarachnoid hemorrhage. Neurosurg Focus. 2006;21:3.

Talke PO, Sharma D, Heyer EJ, Bergese SD, Blackham KA, Stevens RD. Republished: Society for Neuroscience in Anesthesiology and Critical Care expert consensus statement: anesthetic management of endovascular treatment for acute ischemic stroke. Stroke. 2014;45(8):e138–50. https://doi.org/10.1161/STROKEAHA.113.003412.

Powers WJ, Rabinstein AA, Ackerson T, Adeoye OM, Bambakidis NC, Becker K, Biller J, Brown M, Demaerschalk BM, Hoh B, Jauch EC, Kidwell CS, Leslie-Mazwi TM, Ovbiagele B, Scott PA, Sheth KN, Southerland AM, Summers DV, Tirschwell DL. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2018;49(3):e46–99.

Schönenberger S, Uhlmann L, Hacke W, Schieber S, Mundiyanapurath S, Purrucker JC, Nagel S, Klose C, Pfaff J, Bendszus M, Ringleb PA, Kieser M, Möhlenbruch MA, Bösel J. Effect of conscious sedation vs general anesthesia on early neurological improvement among patients with ischemic stroke undergoing endovascular thrombectomy. JAMA. 2016;316(19):1986.

Simonsen CZ, Yoo AJ, Sørensen LH, Juul N, Johnsen SP, Andersen G, Rasmussen M. Effect of general anesthesia and conscious sedation during endovascular therapy on infarct growth and clinical outcomes in acute ischemic stroke. JAMA Neurol. 2018;75(4):470.

Nogueira RG, Jadhav AP, Haussen DC, Bonafe A, Budzik RF, Bhuva P, Yavagal DR, Ribo M, Cognard C, Hanel RA, Sila CA, Hassan AE, Millan M, Levy EI, Mitchell P, Chen M, English JD, Shah QA, Silver FL, Pereira VM, Mehta BP, Baxter BW, Abraham MG, Cardona P, Veznedaroglu E, Hellinger FR, Feng L, Kirmani JF, Lopes DK, Jankowitz BT, Frankel MR, Costalat V, Vora NA, Yoo AJ, Malik AM, Furlan AJ, Rubiera M, Aghaebrahim A, Olivot J-M, Tekle WG, Shields R, Graves T, Lewis RJ, Smith WS, Liebeskind DS, Saver JL, Jovin TG. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. N Engl J Med. 2018;378(1):11–21.

Albers GW, Marks MP, Kemp S, Christensen S, Tsai JP, Ortega-Gutierrez S, McTaggart RA, Torbey MT, Kim-Tenser M, Leslie-Mazwi T, Sarraj A, Kasner SE, Ansari SA, Yeatts SD, Hamilton S, Mlynash M, Heit JJ, Zaharchuk G, Kim S, Carrozzella J, Palesch YY, Demchuk AM, Bammer R, Lavori PW, Broderick JP, Lansberg MG. Thrombectomy for Stroke at 6 to 16 Hours with Selection by Perfusion Imaging. N Engl J Med. 2018;378(8):708–18.

Anesthesiological Challenges During Neuroradiological Interventions

73

Michael Aziz and Ansgar M. Brambrink

Contrast Reactions

Overview

Intravascular contrast medium facilitates visualization of neurovascular structures. Administration of contrast agents can cause severe complications. For all settings the estimated incidence of any reactions is up to 15%. The incidence of life-threatening reactions is 1 in 1000–2000 examinations, and fatal reactions have been reported.

Reactions to contrast media are classified as anaphylactoid or chemotoxic. Anaphylactoid reactions occur at certain threshold levels and are not dose-dependent. Contrast can cause direct release of histamine from mast cells or can activate complement, but the exact mechanism of reaction is poorly understood. Anaphylactoid reactions present as nausea, urticaria, bronchospasm, angioedema, laryngospasm, hypotension, or seizures. Patients at higher risk for anaphylactoid reactions are those with a history of multiple allergies, asthma, or previous reaction to contrast media.

Chemotoxic reactions result from chemical effects of the agent on the vessel or organ perfused. These reactions are dose-dependent (i.e., increased dose; repeated administration = increased likelihood). Types of chemotoxic reactions include fluid shifts due to the hyperosmolar nature of media and renal toxic effects (discussed further below). Patients at risk for these chemotoxic reactions are those with significant medical comorbidities. Patients with renal and cardiovascular disease are at particular risk due to the effects of fluid shifting and nephropathy.

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Prevention

Preparation is paramount to prevention and appropriate treatment of contrast reactions. Administer contrast to patients only in settings equipped for cardiopulmonary resuscitation with skilled providers who know the patient's medical history.

Patients at risk for anaphylactoid reactions should be pretreated with adequate hydration, corticosteroids, and histamine-blocking agents.

Patients at risk for chemotoxic reactions should be adequately hydrated throughout and particularly after administration of contrast. When possible, use lower osmolality, nonionic contrast media. The minimum amount of contrast medium necessary should be administered. Patients at risk for renal complications are discussed below.

Crisis Management

Table 73.1 summarizes the key treatment strategies for contrast reactions.

Key Points

- Contrast reactions can be classified as anaphylactoid or chemotoxic.
- Patients at risk for anaphylactoid reactions include those with multiple allergies, asthma, or previous reaction to contrast media; patients with medical comorbidities are at risk for chemotoxic reactions.
- In preparation, carefully evaluate the patient, and ensure that the facility is equipped for resuscitation and that skilled providers are readily available.
- Reactions can manifest as nausea, bronchospasm, hypotension, or seizures or as large fluid shifts (anaphylactic) and renal toxic effects (chemotoxic).
- Severe reactions should be treated quickly and aggressively according to the manifesting symptoms as some reactions can be fatal.

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Table 73.1 Key treatment strategies for contrast reactions

Reaction	Treatment	Potential adverse effects
Nausea/vomiting	Ondansetron or other 5HT3 agents	Migraine headache
Urticaria	Diphenhydramine	Drowsiness
	Cimetidine or ranitidine	
Bronchospasm – mild	Supplemental oxygen	
	Albuterol	Tachycardia
	Subcutaneous epinephrine	Tachycardia, hypertension, cardiac dysrhythmias
Bronchospasm – severe	Supplemental oxygen	
	Corticosteroid	
	Albuterol or terbutaline	Tachycardia
	IV epinephrine	Tachycardia, hypertension, potentially malignant cardiac dysrhythmia
Angioedema	Secure airway	Tachycardia, hypertension, potentially malignant cardiac dysrhythmia
	Corticosteroid	
	Epinephrine	
Laryngospasm	Positive pressure ventilation	
	Succinylcholine	Paralysis may require endotracheal intubation (provider skilled in airway management should be readily available)
Vagal reaction	IV fluids	Fluid overload
	Elevate patient's legs/Trendelenburg	
	Atropine	Tachycardia, dysrhythmias
Hypotension – mild	IV fluids	Fluid overload
Hypotension – severe	IV fluids	Fluid overload
	Epinephrine	Tachycardia, hypertension, cardiac dysrhythmia
Seizures	Diazepam or other benzodiazepines	Respiratory depression, sedation

Contrast-Induced Nephropathy

Overview

Contrast-induced nephropathy is one of the most common causes of renal failure in hospitalized patients. This nephropathy increases morbidity and mortality of the primary disease, prolongs hospitalizations, increases costs, and may lead to long-term hemodialysis requirement. It occurs in 1–15% of all patients undergoing invasive angiography procedures and in as many as 50% of patients with preexisting renal dysfunction or diabetes mellitus. Definition of nephropathy is often a measured serum creatinine ≥25% above baseline or ≥0.5 mg/dL above baseline.

Table 73.2 Patients at particular risk for contrast-induced nephropathy

Patient risk factors	Chronic kidney disease
	Left ventricular pressure ejection fraction <40%
	Urgent procedure
	Congestive heart failure
	Advanced age
	Hypotension or shock
	Low hematocrit
	Diabetes mellitus
	Hypovolemia
History of exposure to particular drugs	Nonsteroidal anti-inflammatory drugs
	ACE inhibitors/angiotensin receptor blockers
	Aminoglycoside antibiotics
Contrast-related factors	Contrast volume
	Ionic contrast
	Viscosity
	Contrast osmolarity

Contrast agents produce renal dysfunction by several mechanisms. Contrast causes an initial dilation of renal vasculature followed by prolonged renal vasoconstriction, which reduces renal blood flow. Reductions in blood flow, as well as direct osmotic toxicity, can cause necrosis of medullary epithelial cells. Subsequent oxidative radical formation injures the renal tubules. Additional mechanisms for nephropathy are thromboembolic events during arterial cannulation and catheter manipulation.

Patients at particular risk for contrast-induced nephropathy are summarized in Table 73.2.

Prevention

Multiple interventions have been employed to prevent contrast-induced nephropathy both in patients at risk and as global prophylaxis. While many agents have shown some benefit in various experimental models, few agents are proven to have benefits based on human randomized controlled trials. The best prevention likely comes from adequate periprocedure hydration. Table 73.3 summarizes reported interventions, their mechanism, potential side effects, and results from related human trials to date.

Crisis Management

The serum creatinine of patients at risk for contrast-induced nephropathy should be followed 24–48 h after the procedure. Those at low risk may be followed for symptoms of renal dysfunction and evaluated subsequently for problems. Any dysrhythmia, difficulty in breathing, change in neurologic status, weight gain, or other signs of fluid overload should be promptly evaluated. A small rise in serum creatinine may be followed by prolonged hospitalization and

Table 73.3 Reported interventions, mechanisms, effects, and clinical investigations

Intervention	Mechanism	Potential adverse effects	Results of clinical investigations
Hydration	Increases renal blood flow	Volume overload	Study results strongly support this intervention
N-Acetylcysteine (150 mEq in 850 mL D5. Infuse at 3 mL/kg/h for 1 h and then 1 mL/kg/h for 6 h)	Scavenging oxygen-free radicals	Flushing, itching, rash, congestive heart failure, GI side effects	Mostly supportive. May be more protective when given IV
Sodium bicarbonate (600 mg IV BID for 3 doses)	Limits the production of oxygen-free radicals	Metabolic alkalosis	Mostly supportive
Calcium channel blockers	Increases renal blood flow	Excessive vasodilation	Mixed results, but benefits may outweigh risks
Theophylline	Increases renal blood flow	Arrhythmia, GI side effects, headache, tremor, restlessness, seizure	Mixed results
Fenoldopam	Increases renal blood flow	Headache, dizziness, hypotension, flushing, tachycardia	Study results *do not support* this intervention
Dopamine	Increases renal blood flow	Tachycardia, hypertension	Not supportive
Atrial natriuretic peptide	Increases renal blood flow	Volume overload	Not supportive
Allopurinol	Reduces effects of oxygen-free radicals	Skin rash, GI side effects, fatigue	Not supportive
Periprocedural hemodialysis	Removal of contrast media	Hypotension, electrolyte disturbance, bleeding	Mixed results
Furosemide	Diuresis	Hypotension, hypokalemia	Not supportive
Prostaglandin E1	Increases renal blood flow	Flushing, peripheral edema, hypotension	Not supportive
HMG-CoA reductase inhibitors (Statins)	Antioxidant, anti-inflammatory mechanism	Muscle aches, rhabdomyolysis, elevated LFTs	Mostly supportive

repeat creatinine measurements. A significant rise in serum creatinine warrants immediate evaluation by a nephrologist as well as strict monitoring of acid/base status, serum electrolytes, and volume status. Treatment should focus on electrolyte and fluid derangements but may also involve some duration of hemodialysis or necessitate even renal transplantation surgery in some cases.

Key Points

- Patients at risk for renal disease must be identified, and prophylaxis prior to contrast administration should be strongly considered.
- When possible, low volume, nonionic, low osmolality contrast should be used.
- The most effective prophylactic strategy remains adequate IV hydration prior to contrast exposure. Patients at higher risk likely also benefit from preemptive intravenous application of *N*-acetylcysteine and sodium bicarbonate (see doses in Table 73.3).
- Other prophylactic measures have not produced consistent results or were harmful in human randomized controlled trials or meta-analysis.
- Treatment should focus on monitoring, and treatment of fluid, electrolyte, and acid/base disorders may require hemodialysis.

Arterial Hypertension

Overview

Elevated arterial blood pressure is problematic in INR. An acute rise in blood pressure can precipitate rupture of an aneurysm and cerebral edema. In contrast, an acute increase in arterial blood pressure at any time during the procedure may, among other things, indicate an acutely elevated ICP and requires immediate attention. The key to successful anesthetic management is a balance between adequate cerebral blood flow and prevention of aneurysm rupture or the precipitation of hypertensive encephalopathy/brain edema formation. A patient with an unsecured aneurysm requires precise blood pressure control to avoid rises that could precipitate rupture. Conversely, if an aneurysm rupture is suspected and the patient has a declining neurologic status, mean arterial pressure may need to be elevated to overcome a high intracranial pressure.

Prevention

Preparation begins with detailed patient history and preoperative evaluation. Because cerebral vessels are manipulated and blood pressure can change acutely, most providers advocate the use of invasive arterial monitoring. Since the neuroradiologist places an arterial catheter for access, a separate arte-

Table 73.4 Events/problems requiring manipulation of hemodynamics

Events/problems	Patient presentation indication	Therapeutic intervention/diagnostic intervention
Laryngoscopy/ endotracheal intubation	Tachycardia and hypertension	Treatment with esmolol, lidocaine, opioid, IV antihypertensive agent, or deepened anesthesia
Cannulation of the femoral artery	Brief stimulating response	Opioid or short-acting antihypertensive
Carotid occlusion trial	To confirm cerebrovascular reserve in patients undergoing carotid occlusion	Induced hypotension may be necessary
Coil placement in wide-necked aneurysms	Repeated failed attempts	Deliberate hypotension or brief cardiac standstill (adenosine) to facilitate placement are options
Embolization of brain arteriovenous malformations	To prevent embolization or acute hemorrhage from glue dislodging into a draining vein	Deliberate hypotension may facilitate glue placement
Acute rise in intracranial pressure	May present as hypertension and bradycardia (potential causes include aneurysmal rupture, brain edema, intraparenchymal hemorrhage)	Relieve elevated ICP via acute hyperventilation, osmotherapy, ventriculostomy, or emergent surgical intervention. Maintain high MAP to allow adequate CBF – cerebral perfusion pressure-guided
Aneurysmal rupture	May manifest as an acute rise in arterial blood pressure	Evaluate for extravasation of contrast medium. Reverse anticoagulant. Consider emergency surgery
Cerebral edema	Signs of intracranial hypertension	Consider ICP measurement to guide therapy. Osmodiuretics, deepen anesthesia, maintain adequate perfusion pressure
Cerebral vasospasm	Declining neurologic status days after subarachnoid hemorrhage	Medically induced hypertension, hypervolemia, hemodilution. Continue calcium channel blockers; statins. Consider balloon angioplasty and intra-arterial application of vasodilatory drugs

rial catheter is not used by some. However, a preoperative arterial line facilitates a hemodynamically stable anesthetic induction as well as constant monitoring during periods when the femoral arterial pressure is not transduced.

Crisis Management

The evidence to support a specific antihypertensive regimen is weak. Calcium channel blockers may be preferred in patients with aneurysmal subarachnoid hemorrhage as these drugs have been shown to improve long-term outcomes secondary to positive effects on cerebral vasospasm. Otherwise, blood pressure can be controlled with various antihypertensive agents and/or inhalation or intravenous anesthetics. Table 73.4 summarizes several events or problems that may require immediate intervention to manipulate hemodynamics accordingly.

Key Points

- Precise control of blood pressure is crucial to prevent rupture of an aneurysm and cerebral edema.
- Invasive arterial monitoring facilitates precise control.
- For ruptured aneurysms or brain edema, MAP needs to be elevated in order to allow for adequate CBF; consider ICP monitoring for CPP-driven therapy.
- To control hypertensive responses, multiple antihypertensive or anesthetic agents can be used.

Suggested Reading

Contrast Reaction

Bush WH, Swanson DP. Acute reactions to intravascular contrast media: types, risk factors, recognition, and specific treatment. AJR Am J Roentgenol. 1991;157:1153–61.

Contrast-Induced Nephropathy

Merten GJ, Burgess WP, Gray LV, Holleman JH, Roush TS, Kowalchuk GJ, et al. Prevention of contrast-induced nephropathy with sodium bicarbonate: a randomized controlled trial. JAMA. 2004;291:2328–34.

Pannu N, Wiebe N, Tonelli M, Alberta Kidney Disease Network. Prophylaxis strategies for contrast-induced nephropathy. JAMA. 2006;295:2765–79.

Stenstrom DA, Muldoon LL, Armijo-Medina H, Watnick S, Doolittle ND, Kaufman JA, et al. N-acetylcysteine use to prevent contrast medium-induced nephropathy: premature phase III trials. J Vasc Interv Radiol. 2008;19:309–18.

Tepel M, van der Giet M, Schwarzfeld C, Laufer U, Liermann D, Zidek W. Prevention of radiographic-contrast-agent-induced reductions in renal function by acetylcysteine. N Engl J Med. 2000;343:180–4.

Arterial Hypertension

Lee CZ, Young WL. Anesthesia for endovascular neurosurgery and interventional neuroradiology. Anesthesiol Clin. 2012;30(2):127–47.

Osborn IP. Anesthetic considerations for interventional neuroradiology. Int Anesthesiol Clin. 2003;41:69–77.

74 Specific Challenges During Neuroradiologic Interventions in Pediatric Patients

F. Cole Dooley and Timothy W. Martin

Overview

Interventional radiology procedures performed on the brain and spinal cord of children may be diagnostic, therapeutic, or palliative and may be performed on either a "stand-alone" basis or combined with an open surgical procedure. Most procedures are performed with high-speed fluoroscopy and digital subtraction angiography for imaging and the use of microcatheters that permit superselective catheterization of blood vessels.

Although transarterial or transvenous routes can be used, including the umbilical vessels in neonates, the transfemoral arterial approach is selected most commonly. In children, these procedures are typically done under general anesthesia and require endotracheal intubation due to case duration and need for a motionless state. With endotracheal intubation, the airway and ventilation can be controlled to optimize cerebral perfusion and deal with possible periprocedural complications. Laryngeal mask airways are appropriate in some cases. Table 74.1 lists common neuroradiologic diagnostic and therapeutic procedures in children, and Table 74.2 lists possible complications that can occur during or following these procedures.

The anesthetic complications of loss of airway or intravenous access, although not specific to neuroradiologic procedures, may be more likely to occur during these cases due to frequent movement of the patient or radiologic equipment and the typical increased distance of the anesthesia provider from the patient. These complications are not discussed separately in this chapter but are included in Table 74.2 in the interest of creating awareness.

Table 74.1 Common neuroradiologic procedures in children

Diagnostic procedures	
Cerebral angiography	Catheter-based cerebral angiography useful in defining both intra- and extracranial vascular anatomy and pathology
Lumbar puncture (LP)	Guided LP for failed lumbar puncture in patients with spinal deformities or anomalies
Myelography	Evaluation of congenital spinal anomalies, disc disease, and radiculopathy
Image-guided biopsies or aspirations	Biopsies or aspirations of intracranial masses
Therapeutic procedures	
Vascular embolization	Intracranial aneurysm, cerebral arteriovenous malformation, spinal arteriovenous fistula, and malformations
Tumor embolization	Meningiomas, glomus tumor, and nasopharyngeal angiofibroma
Thrombolysis	Local intra-arterial lysis treatment for stroke

Table 74.2 Potential complications of pediatric patients during interventional neuroradiology procedures

Procedural complications
Intracranial hemorrhage
Occlusive complications/thromboembolic stroke
Contrast reactions
Contrast nephropathy
Hematoma and hemorrhage from the vessel puncture site
Anesthetic complications
Hypothermia
Loss or disruption of airway or breathing circuit integrity
Loss of intravenous access
Protamine allergy
Heparin overdose

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Prevention

Most of the complications that may occur in pediatric interventional neuroradiologic procedures can be prevented by thoroughly evaluating the patient's coexisting disease (with particular attention to cardiac, pulmonary, and renal function) and allergy status, having a clear understanding of the planned procedure and anticipated movement of the patient and imaging equipment, and meticulous preparation of all medications (anesthetic and procedure related). Specific preventive measures will be described in the discussion of each potential complication.

Crisis Management: Intracranial Hemorrhage

Intracranial hemorrhage from aneurysm or arteriovenous malformation rupture may occur as a result of pathology of the vessels themselves, acute rise of blood pressure, or intracranial vessel injury, perforation, or dissection directly by vascular manipulation during the procedure. This may result in permanent neurological disability or death (Tables 74.3 and 74.4).

Table 74.3 Signs and symptoms of intracranial hemorrhage

Awake patients may complain of sudden headache, nausea, vomiting, progressive neurologic deficit, confusion, seizure, and/or loss of consciousness
Patients under anesthesia may have a seizure, bradycardia, and/or abrupt rise in mean arterial blood pressure
Extravascular extravasation of contrast agent seen during the procedure

Table 74.4 Management of intracranial hemorrhage

Communicate with the interventional radiologist; call for help
Secure the airway if patient is not intubated for the procedure
Hyperventilate with 100% oxygen to bring $PaCO_2$ between 26 and 30 mmHg. This will induce cerebral vasoconstriction and reduce the bleeding
Immediately stop heparin infusion
Immediately reverse heparin with protamine. Typically, 1 mg of protamine is administered for every 100 units of heparin. This may be done after checking the activated clotting time (ACT). Treat severe hypertension with caution to avoid lowering cerebral perfusion below a safe value
Initiate measures to lower ICP, including optimizing head position, diuresis, and ventricular drainage
Consider antiseizure medications
Order cross matching of blood for possible blood transfusion
Aneurysm perforation may be treated by endovascular placement of coils by the interventional radiologist or by emergency craniotomy through clipping of the aneurysm, though outcomes are usually poor

Key Points

- Intracranial hemorrhage can be life-threatening or result in devastating neurological compromise.
- Ventilate with 100% O_2 and keep pCO_2 between 26 and 30 mmHg to induce cerebral vasoconstriction.
- Reverse any active heparin with protamine.
- Lower the systemic arterial pressure while maintaining adequate cerebral perfusion.
- Blood should be available for possible transfusion.
- Utilize measures to lower ICP (e.g., mannitol; ventriculostomy).
- Avoid anesthetic agents that may raise ICP.

Crisis Management: Occlusive Complications

Occlusive complications can result from embolic material being dislodged from a thrombosed aneurysm site, intraprocedural thrombosis, accidental embolization of occlusive material to an unintended target site, or vasospasm induced by the vascular manipulation. These events can occur during or following the procedure and may compromise cerebral perfusion leading to cerebral ischemic injury and infarction, and the development of new neurologic deficits.

Cyanoacrylate adhesives are embolic agents used in treating arteriovenous malformations that can cause arterial ischemia and microcatheter "gluing," with compromise of the blood supply. Cyanoacrylate can also result in asymptomatic and symptomatic pulmonary emboli and possible respiratory failure.

Most of these complications are diagnosed when the patient recovers from the anesthetic (Table 74.5).

Diagnosis

An occlusive site can be seen and confirmed by an angiogram (Table 74.6).

Table 74.5 Signs and symptoms of occlusive crisis

Change in the mental status in an awake patient pre- or postoperatively
Development of new neurologic deficits
Possible respiratory compromise or failure

Table 74.6 Management of occlusive crisis

Communicate with the interventional radiologist to determine the extent of occlusion; call for help as necessary
Secure the airway to maintain oxygenation and ventilation
Ventilate with 100% oxygen
Decrease the anesthetic depth
Maintain normocarbia to hypercarbia, to increase the cerebral blood flow
Induced hypertension to increase the cerebral blood flow, increase the MAP 30–40% above baseline to drive adequate flow through collaterals
Embolic material compromising the cerebral perfusion may be possibly retrieved by interventional radiologist
Failure to retrieve may require craniotomy by the neurosurgeon
Microcatheter imbedded in glue may be removed by snare or surgically
Thrombus revealed on angiogram may be treated by intra-arterial tissue plasminogen activator

Key Points

- Patient should be ventilated with 100% oxygen.
- Increase the arterial blood pressure to increase collateral blood flow.
- Continuous infusion of heparinized saline should be used during the procedure to prevent thrombosis and maintain catheter patency.
- Removal of embolic material may be attempted by the radiologist or may require surgical intervention.

Table 74.7 Types of contrast reaction

Type of reaction	Mechanism	Remarks
Anaphylactic	IgE mediated	Rare, but life-threatening
Anaphylactoid/ idiosyncratic	Non-IgE-mediated histamine and serotonin release/activation of the complement system	Reactions can be mild to severe
Nonanaphylactoid/ physio-chemotoxic/ nonidiosyncratic	Nonimmunological; dependent upon ionicity and osmolality, volume, and route of administration	Reactions are usually mild to moderate

Table 74.8 Clinical manifestations of contrast reactions

Pruritus, flushing, erythema, urticaria, angioedema, nausea, vomiting, abdominal pain, laryngeal edema, hoarseness, chest tightness, cough, dyspnea, wheezing, light headedness, syncope, tachycardia, dysrhythmias, and hypotension

Table 74.9 Signs of severe reactions under general anesthesia

Cutaneous	Flushing
	Urticaria
	Erythema
	Angioedema
Respiratory	Wheezing
	Cyanosis
	Increase in peak airway pressure
Cardiovascular	Tachycardia
	Hypotension
	Dysrhythmias
	Cardiovascular collapse

Crisis Management: Contrast Reactions

Contrast agents improve the visualization of anatomical structures that are not normally easy to see. They can be administered by intravenous, intra-arterial, or intrathecal routes. The most commonly used intravenous contrast agents are iodinated ionic and nonionic compounds.

Pediatric contrast reactions are usually anaphylactoid, with rates of 0.18–3% for low osmolality contrast media and 3–13% for high osmolality contrast media. Most contrast reactions occur within 3–5 min of injection. Severe hypersensitivity reactions are likely to occur in patients with a history of allergy, atopy, or asthma. Patients with a previous reaction have increased chances of recurrence on re-exposure (Tables 74.7, 74.8, and 74.9).

Prevention of Contrast Reactions

Pretreatment prior to contrast administration is typically prescribed for patients with previous nonimmunologic-mediated radiocontrast reactions to contrast agents of the same class as planned. These patients are usually pretreated with antihistamines (H1 and often H2 antagonists) and corticosteroids according to locally established protocols that normally take several hours for implementation. However, despite premedication, a significant number of reactions still occur, and pretreatment has largely only been shown to decrease the frequency of mild reactions.

Management of Contrast Reaction

The reactions can range from mild to life-threatening events and could be either anaphylactic or anaphylactoid reactions, which may not be clinically distinguished.

A mild reaction of short duration may be treated with antihistamine and intravenous fluid, whereas life-threatening reactions should be treated aggressively and immediately (Tables 74.10 and 74.11). Addition of an H2 antagonist has been shown to improve treatment of cutaneous symptoms better than an H1 antagonist alone.

Table 74.10 Treatment of mild contrast reaction

Stop the administration of contrast agent
Maintain adequate oxygenation and ventilation
IV fluids for volume expansion to treat hypotension
Antihistamines (diphenhydramine 0.5–1 mg/kg) to treat pruritus, flushing, erythema, urticaria
Bronchospasm may be treated with albuterol or terbutaline, and if refractory, with epinephrine
Epinephrine may be used to treat hypotension not responding to volume expansion
Hydrocortisone 1–2 mg/kg, then repeated after 4–6 h

Table 74.11 Treatment of severe contrast reaction

Stop the administration of contrast agent
Secure the airway and ventilate with 100% oxygen
Discontinue all anesthetic agents, since they are cardiovascular depressants
Epinephrine should be 10 mcg/kg body weight IV if patient has cardiovascular collapse. The dose may be repeated as needed. If patient is hypotensive, epinephrine 1–2 mcg/kg may be given and gradually increased every 30–60 s until blood pressure improves
Insert large-bore IV
Rapid intravenous fluid expansion
CPR if needed
Diphenhydramine 0.5–1 mg/kg IV
Hydrocortisone 1–2 mg/kg then repeated after 4–6 h
For persistent hypotension, start epinephrine 0.05–0.1 mcg/kg/min norepinephrine, or dopamine infusion may be used if the clinical condition demands
Invasive arterial line and venous catheter for monitoring and infusion of vasoactive drugs
For persistent hypotension, consider vasopressin
Arrange for PICU monitoring for 24 h, remaining mindful of bimodal distribution of airway-/hypotension-related effects, which may peak again up to 12 h after the original insult
Evaluate the airway for edema before extubation

Key Points

- Contrast reactions can be anaphylactic, anaphylactoid, or chemotoxic and usually cannot be distinguished clinically.
- Life-threatening reactions can occur; as such, all equipment, drugs, and staff should be available to aggressively treat the patient.
- Airway should be secured immediately, before angioedema develops.
- Epinephrine should be used to treat severe hypotension.
- Antihistamines and steroids are used to prevent histamine, serotonin, and complement release.

Crisis Management: Contrast Nephropathy

Contrast nephropathy is the impairment of renal function occurring within 3 days following the administration of intravascular contrast agent. Creatinine increases 25% or 0.5 mg/dl from the baseline within 72 h after the contrast is given. In most cases, the disorder is self-limited; however, the nephropathy can persist for weeks in some patients, leading to renal failure requiring dialysis.

As mentioned earlier, the commonly used contrast media are either ionic or nonionic. Ionic contrast agents have high osmolality (1400–2400 Osm/kg/H_2O). Nonionic contrast agents have a lower osmolality (411–796 mOsm/kg/H_2O). These agents are generally safer, have less toxicity, a lower incidence of adverse events, and are generally better tolerated.

The pathogenesis is probably related to intrarenal endothelin and adenosine-induced vasoconstriction, leading to reduction in glomerular filtration rate and renal ischemia, impaired nitric oxide production, direct cellular toxicity, and oxygen-free radical formation. Patients at risk of developing nephropathy include those with preexisting renal disease, diabetes mellitus, heart failure, volume depletion, use of a high dose of contrast agent, use of high osmolality ionic contrast agent, and use of other nephrotoxic drugs (Tables 74.12 and 74.13).

Key Points

- Patients at risk for contrast nephropathy should be identified.
- Preexisting renal dysfunction should be corrected if possible.
- Nephrotoxic drugs should be avoided or stopped.
- Dehydration or hypovolemia should be corrected.
- Low osmolality contrast agent media should be used.
- Contrast studies should be spaced with a 3-day interval, whenever possible.
- Patients developing renal dysfunction need to be carefully monitored and treated.

Table 74.12 Prevention of contrast nephropathy

Use low osmolality contrast agent media
Use lowest possible dose of contrast agent
Contrast studies should be spaced more than 3 days apart whenever feasible
Discontinue nephrotoxic drugs if possible before the procedure
Hypovolemia should be corrected before the procedure, and the intravascular volume status of the patient should be optimized perioperatively
No current evidence supports use of *N*-acetylcysteine over appropriate intravenous hydration as prophylaxis for contrast nephropathy

Crisis Management: Hemorrhage/Hematoma at Vessel Puncture Site

Bleeding may occur around the catheter site at the time of placement, during the procedure or after decannulation. Even small amounts of blood loss may be significant in infants (Tables 74.14 and 74.15).

Key Points

- Multiple attempts for catheter placement should be avoided.
- Catheter site must be regularly inspected.
- After catheter removal, application of manual pressure for 10–15 min followed by use of a pressure dressing.

Table 74.13 Management and treatment of contrast nephropathy

Patients at risk for the development of nephropathy should be monitored by measuring serum creatinine levels before the procedure and once daily for 5 days post procedure
Any nephrotoxic drugs should be avoided and further contrast studies avoided in this period
The volume status of patients should be optimized, with careful monitoring of fluid input–output and weight gain
Patient needs to be hospitalized with monitoring of serum electrolytes, acid base balance, and volume status
Once the diagnosis of contrast nephropathy is established, the management is the same as with renal failure
Some patients will need hemodialysis

Table 74.14 Prevention of hemorrhage/hematoma at vessel puncture site

Avoid multiple attempts at catheter placement
Catheter site should be checked peri- and postoperatively for any bleeding
Tubing should have tight connections, and preferably, luer-locking connections should be used
Emergence of the patient should be smooth; coughing, straining, or emergence agitation should be avoided

Table 74.15 Management of hemorrhage/hematoma at vessel puncture site

Application of direct pressure for 10–15 min and a temporary pressure dressing at the site after catheter removal will limit hematoma formation
Narcotics or propofol may be given to ensure smooth emergence
Antiemetic should be given to avoid nausea and vomiting on emergence
Residual heparin effect should be ruled out

Crisis Management: Hypothermia During Neuroradiologic Interventions

Hypothermia is defined as core body temperature of less than 35 °C. General anesthesia inhibits thermoregulation, and the cold temperature in the procedure room causes further heat loss. Heat is lost to the environment by conduction, convection, evaporation, and radiation, in addition to the depression of metabolic heat production during anesthesia (Tables 74.16, 74.17, 74.18 and 74.19).

Table 74.16 Etiology of hypothermia in children

Larger surface area-to-body mass ratio compared to adults results in more heat loss
Higher conductivity than adults, less subcutaneous fat
Evaporation is higher due to lower keratin content in skin
Reduced capacity for heat production
Significant heat loss from head, which forms nearly 20% of body surface area in neonates and infants. The head may remain exposed during the procedure
IR procedures may be of prolonged duration
Cool interventional radiology rooms
Use of room temperature fluids

Table 74.17 Diagnosis of hypothermia

Body temperature lower than normal, either in peri- or postoperative period
Temperature should be monitored according to ASA standards. Appropriate site for temperature monitoring depends on the clinical situation, with all sites presenting tradeoffs due to level of invasiveness and accuracy
Shivering may be present in older children although it will be absent in infants
Cutaneous vasoconstriction, piloerection
Delayed awakening, decreased level of consciousness

Table 74.18 Clinical implications of hypothermia

Increased blood viscosity, impaired platelet function, platelet sequestration in portal circulation, abnormal blood coagulation cascade, and increased blood loss
Left shift of oxyhemoglobin dissociation curve, increase in pulmonary vascular resistance, decrease in oxygen consumption, decreased in CO_2 production, and VQ mismatch
Arrhythmias, bradycardia, prolonged PR interval, widened QRS interval, prolonged QT interval, ventricular fibrillation, and asystole when core body temperature is less than 30 °C
Delayed postanesthetic recovery

Table 74.19 Management of hypothermia

Increase the room temperature to reduce radiant heat loss
Use forced air warming blanket
Cover exposed portions of patient whenever possible; the head may be covered with a clear plastic bag
Use warm intravenous fluids
Use low flow of inhaled gases and humidifier
In postoperative period, warming lights may be used for neonates and infants

Key Points

- Infants and particularly neonates are prone to hypothermia during neuroradiologic interventions.
- Mild hypothermia may not impair postanesthesia recovery if the procedure is short.
- Moderate hypothermia causes prolonged drug effects, impaired coagulation, and hemodynamic effects.
- Hypothermia can be prevented or minimized by increasing the temperature in the procedure room, using forced air warming devices, and by intravenous fluid warming in the setting of very small children or for those procedures or patients that might require significant fluid volume resuscitation.

Crisis Management: Heparin Overdosage

Flush solutions containing heparin are used to maintain the patency of catheters during the procedure and to prevent thromboembolic complications. This is accomplished by using a pressurized infusion bag or syringe pump. The concentration of heparin is usually 10 units/ml for infants less than 10 kg in weight and 100 units/ml for patients over 10 kg. Massive doses of heparin can be given because an incorrect amount of concentrated heparin is used to prepare the flush solution. It is important to regulate the volume of flush solution to prevent fluid overload and provide an accurate dose of heparin.

The newborn has increased clearance of heparin because of an increased volume of distribution and accelerated metabolism. The half-life of unfractionated heparin is 25 min at term compared to 70 min in adults (Tables 74.20 and 74.21).

Key Points

- Term neonates have increased heparin requirements, whereas preterm neonates have reduced heparin requirements.
- The concentration of heparin must be rechecked before infusion.
- The infusion must be via syringe pump to regulate the volume and accurate dose of heparin.
- Heparin may be reversed with protamine depending on activated clotting time (ACT).

Table 74.20 Prevention of heparin overdosage

Recheck the concentration of the heparin vial before using it
Use a syringe infusion pump to regulate the volume infused
Record the total dose of heparin
Check baseline activated clotting time (ACT) and check ACT every hour for long procedures

Table 74.21 Management of heparin overdosage

If wrong concentration of heparin infusion is suspected or there is an unexpected hemorrhagic complication, heparin should be immediately stopped
ACT should be checked and heparin can be reversed with protamine
If bleeding has occurred, blood transfusion and supportive measures may be needed

Table 74.22 Clinical presentation of protamine reaction

Hypotension: This usually occurs with rapid administration and is associated with tachycardia and flushing. This results from histamine release and the release of nitric oxide-related substances. This can be avoided by slow IV injection
Pulmonary hypertension: Protamine reaction with heparin can result in complement activation and thromboxane release, ending in pulmonary vasoconstriction, pulmonary hypertension, right heart failure, and systemic hypotension
Allergic reactions: The allergic reactions may range from anaphylactic reactions to anaphylactoid reactions. A true anaphylactic reaction occurs as a result of a specific antiprotamine IgE antibody that is seen in patients who use protamine zinc insulin or who have been previously exposed to protamine. Anaphylactoid reactions are the result of the heparin–protamine complex

Crisis Management: Protamine Reaction

Protamine is a specific heparin antagonist used to neutralize the effects of heparin at the end of a procedure or during the procedure in the event of unanticipated intracranial hemorrhage. The heparin–protamine complex does not have any anticoagulant activity. One hundred units of heparin are antagonized by 1 mg of protamine. Complications are rarely seen in interventional neuroradiology because the doses of heparin are small and rarely need to be neutralized. The most common complication seen with protamine administration is hypotension, and pulmonary hypertension and anaphylaxis are rare (Tables 74.22 and 74.23).

Key Points

- Protamine is given at the end of a procedure to reverse the effect of heparin.
- A protamine reaction can cause mild hypotension to severe cardiovascular collapse.
- It should be given slowly IV.
- The most common reaction is hypotension which can be treated with fluid volume, ephedrine, phenylephrine, and antihistamines.

Table 74.23 Management and treatment of protamine reaction

Protamine should be given by slow IV injection
Hypotension can be treated with increased IV fluid volume, ephedrine, phenylephrine, and antihistamines
In case of severe reaction or cardiovascular collapse, protamine administration should be stopped, and the patient treated as for a severe anaphylactic reaction

Crisis Management: Vein of Galen Malformations

Vein of Galen aneurysmal malformations (VGAM) are among the rarest of intracranial arteriovenous malformations and result from persistent dilation of the distal portion of a fetal venous structure responsible for cerebral tissue drainage. The end result is uneven distribution of circulatory volume that causes congestive heart failure due to work and volume overload, generally with the degree of cardiac failure reflecting the size of the shunt. Open surgical repair and transcatheter embolization are both options for medically refractory cases, with the latter offering a significant survival advantage over open repair. Embolization is usually performed in staged procedures and presents unique challenges to the anesthesiologist, mainly related to management of an infant with heart failure in the setting of possible pulmonary hypertension. As the procedure is performed, additional difficulty can be encountered with migration of the embolizing coils to other organ systems, such as the pulmonary circulation. The goal of this partial embolization is improvement in symptoms of heart failure, which occurs almost immediately as venous return and cardiac work are decreased.

Clinical presentation of vein of Galen malformations:

- Typically occur in the neonatal period with significant heart failure with cranial bruit or later in childhood with persistent headache.
- Heart failure severity varies proportionally with the degree of shunt present. Symptoms refractory to medical management are the primary indication for the transcatheter embolization technique. Medical therapy generally consists of diuretics, dopamine, and/or dobutamine.
- Partial embolization improves symptoms of failure as circulatory volume and cardiac work improve.

Key Points

- Vein of Galen malformations frequently present in the neonatal period with heart failure.
- Transcatheter embolization techniques offer considerable survival advantages for medically refractory cases when compared to open surgical repair and typically occurs in staged procedures.
- Care must be taken during anesthetic management, focusing on appropriate treatment of the infant with heart failure and commonly pulmonary hypertension. Management focuses on maintaining normothermia, normal ventilation or hyperventilation for control of intracranial pressure, and avoidance of hypoxia.
- During embolization coil deployment, the anesthesiologist must remain vigilant for displacement of coils to unintended areas, such as the pulmonary circulation.

Suggested Reading

Ashida Y, Miyahara H, Sawada H, Mitani Y, Maruyama K. Anesthetic management of a neonate with vein of Galen aneurysmal malformations and severe pulmonary hypertension. Paediatr Anaesth. 2005;15(6):525–8.

Bochner BS, Lichtenstein LM. Anaphylaxis. N Engl J Med. 1991;324:1785.

Dillman R, Strouse PJ, Ellis JH, et al. Incidence and severity of acute allergic-like reactions to IV nonionic iodinated contrast material in children. AJR Am J Roentgenol. 2007;188:1643–7.

Lasser EC, Berry CC, Talner LB, et al. Pretreatment with corticosteroids to alleviate reactions to intravenous contrast material. N Engl J Med. 1987;317(14):845–9.

Levy JH. Anaphylactic and anaphylactoid reactions. In: Lobato EB, Gravenstein N, Kirby RR, editors. Complications in anesthesiology. Philadelphia: Lippincott Williams & Wilkins; 2008. p. 701–11.

Singh J, Daftary A. Iodinated contrast media and their adverse reactions. J Nucl Med Technol. 2008;36(2):69–74.

Varma MK, Price K, Jayakrishnan V, et al. Anaesthetic considerations for interventional radiology. Br J Anaesth. 2007;99(10):75–85.

Part XIII

Challenges During Postoperative Anesthesia Care After Neurosurgery

Surgical Emergencies After Neurosurgery

75

Jason D. Walls and R. Alexander Schlichter

Hemorrhage

Overview

Despite apparent hemostasis at the end of a neurosurgical procedure, postoperative hemorrhage can occur, leading to serious and sometimes fatal complications. Given that the cranial vault is a rigid structure with a fixed total volume, bleeding after an intracranial procedure can lead to an increased ICP. Not only can this increase in ICP lead to changes in mental status but also to hematoma formation in extreme situations. In addition, heme can irritate brain parenchyma leading to seizure and vasospasm.

Although the vast majority of cases occur at the primary surgical site, in rare cases, intracranial hemorrhage can occur remote from the surgical site. Case reports describe both supratentorial and cerebellar hemorrhage after both supratentorial and infratentorial procedures. Rapid intraoperative loss of significant amounts of cerebrospinal fluid (CSF) and intracranial hypotension appear to be major mechanisms for the development of this rare phenomenon. In addition, bleeding related to neurosurgical procedures remote from the cranium involves a unique set of complications. Hemorrhage after carotid endarterectomy (CEA) can lead to hematoma formation, compromising the airway and cerebral blood flow. Bleeding after spinal surgery can lead to significant blood loss, pressure on the spine, and spinal ischemia. The multiple etiologies of postoperative hemorrhage are summarized in Table 75.1.

Table 75.1 Causes of postoperative hemorrhage

Inadequate surgical hemostasis	Bucking/coughing at extubation
Coagulopathy	Emesis/retching
Uncontrolled hypertension	Trauma to head when moving patient
Excessive CSF drainage	Intraoperative mechanic brain shifting

Table 75.2 Risk factors for postoperative hemorrhage

Bleeding disorders (hemophilia)	Cirrhosis
Antiplatelet therapy (aspirin, clopidogrel)	
Systemic anticoagulation	Postoperative nausea and vomiting (PONV)
Chronic hypertension	Alcohol use
Respiratory disease (coughing)	Tobacco use
Vascular disease	Illicit drug use (cocaine, PCP, and opioids)

Prevention

A thorough preoperative assessment of the patient can reveal potential risk factors for postoperative hemorrhage (Table 75.2). Perioperative preparation also plays an important role: smooth emergence and extubation should be achieved by optimization of equipment and intraoperative medications, stable blood pressure (intra-arterial blood pressure monitoring and antihypertensive medications), and aggressive anti-emesis. If intraoperative hypothermia was employed during aneurysm clipping, the patient needs to be rewarmed, as hypothermia can worsen coagulopathies. After massive red blood cell transfusions, plasma and platelets should be considered to prevent dilutional coagulopathy (see below). Careful positioning and transferring the patient from OR bed will prevent trauma or stress on the surgical site.

Crisis Management

Crisis management strategies for addressing possible causes of postoperative hemorrhage are listed in Table 75.3.

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Table 75.3 Crisis management for hemorrhage

Risk factor	Treatment	Potential adverse effects
Hypertension	Opioids	Oversedation
	Labetalol	Bradycardia/hypotension
	Esmolol	Bradycardia
	Nicardipine	Hypotension
Emesis/retching	Ondansetron	Migraines
	Haloperidol	Oversedation
		Extrapyramidal side effects
		Sedation
	Compazine	Sedation/loss of airway
	Promethazine	
	Propofol	
Mental status changes	Reverse sedation	Pain/delirium
	Full neurological exam	
	CT scan	
	Surgical reexploration	Risks of surgery and anesthesia
Hypothermia	Warming blankets	Low risk for burns
	Warm IV fluids	Hypervolemia
	Hot lights	
Coagulopathy	See Table 75.5	
Hematoma formation	See Table 75.5	

If the patient has a suspected postoperative hemorrhage after a neurosurgical procedure, a full neurological exam should be performed and the neurosurgical team immediately notified. The intervention performed and imaging obtained depend on the severity of the exam. If a patient has a mild change in neurological exam, a conservative "watch and see" approach is appropriate. Any further changes in mental status or neurological exam warrant imaging, usually a CT scan. If major hemorrhage is suspected (loss of consciousness, obtundation, loss of extremity function), immediate surgical reexploration is likely required. Overall functional outcomes are directly related to early detection, rapid control, and limiting the volume of postoperative hemorrhage.

Key Points

- Postoperative hemorrhage is a serious and sometimes fatal complication of neurosurgery.
- Although the majority of cases occur at the primary surgical site, remote site intracranial hemorrhage has been reported after both supratentorial and infratentorial surgeries.
- Patients should be evaluated preoperatively for risk factors that can lead to postoperative hemorrhage.
- Proper equipment and medications should be available to treat hypertension, prevent coughing, insure a smooth extubation, warm the patient, treat coagulopathy, and prevent and treat PONV.
- Frequent and thorough neurological exams of the patient following surgery can detect changes that might indicate a possible hemorrhage. Communication with the neurosurgical team is important to determine if the patient needs further evaluation or reexploration of the surgical site.

Table 75.4 Common risk factors for postoperative coagulopathy

Hereditary (hemophilia, von Willebrand's)	Dilutional (massive transfusion)
Vitamin K deficiency (malnutrition)	Hypothermia
Antiplatelet therapy	Consumptive (ITP)
Heparin therapy	Cirrhosis
Warfarin therapy	Nitroprusside
Non-vitamin K antagonist oral anticoagulants	
Disseminated intravascular coagulopathy	Hetastarch
Acute head injury	Hyperfibrinolysis

Coagulopathy

Overview

Coagulopathy is a serious complication that can lead to postoperative hemorrhage and hematoma formation. Despite apparent adequate intraoperative hemostasis, a coagulopathy may still be present. If unrecognized and untreated, this coagulopathy has the potential to cause serious hemorrhage or hematoma leading to brain or spinal cord ischemia. Postoperative coagulopathy has many potential causes, including low levels of plasma clotting factors or platelets, breakdowns in enzymatic systems that insure proper coagulation and platelet function, or hyperfibrinolysis. Risk factors are summarized in Table 75.4.

Prevention

A proper history, physical, and laboratory tests are essential in preventing postoperative coagulopathy. Preoperatively, the patient needs to be questioned about known bleeding disorders, easy bruising, abnormal bleeding (epistaxis), medications (clopidogrel, aspirin, Warfarin, non-vitamin K antagonist oral anticoagulants, and heparin), nutrition (vitamin K deficiency), and alcohol use. Appropriate preoperative laboratory tests for coagulopathy include a platelet count, prothrombin time (PT), and partial thromboplastin time

(PTT). Bleeding time, activated clotting time (ACT), fibrinogen level, and thromboelastogram are often not necessary but may be useful when available to follow the patient's coagulation profile intra- and postoperatively. In patients with complex hereditary bleeding disorders, a hematology consult may be warranted to assist in perioperative coagulation management.

If the patient is at an elevated risk for intra- or postoperative coagulopathy, adequate large-bore venous access must be obtained prior to the start of surgery, including possible central venous access. Intra-arterial blood pressure monitoring can be useful if large amounts of colloid are going to be transfused or frequent laboratory tests are drawn to follow the patient's coagulation profile. Current type and crossmatch are necessary to insure appropriate amounts of packed red blood cells and fresh frozen plasma (FFP) are available during the surgical procedure.

Crisis Management

Postoperative coagulopathy requires immediate and rapid intervention to prevent serious morbidity and mortality. Treatment is focused on using the appropriate medications and blood factors as well as correcting any other reversible causes of the coagulopathy. If the patient has an elevated PT/INR, vitamin K intravenously should be considered as an initial therapy. Although vitamin K can correct an elevated INR within 24 h, its delayed onset of action will limit its ability to be the sole therapy in a coagulopathic patient at risk of postoperative hemorrhage. Additionally, if the patient is hypothermic, active warming should be implemented with a warm air blanket or hot lights. All fluids and blood products should be warmed prior to administration.

When postoperative coagulopathy requires blood derivatives for correction, treatment options include FFP, platelets, cryoprecipitate, nonactivated prothrombin complex concentrate (PCC), or recombinant factor VIIa (rFVIIa). Using FFP to correct coagulopathy has a long history with established protocols and local practices. However, this therapy is not without complications including prolonged times to achieve adequate hemostasis, large volumes to deliver appropriate quantities of coagulation factors, and the potential for transfusion related acute lung injury (TRALI). If large volumes of blood products are given, the patient's fluid status needs to be monitored to prevent fluid overload, and diuretics should be used when indicated.

Recent reports describe improved hemostasis and faster INR correction with PCC, especially 4-factor PCC (4PCC), compared to traditional FFP administration in patients taking vitamin K antagonist (VKA) medications as well as those patients with coagulopathy related to TBI. Moreover, recent American guidelines recommend VKA reversal with 4PCC rather than FFP in patients with major bleeding. In a postoperative patient with prior VKA use and ongoing coagulopathy, 4PCC should be considered as a potential therapeutic option. Although PCCs are historically associated with an increased risk of thrombotic complications, current formulations and appropriate dosing regimens have lowered the overall risk of thromboembolism. Advantages of PCC over plasma include shorter time to administration, no need for a crossmatch, viral inactivation, and no risk of volume overload. However, PCCs are not recommended in patients with elevated thrombotic risks. Also, repetitive dosing can potentially lead to an increased thrombotic risk due to accumulation of prothrombin. Concurrent treatment with vitamin K is recommended to decrease the need for PCC repetitive dosing. In the setting of acute coagulopathy and potential for hemorrhage leading to brain or spinal cord ischemia, the risk versus benefit must be weighed for the use of PCC.

Additional potential therapies for postoperative coagulopathy include rFVIIa, desmopressin, and antifibrinolytics. rFVIIa has been found to be successful in patients with acute brain injury and intracerebral hemorrhage not responding to FFP or cryoprecipitate. The benefits of rFVIIa must be weight against the risk of potential thromboembolism. Until future research delineates the specific indications and safety profile of rFVIIa, the off-label use of this medication for management of postoperative coagulopathy should be reserved for cases of life-threatening hemorrhage not responding to conventional therapies. If bleeding is related to a qualitative platelet dysfunction, desmopressin 0.3 mcg/kg can be administered. The role of antifibrinolytics has been studied in the prevention of rebleeding, but not in the active treatment of coagulopathy.

With the advent of the targeted oral anticoagulant medications, specifically the non-vitamin K antagonists dabigatran (direct thrombin inhibitor), apixaban, and rivaroxaban (direct factor Xa inhibitors) and abciximab, a glycoprotein IIb/IIIa receptor antagonist, novel mechanisms of coagulopathy may be present in the postoperative period. Preoperative planning is probably the best way to avoid potential bleeding complications from these newer agents by following guidelines for appropriate withholding of therapy prior to elective procedures. However, in patients who present with neurosurgical emergencies including trauma, holding therapy is not an option, and an alternative approach must be instituted. Unlike traditional VKAs (Warfarin), the oral non-vitamin K antagonist anticoagulants do not have a specific antidote. FFP and PCC have limited ability to reverse the clinical effect of these drugs. Additionally, alternative means to eliminate these drugs to prevent or correct coagulopathy are often not appropriate in the acute postoperative setting. For example, nearly 60% of dabigatran can be removed with hemodialysis, but this therapy takes nearly 2 h to be effective once initiated. However, recent literature shows promising treatments for

Table 75.5 Treatment options for correction of coagulopathy

Blood product	Clotting factors present	Clinical use
Fresh frozen plasma	II, V, VII, IX, X, XI, antithrombin III, proteins C + S	Treating coagulopathy with elevated PT, PTT
	Inadequate fibrinogen, vWF	DIC
		Reversing heparin
		Replacing deficient clotting factors except fibrinogen and VWF
Prothrombin complex concentrate (PCC)	Three-factor PCC (II, IX, X)	Treating congenital factor deficiencies
	Four-factor PCC (II, VII, IX, X)	Reversal vitamin K antagonists
Cryoprecipitate	VIII, XIII, vWF, fibrinogen	Replacement of these factors
		DIC
		Use if FFP is not reversing coagulopathy
Platelets	Platelets	Thrombocytopenia
		Platelet dysfunction
		ITP, TTP
		Replacement for patients on antiplatelet drugs
Recombinant factor VII	Factor VII	DIC
		Hemorrhage in acute brain injury
		Use when FFP, cryoprecipitate not reversing coagulopathy
Idarucizumab	Antibody fragments to dabigatran	Dabigatran reversal

coagulopathy and postoperative bleeding in surgical patients taking these newer oral anticoagulants. Idarucizumab is an antibody fragment specifically developed to reverse the effects of dabigatran. Recent reports show complete reversal of dabigatran within minutes of idarucizumab treatment. Future research needs to specifically look at idarucizumab in the neurosurgical patient taking dabigatran with perioperative coagulopathy and bleeding. Treatment options are summarized below in Table 75.5.

Key Points

- Postoperative coagulopathy can be caused by low plasma levels of clotting factors or platelets, by a breakdown in the enzymatic systems that insure proper coagulation and platelet function, or by hyperfibrinolysis.
- Bleeding disorders, easy bruising, current medications, nutrition, and alcohol use should be assessed preoperatively. Appropriate laboratory tests for coagulopathy include a platelet count, PT, PTT, and INR.
- The appropriate blood components need to be given based on laboratory data, medication history, and clinical exam.
- Hypothermia should be avoided and aggressively reversed.
- Newer targeted oral anticoagulant medications (e.g., dabigatran, rivaroxaban) require further research and novel therapies to prevent perioperative hemorrhage. Idarucizumab, an antibody reversal agent of dabigatran, highlights promising new medical therapies to treat perioperative coagulopathy.

Hematoma

Overview

The combination of coagulopathy and hemorrhage can lead to hematoma formation. Subdural hematomas occur between the brain and the dura and are generally caused by rupture of a sinus or bridging vein. By expanding against other parts of the brain, a subdural hematoma can increase ICP and cause ischemia leading to changes in mental status, hypertension, and bradycardia. Epidural hematomas are caused by rupture of meningeal arteries and place pressure on the adjacent spinal cord (or brain if intracranial) causing spinal ischemia and a change in neurological exam. Postoperative symptomatic spinal epidural hematomas appear to be a rare event occurring in probably less than 0.5% of all cases. Although the current literature varies on exact risk factors, studies suggest that multilevel spine surgery appears to present the highest risk. Other possible risk factors include previous spine surgery, increased daily alcohol consumption, high BMI, exaggerated blood pressure elevation after extubation, preoperative coagulopathy, elevated intraoperative blood loss, prior NSAID use, and advanced age.

Hematomas from neurosurgical procedures not involving the CNS, specifically following CEA, may also lead to postoperative complications. Airway compromise can occur from direct pressure on the trachea or compression of the recurrent laryngeal nerve. Also, a decrease in cerebral blood flow can result from a regional hematoma following a CEA. Often, the patient will present with neck swelling accompanied by a change in voice, difficulty swallowing, or a change in mental status.

Prevention

The prevention of hematoma formation depends on preventing possible sources of bleeding. Strategies include the above for treating hemorrhage (Table 75.3) and coagulopathy (Table 75.5).

Table 75.6 Crisis management in hematoma formation

Hematoma location	Diagnosis	Treatment
Intracranial	Neurological exam	Observation
	Neuroimaging	Surgical evacuation
Carotid	Neurological exam	Secure airway
	Physical exam	Surgical reexploration and evacuation
	Airway exam	
Epidural	Neurological exam	Observation
	Neuroimaging	Surgical evacuation

Crisis Management (Table 75.6)

All hematomas should be treated as serious emergencies. If a hematoma formation is suspected, a quick but thorough neurological exam should be performed immediately. The neurosurgical team should be alerted and an operating room made available for possible surgical exploration. If the patient's neurological exam is stable, the neurosurgical team might initially obtain further imaging including a CT scan or MRI. Rapid detection with prompt surgical evacuation appears to decrease overall morbidity and improve outcomes.

Key Points

- All hematomas should be treated as serious emergencies requiring rapid evaluation and possibly prompt surgical evacuation.
- The combination of coagulopathy and hemorrhage potentiates hematoma formation.
- Hematomas following CEA can compromise the airway and cerebral blood flow.

Suggested Reading

Hemorrhage

Baeesa SS. Remote cerebellar hemorrhage in neurosurgery. Neurosciences. 2012;17(4):305–8.

Borkar SA, Lakshmiprasad G, Sharma BS, Mahapatra AK. Remote site intracranial haemorrhage: a clinical series of five patients with review of literature. Br J Neuro surg. 2013;27(6):735–8.

Friedman M, Piepgras PG, Duke DA, et al. Remote cerebellar hemorrhage after supratentorial surgery. Neurosurgery. 2001;49:1327–40.

Garg K, Tandon V, Sinha S, Suri A, Mahapatra AK, Sharma BS. Remote site intracranial hemorrhage: our experience and review of literature. Neurol India. 2014;62:296–302.

Manninen PH, et al. Early postoperative complications following neurosurgical procedures. Can J Anaesth. 1999;46(1):7–14.

Coagulopathy

Ageno W, Gallus AS, Wittkowsky A, Crowther M, Hylek EM, Palareti G. Oral anticoagulant therapy – antithrombotic therapy and prevention of thrombosis, 9th ed. American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2):44–88s.

Fugate JE, Rabinstein AA, McBane RD, Lanzino G. Dabigatran: a primer for neurosurgeons. World Neurosurg. 2013;79(1):154–8.

Goldstein JN, Refani MA, Milling TJ, Lewis B, Goldberg-Alberts R, Hug BA, Sarode R. Four-factor prothrombin complex concentrate versus plasma for rapid vitamin K antagonist reversal in patients needing urgent surgical or invasive interventions: a phase 3b, open-label, non-inferiority, randomised trial. Lancet. 2015;385:2077–87.

Hartmann M, Sucker C. Pharmacology and clinical use of recombinant activated factor seven in neurosciences. Neurocrit Care. 2007;6:149–57.

Holbrook A, Schulman S, Witt DM, Vandvik PO, Fish J, Kovacs MJ, et al. Evidence-based management of anticoagulation therapy – antithrombotic therapy and prevention of thrombosis, 9th ed. American College of Chest Physicians evidence-based clinical practice guidelines. Chest. 2012;141(2):152–184s.

Joseph B, Pandit V, Khalil M, Kulvatunyou N, Aziz H, Tang A, et al. Use of prothrombin complex concentrate as an adjunct to fresh frozen plasma shortens time to craniotomy in traumatic brain injury patients. Neurosurgery. 2015;76(5):601–7.

Le Roux P, Pollack CV, Milan M, Schaefer A. Race against the clock: overcoming challenges in the management of anticoagulant-associated intracerebral hemorrhage. J Neurosurg. 2014;121:1–20s.

Pollack CV, Reilly PA, Eikelboom J, Glund S, Verhamme P, Berstein RA, et al. Idarucizumab for dabigatran reversal. N Engl J Med. 2015;373(6):511–20.

Roitberg B, et al. Human recombinant factor VII for emergency reversal of coagulopathy in neurosurgical patients: a retrospective comparative study. Neurosurgery. 2005;57(5):832–6.

Sorenson B, Spahn DR, Innerhofer P, Spannagl M, Rossaint R. Clinical review: prothrombin complex concentrates – evaluation of safety and thrombogenicity. Crit Care. 2011;15(201):1–9.

Yuan ZH, Jiang JK, Huang WD, Pan J, Zhu JY, Wang JZ. A meta-analysis of the efficacy and safety recombinant activated factor VII for patients with acute intracerebral hemorrhage without hemophilia. J Clin Neurosci. 2010;17:685–93.

Hematoma

Amiri AR, Fouyas IP, Cro S, Casey ATH. Postoperative spinal epidural hematoma (SHE): incidence, risk factors, onset, and management. Spine J. 2013;13:134–40.

Hou J, et al. Risk factors for spinal epidural hematoma after spinal surgery. Spine. 2002;27(15):1670–3.

Palmer JD, et al. Postoperative hematoma: a 5 year survey and identification of avoidable risk factors. Neurosurgery. 1994;35(6):1061–5.

Self D, et al. Risk factors for post-carotid endarterectomy hematoma formation. Can J Anaesth. 1999;46(7):635–40.

Yamada K, Abe Y, Satoh S, Yanagibashi Y, Hyakumachi T, Masuda T. Large increase in blood pressure after extubation and high body mass index elevate the risk of spinal epidural hematoma after spinal surgery. Spine. 2015;40(13):1046–52.

Postoperative Respiratory Complications

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Classification and Etiology

The full scope of postoperative respiratory complications includes an immense spectrum of disorders of diverse pathophysiologic origin. Outside of classification as being associated with hypoxia or hypercarbia, they can be divided into obstructive and restrictive disease processes.

Upper Airway Obstruction (Supraglottic and Glottic)

Upper airway obstruction is a relatively common early respiratory complication that unless treated promptly, can become a life-threatening emergency. The major risk factors for its development are sleep apnea, residual anesthetic agents (including incomplete antagonism of neuromuscular blocking drugs), and trauma of the upper airway. Airway obstruction due to laryngospasm may be triggered by extubation during light anesthesia, accumulated secretions, and inadequate pain control. Cervical spine surgery may be associated with significant pharyngeal edema. Prolonged upper airway obstruction resulting from overflexion of craniocervical junction has been described after occipitocervical fusion in children.

Lower Airway Obstruction (Subglottic; Obstructive Pulmonary Disorders)

Obstructive pulmonary diseases include asthma, emphysema, chronic bronchitis, and bronchiectasis. Exacerbation of chronic obstructive lung disease, particularly chronic bronchitis, increases the risk of pulmonary infection. Severe disorders may lead to prolonged ventilatory support, increasing the possibility of ventilator-associated pneumonia.

Restrictive Pulmonary Disorders

Restrictive pulmonary diseases include interstitial pulmonary disease, diseases of the chest wall, and neuromuscular disorders. They may be caused by airway trauma (pneumothorax) or pulmonary parenchymal abnormalities with ventilation-perfusion ($\dot{V}_A / \dot{Q}$) mismatch (atelectasis, pulmonary edema, acute respiratory distress syndrome (ARDS), and pneumonia). Any condition that leads to anatomical or functional exclusion of a number of the lung units from the gas exchange creates a predisposition to $\dot{V}_A / \dot{Q}$ mismatch. The etiologic factors are presented in the Table 76.1. The predisposing factors are case-specific. Atelectasis may be caused by the low-volume ventilation, obesity, endobronchial intubation, and prolonged administration of 100% oxygen. Aspiration may follow stomach distention and regurgitation or vomiting. Intracranial hypertension is a risk factor for development of neurogenic pulmonary edema. The pathophysiologic mechanisms and causes of arterial hypoxemia and hypercarbia (hypoventilation) are summarized in Tables 76.2 and 76.3.

Pathophysiology, Clinical Presentation, and Treatment

Upper Airway Obstruction

Obstruction to air flow develops when oropharyngeal tissues lose their baseline tone, swell, or confine the airway by active contraction. Mucus, blood, vomitus, or foreign body (e.g., tooth or throat pack) can also block the airway. Complete obstruction not only causes hypoventilation and arterial desaturation, but the forceful respiratory attempts against a

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Table 76.1 Causes of ventilation-perfusion ($\dot{V}_A / \dot{Q}$) mismatch

Ventilation-perfusion ratio imbalance	
Relative or absolute increase in dead space ventilation	Relative or absolute increase in perfusion of poorly ventilated alveoli
Hypovolemia (blood loss, diuresis)	Hypocapnia:
Decreased cardiac output (CHF, pharmacological vasodilatation)	Mechanical hyperventilation (to treat increased ICP). May cause bronchospasm and suppress hypoxic pulmonary vasoconstriction
	Spontaneous as a response to pain or as a sign of respiratory distress
Pharmacological influence on the airways (atropine)	Loss of alveolar space
	Pulmonary edema:
	Postobstructive (negative pressure)
	Neurogenic
	Cardiogenic
	Transfusion-related acute lung injury (TRALI)
Pulmonary vasoconstriction (pulmonary embolism)	Acute lung injury/acute respiratory distress syndrome (ARDS)
	Aspiration pneumonitis
	Pneumonia
Supine position	Atelectasis
	Pneumothorax
Abdominal obesity	Modest decrease of hypoxic pulmonary vasoconstriction by volatile agents with increase of intrapulmonary shunt fraction

Table 76.2 Pathophysiologic mechanisms of arterial hypoxemia

Arterial hypoxemia				
Decreased P_iO_2	Alveolar hypoventilation	Impaired alveolar-capillary diffusion	Ventilation-perfusion mismatch	Pulmonary shunt
Unlikely in monitored environment	See Table 76.3	Very rare within clinically significant limits, usually accompanies restrictive lung disease	See Table 76.1	An extreme example of $\dot{V}_A / \dot{Q}$ mismatch where $\dot{V}_A = 0$

Table 76.3 Causes of alveolar hypoventilation

Mechanisms of alveolar hypoventilation		
Obstructive mechanisms	Impaired regulatory mechanisms	Restrictive mechanisms
Supraglottic: tongue/soft tissues	CNS suppression by trauma/swelling	Parenchymal lung abnormalities (pneumonia, ARDS)
Glottic: laryngospasm	CNS suppression by residual anesthetics/opioids	Pleural abnormalities (effusion, pneumothorax)
Subglottic: bronchospasm		Muscle weakness (cervical spine injury, residual neuromuscular blockade)
COPD		Thoracic cage abnormalities (obesity, flail chest)

closed glottis may result in the rapid development of negative-pressure pulmonary edema.

The clinical picture of an upper airway obstruction is usually very obvious, unless the initial presentation was missed and respiratory distress progressed to apnea. Snoring, gurgling, and high-pitched stridorous sounds accompany the labored breathing. Nasal flaring and sternal or intercostal muscle retractions represent the use of the accessory muscles. In the case of a complete obstruction, no noise may be present since the effective respiration has ceased. Forced expiration efforts using accessory muscles may be observed with a foreign body in the airway or tracheomalacia. If conscious, the patient may appear diaphoretic and agitated. With the ongoing hypoxemia, agitation may progress to stupor. Initially, hypoxemia and hypercarbia cause profound autonomic discharge resulting in tachycardia and hypertension; severe hypoxemia ultimately leads to a myocardial failure and circulatory arrest.

If upper airway obstruction develops, start with oxygen treatment prior to any other intervention, and establish monitoring if not already present. Monitoring oxygen saturation, respiratory rate, and end-tidal CO_2 during the event is crucial. For differential diagnosis of airway obstruction, refer to Fig. 76.1. An arterial blood gas measurement is useful when the obstruction persists and reintubation is considered. If the cause of the upper airway obstruction cannot be easily found, fiber-optic laryngoscopy may be indicated to rule out vocal cord paralysis or the presence of a foreign body.

Head and neck surgery can drastically change intubating conditions and convert a previously "easy" airway into a difficult one. Conditions such as cervical spine fusion, halo traction device, and soft tissue edema can impede both bag-mask ventilation and intubation. Immediate availability of help and additional resources such as laryngeal mask airway,

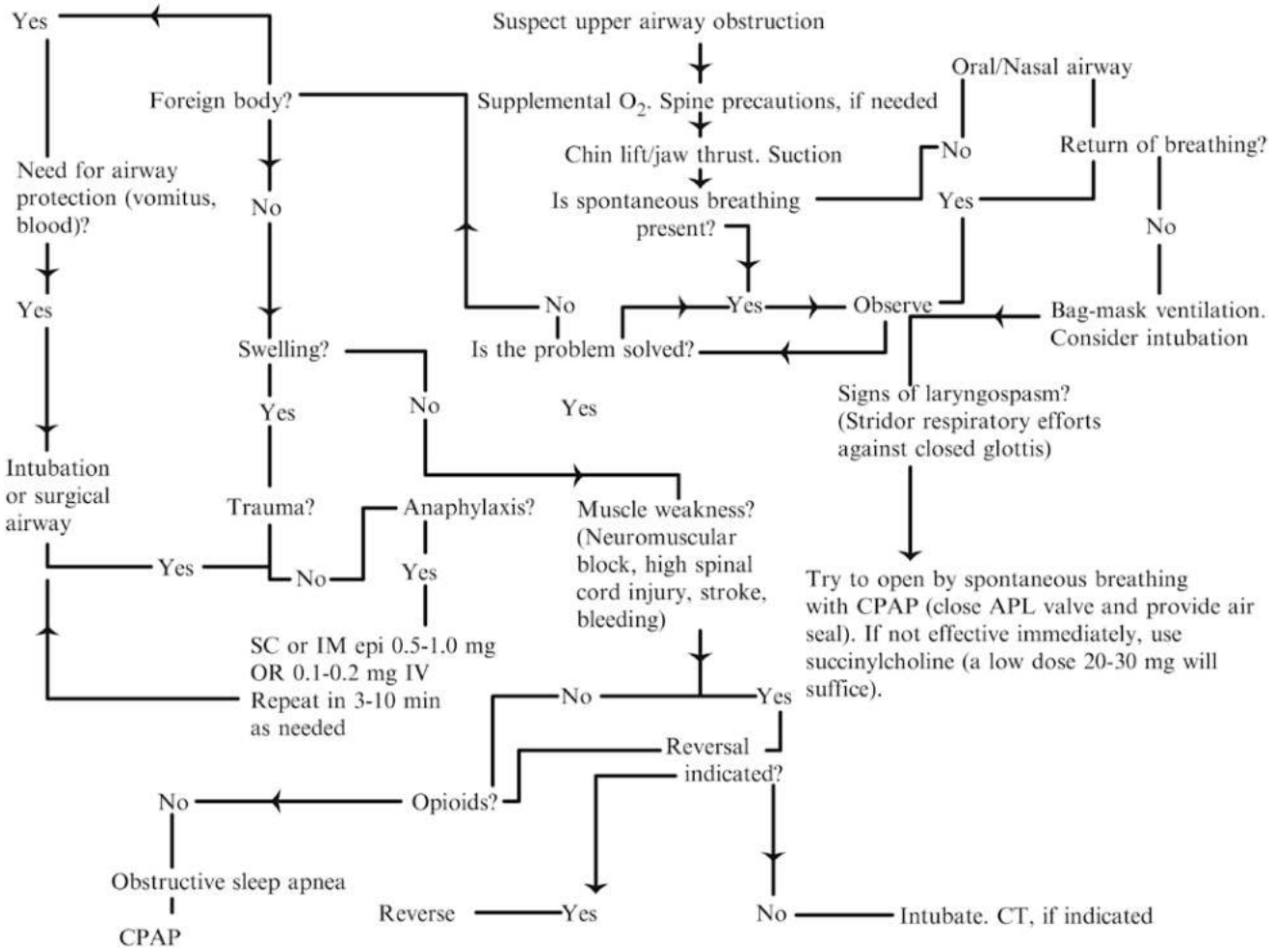

Fig. 76.1 Differential diagnosis and treatment of upper airway obstruction

videolaryngoscope, and emergent cricothyrotomy supplies is crucial when encountering a "can't ventilate, can't intubate" situation that calls for initiation of American Society of Anesthesiologists Difficult Airway Algorithm.

Lower Airway Obstruction

The airway smooth muscle contraction is regulated by release of (a) acetylcholine by vagal nerves, (b) catecholamines by adrenal glands, and (c) histamine by mast cells. Adequate anesthesia with selection of appropriate opioids may prevent excessive vagal stimulation from intubation and surgery. Acetylcholine leads to contraction of smooth muscle by release of intracellular Ca^{2+}. β_2 agonists administration can effectively block this mechanism. Anesthetic agents that possess histamine-releasing qualities should be avoided if possible.

Clinical manifestations in the postoperative period include dyspnea, tachypnea, expiratory wheezing, prolonged expiratory time, and hypercapnia. Intubated patients may have increased peak airway pressure and steep expiratory slope on capnogram.

Differential diagnosis of disorders associated with dyspnea is represented in Fig. 76.2.

First line of bronchospasm treatment consists of 100% oxygen, inhaled β_2 agonists, and anticholinergic agents. If these treatments fail, adjuncts such as intravenous ketamine, magnesium, and inhaled oxygen-helium mixtures can be employed. Steroids may be given to decrease an inflammatory response.

COPD exacerbation may manifest itself as worsening of respiratory symptoms, increased dyspnea, cough, sputum production, and oxygen desaturation. Clinical presentation may give important cues for diagnosis; nevertheless, similar symptoms may accompany other clinical conditions, so additional tests such as chest X-ray and arterial blood gases are often needed.

When diagnosis is confirmed, short-acting bronchodilators and systemic corticosteroids should be administered. Short-term noninvasive positive ventilation could be used as

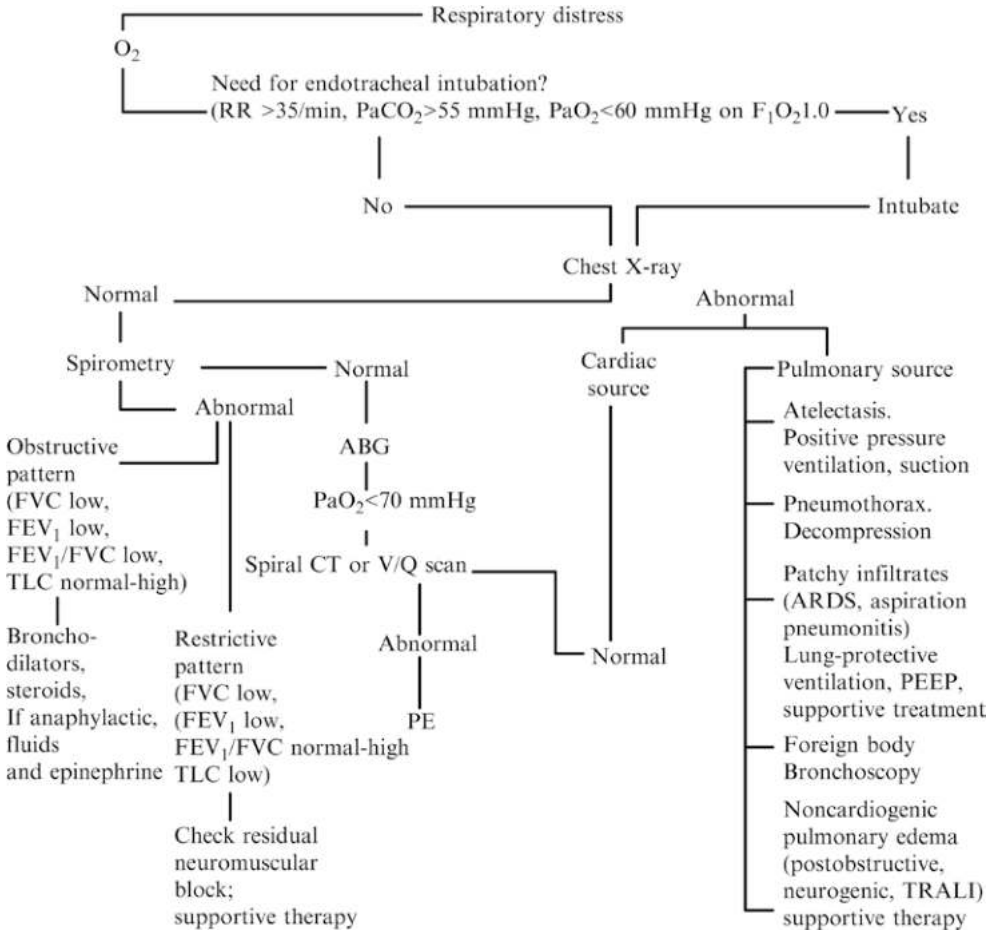

Fig. 76.2 Differential diagnosis of disorders associated with dyspnea

a ventilator weaning strategy and may reduce mortality and rates of ventilator-associated pneumonia.

Since any mode of positive pressure ventilation increases the risk of barotrauma and pneumothorax, implementation of preventive strategies is helpful. This includes utilizing pressure-controlled ventilation, minimization of the peak inspiratory pressure, prevention of air trapping and auto-PEEP by optimization of the expiratory time, and synchronization of the pressure assistance with the patient's respiratory efforts. Continuous monitoring is necessary for quick detection and treatment of positive pressure associated complications.

Postoperative Pulmonary Complications with Restrictive Mechanism

While idiopathic restrictive pulmonary disorders such as pulmonary fibrosis are uncommon, many serious postoperative respiratory complications such as pneumonia, pulmonary edema, and ARDS also are restrictive by nature. Their incidence is particularly high in trauma patients, with ARDS rate reported as high as 20% in patients with traumatic head injury. Hypoxia resulting from respiratory failure may aggravate secondary brain injury, significantly increasing risk of dying or developing permanent vegetative state.

Anesthesia- and surgery-related events such as hypoventilation due to altered consciousness or muscle weakness, decrease in functional residual capacity (FRC) with supine position and muscle relaxation, and oxygen reabsorption from alveoli all contribute to development of atelectasis, the most common culprit of postoperative hypoxemia and one of the main mechanisms contributing to development of acute lung injury.

Most of serious pulmonary complications are associated with development of ventilation-perfusion ($\dot{V}_A / \dot{Q}$) mismatch.

The severity of $\dot{V}_A / \dot{Q}$ mismatch may be established based on the response to O_2 treatment. In the case of mild to moderate $\dot{V}_A / \dot{Q}$ mismatch, PaO_2 will increase with oxygen treatment. However, in the extreme of $\dot{V}_A / \dot{Q}$ mismatch, when some areas of the lung receive zero ventilation (true shunt), oxygen will not have much effect on PaO_2. The higher is the shunt fraction, the less the response to oxygen will be.

The shunt magnitude is estimated by the shunt equation:

$$\dot{Q}s / \dot{Q}t = \left(CcO_2 - CaO_2\right) / \left(CcO_2 - CvO_2\right),$$

where $\dot{Q}s/\dot{Q}t$ is a shunt fracture in %, CcO_2 is the end-capillary blood and ideally equals P_AO_2, and CaO_2 is the arterial oxygen content.

P_AO_2 is calculated using alveolar gas equation: [$P_AO_2 = Fi O_2 \times (P_B - P_{H2O}) - P_ACO_2$]

CaO_2 is calculated as:

$$CaO_2 = Hb(g/dL) \times 1.34\,ml\,O_2/g\,Hb \times SaO_2 + PaO_2 \times (0.003\,ml\,O_2/mm\,Hg/dL).$$

CvO_2 represents the venous oxygen content and is calculated accordingly as CvO_2 = Hb (g/dL) × 1.34 ml O_2/g Hb × SvO_2 + PvO_2 × (0.003 ml O_2/mm Hg/dL). It could be measured in the blood aspirated through the distal port of pulmonary artery catheter.

$\dot{V}_A/\dot{Q}$ mismatch can worsen in patients with brain injury as a result from hypothalamus-regulated regional perfusion redistribution, pulmonary microembolic events, and surfactant depletion. Following release of inflammatory mediators and infection contribute to development of pulmonary structural parenchymal abnormalities.

The clinical presentation depends on the primary pathology, though hypoxia is the universal feature. Aspiration may present with cough and wheezing. In severe cases pulmonary edema will manifest itself with respiratory distress, cyanosis, tachypnea, copious frothy secretions, or hemoptysis. Pneumonia is diagnosed in the presence of a new or progressing infiltrate on the chest radiograph in a combination with either fever over 38 °C, or leukocytosis or leucopenia, or an isolation of a pathogenic microorganism. The difference between obstructive and restrictive lung disease is presented in the Table 76.4.

Table 76.4 Obstructive versus restrictive lung disease

–	Obstructive lung disease	Restrictive lung disease
Risk, incidence, epidemiology	Risk increases with preexisting lung disease and prolonged surgery	Risk increases with obesity, high spinal cord injury, chest wall deformities, intrinsic restrictive lung disease, and long surgery, residual neuromuscular blockade
Etiology, pathophysiology	Increase of airway resistance due to (a) narrowing of the airways with inflammation, secretions, compression or contraction of the smooth muscles, and (b) dynamic compression of the airways with the forceful expiration, when pleural pressure exceeds airway pressure	Decrease of lung expansion and increase of work of breathing due to (a) intrinsic increase of elastic lung recoil or (b) extrinsic obstacle to chest expansion (pleural effusion, obesity, chest wall deformity, muscle weakness)
Clinical presentation	Dyspnea, cough, wheezing, prolonged exhalation, distress	Rapid shallow respirations, respiratory distress, dry cough, muscle weakness in cases of neuromuscular disorders

Treatment starts with oxygen administration. A shunt of 15–30% requires various levels of oxygen support, and shunt over 30% causes profound hypoxemia that usually requires mechanical ventilation and positive end-expiratory pressure. If atelectasis is present, chest physiotherapy should be the first line of treatment (e.g., incentive spirometry, chest percussion), and if that does not help, consider the noninvasive positive pressure ventilation (NPPV), namely, continuous positive airway pressure (CPAP) and bi-level positive airway pressure (BiPAP). The advantages of NPPV over traditional ventilation through endotracheal tube include elimination of intubation-related stress and trauma, decreased incidence of ventilator-associated pneumonia, shorter hospital stay, and lesser expenditures. NPPV is more effective in a relaxed and cooperative patient. It is contraindicated when respiratory arrest, hemodynamic instability, increased aspiration risk, facial fractures, severe hypoxemia, or impaired mental status is present. If NPPV trial failed, or could not be employed, intubation and invasive positive pressure ventilation should be performed. ARDS patients may benefit from pressure and volume limitation that prevent further lung injury. Positive end-expiratory pressure (PEEP) >5 cmH_2O and prone position may be utilized in severe cases. When infection is suspected, respiratory tract and blood cultures should be obtained followed by a broad-spectrum antibiotic regimen.

Prevention

Preexisting pulmonary disease, older age, and prolonged surgery are the major independent risk factors for postoperative pulmonary complications and extubation failure. Thus, preoperative medical management of chronic medical conditions as well as minimizing the surgical and anesthesia time are important. Thorough preoperative evaluation is paramount; history should include activity tolerance, presence of symptoms indicative of infectious symptoms, medications, and comorbidities. Risk of postoperative COPD exacerbation increases with positive history of previous treated events. In such patients, severity of air flow impairment could be evaluated with spirometry. However, routine pulmonary function testing is currently not recommended.

Regimen of inhaled corticosteroids in combination with short-acting β_2 agonist is beneficial for patients with asthma. Patients that have been treated with systemic corticosteroids within 6 months before the surgery should receive systemic corticosteroid (hydrocortisone) coverage (stress dose) intra-

operatively with tapering it down postoperatively. In COPD patients, smoking cessation 2 to 4 weeks preoperatively is one of the most effective ways of preventing possible exacerbation by decreasing secretions and airway hyper-reactivity. Pharmacologic treatment may consist of combination of bronchodilators, anticholinergic drugs, and inhaled corticosteroids. Prophylactic antibiotic administration, usually second-generation cephalosporins, may be useful in pneumonia prevention. However, the most significant reduction in the infection risk comes from prevention and aggressive treatment of postoperative atelectasis. Reduction in ventilator-associated pneumonia, especially in patients with traumatic brain injury, may be achieved by upright positioning and oropharyngeal hygiene.

Ventilation-perfusion misbalance prevention mostly consists of maintaining optimal ventilation and perfusion. Preservation of euvolemia, treatment of hypotension, and deep venous thrombosis/pulmonary embolism prophylaxis will help to avoid hypoperfusion. Moderate levels of PEEP are beneficial for atelectasis prevention. Postoperative lung expansion with incentive spirometry, chest physical therapy, postural drainage, and continuous positive airway pressure are useful for prevention of the uneven ventilation. $\dot{V}_A / \dot{Q}$ matching is improved in the prone position compared to the supine position. Volutrauma can contribute to lung injury and should be avoided. Tidal volume should be limited to 6–7 ml/kg in high-risk patients, and airway plateau pressure should not exceed 20 cm H_2O.

The best prevention of postoperative upper airway obstruction is a thorough assessment prior to extubation. An awake and alert patient with no signs of respiratory depression or excessive swelling of the airway has a low chance for airway obstruction. A "leak" test should be performed prior to extubation in prone cases and in those who have received a significant amount of crystalloid solutions. Discussion with the surgeon regarding possible upper airway compromise is particularly important in prone cervical spine and posterior fossa cases.

Strength is one of the important parameters to be tested prior to extubation. Forced vital capacity of 10 ml/kg of ideal body weight, 5-second head lift, and handgrip have been traditionally employed for clinical strength assessment. However, they require full patient's cooperation. Negative inspiratory force is reliable in the absence of cooperation; value of 30 cm H_2O is considered adequate for most patients.

The most accurate assessment of neuromuscular blockade reversal and strength recovery is achieved by neuromuscular monitoring with train-of-four (TOF) ratio determination. Adductor pollicis TOF >0.9 reliably indicates full recovery of the pharyngeal function. Implementation of quantitative TOF ratio measurement is more objective and superior to the qualitative method.

Key Points

- Assess pulmonary function prior to the surgery, primarily based upon history and physical examination. Chest X-rays, spirometry, and arterial blood gases are not routinely recommended for the preoperative evaluation; use only when indicated.
- Chronic lung disease, particularly chronic bronchitis, is a risk factor for postoperative infection. Preexisting restrictive lung disease combined with postoperative respiratory depression by opioids and anesthetics may lead to severe hypercapnia and respiratory failure.
- Plan for extubation ahead of time. Extubate the patient only if all of standard extubation criteria are met.
- Airway obstruction may lead to rapid deterioration. Give oxygen immediately and restore assisted ventilation as soon as possible. If the obstruction was not relieved by the therapeutic maneuvers such as chin lift, jaw thrust, or supraglottic airway, do not hesitate to insert an LMA or reintubate. You can always remove the endotracheal tube later.
- Prophylactic administration of albuterol and possibly ipratropium bromide helps reduce reflex-induced bronchospasm associated with endotracheal intubation.
- $\dot{V}_A / \dot{Q}$ mismatch and shunt are the most common reasons for decreased PaO_2 (think atelectasis). Oxygen will help in the case of $\dot{V}_A / \dot{Q}$ mismatch, but oxygenation will not improve with true shunt.

Suggested Reading

Barbosa FT, Castro AA, de Sousa-Rodrigues CF. Positive end-expiratory pressure (PEEP) during anaesthesia for prevention of mortality and postoperative pulmonary complications. Cochrane Database Syst Rev. 2014;6:CD007922.

Bratton SL, Davis RL. Acute lung injury in isolated traumatic brain injury. Neurosurgery. 1997;40(4):707–12; discussion 12.

Burns KE, Meade MO, Premji A, Adhikari NK. Noninvasive positive-pressure ventilation as a weaning strategy for intubated adults with respiratory failure. Cochrane Database Syst Rev. 2013;12:CD004127.

Canet J, Gallart L. Postoperative respiratory failure: pathogenesis, prediction, and prevention. Curr Opin Crit Care. 2014;20(1):56–62.

Claesson J, Freundlich M, Gunnarsson I, Laake JH, Vandvik PO, Varpula T, et al. Scandinavian clinical practice guideline on mechanical ventilation in adults with the acute respiratory distress syndrome. Acta Anaesthesiol Scand. 2015;59(3):286–97.

Ferreyra G, Long Y, Ranieri VM. Respiratory complications after major surgery. Curr Opin Crit Care. 2009;15(4):342–8.

Hans GA, Sottiaux TM, Lamy ML, Joris JL. Ventilatory management during routine general anaesthesia. Eur J Anaesthesiol. 2009;26(1):1–8.

Huang M, Gonda DD, Briceno V, Lam SK, Luerssen TG, Jea A. Dyspnea and dysphagia from upper airway obstruction after occipitocervical fusion in the pediatric age group. Neurosurg Focus. 2015;38(4):E13.

Laffey JG, Kavanagh BP. Hypocapnia. N Engl J Med. 2002;347(1):43–53.

Manninen PH, Raman SK, Boyle K, el-Beheiry H. Early postoperative complications following neurosurgical procedures. Can J Anaesth. 1999;46(1):7–14.

Missios S, Kalakoti P, Nanda A, Bekelis K. Craniotomy for glioma resection: a predictive model. World Neurosurg. 2015;83(6):957–64.

Muscedere J, Dodek P, Keenan S, Fowler R, Cook D, Heyland D, et al. Comprehensive evidence-based clinical practice guidelines for ventilator-associated pneumonia: prevention. J Crit Care. 2008;23(1):126–37.

Pelosi P, Severgnini P, Chiaranda M. An integrated approach to prevent and treat respiratory failure in brain-injured patients. Curr Opin Crit Care. 2005;11(1):37–42.

Reddel HK, Bateman ED, Becker A, Boulet LP, Cruz AA, Drazen JM, et al. A summary of the new GINA strategy: a roadmap to asthma control. Eur Respir J. 2015;46(3):622–39.

Schoenfeld AJ, Carey PA, Cleveland AW 3rd, Bader JO, Bono CM. Patient factors, comorbidities, and surgical characteristics that increase mortality and complication risk after spinal arthrodesis: a prognostic study based on 5,887 patients. Spine J. 2013;13(10):1171–9.

Shalev D, Kamel H. Risk of reintubation in neurosurgical patients. Neurocrit Care. 2015;22(1):15–9.

Shi Z, Xie H, Wang P, Zhang Q, Wu Y, Chen E, et al. Oral hygiene care for critically ill patients to prevent ventilator-associated pneumonia. Cochrane Database Syst Rev. 2013;8:CD008367.

Vestbo J, Hurd SS, Agusti AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2013;187(4):347–65.

Wong JJ, Lee JH, Turner DA, Rehder KJ. A review of the use of adjunctive therapies in severe acute asthma exacerbation in critically ill children. Expert Rev Respir Med. 2014;8(4):423–41.

Yamakage M, Iwasaki S, Namiki A. Guideline-oriented perioperative management of patients with bronchial asthma and chronic obstructive pulmonary disease. J Anesth. 2008;22(4):412–28.

Neurologic Emergencies After Neurosurgery

77

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Neurosurgical operations are sometimes associated with unexpected postoperative complications which may be emergent in nature. The overall complication rate of neurosurgical procedures is approximately 14%, but these are commonly systemic complications (e.g. bleeding requiring transfusion, need for mechanical ventilation). Brain oedema, elevated intracranial pressure (ICP), seizures, intracranial haemorrhage, ischemic infarction, and cranial nerve palsies are more common neurologic complications.

In this chapter the authors try to summarise acute neurological problems in the postoperative period that confront neuro-anaesthesiologists and intensivists. These complications are discussed under the headings of (A) General Complications, (B) Specific Complications, and (C) Complications Related to Specific Surgical Procedures.

General Complications

Hypotension

Hypotension following neurosurgery could be due to blood loss, injury to the vital structures like the hypothalamus or brainstem, or acute withdrawal of steroids. Correction of hypotension involves assessment of blood loss and replacement of adequate blood products. If the patient has been on corticosteroids for brain oedema treatment, inadvertent missing of the dose during prolonged surgery is a possibility. Acute intravenous administration of hydrocortisone will quickly correct hypotension, but it could take hours to correct associated electrolyte abnormalities. Hypotension caused by injury to the hypothalamus or brainstem has to be treated with inotropes or vasopressors.

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Airway Obstruction

Persistent anaesthetic (sedatives, analgesics, neuromuscular blockers) effect is the most common cause of airway obstruction. Other neurological causes are unconsciousness due to postoperative raised ICP, injury to brain structures, nasal packing following transsphenoidal surgery, tongue swelling after posterior fossa surgery (particularly when using an oral-pharyngeal airway), and pharyngeal and laryngeal oedema after transoral surgery for craniovertebral anomalies. Tracheal intubation should be carried out immediately in order to prevent hypoxia and also to avert intracranial problems associated with laboured breathing.

Hypoventilation

The causes for postoperative hypoventilation are persistent anaesthetic effect and injury to the vital brain centres. Mechanical ventilation is required until such time as the patient's spontaneous respiration is restored.

Polyuria

Polyuria may be due to excess fluids administered during the surgery. Alternatively, it may be due to diabetes insipidus (DI) following surgery on pituitary. DI may be transient or permanent. Diagnosis is established by measuring the serum sodium and osmolarity and urinary sodium and osmolarity and urinary specific gravity. High serum sodium with low urinary sodium levels and a low urinary specific gravity confirms DI. Administration of Pitressin or nasal spray of desmopressin is the treatment along with appropriate maintenance of fluid and electrolyte balance. This condition has to be differentiated from cerebral salt wasting which is characterised by excessive urinary sodium loss and hyponatremia.

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Hypothermia

Postoperative hypothermia generally results from improper temperature maintenance intraoperatively. Hypothermia in the intraoperative and postoperative periods is associated with increased cardiac risk, coagulation problems, postoperative infections, and poor wound healing. It is also a cause of delayed awakening from anaesthesia and generalised reduced metabolism of pharmacologic agents. Intraoperative and postoperative use of forced air warming blanket would resolve the problem. Rarely, hypothalamic injury may be a cause of postoperative hypothermia.

Hyperthermia

Fever frequently develops after intraventricular neuroendoscopic procedures in children. Fever in the early postoperative period of subarachnoid haemorrhage is associated with development of delayed cerebral ischemia (DCI) and a poor outcome. Reactivation of herpes simplex virus encephalitis must be considered in neurosurgical patients who develop postoperative seizures and fever. Excision of lesions in thalamus or hypothalamus and hemispherotomy may lead to hyperthermia.

Specific Complications

Postoperative Seizures

Postoperative seizures can happen because of cortical injury, intraparenchymal haematoma, acute hydrocephalus, pneumocephalus, and prior history of seizures, following epilepsy surgery and cerebral ischemia.

Incidences and predictive factors for occurrence of postoperative seizures have been inconsistent among authors. In general intra-axial primary and metastatic brain tumours, age $\geq$60 years, total tumour/oedema volume $\leq$64 cm^3, complete resection, diencephalic location, and high-grade tumours had significant predictive value for postoperative seizures. Among patients with meningiomas, with a 40% risk of preoperative seizures, the risk factors for postoperative seizures are preoperative seizures, tumour location, and extent of tumour removal. Among patients who underwent surgery for gliomas, DNA repair protein O^6-methylguanine-DNA methyltransferase (MGMT) expression ($P = 0.05$), epidermal growth factor receptor (EGFR) expression ($P = 0.001$), and anaplastic oligodendroglioma/anaplastic oligoastrocytoma (AO/AOA) ($P = 0.038$) are independent factors predicting postoperative seizure. Patients with lower MGMT and EGFR expression and higher AO/AOA showed more frequent postoperative seizures. Postoperative seizure had no statistical correlation with survival and progression-free survival.

Following posterior fossa surgery too, the incidence of seizures was 5.9% in patients who were on antiepileptic coverage. The seizures occurred within 2 weeks postoperatively and were generalised tonic-clonic in nature. Risk factors for developing seizures included acoustic schwannoma, medulloblastoma and astrocytoma, intraoperative venous air embolism, pneumocephalus and sitting position, and preoperative ventriculoperitoneal shunt.

Intraoperative and postoperative drugs may be responsible for postoperative seizures. Nefopam, used to control postoperative pain, causes focal, generalised, myoclonic type of seizures, or status epilepticus, and the occurrence of seizures is not dose-related. Seizure rate with a 2 g cefazolin intraoperative irrigation was 32.9%.

There is little evidence to suggest that antiepileptic drug (AED) treatment administered prophylactically is effective in preventing post-craniotomy seizures.

Non-convulsive status epilepticus (NCSE) is a condition where electrical seizures occur with subtle or no overt clinical manifestations. It is an important cause for prolonged postoperative unconsciousness. It can be diagnosed by an electroencephalogram (EEG), and early treatment is associated with better prognosis.

Haematomas

Postoperative intracranial haematoma can result in permanent neurological deterioration. Various types of haematomas are reported following intracranial surgeries – extradural haematoma (EDH), subdural haematoma (SDH), operative site haematoma, and remote site haematoma.

Extradural Haematoma

The incidence of EDH, in a single surgeon's experience, is 0.8%. A haematoma volume >40 mL manifests with symptoms and requires intervention. Remote EDH occurs following supratentorial surgery and transsphenoidal surgery especially when there is a sudden leakage of a large volume of cerebrospinal fluid (CSF) from ventricles/lumbar CSF drainage. The majority of EDHs occur within 6 h after the primary surgery.

Postoperative EDHs are also described after surgery for acute traumatic SDH. Surgical decompression of SDH results in a sudden decrease in ICP, which facilitates formation of EDH on the contralateral side. Postoperative EDH has also been described following burr-hole craniotomy and closed system drainage for chronic subdural haematoma. When the skull bone is thinned out as seen in long-standing meningioma, even placing skull pin headrest can cause an acute EDH.

Subdural Haematoma

Supratentorial subdural haematomas have been reported following microvascular decompression. The authors advocate

against excessive CSF aspiration to avoid this complication. Four cases of SDH following deep brain stimulation (DBS) lead implantation have been reported out of 500 DBS procedures. Two patients were clinically symptomatic. The other two cases were discovered on routine postoperative imaging. There are reports of SDH as a cause of postoperative cognitive dysfunction or headache, especially when dura was torn accidentally in spinal surgery. Acute SDH has occurred after transsphenoidal decompression of a pituitary adenoma followed by a lumbar drain to manage postoperative CSF rhinorrhoea.

Intraparenchymal Haematoma

Risk factors for postoperative intracranial haematoma include preexisting medical comorbidities such as hypertension, coagulopathies and haematological abnormalities, intraoperative hypertension and blood loss, tumour bed bleeding, venous obstruction, subdural bleed from ruptured veins (because of excessive brain relaxation), and deficiencies in haemostasis.

Epidermoid cysts seem to have greater predilection to cause postoperative haematomas. Out of the 428 surgically treated epidermoids, the incidence of postoperative haemorrhage and delayed postoperative haemorrhage were 5.61% and 4.91%, respectively, significantly higher than the figures for postoperative haemorrhage in all intracranial tumours, which is 0.91%.

Remote Intracranial Bleed

In a report of 2500 cranial surgeries, 5 patients developed remote ICH (0.002%). This complication has been described in patients undergoing transsphenoidal surgery, neuroendoscopy, and burr-hole evacuation for chronic SDH. The postulated mechanism is excessive CSF drainage resulting in traction on the veins. Patients present with headache, neurological deficits, and deterioration.

Postoperative Brain Swelling

Postoperative brain swelling may occur because of brain oedema or hyperemia. Brain swelling raises the ICP and leads to herniation. The patients may progressively become cognitively depressed or unconscious and develop lateralising signs like hemiparesis and pupillary dilatation. Postoperative ICP monitoring may help to identify the condition. When it fails to respond to mannitol or hypertonic saline, decompressive craniectomy is the most appropriate care option.

Prolonged Postoperative Unconsciousness

After excluding anaesthetic and metabolic causes for prolonged unconsciousness following anaesthesia, one must look for common neurological causes like postoperative haematoma and seizures/non-convulsive status epilepticus. An immediate CT scan would be helpful in ruling out a haematoma. An EEG would rule out non-convulsive status epilepticus. Injury to the vital areas of the brain such as brainstem and hypothalamus is another cause. Other causes for prolonged postoperative unconsciousness are as follows.

Intracranial Hypotension

Intracranial hypotension, caused by excessive CSF leak, has been recognised as a cause of prolonged unconsciousness after neurosurgery.

Intracranial hypotension following lumbar drain-assisted skull-base surgery has been reported during surgery for a spheno-orbital meningioma and osteosarcoma of the orbit. Severe postural headache and a deteriorating consciousness level were observed in the early postoperative course. Neuroimages demonstrated epidural fluid collections, severe midline shift, and tonsillar sag compatible with intracranial hypotension. Epidural blood patch completely reversed the clinical and radiologic findings.

Intracranial haematomas occur due to intracranial hypotension after cervical spine surgeries. Bilateral intracranial extradural haematomas following excision of the C4 subdural schwannoma and cerebellar haematoma after removal of the C2–C5 subdural schwannoma have been reported. In both the cases, spinal dura was partially removed together with the tumour, and the dural sac could not be repaired, resulting in large amounts of intraoperative CSF loss. Likewise, intracranial hypotension has been reported, 3 weeks after a lumbar puncture in a patient who underwent an elective craniotomy for an aneurysm. In that situation, lumbar blood patch resulted in a dramatic improvement in the patient's status.

Pseudohypoxic Brain Swelling

Pseudohypoxic brain swelling (PHBS) is characterised by an early postoperative clinical deterioration, in association with typical CT or MRI changes (hypodensities or altered intensities in basal ganglia and/or thalamus). These changes are induced by suction drainage of the operative wound.

Tension Pneumocephalus

Skull pin penetration and lumbar CSF drain can result in excess accumulation of air within cranial cavity leading to tension pneumocephalus and prolonged postoperative unconsciousness. It is also seen after surgery in the sitting position.

Pharmacologic

Postoperative coma has been described in children who received intrathecal baclofen pump. The aetiology is likely to be inadvertent bolus of baclofen given into the subarachnoid space. Valproate intolerance resulted in immediate postoperative coma. Recovery occurred in 1–5 days.

Sustained increase in the cerebral state index within 6 h predicts awakening from coma.

Postoperative Visual Loss

Postoperative visual loss is a complication that is reported mostly after spinal surgery in prone position. A retrospective study addressing this problem included patients from 1993 to 2002 who underwent spine surgery and had ischemic optic neuropathy (ION), central retinal artery occlusion (CRAO), or non-ION non-CRAO perioperative visual impairment. The overall incidence of visual disturbance was 0.094%. Spine surgery for scoliosis correction and posterior lumbar fusion had the highest rates of visual loss of 0.28% and 0.14%, respectively. Paediatric patients (<18 years) were 5.8 times and elderly patients (>84 years) were 3.2 times more likely than patients 18–44 years of age to develop non-ION non-CRAO visual loss. Patients with peripheral vascular disease and hypertension and those who received blood transfusion were more likely to develop non-ION non-CRAO vision loss. ION was present in 0.006% of patients. Hypotension, peripheral vascular disease, and anaemia were the strongest risk factors for development of ION.

Postoperative Autonomic Dysfunction

Acute postoperative autonomic dysfunction is rare. However, there is a report of a patient with cerebellar haematoma and acute hydrocephalus who underwent a vermian and partial right cerebellar hemisphere resection and had postoperative orthostatic hypertension. On standing the patient's systolic BP rose over 60 mmHg with a fivefold increase in plasma noradrenaline. The condition improved after 8 weeks. Transient impairment of cerebellar autonomic modulation or dysfunction of the baroreflex medullary circuit might have resulted in orthostatic hypertension. Autonomic disturbance due to hypothalamic injury that resulted in postoperative death has been reported after craniopharyngioma surgery.

Complications Related to Specific Surgical Procedures

Epilepsy Surgery

A common emergency problem in the postoperative period following seizure surgery is refractory seizures requiring anaesthetics and elective ventilation. An association has been found between acute postoperative seizures and poor outcome in both temporal and extra-temporal paediatric epilepsy surgeries.

Posterior Fossa Surgeries

Surgeries closer to the brainstem can sometimes lead to rapid deterioration, and the causes include acute hydrocephalus, cerebellar haematoma, damage to the major venous system and haemorrhagic infarcts, brainstem stroke, and tumour bed haematoma. In a retrospective study of 500 patients, overall complication rates were 31.8%. But serious complications like cerebellar oedema and haemorrhage occurred only in patients who underwent surgery for cerebellopontine angle tumours. Mortality rate in this series was 2.6%.

Spinal extramedullary haemorrhage spreading to the entire spinal regions, just sparing the cauda equina, has been reported in a patient who underwent a posterior fossa tumour removal in the prone position.

Transsphenoidal Pituitary Surgery

CSF leaks and diabetes insipidus are common complications following pituitary surgery through transnasal endoscopic route. Ischemic complications involving anterior communicating artery and basilar artery are reported. Patients who develop vascular complications have a poorer outcome and remain unconscious. In a case report, the patient developed progressive loss of consciousness in the immediate postoperative period due to a huge haematoma in the operative site causing a stroke due to bilateral internal carotid artery compression. Sudden massive haemorrhage during endoscopy is difficult to control. One safe option would be to pack the operative site and re-explore after 24–48 h.

Two cases of neurological deterioration and coma after the transsphenoidal decompression of a pituitary adenoma with marked suprasellar extension and invasion of the third ventricle are reported. Emergency ventricular shunting led to prompt neurological improvement.

Negative pressure pulmonary oedema has been reported in the immediate postextubation period following transnasal transsphenoidal surgery, which required intubation and mechanical ventilation.

Neuroendoscopic Procedures

In a recent review on endoscopic third ventriculostomy involving 250 patients, overall complication rate was 3.6%, and 2% were serious. When the surgeon approaches the floor of the third ventricle and tries to create a communication, there is a potential for injury to basilar artery or perforators of the circle of Willis. This can lead to torrential bleeding with haemodynamic instability, cranial nerve palsies, and parenchymal infarcts. Sometimes this procedure can lead to fatal subarachnoid haemorrhage which can manifest a few hours later postoperatively. Bleeding can result in accumulation of blood in the ventricles requiring external ventricular drain and shunt at a later period. Rarely, the patient can present with pseudoaneurysm of the injured vessel later. The incidence of internal carotid artery injury following endoscopic skull base surgery is reported as 0.3% with no direct mortality. Major complications following endoscopic biopsies of ventricular tumours have an incidence of 2.2%.

Decompressive Craniectomy

Complication rates of 89 patients who underwent decompressive craniectomy over a 5-year period were analysed in a study. Neurological deterioration occurred, which is aetiology specific at different times of presentation – contralateral epidural/subdural haematoma at 1.5 ± 0.9 days, contusion expansion at 2.2 ± 1.2 days, epilepsy at 2.7 ± 1.5 days, external herniation at 5.5 ± 3.3 days, and CSF leak at 7 ± 4.3 days. Patients with poor GCS and elderly patients are susceptible to these complications.

Ventriculoperitoneal (VP) Shunt Procedures

Shunt obstruction and malfunction can result in recurrence of symptoms of raised ICP. In tuberculous meningitis it is very common due to high protein content in the CSF. Rarely patients can have neurological deterioration at the end of surgery due to operative site haematoma. CSF leak can result in meningitis and ventriculitis which have a bad prognosis. Sudden drainage of CSF through lumbar drain can result in cardiovascular instability due to cerebral herniation. Even after immediate resuscitation and clamping of the drain, it might take up to 48 h to reverse the herniation.

Cranioplasty

With increasing number of patients undergoing decompressive craniectomy for head injury and malignant stroke infarcts, the requirements for cranioplasty are also increasing. Two case series reported on 348 and 108 patients who underwent decompressive craniectomy. Common complications noted include seizures, reoperation for haematoma evacuation, hydrocephalus, and infections.

Vascular Procedures

Moyamoya Disease

Intracranial to extracranial anastomosis done to prevent stroke per se can result in stroke and delayed awakening. Patients with preoperative infarcts and poor cerebrovascular reserve are more prone to develop the ischemic complications. In a review of patients with adult Moyamoya disease, who underwent direct bypass surgery over 6 years, ischemic complications occurred in 4 of 79 (5.1%) patients. In patients with advanced Moyamoya disease and involvement of the posterior cerebral artery, intentional hypotension could result in ischemic stroke in the hemisphere contralateral to the one operated on.

In 165 surgically treated adult-onset Moyamoya disease patients, there were 19 (7.7%) perioperative ischemic complications (4 infarctions with neurological sequelae and 15 reversible ischemic neurological deficits with a new lesion). Multiple preoperative ischemic episodes, presence of a low-density area on CT scanning, and a high signal intensity on diffusion-weighted magnetic resonance imaging were significantly correlated with perioperative ischemic complications.

Intracranial Aneurysm

One of the main complications following aneurysm clipping is ischemia resulting in neurological deficit. Poor SAH grade and brain herniation are the risk factors. Intraoperative monitoring by microvascular Doppler, indocyanine green videoangiography, and intraoperative neuromonitoring can prevent this complication.

Other complications of aneurysmal subarachnoid haemorrhage are loss of consciousness due to seizures, hydrocephalus, and vasospasm.

Predictors of Postoperative Neurological Deterioration Following Aneurysm Surgery

The subjects of the Intraoperative Hypothermia for Aneurysm Surgery Trial (IHAST), which was a multicentre randomised clinical trial that enrolled 1001 patients, were analysed for postoperative deterioration. Acute postoperative neurological deterioration was observed in 42.6% of the patients. New focal motor deficit accounted for 65% of postoperative neurological deterioration, while 60% was accounted for by the National Institutes of Health Stroke Scale score change and 51% by Glasgow Coma Scale score change. Factors associated with postoperative neurological deterioration included age, Fisher grade on admission, ventriculostomy prior to aneurysm surgery, timing of surgery, systolic blood pressure during surgery, ST-segment depression during surgery, history of abnormality in cardiac valve function, use of intentional hypotension during surgery, duration of anterior cerebral artery occlusion, intraoperative blood loss, and difficulty of aneurysm exposure. Of the 426 patients with postoperative neurological deterioration, only 46.2% had a good outcome (GOS score of 1) at 3 months, while 77.7% of those without postoperative neurological deterioration had a good outcome.

Surgery for Parkinsonism

The results of a retrospective study of 796 patients with parkinsonism are as follows: the overall complication rate was 15.3% of 884 operations. Permanent complications occurred in 3.6% of patients. Intracranial haemorrhage occurred in 24 operations (2.7%). In seven of them, the patients required craniotomy and haematoma evacuation and sustained a disabling motor deficit (0.8%). Intracranial haemorrhage occurred more often in patients who underwent microelectrode recording and had a history of chronic hypertension. Hemiparesis without intracranial haematoma occurred in 12 operations (1.4%); microelectrode recording was the risk factor. In 55 operations (6.2%), patients developed postoperative confusion. This occurred more often in elderly patients and those with advanced disease. In 17 operations

(1.9%), patients required observation in the intensive care unit because of postoperative hypotension.

Spine Surgeries

Airway obstruction occurs sometimes following cervical spinal surgery. The causes are upper airway collapse, retropharyngeal haematoma, and even surgifoam expansion. Oesophageal and pharyngeal perforations occur during cervical spine surgery.

Intracranial complications are reported after spinal surgery. One review had 1113 consecutive patients. Neurologic change warranted either a CT or an MR imaging in 59 (4.2%) patients. Six patients (0.4%) had subdural hygroma (four patients), remote cerebellar haemorrhage (one patient), or subdural haematoma (one patient). The haematomas presumably resulted from dural dynamic changes secondary to cerebrospinal fluid loss and intracranial hypotension. In another series of 1077 patients who underwent lumbar spinal surgery, 4 intracranial haematomas occurred.

To conclude, neurosurgical procedures are sometimes associated with life-threatening complications in the postoperative period. Clinicians must be able to recognise them in time and take appropriate steps so that the damage done to the patient is minimised.

Key Points

- Systemic complications are more common than the neurologic complications in the postoperative neurosurgical patient.
- Systemic complications can worsen the neurological insult, e.g. opioid-induced postoperative hypoventilation can worsen brain oedema.
- Some of the neurologic complications are life-threatening and need reexploration, e.g. intracranial haemorrhage.
- Diagnostic imaging studies are required to diagnose life-threatening intracranial complications.

Suggested Reading

Bahuleyan B, Menon G, Nair S. Immediate postoperative death due to hypothalamic injury following surgery for craniopharyngioma. J Clin Neurosci. 2009;16:850–1.

Borkar SA, Lakshmiprasad G, Sharma BS, Mahapatra AK. Remote site intracranial haemorrhage: a clinical series of five patients with review of literature. Br J Neurosurg. 2013;27:735–8.

Dubey A, Sung WS, Shaya M, Patwardhan R, Willis B, Smith D, Nanda A. Complications of posterior cranial fossa surgery – an institutional experience of 500 patients. Surg Neurol. 2009;72:369–75.

Fugate JE. Complications of neurosurgery. Continuum (Minneap Minn). 2015;21(5 Neurocritical Care):1425–44.

Hirono S, Kawauchi D, Higuchi Y, Setoguchi T, Kihara K, Horiguchi K, Kado K, Sato M, Fukuda K, Nakamura T, Saeki N, Yamakami I. Life-threatening intracranial hypotension after skull base surgery with lumbar drainage. J Neurol Surg Rep. 2015;76:e83–6.

Magro E, Graillon T, Lassave J, Castinetti F, Boissonneau S, Tabouret E, Fuentes S, Velly L, Gras R, Dufour H. Complications related to endoscopic endonasal transsphenoidal approach for nonfunctioning pituitary macroadenomas in 300 consecutive patients. World Neurosurg. 2016;89:442–53.

Mahaney KB, Todd MM, Bayman EO, Torner JC, IHAST Investigators. Acute postoperative neurological deterioration associated with surgery for ruptured intracranial aneurysm: incidence, predictors, and outcomes. J Neurosurg. 2012;116:1267–78.

Patil CG, Lad EM, Lad SP, Ho C, Boakye M. Visual loss after spine surgery: a population-based study. Spine (Phila Pa 1976). 2008;33:1491–6.

Pham MH, Tuchman A, Platt A, Hsieh PC. Intracranial complications associated with spinal surgery. Eur Spine J. 2016;25:888–94.

Sayegh ET, Fakurnejad S, Oh T, Bloch O, Parsa AT. Anticonvulsant prophylaxis for brain tumor surgery: determining the current best available evidence. J Neurosurg. 2014;121:1139–47.

Skardelly M, Brendle E, Noell S, Behling F, Wuttke TV, Schittenhelm J, Bisdas S, Meisner C, Rona S, Tatagiba MS, Tabatabai G. Predictors of preoperative and early postoperative seizures in patients with intra-axial primary and metastatic brain tumors: a retrospective observational single center study. Ann Neurol. 2015;78:917–28.

Zanaty M, Chalouhi N, Starke RM, Clark SW, Bovenzi CD, Saigh M, Schwartz E, Kunkel ES, Efthimiadis-Budike AS, Jabbour P, Dalyai R, Rosenwasser RH, Tjoumakaris SI. Complications following cranioplasty: incidence and predictors in 348 cases. J Neurosurg. 2015;123:182–8.

Hemodynamic Complications After Neurosurgery

78

Jeffrey Yoder, Umeshkumar Athiraman, and René Tempelhoff

Neurogenic Pulmonary Edema

Overview

Neurogenic pulmonary edema (NPE) may result following multiple different types of neurologic injury and results in significant morbidity and mortality in affected patients. Insults such as traumatic brain or spinal cord injury, intracranial hemorrhage, intracranial hypertension, epileptic seizure, and SAH are all associated with the development of NPE. Tachypnea, tachycardia, hypoxemia, and diffuse bilateral pulmonary infiltrates are typical findings. Pulmonary vascular congestion, accumulation of protein-rich alveolar fluid, and intra-alveolar hemorrhage often result in significant hypoxemia. Treatment is primarily supportive.

NPE usually happens during the initial 24–48 h after injury and is usually a self-limited phenomenon. Multiple pathophysiologic mechanisms have been proposed, although this process is not completely understood. Trigger zones consisting of specific vasomotor centers have been identified in the brainstem and hypothalamus. Injury to these regions and increased ICP are thought to elicit NPE through destabilization of pulmonary autonomics, massive catecholamine surge, and release of other vasoactive substances. Rapid sympathetic activation, as well as increased pulmonary capillary permeability, results in intra-alveolar exudates. Neurogenic stunned myocardium and cardiac failure may also contribute to the formation of pulmonary edema in some patients.

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Prevention

There are no proven prophylactic measures to prevent NPE in man. In laboratory animals, lesions which produce NPE are much less likely to do so when the animal is concurrently anesthetized with high concentrations of volatile anesthetics. It is possible that tight hemodynamic control and blunting of the response to catecholamines may limit the generation of NPE. Treatment of the underlying condition (such as surgical clipping of an aneurysm) may also improve NPE outcome.

Crisis Management (Table 78.1)

Key Points

- NPE may be elicited by multiple different injuries to the CNS.
- Significant hypoxemia may develop, and morbidity is high.
- Treatment is supportive.

Table 78.1 Presentation/assessment/intervention

Presentation	Assessment	Intervention
Tachycardia	Check vital signs	Treatment is supportive
Tachypnea/ dyspnea	Arterial blood gas – hypoxemia is the most common finding	Supplemental oxygen and mechanical ventilation if required
Hypoxemia	Chest X-ray – typically diffuse bilateral infiltrates	Hemodynamic support as necessary
Respiratory failure	Differentiate from other causes of pulmonary edema. Consider TTE to assess cardiac function	Self-limited, expect clearance within 24–48 h. Rule out other etiology if the edema persists after 48 h. NPE is mostly a diagnosis of exclusion
	Assess need for mechanical ventilation	

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Pulmonary Embolism

Overview

Patients undergoing craniotomy or major spine surgery are at increased risk for the development of deep venous thrombosis (DVT) and venous thromboembolism (VTE). Specific risk factors include immobility secondary to neurologic deficit and/or prolonged surgery, malignancy, advanced age, venous stasis, and avoidance of pharmacologic DVT prophylaxis due to concern of increased risk of bleeding. A state of relative hypercoagulability has been described following many neurologic events.

The reported incidence of lower extremity DVT and VTE varies based on patient population, risk factors, type of screening, and presence and type of prophylaxis. DVT is unfortunately quite common in the neurosurgical patient population with a reported incidence as high as 20–40% during hospital stay. Clinically significant VTE is more rare, with a reported incidence of <5% in most studies, although it is thought that the majority of VTE are "silent." Practices that support the routine use of PICC lines also observe an increased frequency of DVT and VTE in the upper extremity.

Prevention

Various prophylactic measures against DVT are employed in hospitalized patients. Commonly used techniques include elastic stockings, intermittent pneumatic compression (IPC) devices, subcutaneous unfractionated heparin, and low-molecular-weight heparin. Elastic stockings and IPCs are generally the only prophylactic measures taken during the perioperative period due to concerns that heparin could increase the risk of bleeding. In recent meta-analysis of mixed neurosurgical patients, IPCs appear of similar efficacy to low-molecular-weight heparin in prevention of VTE during the immediate perioperative period. However, it is likely that patients with multiple risk factors might benefit from a combined regimen. During surgery, patients should be positioned such that venous return is not impeded (avoidance of excessive flexion of the hips/knees in prone patients). Postoperatively medical prophylaxis should be resumed as soon as it is deemed safe to do so by the surgical team. Concerns about the appropriate timing of pharmacologic thromboprophylaxis remain particularly high for patients after intracranial hemorrhage due to their high risk for both rebleeding and thrombus formation. Currently, clinical practice of DVT prophylaxis in this patient population is guided by personal experience rather than by scientific evidence, secondary to a paucity of reliable data. The avoidance of PICC lines in the absence of pharmacologic prophylaxis may be an important consideration to reduce the incidence of upper extremity DVT.

Crisis Management (Table 78.2)

Key Points

- Neurosur.gical patients are at high risk for DVT.
- IPC and/or compression stockings are the most commonly employed prophylaxis during the perioperative period.
- Clinically significant VTE present with hypoxemia and tachycardia.
- IVC filter placement should be considered in patients with VTE and DVT, given bleeding risk from early anticoagulation.

Table 78.2 Presentation/assessment/intervention

Presentation	Assessment	Intervention
Tachycardia	Check vital signs	Supportive care
Tachypnea/dyspnea	Assess oxygenation and ventilation, check for change in $ETCO_2$ in intubated patients	Supplemental oxygen and/or mechanical ventilation as necessary
Hypoxemia	ABG – typically shows hypoxemia. $PaCO_2$ may be significantly higher than $EtCO_2$	Hemodynamic support if required
Increased gradient between $EtCO_2$ and $PaCO_2$	Differentiate from other causes of hypoxemia including pulmonary edema, atelectasis, etc.	Consider IVC filter placement (particularly if LE venous Doppler studies demonstrate clot)
Anxiety	Chest X-ray – often negative in PE	Consider anticoagulation (heparinization) depending upon type and duration out from surgical procedure
Hemodynamic instability	PE protocol CT (or V/Q scan in patients with significant renal impairment)	Consider intravascular clot retrieval by skilled interventional radiologist
	Consider lower extremity Doppler's (may influence decision for early IVC filter if positive)	

Blood Pressure Dysregulation

Overview

Blood pressure lability is common in postoperative neurosurgical patients and may result from a variety of neurogenic, cardiogenic, or systemic causes. Emergence hypertension, pain, and agitation are common. Cushing's response to raised ICP or cerebral ischemia can result in significant increases in blood pressure. Patients with spinal cord lesions whether acute (spinal shock) or chronic (autonomic hyperreflexia) may develop blood pressure instability in the perioperative period. Seizures may result in labile blood pressures. Following carotid endarterectomy (CEA), many patients experience blood pressure dysregulation, as a result of baroreceptor dysfunction. Hypertension is a dreadful complication post CEA due to the increased risk of reperfusion injury.

Systemic causes of hemodynamic instability are numerous and include hypovolemia, anemia, and pulmonary embolism. Myocardial infarction, arrhythmias, and cardiac failure can also present with significant hemodynamic instability.

Careful attention to blood pressure must always be paid in order to ensure adequate perfusion pressure to critical organs such as the brain and myocardium, but hypertension cannot be allowed to go unchecked. Emergence from anesthesia is frequently accompanied by postoperative hypertension and cerebral hyperemia. There is a significant association between postoperative hypertension and intracranial hemorrhage; thus this response should be controlled by beta-blockers and other antihypertensives.

Prevention

Postoperative blood pressure lability may be limited by careful intraoperative management of blood pressure, volume status, and hematocrit. Significant emergence hypertension should prompt early treatment with beta-blockers (which have the advantage of not effecting ICP) and other antihypertensives, as well as effective treatment of pain and agitation. Dexmedetomidine has shown promise in preliminary studies in reducing hypertensive events in the perioperative period in patients undergoing craniotomy.

Crisis Management (Table 78.3)

Key Points

- Postoperative blood pressure instability can present secondary to multiple neurogenic or cardiac causes.
- Blood pressure should be carefully regulated in the postoperative period to ensure effective perfusion to organs and reduce the risk of hemorrhage.

Table 78.3 Cause/assessment/intervention

Cause	Assessment	Intervention
Pain	Check vital signs, neurologic assessment, and pain score	Supportive care for patient
Agitation	Assessment of volume status, recent drugs administered, hematocrit	Identify and treat underlying cause (if possible)
Emergence hypertension	Consider underlying etiology – neurogenic, cardiogenic, metabolic	Antihypertensive therapies
Elevated ICP		β blockade (i.v. esmolol 10–50 mg, metoprolol 1–5 mg, labetalol 5–20 mg)
Cerebral ischemia		Hydralazine (5–15 mg i.v.)
Seizure		Nicardipine (0.25–2 mcg/kg/min i.v. infusion)
Spinal cord injury		Antihypotensive therapies
Baroreceptor dysfunction		Treat significant bradycardia with anticholinergics
Essential hypertension		Ephedrine (5–10 mg i.v.)
Drug effect		Phenylephrine (0.25–2 mcg/kg/min i.v. infusion) Caution in the context of bradycardia
Hypovolemia/anemia		Norepinephrine (0.02–0.2 mcg/kg/min i.v. infusion)
Myocardial infarction/cardiac failure		
Arrhythmia		
Pulmonary embolism		

Bradycardia

Overview

Bradycardia is frequently noted in neurosurgical patients during the perioperative period. Identification of cause is important for effective therapy. This response may be elicited by multiple neurogenic, cardiac, or metabolic factors.

The conditions which elevate the intracranial pressure such as tumor, edema, intracranial hemorrhage, or acute hydrocephalus can result in brain herniation which may result in the Cushing's triad of bradycardia, hypertension, and irregular respiration. Bradycardia may also occur in association with spinal cord injury (SCI), such as acute spinal shock secondary to transection of sympathetic pathways or autonomic dysreflexia in chronic SCI patients. Bradycardia may also be seen with seizures and can be triggered via reflex pathways such as the baroreceptor or trigeminal cardiac reflex.

Cardiac etiologies of bradycardia may include nodal or conduction deficits, as well as other arrhythmias. Myocardial ischemia and cardiac failure can also precipitate bradycardia. Metabolic causes are numerous. Many drugs may produce bradycardia through direct or indirect effects. Electrolyte disturbances may be precipitated by diuretics or hyperosmolar therapy. Endocrine disorders such as hypothyroidism may also contribute to bradycardia.

Prevention

As significant bradycardias are not infrequent in neurosurgical patients, resuscitative drugs, particularly atropine, should always be readily available. Patients at high risk for such complications include those after surgeries on/and around the brain stem or the cerebral pontine angle and those after endovascular carotid stenting. In high-risk cases or when bradycardias are frequently noted, prophylactic administration of anticholinergics such as glycopyrrolate may be beneficial.

Crisis Management (Table 78.4)

Key Points

- Bradycardia is frequent and has multiple potential etiologies in neurosurgical patients.
- Bradycardia may be a sign of impeding clinical deterioration of the patient.
- Treatment involves identifying cause, anticholinergics, and pacing in refractory cases.

Table 78.4 Cause/assessment/intervention

Cause	Assessment	Intervention
Increased ICP	Check vital signs, including BP and oxygenation, and neurologic assessment	Anticholinergics (e.g., glycopyrrolate 0.2–1.0 mg IV or PO; atropine 1 mg i.v. for significant bradycardia) – avoid lower doses in adult patients due to risk of paradoxical bradycardia
Edema		
Hemorrhage		
Hydrocephalus	Check rhythm strip (p wave, narrow/wide complex)	
Pneumocephalus (tension)		
Vagal	Evaluate for cause	Support hemodynamics and oxygenation
Spinal cord injury	Drug administration	Identify/treat underlying cause (if possible)
Cardiac, nodal/ conduction deficits	Reflex	Consider temporary pacing (transvenous) in refractory cases
Drug effect	Cardiac	
Metabolic	Increased ICP	
	Consider imaging (head CT)	

Myocardial Infarction

Overview

Postoperative myocardial infarction (MI) is fortunately a rare event. Often affected patients have preexisting medical comorbidities such as coronary artery disease or its risk factors such as smoking, diabetes, or others. Coronary insufficiency can lead to infarction when stress of surgery is superimposed. Independent of surgery, severe brain injury states may also cause significant elevations in catecholamines which can precipitate ischemia and infarction. EKG changes suggestive of myocardial injury or stress occur in up to 80% of patients following subarachnoid hemorrhage. While these patients often exhibit elevation of cardiac enzymes and regional wall motion abnormalities, this form of myocardial injury is more commonly neurogenic stress cardiomyopathy than traditional myocardial infarction. The myocardial dysfunction will recover within 2–4 weeks. Neurogenic cardiomyopathy is associated with non-coronary distribution wall motion abnormalities, diffuse ST changes on EKG and takotsubo's appearance of the left ventricle.

In patients with risk factors or known coronary artery disease, preoperative optimization is often limited to medical therapies. Invasive coronary interventions typically require anticoagulation and wait times for stent stabilization. Given the often urgent nature of neurosurgery and the risk of significant complications with surgical bleeding, coronary intervention may not be feasible or able to effectively reduce risk. These limitations can also complicate management of active myocardial ischemia in the patient immediately postop

from brain or spine surgery. Furthermore in patients with preexisting coronary stents, perioperative discontinuation of aspirin and/or clopidogrel may precipitate acute coronary syndromes from in-stent thrombosis.

Prevention

Guidelines for preoperative cardiac evaluation are published by the American Heart Association and frequently updated. Currently, diagnostic testing (such as stress testing) is recommended only in high-risk patients, and only if results will significantly affect the surgical decision or perioperative management. Urgent surgeries generally should be delayed for medical optimization in patients with active cardiac conditions such as myocardial ischemia, decompensated heart failure, or significant arrhythmias. Patients with a history of coronary artery disease should be evaluated to ensure that they are medically optimized, such as effective beta-blockade and heart rate control. Perioperatively, patients with significant risk of cardiac ischemia should be carefully monitored and their hemodynamics aggressively controlled. Prevention of tachycardia and maintenance of an effective blood pressure are the primary goals.

Crisis Management (Table 78.5)

Key Points

- In neurosurgical patients, preoperative cardiac optimization is predominantly medical.
- Avoidance of tachycardia and maintenance of adequate coronary perfusion pressure are primary goals to prevent myocardial ischemia.
- Beta-blockade and other supportive care are first-line therapies.

Treatment of MI in the early postoperative period with antiplatelet agents and heparinization is complicated by the increased risk of bleeding.

Table 78.5 Presentation/assessment/intervention

Presentation	Assessment	Intervention
Chest pain and/or dyspnea	Check vital signs with attention toward HR, BP, and oxygenation	Limit tachycardia – treat pain, β blockade as tolerated (i.v. metoprolol)
ECG abnormalities (ST segment depression or elevation)	Obtain 12 lead ecg	Ensure adequate oxygenation
Hemodynamic instability	Obtain labs for serum troponin-I, Hgb/Hct, and electrolytes	Ensure an adequate blood pressure (for coronary and cerebral perfusion)
Arrhythmia or cardiac failure		Consider nitrates (however, these may increase CBF and ICP in at risk patients)
		Early cardiology consultation for discussion of anticoagulation and/or invasive intervention

Hypovolemia

Obviously the results of intentional fluid restriction during the surgery compounded by the use of osmotic diuretics such as mannitol usually manifest itself in the postoperative period by relative hypotension and tachycardia. It can also be due to other etiologies such as insufficiently compensated intraoperative blood loss and other rarer conditions, but requiring attention are the onset of diabetes insipidus and cerebral salt-wasting syndrome. In general, adequate amount of intravenous fluids should be given in the postoperative period to prevent extreme hypovolemia in an effort to maintain an adequate cardiac output and optimal cerebral blood flow. However, in patients whose elastance curve of the brain is already overwhelmed, any fluid therapy will only worsen the situation. This is particularly true after treatment of subarachnoidal hemorrhage that is often followed by a dangerous period of vasospasm of the vessel bearing the aneurysm or even in a different territory. This complication is best managed by increasing both the intravascular volume and the cerebral perfusion pressure in an attempt to "push" the CBF.

Diabetes Insipidus

Overview

Central or neurogenic diabetes insipidus (DI) is a condition characterized by the excessive excretion of dilute urine in the presence of normal or high plasma osmolality. It is caused either by the decreased secretion or action of AVP (arginine vasopressin) also called ADH (antidiuretic hormone). ADH is produced in the supraoptic and paraventricular nuclei of the hypothalamus and stored in the posterior lobe of the pituitary gland for release when needed. DI after neurological surgery can be transient or permanent and may be caused by various conditions affecting the hypothalamus and posterior pituitary unit. Early diagnosis and management of DI is critical as it might lead to severe dehydration, hypovolemia, and hypotension if left untreated.

Table 78.6 Presentation/assessment/intervention

Presentation	Assessment	Intervention
Large amount of very dilute urine	Hourly urine measurement in the perioperative period. 24-h urine collection for the determination of urine volume is the gold standard	Early intervention with isotonic fluids such as normal saline until the patient is euvolemic and then plasma osmolality is corrected with hypotonic IV fluids (5% dextrose in water/half normal saline)
	Serum electrolytes for sodium concentration: elevated	Serum sodium should be corrected slowly at the rate of 0.5 mEg/l every hour
	Urine specific gravity: 1.005 or less	Desmopressin is the drug of choice and alternatives include synthetic vasopressin. Desmopressin (DDAVP) can be administered through different routes, namely, by nasal inhalation, IV, SC injection, or oral tablet. The doses usually range from 1 to 2 μg qd or bid by injection, 10–20 μg bid or tid by nasal spray, or 100–400 μg bid or tid orally
	Plasma/urine osmolality: greater than 287 mOsm/kg/ less than 200 mOSm/kg	

Prevention

There are no proven ways to prevent DI. Having a high suspicion when dealing with patients who are at risk and treating them promptly is important in preventing hemodynamic complications.

Crisis Management (Table 78.6)

Key Points

- DI can occur after multiple neurological interventions.
- DI can result in significant hemodynamic instability.
- Prompt diagnosis and treatment of DI is critical.

Cerebral Salt-Wasting Syndrome (CSW)

Overview

It is a disorder of sodium and water homeostasis caused by cerebral disease in the setting of normal kidney function. It can be caused by several conditions such as subarachnoid hemorrhage, head trauma, intracranial or metastatic neoplasm, carcinomatous or infectious meningitis, encephalitis, and central nervous system surgery. It is characterized by hyponatremia in association with hypovolemia. This condition has to be differentiated from syndrome of inappropriate antidiuretic hormone (SIADH) as both conditions share many clinical and laboratory findings and the treatment is entirely different. The mechanism beyond CSW is not clear, but the following are postulated: (1) disruption of sympathetic neural input to the kidney and (2) natriuresis induced by natriuretic peptides. Prompt diagnosis and treatment of CSW is essential as it might lead to severe hemodynamic complications.

Table 78.7 Presentation/assessment/intervention

Presentation
Polyuria, dehydration, and hypotension
Signs of hyponatremia: lethargy, apathy, disorientation, muscle cramps, anorexia, agitation
Assessment
Urinary sodium level >40 mEg/l
Urinary osmolality: high
Serum osmolality: low
Central venous pressure: low
Extracellular fluid volume: low
Brain natriuretic peptide level: high
Intervention
Isotonic or hypertonic solutions are given to treat the hyponatremia based on the acuity and the level of symptom presentation
Rapid correction of serum sodium >12 mmol/d should be avoided
Fludrocortisone (0.1–1 mg/day) a mineralocorticoid has been used to restore the extracellular fluid volume status

Prevention

There are no proven ways to prevent CSW. Prompt diagnosis and treatment of the patients at risk is important in preventing hemodynamic complications.

Crisis Management (Table 78.7)

Key Points

- CSW can occur after multiple neurological interventions.
- It is essential to differentiate between the CSW and SIADH as the management is different.
- Prompt diagnosis and treatment of CSW is critical to avoid significant hemodynamic instability.

Suggested Reading

Adamczyk P, He S, Amar AP, Mack WJ. Medical management of cerebral vasospasm following aneurysmal subarachnoid hemorrhage: a review of current and emerging therapeutic interventions. Neurol Res Int. 2013;2013:462491.

Agrawal A, Timothy J, Cincu R, Agarwal T, Waghmare LB. Bradycardia in neurosurgery. Clin Neurol Neurosurg. 2008;110:321–7.

Bekker A, Sturaitis M, Bloom M, Moric M, Golfinos J, Parker E, et al. The effect of dexmedetomidine on perioperative hemodynamics in patients undergoing craniotomy. Anesth Analg. 2008;107:1340–7.

Busl KM, Bleck TP. Neurogenic pulmonary edema. Crit Care Med. 2015;43(8):1710–5.

Collen JF, Jackson JL, Shorr AF, Moores LK. Prevention of venous thromboembolism in neurosurgery. Chest. 2008;134:237–49.

Fleisher LA, Beckman JA, Brown KA, Calkins H, Chaikof E, Fleischmann KE, et al. ACC/AHA 2007 guidelines on perioperative cardiovascular evaluation and care for noncardiac surgery: a report of the American College of Cardiology/American Heart Association task force on practice guidelines. Circulation. 2007;116:e418–99.

Goma HM, Ali MZ. Control of emergence hypertension after craniotomy for brain tumor surgery. Neurosciences (Riyadh). 2009;14(2):167–71.

Jeraq M, Cote DJ, Smith TR. Venous thromboembolism in brain tumor patients. Adv Exp Med Biol. 2017;906:215–28.

Loscalzo J, Kasper D, Jameson J, Hauser S, Fauci A, Longo D. Harrison's principles of internal medicine 19/E (vol 1 & vol 2). Part 16: Endocrinology and Metabolism: McGraw-Hill Professional Publishing; 2015.

Momi J, Tang CM, Abcar AC, Kujubu DA, Sim JJ. Hyponatremia-what is cerebral salt wasting? Perm J. 2010;14(2):62–5.

Schubert A. Cardiovascular therapy of neurosurgical patients. Best Pract Res Clin Anaesthesiol. 2007;21:483–96.

Sedy J, Zicha J, Kunes J, Jendelova P, Sykova E. Mechanisms of neurogenic pulmonary edema development. Physiol Res. 2008;57:499–506.

Stoneham MD, Thompson JP. Arterial pressure management and carotid endarterectomy. Br J Anaesth. 2009;102:453–62.

Endocrinologic Emergencies After Neurosurgery

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Ola Harrskog and Robert E. Shangraw

Overview

Severe and potentially life-threatening endocrine conditions in neurosurgical patients most often are secondary to dysfunction of the hypothalamic-pituitary-adrenal axis. The pituitary gland, frequently called the "master endocrine gland," is confined within a bony space – the sella turcica – and is subdivided, both anatomically and functionally, into anterior (anterior pituitary) and posterior (neurohypophysis) components. The anterior pituitary has a vulnerable portal blood supply. The posterior portion connects to the hypothalamus via long sensitive nerve endings. This arrangement makes the pituitary especially susceptible to traumatic brain injury, brain edema, space-occupying intracranial lesions, and surgery.

Hormones secreted by the pituitary regulate metabolic homeostasis, fluid and electrolyte balance, and circulatory stability. The anterior pituitary secretes six hormones: growth hormone, adrenocorticotropic hormone (ACTH), thyroid-stimulating hormone (TSH), follicle-stimulating hormone (FSH), luteinizing hormone, and luteotropic hormone. Control of the anterior pituitary comes from the hypothalamus, via releasing factors secreted into the hypothalamic-hypophyseal portal system. There is a negative feedback control system, by which end products of anterior pituitary activity inhibit corresponding stimulatory hormone secretion by anterior pituitary and the upstream releasing factor secretion by the hypothalamus, to maintain homeostasis. ACTH released from the anterior pituitary stimulates the adrenal cortex to release cortisol and to a much lesser extent mineral corticosteroid (aldosterone) and androgen dehydroepiandrosterone (DHEA). Circulating cortisol feeds back to both the pituitary and hypothalamus to reduce stimulatory activity. Cortisol is vital to cellular homeostasis and metabolism and is needed for both catecholamine-mediated and angiotensin-mediated maintenance of vascular tone, which is essential for hemodynamic stability.

The posterior pituitary secretes antidiuretic hormone (ADH), also known as vasopressin, and oxytocin. Its function is more directly regulated by the hypothalamus through neural connections. Through ADH secretion, the posterior pituitary (neurohypophysis) regulates both intravascular volume and serum osmolarity. ADH is a nonapeptide which acts on aquaporin 2 in the renal collecting tubule to increase water permeability and, in turn, retain water from the urinary space (antidiuretic effect). Physiologic control of ADH secretion is maintained via osmoreceptors located in the hypothalamus that increase ADH secretion in response to hyperosmolarity (most often hypernatremia). ADH plays a vital role in maintaining salt and water balance. ADH also has direct vasoconstrictor activity and is an effective non-catecholamine pressor agent when administered in pharmacological dosage. Its role in maintaining normal vascular tone under physiological conditions is less clear.

Anterior Pituitary Insufficiency

Severe illness, trauma, or other insults trigger a metabolic "stress" response, mediated in large part by the neuroendocrine system. Under some circumstances, the stress response can be maladaptive and may need to be inhibited. During anesthesia, the stress response may be altered if not prevented.

Adrenal insufficiency, the inability to mount an appropriate level of cortisol secretion, can be relative or absolute. An intact hypothalamic-pituitary-adrenal axis, with cortisol as the centerpiece, is essential to maintaining stable hemodynamics during stress. Patients who receive pre-existing glucocorticoid treatment are at risk for developing an absolute adrenal insufficiency secondary to adrenal gland atrophy. If, as in most cases, the glucocorticoid supplement is low, it cannot provide the higher glucocorticoid concentration needed during a stress state. Less common causes of absolute adrenal insufficiency are congenital adrenal

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hypoplasia or destruction of the adrenal gland secondary to infection (e.g., Addison's disease) or surgery. The common endpoint of these conditions is an inability to increase cortisol production in response to stress.

Relative adrenal insufficiency is associated with critical illness, especially sepsis, and with head trauma, systemic inflammatory response, advanced age, and certain drugs. Among drugs associated with relative adrenal insufficiency, the sedative-hypnotic etomidate deserves special mention. Since its US release in 1972, etomidate has been known to attenuate the hypercortisolemic response to surgery. Although it was initially thought to produce a "stress-free" surgery, etomidate directly inhibits cortisol synthesis by the adrenal gland. Etomidate infusion in the intensive care unit is associated with increased mortality secondary to adrenal suppression, and even a single induction dose of etomidate can suppress cortisol secretion for 4–12 h. Etomidate exposure is an important risk factor for relative adrenal insufficiency in critically ill, septic patients, and is associated with higher mortality in these patients unless supplemental steroids are administered. Physiological doses of glucocorticoids improve outcome in septic patients, but supraphysiological doses provide no definite advantage. For non-septic high-risk patients, the value of any glucocorticoid administration on outcome is less clear.

Incidence

Adrenal insufficiency, as indexed by cortisol response, has an incidence of 30–40% in the general critically ill population and about 25% after traumatic brain injury. The underlying medical condition and the magnitude of stress stimulus are important for defining relative risk.

Prevention

Patients with a history of current or recent (within 2 months) glucocorticoid therapy should be considered at risk for relative adrenal insufficiency, even if signs or symptoms are absent. A daily dose of prednisolone 7.5 mg, or its equivalent, for 2 weeks or longer is sufficient to suppress the adrenal stress response; and hyporesponsiveness can persist for 2 months after steroid therapy has been discontinued. Depending on the anticipated stress event, one should consider supplemental prophylactic glucocorticoid administration ("stress steroids"). Reasonable choices before major surgery are hydrocortisone 100 mg q 8 h × 3 doses or dexamethasone 8–10 mg with the same dosing regimen.

Clinical Presentation

An unstressed patient with an underlying adrenal insufficiency may be asymptomatic, with no revealing signs. Clinical signs, if present, are constitutional and vague: asthenia, muscle weakness, anorexia, abdominal pain, or other referred gastrointestinal complaints. More pronounced insufficiency can lead to hypoglycemia, hyponatremia, and/or hyperkalemia. The electrolyte abnormalities may induce severe muscle weakness.

Diagnosis of a relative adrenal insufficiency, where the signs and symptoms are vague, requires a high level of suspicion. Superimposition of physiological stress (e.g., trauma, infection, surgery) or sudden cessation of chronic steroid intake can trigger an acute crisis. In an acute adrenal crisis, the patient often develops a profound and refractory hypotension in addition to muscle weakness and hypoglycemia. Hypotension in this setting is due to a confluence of impaired catecholamine synthesis, hyporesponsive beta-adrenoreceptors, and an inability of vascular smooth muscle to contract in response to either circulating catecholamines or angiotensin. Differential diagnosis of refractory arterial hypotension without obvious cause should include suspicion of acute adrenocortical insufficiency.

Patient Assessment

A random cortisol concentration level is the definitive diagnostic test. The serum specimen should be collected before empirical steroid therapy commences; otherwise, timing is not important. Critically ill patients do not exhibit predictable diurnal cycling of cortisol secretion. In general, a cortisol value >35 μg/dL is normal in the critically ill patient with normal adrenal function, whereas a value <15 μg/dL is consistent with adrenal insufficiency. Intermediate results may indicate further testing. If the results are borderline, the corticotrophin stimulating test may help to identify patients who may benefit from chronic glucocorticoid supplements. Serial measurements of serum electrolytes and glucose concentrations are indicated to detect hyponatremia, hyperkalemia, and/or hypoglycemia. Urine electrolytes concentrations are also useful because high urine sodium excretion may occur despite functional hypovolemia. An arterial blood gas will reveal whether there is an accompanying metabolic or respiratory acidosis.

Crisis Management

Treatment of an acute Addisonian crisis is often empirical because the turnaround time for serum cortisol analysis is often on the order of 24 h. Hydrocortisone 100 mg IV q 8 h or dexamethasone 10 mg IV q 8 h are both good choices. Hemodynamic support, fluid administration, and vasopressor(s) are given as necessary. Other potential causes for hypotension, such as myocardial dysfunction (ischemia, infarction) or sepsis, should be evaluated and ruled out. If hypotension is, in fact, precipitated by adrenal insufficiency, the patient will become quickly responsive to inotropes such as ephedrine or epinephrine within an hour after steroid supplementation.

If it appears that a critically ill patient may have an adrenal insufficiency, treatment with stress doses of hydrocortisone

should be given. Patients with suspected relative adrenal insufficiency should be treated with titrated doses, i.e., in most nonseptic patients, the equivalent of dexamethasone 2–10 mg should suffice. Because cortisol is much more potent as a glucocorticoid than as a mineralocorticoid, the volume deficit in patients with adrenal crisis is rarely more than 10% of the total body water. Normal saline is the usual fluid for volume expansion. Hypoglycemia, which is usually mild, is treated by titration of glucose 5% added to the normal saline infusion.

Monitoring

Frequent electrolyte, glucose, and arterial blood gas measurements are important. Invasive hemodynamic monitoring via arterial line and central venous line may be necessary to guide treatment in unstable patients.

Posterior Pituitary (Neurohypophysis) Dysfunction

Posterior pituitary dysfunction most often presents as disorders of water and salt balance. These are common in patients with traumatic brain injury or disease in the area of the hypothalamus and the pituitary gland. Dysfunction of the neurohypophysis can result in either overproduction or underproduction of ADH. Some extracranial diseases, such as pulmonary diseases (e.g., oat cell carcinoma) or extraneural neoplasms, are associated with ectopic production of ADH. Three conditions have important implications for salt and water homeostasis in patients with cerebral disease processes: diabetes insipidus (DI), syndrome of inappropriate ADH secretion (SIADH), and cerebral salt-wasting syndrome (CSWS). It is extremely important to recognize these conditions and their pathophysiology early to maximize the potential for recovery.

Diabetes Insipidus (DI)

DI is a syndrome characterized by polyuria, polydipsia, and excessive thirst. Patients with DI experience excessive loss of free water into the urine causing increased concentration of solutes throughout the body and hemodynamic instability secondary to hypovolemia. DI is divided into two subtypes, (1) nephrogenic and (2) central (or neurogenic).

Nephrogenic DI is due to failure of the kidney to appropriately respond to physiological levels of ADH in the circulation and involves dysfunction of aquaporin 2, the intrinsic receptor that increases renal collecting tubule permeability to water. Central DI, the more common subtype in the neurosurgical patient, results from insufficient ADH secretion by the posterior pituitary gland.

Normally, up to 12% of glomerular filtrate is reabsorbed under the influence of ADH. Complete absence of ADH results in profound loss of free water (~20 L/24 h) into the urine, leading to polyuria of extremely low urine osmolality. ADH deficiency is more commonly incomplete, with volume of hypotonic urine 5–10 L/24 h. DI is usually transient but can be permanent.

Incidence

Transient DI after traumatic brain injury occurs in up to 50% of patients and is permanent in up to 10% of all cases. After transsphenoidal hypophysectomy, 18% of patients are affected at least transiently, and 2% require long-term treatment. In general, any prolonged episode of increased intracranial pressure, such as intracranial hemorrhage or a tumor, can impair ADH secretion by the neurohypophysis, independent of etiology.

Clinical Presentation

Onset of polyuria is usually sudden after trauma, regional surgery, or sella radiotherapy. If the patient is awake and alert, this will manifest as polydipsia. If the patient is not fully conscious, however, inadequate fluid intake may result in hypovolemia and hypernatremia. Replacement of lost water with a balanced intravenous salt solution leads to apparent sodium accumulation, and serum hypernatremia worsens. Severe hypernatremia induces central nervous system dysfunction, presenting progressively as delirium, confusion, somnolence, and finally coma. Marked interindividual variability in CNS response to hypernatremia precludes assigning trigger sodium concentrations at which specific symptoms will occur. Caution should be exercised during correction of hypernatremia because too rapid correction of hyperosmolality can produce cerebral edema.

Patient Assessment

Fulminant DI produces copious and very hypotonic (50–200 mOsm/kg) urine. Incomplete DI is still characterized by polyuria, but urine sodium concentration can be high (up to 700 mOsm/kg), especially if the patient is hypovolemic and/or if intravenous saline has been given. The most important finding is that urine osmolality is inappropriately low compared to plasma osmolality (ratio less than 2). If plasma Na >145 mmol/L and plasma osmolality >300 mOsm/kg, in concert with diluted polyuria (>3.5 L/24 h), the most likely diagnosis is DI. Free water deficit can be estimated by the equation: Water deficit = 0.6 × premorbid weight (− kg) × (1 – 140/[Na]mEq/L).

The definitive test to discern central DI from nephrogenic DI is to assay serum ADH concentration. ADH is low in central DI but normal in nephrogenic DI (Table 79.1).

Table 79.1 Summary of differences in volume status and laboratory tests in the postoperative time period in neurosurgical patients

Dysfunction	Body water (fluid status, CVP)	Urine output	Serum-[Na^+]	Urine-[Na^+]	Serum-[ADH]
CSWS	↓	↑	↓	↑	↑ or →
SIADH	↑ or →	↓ or →	↓	↑	↑
Central DI	↓	↑↑	↑	↓ or →	↓
Nephrogenic DI	↓	↑↑	↑	↓ or →	↑ or →

CSWS cerebral salt-wasting syndrome, *SIADH* syndrome of inappropriate release of antidiuretic hormone release, *DI* diabetes insipidus, ↓ lower than normal, ↑ higher than normal, → no difference from normal

Crisis Management

Interventional goals are to (1) correct intravascular volume and total body water deficits, (2) replace ongoing water losses, (3) reduce ongoing water losses, and (4) prevent hyperosmolality. Given these guidelines, treatment is individualized based on the severity and anticipated duration of the dysfunction. In an awake patient with an intact thirst mechanism (with free access to water), observation and monitoring may suffice.

If DI is prolonged or diuresis outstrips practical oral water intake, modified ADH (desmopressin, DDAVP) is the agent of choice to restore more normal renal water reabsorption. DDAVP can be administered by oral, nasal, or intravenous route. For acutely ill patients, parenteral administration is preferred, and the recommended dose is 1–4 μg q 8–12 h. Alternatively, unmodified vasopressin may be used, to help retain free water, but its short half-life limits utility.

Intravenous fluid replacement should maximize free water and limit sodium concentration because the goal is to compensate for loss of free water. Aqueous glucose (D5%W) is usually the first choice in patients who cannot take in adequate oral fluid to cover the losses and deficits. Careful glycemic management is warranted to prevent iatrogenic hyperglycemia risking consequent brain injury.

Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

SIADH is a condition of excessive ADH secretion. High ADH concentration in plasma pathologically increases renal free water reabsorption, leading in turn to hypervolemia and hyponatremia. Concomitant renal sodium excretion may be normal or increased. The neurohypophysis is the source of excessive ADH secretion in disease states such as intracranial infection, trauma, bleeding, or infection. Alternatively, tumors of extra-neural origin, such as oat cell lung carcinoma, can also be a pathologic ectopic source of ADH.

Incidence

In patients suffering traumatic brain injury, the incidence of SIADH is reported to be 2.3–37%. Single case series place the incidence of SIADH at 12.8% after transsphenoidal hypophysectomy and 6.9% after major spine surgery.

Clinical Presentation

CNS manifestations of SIADH-induced hyponatremia are usually mild as long as plasma Na^+ concentration >125 mmol/L. Plasma Na^+ concentration <120 mmol/L is associated with increased risk of pronounced CNS signs and symptoms. The mildest presentation is headache, which may progress to nausea, confusion, coma, and seizures. The sensitivity of patients to hyponatremia depends in large part to the speed with which it unfolds. Very rapid progression of hyponatremia raises the risk of cerebral edema and its consequent events. Some individuals may tolerate a chronic serum sodium concentration <115 mmol/L without clinical symptoms if the onset is gradual, such as over months.

Patient Assessment

Patients with SIADH have hypotonic hyponatremia in context with urine osmolality greater than plasma osmolality. Sodium excretion in urine exceeds 20 mmol/L, while serum osmolality is <280 mOsm/kg. Circulatory instability is unlikely unless the patient has a history of congestive heart failure, which could be exacerbated by hypervolemia. Symptomatic hyponatremia is typically produced by coincidence of overhydration (positive 6–8 L) and a sodium deficit of 200–400 mmol.

Crisis Management

The treatment strategy depends upon presence or absence of clinical manifestations. If the patient is asymptomatic, the condition is treated by fluid restriction and identification of precipitating factor(s). If CNS manifestations are present, serum sodium concentration must be increased to target approximately 130 mmol/L, but at a rate less than or equal to 1–2 mmol/L/h. Normal (0.9%) saline or hypertonic saline 3% is administered to correct hyponatremia at a rate that does not exceed urinary losses. Too rapid correction of hyponatremia carries the risk of brain demyelination (central pontine myelinolysis) . On the other hand, if the patient has seizures, it is important to treat not only the seizures but also to begin prompt treatment of cerebral edema and a more rapid correction of hyponatremia, usually with bolused hypertonic saline 3%. Mannitol (500 mL, 20%) is a reasonable alternative to increase serum osmolality in the setting of seizures. A recent addition to the therapeutic armamentarium to consider is administration of vasopressin receptor antagonist (e.g., conivaptan), to increase plasma free water content, although clinical experience with this class of drug to date is limited.

Cerebral Salt-Wasting Syndrome (CSWS)

CSWS also causes hyponatremia in patients suffering neurological disease. CSWS and SIADH have many similar laboratory characteristics. They differ, however, in that patients with SIADH are euvolemic or slightly hypervolemic, whereas those with CSWS are hypovolemic. The molecular mechanism by which CSWS causes excessive urinary sodium loss in the setting of intracranial disease is unclear. One hypothesis is that as-yet unidentified natriuretic factor(s) is/are released by the injured or dysfunctional brain. Candidates for the diuretic factor include atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP). Circulating ADH concentration is normal in patients with CSWS, in contrast to elevated ADH concentration in patients with SIADH.

Incidence

The incidence of CSWS following traumatic brain injury is 0.8–34.6%, but remains unknown in other clinical states.

Clinical Presentation

CSWS usually appears in the 1st week after a brain insult, whether trauma, tumor, infection, or surgery. It usually persists for a few weeks and is self-limited. Clinical characteristics are polyuria, increased urinary sodium loss, hyponatremia, and hypovolemia. Differentiating between SIADH and CSWS can be challenging, but must be established before beginning clinical treatment.

Patient Assessment

The main clinical challenge is to distinguish CSWS from SIADH. Plasma ADH concentration in CSWS is either within normal limits or may be increased as part of the physiological response to hypovolemia. Distinguishing features of the syndromes affecting salt and water balance are summarized in Table 79.1.

Crisis Management

Once the diagnosis of CSWS is made, treatment goals are to maintain adequate fluid hydration plus replace sodium losses. This regimen contrasts from treatment of SIADH, the other major etiology featuring hyponatremia, which restricts fluid intake, perhaps coupled with promoting free fluid loss with vasopressin antagonist (vaptan - class) therapy. Vaptans are contraindicated in the setting of CSWS. Exacerbating the pre-existing hypovolemia of CSWS, either by limiting fluid intake or pharmacologically stimulating free water loss, risks hypoperfusing an already compromised brain. Hypovolemia-induced mechanisms of worsened CNS status are cerebral vasospasm, ischemic cerebral infarction, or myocardial ischemia and secondary diminished cardiac output leading to systemic hypoperfusion. Since a major endpoint of CSWS therapy is to preserve or expand intravascular volume, invasive hemodynamic monitoring including arterial and central venous pressure (CVP) monitoring may be indicated, even if the patient appears to be hemodynamically stable. Concomitantly, hyponatremia must be corrected, with either isotonic or hypertonic (3%) saline infusion. Infusions should be guided by frequent measures of plasma electrolyte concentrations. Severe CSWS may indicate addition of a mineralocorticoid supplement to the treatment plan.

Key Points

- The hypothalamic-pituitary-adrenal axis underlies most critical endocrine conditions in the neurosurgical patient.
- Stress increases the requirement for cortisol, and stressed patients at risk for insufficient cortisol response should receive glucocorticoid supplement.
- Short-term steroid treatment has few negative effects and may be life-saving in the neurosurgical population.
- The patient at risk for adrenal insufficiency with circulatory instability should be treated empirically with steroids.
- Patients with intracranial injury should have serum electrolytes, urine electrolytes, plasma glucose, body weight, and water balance monitored frequently to detect postoperative endocrine problems early.

Suggested Reading

Aditya S, Rattan A. Vaptans: a new option in the management of hyponatremia. Int J Appl Basic Med Res. 2012;2(2):77–83.

Bloomfield R, Noble DW. Etomidate, pharmacological adrenalectomy and the critically ill: a matter of vital importance. Crit Care. 2006;10(4):16. https://doi.org/10.1186/cc5020.

Capatina C, Paluzzi A, et al. Diabetes insipidus after traumatic brain injury. J Clin Med. 2015;4(7):1448–62.

Cardoso AP, Dragosavac D, et al. Syndromes related to sodium and arginine vasopressin alterations in post-operative neurosurgery. Arq Neuropsiquiatr. 2007;65(3B):745–51.

Clapper A, Nashelsky M, et al. Evaluation of serum cortisol in the postmortem diagnosis of acute adrenal insufficiency. Am J Forensic Med Pathol. 2008;29(2):181–4.

Cooper MS, Stewart PM. Corticosteroid insufficiency in acutely ill patients. N Engl J Med. 2003;348(8):727–34.

Cotton BA, Guillamondegui OD, et al. Increased risk of adrenal insufficiency following etomidate exposure in critically injured patients. Arch Surg. 2008;143(1):62–7; discussion 67.

Dumont AS, Nemergut EC 2nd, et al. Postoperative care following pituitary surgery. J Intensive Care Med. 2005;20(3):127–40.

Gibson SC, Hartman DA, et al. The endocrine response to critical illness: update and implications for emergency medicine. Emerg Med Clin N Am. 2005;23(3):909–29, xi.

Jackson WL Jr. Should we use etomidate as an induction agent for endotracheal intubation in patients with septic shock?: a critical appraisal. Chest. 2005;127(3):1031–8.

Leonard J, Garrett RE, et al. Cerebral salt wasting after traumatic brain injury: a review of the literature. Scand J Trauma Resusc Emerg Med. 2015;23:98. https://doi.org/10.1186/s13049-015-0180-5.

Mohammad Z, Afessa B, et al. The incidence of relative adrenal insufficiency in patients with septic shock after the administration of etomidate. Crit Care. 2006;10(4):R105. https://doi.org/10.1186/cc5020.

Nemergut EC, Dumont AS, et al. Perioperative management of patients undergoing transsphenoidal pituitary surgery. Anesth Analg. 2005;101(4):1170–81.

Nielsen S, Chou C-L, et al. Vasopressin increases water permeability of kidney collecting duct by inducing translocation of aquaporin-CD water channels to plasma membrane. Proc Natl Acad Sci U S A. 1995;92(2):1013–7.

Powner DJ, Boccalandro C. Adrenal insufficiency following traumatic brain injury in adults. Curr Opin Crit Care. 2008;14(2):163–6.

Schneider HJ, Kreitchmann-Andermahr I, et al. Hypopituitary dysfunction following traumatic brain injury and aneurismal subarachnoid hemorrhage: a systematic review. JAMA. 2007;298(12):1429–38.

Tanriverdi F, Schneider HJ, et al. Pituitary dysfunction after traumatic brain injury: a clinical and pathological approach. Endocr Rev. 2015;36(3):305–42.

Ullian ME. The role of corticosteroids in the regulation of vascular tone. Cardiovasc Res. 1999;41(1):55–64.

Venkataraman S, Munoz R, et al. The hypothalamic-pituitary-adrenal axis in critical illness. Rev Endocr Metab Disord. 2007;8(4):365–73.

Verbalis JG. Management of disorders of water metabolism in patients with pituitary tumors. Pituitary. 2002;5(2):119–32.

Zaloga GP, Marik P. Hypothalamic-pituitary-adrenal insufficiency. Crit Care Clin. 2001;17(1):25–41.

Postoperative Paralysis, Skin Lesions, and Corneal Abrasions After Neurosurgery

80

Martin H. Dauber and Steven Roth

Postoperative Paralysis

Overview

Paralysis is the loss of voluntary control of skeletal muscle function caused by failure of nerve conduction of electrical impulse. This can occur centrally or be a result of peripheral nerve problems, and the differential diagnosis is critical in the postoperative period. Paralysis following intracranial surgery may be anticipated as a result of resection of tumor in proximity to the motor cortex. Similarly, following peripheral nerve resection, an element of local paralysis may manifest.

Preexisting paresis or paralysis poses the greatest risk factors for paralysis presenting in the PACU. Many of these patients will indeed be weak or paralyzed after the surgery. A preanesthetic history and physical should thoroughly document the degree of neurologic impairment of all patients. This is particularly so in neurosurgical spine and intracranial procedures where, due to their typical long duration, it is common for the anesthesia team present upon emergence to be different from the team which started the case.

It is rare to have any paralysis in the PACU patients, in general, and the incidence may be higher in patients following neurosurgery. This elevated risk is due to three primary factors:

1. Location and nature of surgical site
2. Patient position during surgery (full or partially prone, sitting, lateral, etc.)
3. Long duration

The location of surgery may increase the risk for central paralysis, whereas the other factors may elevate risk for peripheral neuropathies. It is these peripheral neuropathies that are most under the control of the anesthesiologist.

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Prevention

Surgical attention to the possibility of paralysis both in the head and in the spine is the key to preventing the paralysis seen in the PACU that is related to surgical site. Details of this are beyond the scope of anesthesia practice, except in the broadest sense. Peripheral neuropathies leading to paralysis, however, are very much the concern of anesthesiologists. Although studies have failed to confirm with scientific certainty the relationship of positioning to peripheral neuropathies, the American Society of Anesthesiologists issued a practice advisory for the prevention of perioperative neuropathies.

Crisis Management and Assessment

Immediate diagnosis of paralysis upon emergence is the shared responsibility of the nurses caring for the PACU patient as well as of the neurosurgical and anesthesia teams. Centrally related paralysis needs to be differentiated from peripherally caused problems. Timely diagnosis is critical in these cases as certain causes indicate immediate surgical intervention. As soon as the finding of paresis or paralysis is revealed, both the surgeons and anesthesiologists need to be aware; the surgeons so they can pursue diagnosis or reexploration and the anesthesiologists so they can facilitate the emergency anesthetic.

Peripheral neuropathies are less likely to be surgical emergencies, unless they are as a result of arterial embolic phenomenon. Accordingly, the affected extremity must be examined for pulses, pain, and pallor.

Hemodynamic stability and oxygenation status are always important in the PACU and even more so in the patient who may be required to go back to the operating room. Raising systemic arterial blood pressures to the high end of normal may increase perfusion to neural cells at ischemic risk, thereby protecting them and minimizing permanent injury. In the setting of presumed spinal cord injury, as the cause of new paralysis/paresis, high-dose corticosteroids have been

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advocated by many, though there is little evidence upon which to base this. Methylprednisolone 30 mg/kg intravenously bolused over 15 min followed by a 23 h infusion of 5.4 mg/kg/h is the recommended dose.

Key Point

- Postoperative paralysis is a potentially devastating complication of neurosurgical procedures that may first manifest in the PACU. Central or surgical field-related etiologies are the most likely, though peripheral neuropathies can cause more localized paralysis. Anesthesiologists must be aggressive in the maintenance of hemodynamics and oxygen-carrying capacity to prevent further deterioration of paresis or paralysis. Operating room care and early PACU diagnosis in the event of problems can lead to improved outcomes.

Anemia and electrolyte imbalance must be aggressively addressed to rule out these as causes or contributing factors. Aggressive transfusion of red blood cells should be performed to raise hemoglobin concentrations over 10 g/dL, although the critical hematocrit has not been determined for this patient population. Depending on neurosurgical impressions, emergency imaging, such as MRI, may be indicated, and this may require the presence of the anesthesiologist if the patient has not made adequate progress toward recovery.

Skin Lesions

Overview

Dermatologic complications following neurosurgical procedures seem to occur with higher frequency than following surgery to other systems. However, there is sparse literature to support this impression. Since skin lesions can be painful, alarming for patients and others to see, and potential sources of infection, they can be troublesome. Nonetheless, skin problems following these cases can be divided into three broad categories:

1. Minor abrasions
2. Deep dermal damage
3. Complete skin disruption

Most of these injuries occur through excess pressure over long time periods. Iatrogenic skin disruption during removal of electrodes or tape may also occur. This section discusses these various types of injuries and their diagnosis and treatment.

Presentation and Treatment

In the PACU after the basic recovery issues are handled; the nurse who performs the complete secondary survey will identify any dermal lesions. Additionally patients may complain of pain or burning sensation at affected areas. Erythema, bleeding, and tenderness may be present. In cases of complete skin disruption due to the skin's adherence to tape or the like, immediate diagnosis is important, as salvage of autogenous skin is possible. If the removed skin can be located, it should rapidly be cleaned and then replaced in situ and secured with staples and sutures. A loose Vaseline dressing can then be applied. Infection is extremely rare eliminating the need for prophylactic antibiotics.

Prevention

Neurosurgical procedures are often performed in positions that put patients at risk for dermal damage and have a long duration, further exacerbating any problems. Intraoperative attention to positioning can be the most protective mechanism against perioperative skin changes. Soft surfaces should be provided in any area of contact with the patient and bed, supports, or other equipment. Pressure at boney prominences should be minimized as much as possible. Many use gel-filled pads where contact pressure is high, such as under the iliac crests and knees in prone patients. There are many pillows and other devices to position the head for prone cases that are nonabrasive, in addition to the other purported benefits. The female breasts should be positioned midline toward the head to allow adequate perfusion which primarily comes from the internal thoracic and internal mammary arteries.

Anesthesiologists often use tape and adhesives that may cause complete skin disruption upon removal. Additionally, neurosurgical patients are often subject of peripheral neurological monitoring, and neurophysiologists need to be attentive to this risk. Some patients, such as the elderly or those with "fair skin," may be more susceptible.

Key Point

- Skin lesions can be a nuisance-type complication following any surgery, and neurosurgical patients seem to be at higher risk. Proper equipment to aid positioning and meticulous attention to the comfort of the anesthetized patient as well as protection of the skin may decrease the incidence. Visible skin lesions never threaten life but can cause disfigurement that is permanently bothersome to the patient who suffers this problem.

Corneal Abrasions

Overview

A corneal abrasion is a painful scrape or scratch of the surface of the clear part of the eye known as the cornea. This transparent window covers the iris, the circular-colored portion of the eye. The cornea has many nerve endings just under the surface, so that any disruption of the surface may be painful. Anytime a foreign body contacts the eye, an abrasion is a possibility, particularly under general anesthesia when the eye does not have its protective reflexes. Corneal abrasions may also occur during anesthesia when the eye is not taped closed properly and the cornea becomes dry because the patient will not blink during anesthesia. The true incidence of corneal abrasions is not well documented for neurosurgical patients, but due to the exposure of the face and eyes to potential contact, it is assumed to be higher than for non-neurosurgical patients. In addition, during craniotomy or during prone cases, the anesthesiologist is unable to monitor the eyes during the case to make sure the eyes remain completely closed during the entire case. Some patients also experience an itching sensation in their eyes upon awakening. In an attempt to alleviate the discomfort, the still drowsy patient may try rubbing the eyes, which can easily result in corneal damage. The neuroanesthesiologist should be aware of any preexisting vision-related problems.

Crisis Management

Presentation

Following a neurosurgical procedure, a patient may complain of:

1. Sensation of a foreign body in the eye
2. Tearing of the eyes
3. Blurred vision or distortion of vision
4. Photophobia, especially to bright lights
5. Spasm of the periocular muscles causing squinting

Any or all of these findings should lead to consideration of the possibility of a corneal abrasion. Although many advocate for immediate ophthalmologic evaluation, this can be difficult in some settings especially later in the evening when many neurosurgical cases are arriving in PACU.

Assessment

There are two principal parts of the diagnosis of corneal abrasion:

1. Ruling out the presence of a foreign body
2. Fluorescein ophthalmoscopic examination of the cornea

Patients with corneal abrasions will be in pain, and this may make a proper examination difficult. The clinician must be relentless in his pursuit of diagnosis, nonetheless. The use of topical 1% tetracaine to the eye prior to exam has been recommended but has been associated with the potential for worse healing. The upper and lower eyelids must be inverted and the fossae inspected. Then with either a drop of ophthalmic fluorescein (0.25%) or a fluorescein strip applied to the eye, an examination of the cornea can be performed under cobalt blue-filtered light. An abrasion will show as a disruption of the regular smooth surface of the cornea.

Management

If a foreign body is present on the eye, removal by irrigation may be possible. If not readily performed, emergency ophthalmologic consultation should be sought. In the case of a corneal abrasion:

1. Antibiotic eyedrops or ointment (such as erythromycin, tobramycin, or ciprofloxacin) may be applied. Some ophthalmologists advocate the addition of steroids to reduce inflammation and to avoid potential scarring.
2. The eye should not be patched. Recent evidence shows that patching the eye does not help and may actually have a negative impact on the healing process.
3. Mydriatics are no longer indicated.
4. Analgesics appropriate to patient's overall postoperative condition.
5. Follow-up examination by ophthalmologist after 24 h to assess the degree of healing and prognosticate about potential long-term sequellae.

Prevention

It is probably more true of the prevention of corneal abrasions that of many other iatrogenic injuries, that concern for the potential is the cornerstone of prevention. Many techniques have been advocated over the years, yet none has proven itself. Taping of the eyes early in peri-induction period may decrease the eyes' exposure to foreign bodies such as ID tags, endotracheal tube pilot balloons, or laryngoscopes.

For craniotomies many use lubricants (lanolin based) to protect the corneas as well as to dilute any surgical prep solution that may enter under the tape. For prone cases where large volume shifts may occur, some use hypertonic 3% saline ointment (e.g., Muro 128). Transparent adhesive medical dressings (e.g., Tegaderms) are occasionally put over the eyes for their protection, but skin abrasions have been noted. There is no foolproof method for absolute prevention that is standard of care.

Key Points

- Corneal abrasions can be bothersome to patients emerging from neurosurgical procedures. Although the incidence is low, these patients may be at higher risk because of the non-face-up positions that they may be in. Most anesthesia-related corneal abrasions heal within 24 h though rarely can persist ophthalmoscopically for 3–4 months. Attention to prevention and rapid treatment and analgesia can improve the care of these patients.
- Although many anesthesia-related complications are noted in the operating room during the administration of general anesthesia, some are not noted until later. During emergence from anesthesia in the PACU, major complications such as paresis or paralysis and minor ones such as corneal abrasions and skin lesions may manifest. Rapid attention to these complications can prevent further deterioration and possibly good outcomes.

Suggested Reading

Cheney FW, Domino KB, Caplan RA, Posner KL. Nerve injury associated with anesthesia. Anesthesiology. 1999;90:1062–9.

Roth S, Thistead RA, Erickson JP, Black S, Schreider BD. Eye injuries after nonocular surgery; a study of 60,965 anesthetics from 1988–1992. Anesthesiology. 1996;85:1020–7.

Postoperative Pain Management in Patients After Neurosurgical Operations

81

Mary Newton and Tacson Fernandez

Introduction

Despite the diversity of neurosurgical procedures and the multiplicity of pain presentations in this population, effective and safe pain relief is possible for the vast majority of patients.

Sound knowledge of the underlying pathophysiology relating to the specific neurosurgical condition and an understanding of the associated complications are essential for optimizing safe post-operative analgesia.

Many neurosurgical conditions are highly dynamic. A decrease in the Glasgow Coma Scale (GCS) must be carefully investigated as many neurosurgical complications may require urgent surgical and/or therapeutic intervention (Table 81.1). A deterioration in GCS must not be attributed solely to a relative opioid 'overdose' until other causes have been excluded.

Analgesia for major spinal surgery may be especially challenging. Many of these patients suffer from chronic pain and may present with a combination of nociceptive and neuropathic pain. A significant number of these patients may be on opioid medication and/or a combination of drugs preoperatively, which may have effects on cognitive function, alertness, and wake-up times following anaesthesia. Acute on chronic pain is typically more difficult to manage than isolated acute pain.

Neuraxial opioids, alone or in combination with local anaesthetics, can be very effective following spinal surgery. However, the approach requires careful considerations; neuraxial local anaesthetic/opioids may be contraindicated if there is a significant risk of an intraoperative dural tear which could result in unpredictable amounts of local anaesthetic/opioid reaching the cerebrospinal fluid (CSF). In some centres, administration of opioids (particularly those that are long-acting and water soluble) into the CSF would commit the patient to high dependency (HDU) care post-operatively. Additionally, local anaesthetic-induced motor block may mask neurological deterioration secondary to spinal cord compression by, for example, haematoma or tissue swelling. If this analgesic technique is used, it is imperative that the patient is monitored by nursing staff familiar with its use in this specialized population of patients. There must be a strict local protocol for action to be taken in the event of onset of reduced limb power.

Increasing or uncontrolled pain post-operatively requires reassessment and consideration of alternative causes (Table 81.2), for example, a surgical complication or neuropathic pain.

Table 81.1 Common causes of post-operative/post-procedure decrease in GCS

Common neurosurgical conditions	Potential causes of decreasing Glasgow Coma Scale (GCS)
Subarachnoid haemorrhage (SAH) (post-clipping/ post-coiling)	Re-bleed
	Acute hydrocephalus
	Cerebral vasospasm
	Seizure
Traumatic brain injury (TBI)	Reaccumulation of haematoma
	Haemorrhage into contusion
	Oedema
	Seizure
Craniotomy	Haematoma (subdural/ intracerebral, etc.)
	Oedema
	Seizure
	Air encephalocoele
	Infection – e.g. meningitis, etc.

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Table 81.2 Post-operative complications which may increase pain

Complication	Cause of pain
Subarachnoid haemorrhage (SAH) (post-clipping/ post-coiling)	Re-bleed
	Hydrocephalus
	Infection
Traumatic brain injury (TBI)	Wound infection
	Reaccumulation of haematoma
Craniotomy	Haematoma (e.g. subdural/ intracerebral)
	Air encephalocoele
	Low ICP headache/CSF leak
	Infection – e.g. meningitis
Spinal decompression/fusion	Nerve root compression by disc remnant/haematoma/oedema
	Neuropraxia (C2 root especially common)
	Infection
	Malpositioned instrumentation
	Muscle spasm
Intradural/intramedullary spinal cord surgery	Wound infection
	Haematoma formation
	Meningitis
	Low ICP headache/CSF leak

Prevention

Pain is the fifth vital sign and requires regular evaluation in combination with appropriate intervention to maximize pain relief. Effective management of acute post-operative pain reduces the incidence of chronic pain; additionally, it aids early mobilization and may decrease morbidity associated with immobility (e.g. venous thrombosis and pulmonary atelectasis). Education of patients and clinical staff is vital to optimize acute post-operative pain management.

Pain Scores

Pain is a subjective experience and most measures of pain are based on self-report. Numerous pain scales exist. Descriptive scales, where pain is described as 'none, mild, moderate or severe' are easy to use. Numerical scores are less easy to use but are more accurate at assessing the response to an intervention. The most popular numerical scale is the visual analogue score (VAS); it consists of a 100 mm line where 0 mm correlates with no pain and 100 mm correlates with 'worst pain possible'. The patient is asked to mark the line to 'score' their pain. VAS ratings of >70 mm are indicative of 'severe pain'. *Because of the subjective nature of pain scales, most clinicians may have observed patients who report very high pain scores but who, at the same time, do not demonstrate typical physiological evidence of pain (e.g. tachycardia, hypertension).*

Education

Education of patients preoperatively can help to reduce anxiety, post-operative pain, and other associated symptoms. Ideally, it should begin preoperatively with information about the planned surgical procedure, expected pain relating to it, the hospital's pain-scoring system (see below), and the importance of effective analgesia to aid early mobilization to reduce the clinical risks associated with immobility. Patients should be made aware of the analgesic modalities available to them; this information will need to be reinforced repeatedly in the preoperative and early post-operative phase.

All clinicians involved in the post-operative care of neurosurgical patients need ongoing education in acute pain management and specific considerations for this patient group. Familiarity with the operative procedure and associated complications is particularly important. Clinical staff must be familiar with the hospital's pain-scoring system and the application of this to optimize analgesia. Standardized prescriptions for analgesia used in conjunction with frequent assessment of pain scores can improve post-operative pain management.

Recommended Analgesic Regimes

The World Health Organization (WHO) pain ladder (Fig. 81.1) describes a simplistic guide to the optimization

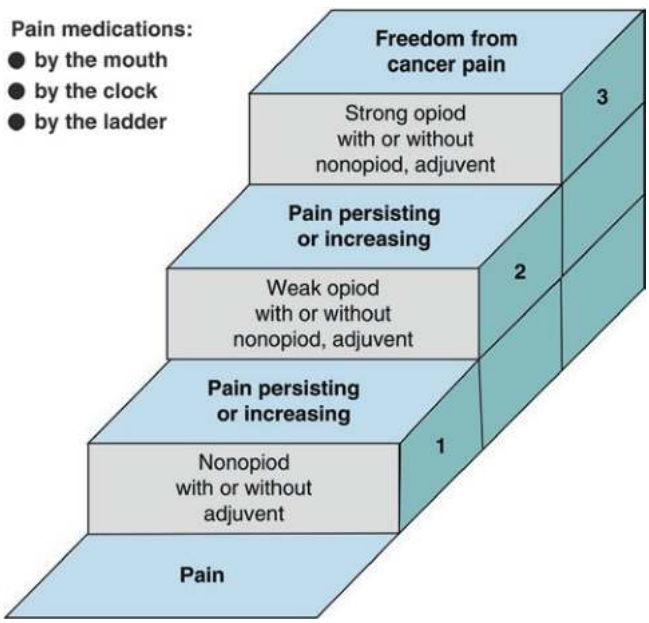

Fig. 81.1 WHO pain ladder. (Source: www.who.int/cancer/palliative/painladder/en)

Table 81.3 Guidelines for multimodal analgesia following *intracranial surgery* – timing and analgesic considerations

Post-operative period	Recommended analgesia (aim for pain score ≤3)	Analgesic considerations	Evaluation of analgesia
Immediate (1–60 min)	Intravenous (i.v.) paracetamol +/− i.v. morphine	Severe pain post-craniotomy refractory to paracetamol and small amounts of i.v. morphine should prompt formal exclusion of complications	Frequent reassessment of
	Remember adjuncts (e.g. position, cool packs)		Pain score
			Response to intervention
			Re-evaluate analgesic doses
Early (60 min–6 h)	Regular i.v. paracetamol 1 g 6-hourly	Paracetamol i.v. 6-hourly for first 48 h post-op for painful surgery	Frequent reassessment of
	Regular oral or PCA morphine	Continuing severe pain – exclude complications	Pain score
	Remember adjuncts (e.g. position, cool packs)		Response to intervention
			Re-evaluate analgesic doses
Intermediate (>6–24 h)	Regular i.v. paracetamol 1 g 6-hourly	Paracetamol i.v. 6-hourly for first 48 h post-op for painful surgery	Frequent reassessment of
	Oral or PCA morphine	∗*NSAIDs* see particular cautions relating to use in neurosurgical patients	Pain score
	Remember adjuncts (e.g. position, cool packs)	Continuing severe pain – exclude complications	Response to intervention
	Consider regular: oral/rectal/i.v. NSAIDs∗		Re-evaluate analgesic doses
Late (>24 h)	Regular i.v. paracetamol 1 g 6-hourly	Paracetamol i.v. for first 48 h post-op for painful surgery	Frequent reassessment of
	Oral or PCA morphine	∗*NSAIDs* see particular cautions relating to use in neurosurgical patients	Pain score
	Remember adjuncts (e.g. position, cool packs)	Continuing severe pain – exclude complications	Response to intervention
	Consider regular: oral/rectal/i.v. NSAIDs∗	Consider introduction gabapentin 100 mg three times/day or pregabalin 25 mg twice daily and titrate according to response	Re-evaluate analgesic doses
	+/− gabapentin		Reduce analgesia as pain improves (opioids first)

of analgesia. Urgent action is required for patients in severe pain which frequently requires all three steps of the pain ladder to be initiated simultaneously, in combination with pharmacological adjuncts (Tables 81.3 and 81.4) and non-pharmacological adjuncts (e.g. reassurance, explanation of the cause of the pain and the intended management of it, careful positioning, cool/warm packs, and eye shades). Prompt action in the provision of good pain relief reduces anxiety. Anxiety is known to exacerbate pain.

Table 81.5 is a guide to appropriate post-operative prescribing of multimodal analgesia in our unit where commonly performed neurosurgical procedures are categorized according to the *predicted* pain (VAS) in the post-operative period. Details of the timed introduction of multimodal analgesia for intracranial surgery are shown in Table 81.3 and for non-intracranial surgery in Table 81.4.

Preventive Analgesia

This describes a reduction in post-operative pain following the administration of a drug that has an effect longer than the expected duration of that agent. There is no evidence to support the best timing of this therapy in the perioperative period. The use of NMDA receptor antagonists has been advocated as preventive analgesic regime in the context of abdominal, gynaecological, orthopaedic, and dental surgery. However, general concerns remain regarding the use of ketamine in neurosurgical patients because of its effect on intracranial pressure. Studies have suggested a similar benefit following the use of gabapentin which would be more suitable in the context of neurosurgical interventions. Likewise pregabalin has also been found to be beneficial. Scalp blocks may provide effective and long-standing analgesia post-craniotomy; they are safe and simple to perform. As mentioned above, great care needs to be taken with the use of neuraxial opioids and local anaesthetic in spinal surgery. Potential preventive analgesic therapies that could be considered in expected 'Major' and 'Complex Major Pain' patient groups are shown in Table 81.6.

Relative Contraindications for Commonly Used Analgesics in the Neurosurgical Population

NSAIDs

The use of NSAIDs in neurosurgical patients is controversial. There are no published studies about their use in this

Table 81.4 Guidelines for multimodal analgesia following *non-intracranial surgery* – timing and analgesic considerations

Post-op period and recommended analgesia (aim for pain score ≤3)	Analgesic considerations	Evaluation of analgesia
Immediate (1–60 min)	*Midazolam* – useful post-spinal surgery if other analgesia unsuccessful. Use very low dose (0.5 mg) and be aware of intense synergism with opioids	Frequent reassessment of
Intravenous (i.v.) paracetamol	*Clonidine* – slow i.v. increments (15 μg) to maximum 150 μg. Monitor BP carefully	Pain score
+/− i.v. morphine	*Ketamine* – dysphoria unlikely with very low bolus dose (0.1 mg/kg)	Response to intervention
If severe pain persists consider	*Dexamethasone* (4–8 mg) – may be helpful for acute neuropathic pain. Continue 4 mg four times daily for 48 h. Caution in diabetes	Re-evaluate analgesic doses
Low-dose midazolam		Severe pain?
Clonidine		Consider post-op complications
Low-dose ketamine		
For acute neuropathic pain consider		
Dexamethasone		
Early (60 min–6 h)	As above	As above
As above but substitute i.v. morphine for regular oral *or* PCA morphine	*Paracetamol* i.v. 6 hourly for first 48 h post-op for painful surgery	
Intermediate (6–24 h)	As above	As above
As above	∗ *NSAIDs* see particular cautions relating to use in neurosurgical patients (above)	
Consider regular	*Gabapentin* – depending on age start at 100–300 mg three times daily or pregabalin at 75–150 mg/twice daily	
Oral/rectal/i.v. NSAIDs∗	*Clonidine* – start at 50–100 μg orally twice daily	
If severe pain persists consider		
Gabapentin		
Clonidine		
Late (24 h)	As above	As above
As above	*Benzodiazepine* – low dose for 48–72 h, e.g. oral diazepam 2 mg three times daily	Severe pain?
If high opioid requirement consider switching to slow-release formulation		Consider post-op complications
Consider regular		Consider reduction in analgesia as pain improves (opioids first)
Oral benzodiazepine for muscular wound pain		

Table 81.5 Some common neurosurgical procedures are listed according to the *predicted* pain (VAS) in the post-operative period to guide appropriate post-operative prescribing of multimodal analgesia

Predicted pain scores without analgesia	Examples of surgical procedures in this category	Regular paracetamol (acetometophen)	Regular NSAID[a]	Regular oral or PCA morphine	'Rescue' opioid if required	Consider pharmaceutical adjunct (Table 81.4)
Minor pain (VAS 1–3)	Carpal tunnel	Yes	Yes	No	Yes	No
Intermediate pain (VAS 3–6)	Craniotomy/lumbar microdiscectomy	Yes (i.v. first 24 h post-op)	≥6 h[a] post-op	Yes	Yes	No
Major pain (VAS 7–10)	Lumbar/cervical laminectomy	Yes (i.v. first 48 h post-op)	≥6 h[a] post-op	Yes (if no PCA consider slow-release morphine preparation)	Yes (not with PCA)	No
Complex major pain (VAS 7–10)	Posterior spinal fusion, thoracic discectomy	Yes (i.v. first 48 h post-op)	≥6 h[a] post-op	Yes (if no PCA consider slow-release morphine preparation)	Yes (not with PCA)	Yes

[a]If no neurosurgical or medical contraindication

population. Theoretically, they increase the risk of post-operative bleeding due to their inhibitory effect on platelet function; thus neurosurgeons have great concerns regarding their use, particularly in the context of craniotomies and spinal surgery. Following elective supra-tentorial surgery, it is highly unusual for patients to present with an intracranial

Table 81.6 Preventive analgesic therapies that could be considered in expected 'Major' and 'Complex Major Pain' patient groups

Timing of adjunct	Dosage guidelines	Precautions
Preoperative	Gabapentin 2 h pre-op 200–600 mg single dose/ pregabalin 75–150 mg single dose	High-dose *gabapentin/pregabalin* may cause drowsiness. Dose reduction in renal failure
	(Titrate dose according to age, weight)	
	Ketamine – not for intracranial surgery	*Ketamine* – not for intracranial surgery
	5 min before skin incision – (0.1–0.5 mg/kg)	Psychosis not usually a problem with low-dose ketamine
	Local anaesthetic block (LA)	LA – see notes in 'Overview'
Intraoperative	*Ketamine* – not for intracranial surgery	*Ketamine* – not for intracranial surgery
	(0.1–0.25 mg/kg repeated at 1 h intervals)	Psychosis not usually a problem with low-dose ketamine
	Local anaesthetic block (LA)	LA – see notes in 'Overview'
Post-operative	Gabapentin in three divided doses at 200–1800 mg/day or pregabalin in two divided doses at 25–150 mg/day (titrate dose according to age, weight)	Gabapentin/pregabalin – dose reduction in renal failure. Continue for 2 weeks to 1 month post-op. Wean off over 2 weeks
	Caution in renal failure	
	Ketamine – not for intracranial surgery	*Ketamine* – not for intracranial surgery
	Avoid if possible in all patients post-op	Psychosis not usually a problem with low doses
	(10–50 mg orally three times daily)	

haematoma if they have regained their preoperative status by 6 h post-surgery. In our institution, we have applied this finding to our entire neurosurgical population and introduce NSAIDs after 6 h, if the post-operative course of any type of elective surgery has been uncomplicated and there is nothing to suggest a clotting disorder. Introduction of NSAIDs may be delayed in high-risk cases (e.g. spinal cord tumours, large meningioma resections, and 'deep brain' surgery).

Another concern with the use of NSAIDs is possible impairment of bone fusion (through interference with the complex regulatory system of bone formation that includes prostaglandins) which could be significant following spinal fusion. There is no evidence in humans to support this.

Opioids

If used in doses just sufficient to relieve pain, they will not significantly affect respiratory drive, thus avoiding an increase in $PaCO_2$ with consequent effects on increasing ICP.

Careful titration is the key to the safe use of opioids. Following craniotomy very small doses may be highly effective (e.g. 1–2 mg morphine repeated if necessary at 5 min intervals in the immediate post-operative phase followed by 5–10 mg orally at later stages). This is in contradistinction to patients in the 'Major' and 'Complex Major Pain' categories who invariably require much higher doses.

Patient-controlled analgesic (PCA) devices have been used successfully without complication following craniotomy and subarachnoid haemorrhage. For the use of morphine-PCA, some practitioners suggest low 4 h limits (e.g. 15 mg) and re-evaluate the patient before further dose increase. Patients after major spinal surgery frequently benefit from additional oral slow-release morphine preparations as supplementation of the PCA treatment due to more extensive pain levels; however, this requires a high level of patient supervision, such as an HDU environment. End-tidal CO_2-feedback-control PCA devices have been introduced in an attempt to improve patient safety when opioid self-administration is desired.

Crisis Management

Nociceptive Pain

Severe nociceptive pain is easier to treat than severe neuropathic pain. Whenever severe pain is present, the cause of the pain should be actively sought. There should be a low threshold for further investigation, if it persists or is difficult to control. In the late post-operative phase, this may require admission to an HDU for rapid control of pain by intravenous boluses of opioids and other adjuncts.

Neuropathic Pain

Neuropathic pain is classically described as aching, burning, shooting, or stabbing. It may be paroxysmal or spontaneous with no precipitating cause and may be associated with hyperalgesia or allodynia. It may be a new phenomenon post-operatively or an exacerbation of pre-existing neuropathic pain. It can be very difficult to relieve. Although classically resistant to opioids, these should be tried to assess whether they are of any benefit. Dexamethasone (4 mg four times daily for 48 h) can be effective in the early post-operative phase, if oedema of nerve roots is thought a probable cause. There should be a low threshold to the intro-

duction of gabapentin/pregabalin or amitriptyline if significant neuropathic pain persists. Carbamazepine is the most effective treatment for trigeminal neuralgia (sometimes exacerbated following microvascular decompression) but has a poor side effect profile. There are successful reports of the use of intranasal sumatriptan in refractory cases of trigeminal neuralgia (caution should be exercised in patients with ischaemic heart disease).

Neuropathic pain following spinal cord injury and brachial plexus avulsion is common and can be severe. There is evidence to support benefit from opioids, ketamine infusion, and intravenous lidocaine. The latter two have to be administered in an HDU environment. Benzodiazepines may contribute to the management of refractory pain. Their use should be strictly short term and over-sedation and its attendant risks avoided.

Side Effects of Treatment

Constipation, nausea, and so on are common post-operatively. They should be anticipated and active measures taken to prevent them. Several analgesics have sedative effects on the patients, particularly opioids. Awareness of the possible confounding effects of the analgesic treatment on mental status and neurologic presentation is of paramount importance in the perioperative management of neurosurgical patients. Overmedication with analgesics may result in differential diagnostic problems, which should trigger an immediate neurologic evaluation and frequently require emergency CT imaging of the cranium.

Key Points

- Acute pain management education of patients/clinical staff reduces the incidence of severe post-operative pain.
- Post-operative pain management should be planned preoperatively.
- Consider the use of preventive analgesia in relevant patient groups.
- Multimodal analgesia may improve the quality of analgesia and reduce the incidence of side effects.
- PCA has a high patient satisfaction.
- Be specific about site of pain and its potential causes.
- Assess pain and the effect of interventions frequently.
- Increasing or severe pain should prompt further investigation.
- Monitoring in an HDU environment may be necessary for prompt and safe management of severe pain.
- As pain reduces, it would be appropriate to wean analgesia to prevent dependence.

Suggested Reading

Acute Pain Management. Scientific evidence – Australian and New Zealand College of Anaesthetists and Faculty of Pain Medicine. 2nd ed. 2005. https://www.ncbi.nlm.nih.gov/pubmed/27125806.

de Gray LC, Matta BF. Acute and chronic pain following craniotomy: a review. Anaesthesia. 2005;60:693–704.

Zeiler FA, AlSubaie F, Zeiler K, Bernard F, Skrobik Y. Analgesia in neurocritical care: an international survey and practice audit. Crit Care Med. 2016;44(5):973–80.

Harmer M, Davies KA. The effect of education, assessment and a standardised prescription on postoperative pain management. Anaesthesia. 1998;53:424–30.

Kehlet H, Jensen TS, Woolf CJ. Persistent postsurgical pain: risk factors and prevention. Lancet. 2006;367:1618–25.

Pandey CK, Navkar DV, Giri PJ, et al. Evaluation of the optimal preemptive dose of gabapentin for postoperative pain relief after lumbar diskectomy: a randomized, double-blind, placebo-controlled study. J Neurosurg Anesthesiol. 2005;17:65–8.

Shimony N, Amit U, Minz B, Grossman R, Dany MA, Gonen L, Kandov K, Ram Z, Weinbroum AA. Perioperative pregabalin for reducing pain, analgesic consumption, and anxiety and enhancing sleep quality in elective neurosurgical patients: a prospective, randomized, double-blind, and controlled clinical study. J Neurosurg. 2016;12:1–10.

Taylor WA, Thomas WM, Wellings JA, Bell BA. Timing of post-operative intracranial hematoma development and implications for the best use of neurosurgical intensive care. J Neurosurg. 1995;82:48–50.

Management of Postoperative Nausea and Vomiting After Neurosurgery

82

Concezione Tommasino

Overview

Postoperative nausea and vomiting (PONV) constitutes a major unpleasant symptom after anesthesia and surgery. The current overall incidence of PONV for all surgeries is estimated to be 25–30% whereas after craniotomies is more than 50%. In the absence of prophylactic antiemetics, in retrospective analysis, the incidence has been as high as 39% for emesis and 67% for nausea, while in prospective studies, PONV incidence has been reported from 55% to 70%. The reasons for the high incidence of PONV in neurosurgical patients may relate to surgery being performed in close proximity to emetic centers of the brainstem or on the structures integral to maintenance of equilibrium.

The exact etiology of PONV is unknown, but research suggests a multifactorial origin and risk factors are well established (Table 82.1). Other possible risk factors include history of migraine, better ASA physical status, anxiety, obesity, decreased perioperative fluids, general versus regional anesthesia or sedation, balanced versus total i.v. anesthesia, and use of longer-acting versus shorter-acting opioids.

Although PONV is almost always self-limiting and nonfatal, it can cause significant morbidity.

In addition to causing patient discomfort, protracted nausea and vomiting may cause dehydration, acid–base disturbances, and electrolyte imbalance. Despite the lack of documented cases of harm caused by postcraniotomy PONV, the physical act of vomiting may result in an increase in arterial, venous, and intracranial pressures, thereby potentially increasing the risk of intracranial hemorrhage and neurologic dysfunction. In patients with depressed airway reflexes during the early postoperative period, vomiting can cause pulmonary aspiration. The peak incidence of vomiting after neurosurgery is within the first few postoperative hours, rendering this complication one of the most frequent in the postanesthesia care unit (PACU) in this patient population, and each vomiting episode delays discharge from the recovery room by about 20 min.

Table 82.1 Risk factors for postoperative nausea and vomiting

Patient-specific risk factors	Age
	Female gender
	Nonsmoking status
	History of PONV/motion sickness
Anesthesia-related independent predictors	Mask ventilation
	Volatile anesthetics
	Nitrous oxide
	Intraoperative and postoperative opioids
	Large-dose neostigmine
	Long duration of anesthesia
	Awake craniotomy *lower* risk than general anesthesia
Neurosurgical risk factors	Infratentorial > supratentorial > transsphenoidal procedures
	High risk in surgery near the area postrema at the floor of the fourth ventricle (vomiting center located nearby)
	Decompression of cranial nerves
	Long duration of surgery
Emergence	Rapid awakening
	Movement
Other factors	Hypotension
	Pain

Updated guidelines for managing PONV suggest that *prophylaxis* and *treatment* of nausea and vomiting improve patient comfort and satisfaction, reduce time to discharge, and should be done selectively.

No single drug or class of drug is fully effective in controlling PONV, presumably because none blocks all pathways to the vomiting center. However, because of the multi-receptor origin of PONV, combination therapy is being more widely employed.

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The successful management of nausea and vomiting is a fundamental part of perioperative anesthesia treatment in neurosurgery and requires several steps:

1. Recognition of patients at risk for PONV
2. Avoidance, when possible, of factors precipitating PONV
3. Prophylaxis
4. Treatment

Prevention

Identification of patients at moderate to severe risk for PONV enables targeting prophylaxis to those who will benefit most from it. Patient, anesthesia, and surgery-related risk factors have been identified (Table 82.1), and a number of PONV risk-scoring systems have been developed. Very simplified risk scores consider only few predictors, and Tables 82.2 and 82.3 indicate the PONV incidence according to the presence of four or five of these predictors.

Both scores are very simple to use and have demonstrated equivalent or superior discriminating power compared with more complex formulas. Koivuranta et al. simplified system (Table 82.3) has a statistically higher predictive value.

In children, risk of nausea and vomiting is highly associated with the type of surgery. Validated PONV-scoring systems are not available for children, but surgery lasting longer than 30 min, age of 3 years and older, a personal history, and even a history of PONV in a close relative are all risk factors. The presence of all four factors increases the risk by 70%.

Table 82.2 Simplified risk score for PONV in adults based on four predictors: range of possible score 0–4

Predictors ($n = 4$)	Predictors	PONV risk by score (%)
	0	10
Female gender	1	21
History of motion sickness or PONV	2	39
Nonsmoking status	3	61
Postoperative opioids	4	79

Table 82.3 Simplified risk score for PONV in adults based on five predictors: range of possible score 0–5

Predictors ($n = 5$)	Predictors	Risk of nausea by score (%)	Risk of vomiting by score (%)
	0	17	7
Female gender	1	18	7
History of PONV	2	42	17
History of motion sickness	3	54	25
Nonsmoking status	4	47	38
Duration of surgery >60 min	5	87	61

Table 82.4 Strategies to reduce baseline risk

Risk factors	Strategies
Anesthesia-related	Awake craniotomy whenever applicable
	Regional anesthesia whenever applicable
	Propofol for induction and/or maintenance of anesthesia
	Avoidance of high-dose volatile anesthetics[a]
	Avoidance of nitrous oxide
	Minimization of intraoperative and postoperative opioids[a]
	Minimization of neostigmine (<2.5 mg)
	Reduce duration of anesthesia
Surgery-related	Reduce duration of surgery
Emergence-related	Perform gastric aspiration/decompression
	Plan a smooth awakening
	Avoidance of sudden movements
Other factors	Maintenance of hemodynamic stability
	Adequate oxygenation
	Adequate hydration
	Adequate pain treatment

[a]Emetogenic effect of inhaled anesthetics and opioids appears to be dose-related

The simplified scoring systems obviate laborious calculations and may reduce the scope of required detailed history-taking. No risk model, however, can accurately predict the likelihood of an individual having PONV; risk models only allow clinicians to estimate the risk for PONV among patient groups.

The logical consequence of these risk scores is "the higher the risk, the more aggressive prevention should be," starting from strategies to reduce baseline risks (Table 82.4).

PONV is less common using propofol (induction and maintenance) and avoiding nitrous oxide. Hypotension causes brain stem hypoxia (vomiting center) and decreases blood flow to the chemoreceptor trigger zone (CTZ), both of which can induce nausea and vomiting. Keeping the patient well hydrated has been shown to reduce the incidence of PONV. Pain itself causes nausea and vomiting, and adequate control of pain is essential: the patient must not be deprived of analgesics under the false assumption that the medications are the only cause of PONV. It will be mandatory, however, to prevent opioid-induced emesis. Experienced PACU nurses are well aware that sudden changes of position and motion, including transportation by stretcher, may trigger vomiting. Upright positioning of a patient with hypotension can also cause nausea. Controlling movement and surrounding activity and decreasing noise and brightness will also reduce stimulation of the vestibular apparatus.

Nonpharmacologic Measures

Acupuncture, acupressure, and electrical stimulation of the P6 point have been shown to be effective in reducing nausea, at least in adults, which has been explained by

endogenous β-endorphin release in the cerebrospinal fluid or a change in serotonin transmission, via the activation of serotonergic and noradrenergic fibers. It is unlikely that this approach will be the mainstay of reducing PONV, but it may have an effect when used as part of a multimodal approach.

Pharmacologic Prophylaxis

Prophylactic antiemetics should be used only when the patient's individual risk is sufficiently high (Tables 82.2 and 82.3). This can be estimated by multiplying the expected incidence (baseline risk) by the relative risk reduction resulting from prophylaxis. As a rule of thumb, each effective antiemetic intervention will lead to a relative risk reduction of approximately 30%.

More aggressive prophylaxis is appropriate for patients in whom vomiting poses a particular medical risk, including those at risk for or with increased intracranial pressure, and when the anesthesia care provider determines the need or the patient has a strong preference to avoid PONV. Many patients are willing to pay out of pocket to avoid PONV or would prefer to suffer pain over nausea and vomiting.

Available antiemetic agents work on different types of receptors involved in the etiology of PONV (Table 82.5). Clinicians, however, must carefully select an antiemetic for patients undergoing craniotomy. The need for ongoing neurocognitive monitoring makes the use of sedating antiemetics (such as anticholinergics, antihistamines, benzamides, and butyrophenones) undesirable (Table 82.5).

Because multiple receptor stimulation is usually involved, in patients at high risk, several studies demonstrate better prophylaxis by the use of two or more antiemetics acting at different receptors compared with monotherapy. Combination therapy is recommended for both adults and children to prevent and manage PONV (Table 82.6).

In adults, 5-HT3-receptor antagonists, dexamethasone and droperidol, are equally effective, each reducing risk of nausea and vomiting by about 25%. In children, the 5-HT3-receptor antagonists are the drugs of choice (ondansetron, children <40 kg = 0.1 mg/kg i.v.; >40 kg = 4 mg i.v.).

Dexamethasone, a corticosteroid, is an effective antiemetic drug. It reduces the incidence of PONV with delayed but prolonged efficacy. The antiemetic effect can be attributed to its strong anti-inflammatory action, which reduces the ascending impulses to the vomiting center. Other mechanisms discussed include decreased production of prostaglandins, blockade of the corticoreceptors in the nucleus tractus solitarius, release of endorphins, and reduction in the serotonin concentration in the brain and the gut. It should be administered before induction. Droperidol has been extensively used in neurosurgery. Nevertheless, in 2001, reports of cardiac rhythm changes after "large dose" droperidol led the Food and Drug Administration to insert a black box warning in the package insert, although doses used for PONV management have never been associated with fatal cardiac arrhythmias.

The widespread use of drugs with pure 5-HT3 (serotonin) receptor antagonism in neurosurgical patients is based on their efficacy on vomiting and lack of side effects of sedation and extrapyramidal reactions. There is no evidence that any of the 5-HT3 antagonists are superior to or have less side

Table 82.5 Receptor site activity of antiemetic drugs and suggestions from the literature for their use in neurosurgery

Pharmacologic group	Dopamine receptors	Muscarinic cholinergic receptors	Histamine receptors	Serotonin receptors	Literature suggestions
Butyrophenones					
Droperidol	++++	–	+	+	≤1.25 mg no sedative effects
Haloperidol	++++	–	+	–	
Phenothiazines					Not supported
Chlorpromazine	++++	++	++++	+	
Fluphenazine	++++	+	++	–	
Antihistamines					Not supported
Diphenhydramine	+	++	++++	–	
Promethazine	++	++	++++	–	
Anticholinergics					Not supported
Scopolamine	+	++++	+	–	
Benzamides					Supported
Metoclopramide	+++	–	+	++	≤10 mg no sedative effect
Antiserotonin					Supported
Ondansetron	–	–	–	++++	4 mg end of case
Granisetron	–	–	–	++++	1 mg end of case
Tropisetron	–	–	–	++++	2 mg end of case
Ramosetron	–	–	–	++++	0.3 mg end of case

The number of positive signs (+) indicates activity to the receptor type and negative sign (–) no activity

effects than any other drug of that class. The evidence supports the administration of 5-HT3 antagonists at the end of surgery rather than prior to induction (Table 82.5).

Other antiemetics may be used, although the evidence supporting their use is less robust.

Multimodal Approach

A multimodal approach has been very effective in reducing early PONV in the highest-risk group (PONV from 41% with no therapy to 2% with multimodal therapy). This approach is based on avoiding *all* factors known to increase PONV and the combined administration of drugs known to reduce PONV (propofol, steroids, 5-HT3 antagonists, liberal intravenous fluids) (Tables 82.4 and 82.6). Figure 82.1 illustrates a suggested algorithm for PONV multimodal approach.

Table 82.6 Guidelines for identification and management of PONV

Risk	Management
Low (no risk factors)	Prophylaxis not recommended
Moderate (1–2 risk factors)	Use single agent prophylactic therapy such as dexamethasone, ondansetron, or droperidol
High (3–4 risk factors)	Treatment includes dexamethasone plus ondansetron or droperidol plus ondansetron
Very high (4 risk factors)	Treatment includes combination antiemetics plus total intravenous anesthesia with propofol

Crisis Management

Pathophysiology and Clinical Presentation

Nausea and vomiting are caused by the stimulation of neurologic mechanisms in the brain and the gastrointestinal tract (GIT). The complex act of vomiting involves coordination of the respiratory, gastrointestinal, and abdominal musculature. It is controlled by the vomiting center which is not a discrete anatomical site but represents interrelated neuronal networks. The nucleus tractus solitarius, the dorsal motor nucleus of the vagus, and the nucleus ambiguous are the three nuclei that comprise the vomiting center. Inputs to the vomiting center include vagal sensory pathways from the GIT and neuronal pathways from the labyrinths, higher centers of the cortex, intracranial pressure receptors, and the CTZ, which is located in the area postrema, on the dorsal surface of the medulla oblongata at the caudal end of the fourth ventricle. The vomiting center is stimulated by histamine, dopamine, serotonin, and acetylcholine.

The vomiting reflex has two main detectors of the need to vomit: the GIT and the CTZ. The vagus is the major nerve involved in the detection of emetic stimuli from the GIT and has two types of afferent fibers involved in the emetic response: mechanoreceptors, located in the muscular wall of the gut, which are activated by contraction and distension of the gut, and chemoreceptors, located in the mucosa of the upper gut, which are sensitive to noxious chemicals. Stimulation of the vagal afferents leads to activation of the CTZ in the area postrema. CTZ can initiate vomiting independent of the vomiting center, is

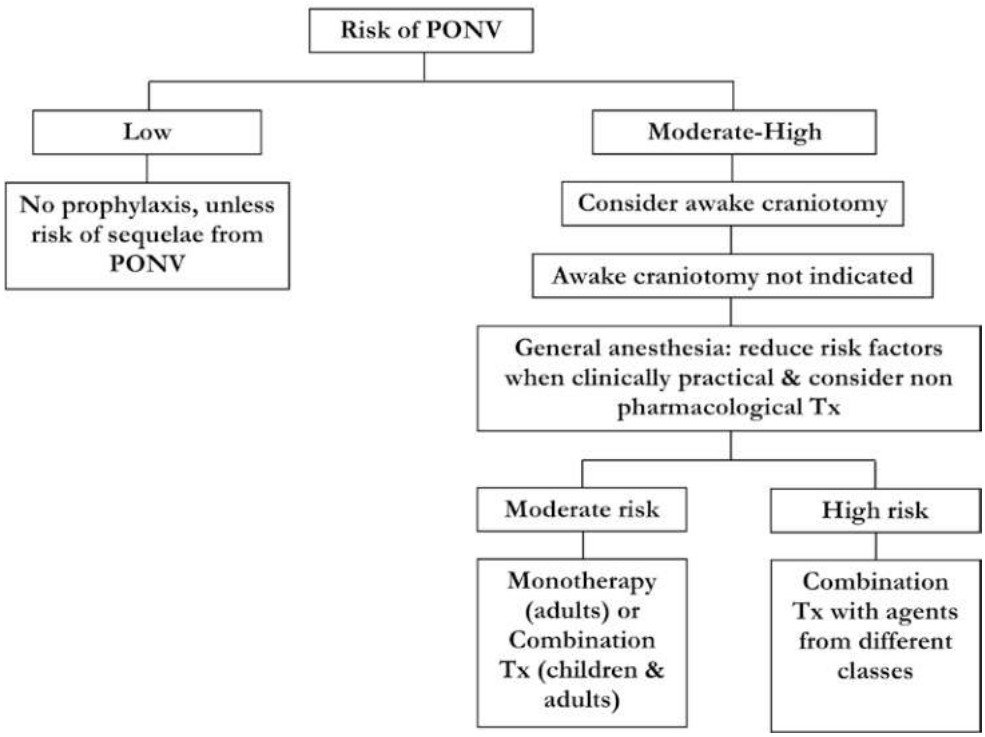

Fig. 82.1 Algorithm for PONV prophylaxis

not protected by the blood–brain barrier, and thus can be activated by chemical stimuli received through the blood as well as the cerebrospinal fluid. The CTZ is stimulated by dopamine, serotonin, opioids, and certain anesthetic agents. Gastrointestinal stimulation of mechanoreceptors in the wall of the gut from distention and manipulation results in the release of serotonin.

Several other stimuli can affect the vomiting center including afferents from the oropharynx, mediastinum, peritoneum, and genitalia as well as afferents from the CNS (cerebral cortex, labyrinthine, visual, and vestibular apparatus). The labyrinth vestibular center can send input to the vomiting center in response to sudden changes in motion and pressure or initiated by the use of nitrous oxide. Hypotension causes brain stem hypoxia and triggers the vomiting center and can decrease blood flow to the CTZ, which can also induce nausea and vomiting.

PONV encompasses three main symptoms that may occur separately or in combination after surgery: nausea, retching, and vomiting.

- *Nausea* is the subjective sensation of an urge to vomit, in the absence of expulsive muscular movements; when severe, it is associated with increased salivary secretion, vasomotor disturbances, and sweating. Loss of gastric tone, duodenal contractions, and the reflux of intestinal contents into the stomach often accompany nausea. The arterial hypertension, which occurs while being nauseated, can complicate efforts to keep the blood pressure within a safe range for a patient after neurosurgery.
- *Retching* follows nausea and comprises labored spasmodic respiratory movements against a closed glottis with contractions of the abdominal muscles, chest wall, and diaphragm without any expulsion of gastric contents. Retching can occur without vomiting, but normally it generates the pressure gradient that leads to vomiting.
- *Vomiting* is caused by the powerful sustained contraction of the abdominal and chest wall musculature, which is accompanied by the descent of the diaphragm and the opening of the gastric cardia. This is a reflex activity that is not under voluntary control. It results in the rapid and forceful evacuation of stomach contents up to and out of the mouth. During active retching and vomiting (*emesis*), intra-abdominal and intrathoracic pressures increase and translate into elevated intracranial pressure. Despite the lack of documented cases of intracranial bleeding due to retching and vomiting, it is reasonable to assume that this is a realistic threat.

Patient Assessment

Periodic assessment of nausea and vomiting should be performed routinely during emergence and recovery and should be part of the "standard" evaluation of neurosurgical patients (Table 82.7).

Table 82.7 Nausea and vomiting score

Score	Description
0	No nausea or vomiting
1	Nausea but not vomiting
2	Nausea and retching
3	Nausea and vomiting

Table 82.8 Treatment of established PONV, ≤6 h postoperatively

Prophylaxis: yes	Prophylaxis: no
Antiemetic different from the drug used for prophylaxis	Low-dose 5-HT3 antagonist:
	Ondansetron 1.0 mg
	Dolasetron 12.5 mg
	Granisetron 0.1 mg
	Tropisetron 0.5 mg
Dexamethasone 2–4 mg	
Droperidol 0.625 mg[a]	
Propofol 20 mg[a]	

[a]In neurosurgical patients single dose to avoid sedative effects

Intervention/Treatment

There are only few trials on the efficacy of drugs in controlling established PONV in the PACU in adults and even fewer in children, compared with the multitude of trials on prophylaxis of this complication. Paucity of data particularly exists in the context of neurosurgical operations, and we have to rely on the information that is derived from trials in other groups of patients (Table 82.8).

When PONV occurs within 6 h postoperatively, the antiemetic should be chosen from a different therapeutic class than the drugs used for prophylaxis. If no prophylaxis was given, the recommended treatment is a low-dose 5-HT3 antagonist, the only drugs that have been adequately studied for the treatment of existing PONV: ondansetron 1.0 mg, dolasetron 12.5 mg (smaller doses have not been studied), granisetron 0.1 mg, and tropisetron 0.5 mg. Studies in adults suggest that ondansetron has greater efficacy than metoclopramide in controlling established PONV.

Alternative treatments for established PONV include dexamethasone, 2–4 mg i.v., or droperidol, 0.625 mg i.v. Propofol, 20 mg as needed, can be considered for rescue therapy in patients still in the PACU and has been found as effective as ondansetron, although its antiemetic effect is probably brief. In neurosurgical patients, however, propofol should be used only after communication with the neurosurgical team, since sedative side effects can alter the neurologic exam.

Beyond 6 h, PONV can be treated with any of the agents used for prophylaxis except dexamethasone, which is longer acting.

Key Points

- Main determinant factors for PONV: patient-associated risk factors, duration and type of anesthesia, postoperative opioids.
- Risk of PONV in a given patient should be established first using established scoring systems.
- Consider acupressure.
- No prophylaxis in minimal risk patients, free from medical sequelae of vomiting.
- Prophylaxis for patients at moderate to high risk for PONV.
- Antiemetic combinations for patients at high risk for PONV.
- Avoid two drugs from the same group (e.g., metoclopramide and domperidone).
- Do not use combinations with antagonistic actions (e.g., cyclizine and metoclopramide, as cyclizine antagonizes the prokinetic effect of metoclopramide).
- Children at moderate or high risk for PONV should receive combination therapy with a 5-HT3 antagonist and a second drug (e.g., dexamethasone).
- Rescue therapy <6 h post-op: antiemetic chosen from a different therapeutic class than the drugs used for prophylaxis.
- Rescue therapy >6 h post-op: any of the drugs used for prophylaxis.
- Strategy to reduce baseline risk and the adoption of a multimodal approach will most likely ensure success in the management of PONV.

Suggested Reading

Apfel CC, Laara E, Koivuranta M, et al. A simplified risk score for predicting postoperative nausea and vomiting. Anesthesiology. 1999;91:693–700.

Arnberger M, Stadelmann K, Alischer P, et al. Monitoring of neuromuscular blockade at the P6 acupuncture point reduces the incidence of postoperative nausea and vomiting. Anesthesiology. 2007;107:903–8.

Eberhart LH, Morin AM, Kranke P, et al. Prevention and control of postoperative nausea and vomiting in post-craniotomy patients. Best Pract Res Clin Anaesthesiol. 2007;21:575–93.

Fabling JM, Gan TJ, EI-Moalem HE, et al. A randomized, double-blinded comparison of ondansetron, droperidol, and placebo for prevention of postoperative nausea and vomiting after supratentorial craniotomy. Anesth Analg. 2000;91:358–61.

Gan TJ, Meyer T, Apfel CC, et al. Consensus guidelines for managing postoperative nausea and vomiting. Anesth Analg. 2003;97:62–7.

Neufeld SM, Newburn-Cook CV. The efficacy of 5-HT3 receptor antagonists for the prevention of postoperative nausea and vomiting after craniotomy: a meta-analysis. J Neurosurg Anesthesiol. 2007;19:10–7.

Ryu JH, Lee JE, Lim YJ, Hong DM, Park HP, Han JI, Baik HJ, Kim HZ, Min KT, Do SH. A prospective, randomized, double-blind, and multicenter trial of prophylactic effects of ramosetron on postoperative nausea and vomiting (PONV) after craniotomy: comparison with ondansetron. BMC Anesthesiol. 2014;14:63.

The Intrahospital Transport of Neurosurgical Patients

83

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Overview

Critically ill patients are at increased risk of mortality and morbidity during transport, with complications arising in as many as 70% of transports. These complications range from trivial to catastrophic including severe hypotension, accidental extubation, increased intracranial pressure (ICP), and central line displacement affecting administration of inotropes. Known patient risk factors for adverse events during transport include pre-existing PEEP requirement, catecholamine support, emergent transports, the amount of time out of the ICU, and treatment modification prior to transport.

Equipment failures are common during the transport of critically ill patients, occurring in up to 45% of transports. Many of these failures can be quite minor, such as electrocardiogram or pulse oximetry disconnects. Others can be potentially catastrophic, however, such as loss of monitor power.

During transport of critically ill patients, respiratory complications can be particularly dangerous. Not surprisingly, hypoxia during transport is more common in those patients requiring PEEP. Furthermore, in one study of combined medical and surgical ICU patients, hypotension and arrhythmias were associated with episodes of inadvertent hypoventilation or hyperventilation with individual changes in $PaCO_2$ as great as 27 mmHg. This finding has ramifications for patients with increased ICP. There is evidence that, as a group, end-tidal CO_2 is well-maintained for intubated patients being hand-ventilated by caretakers. However, variability among individual patients is greater than may be acceptable for patients with abnormal intracranial compliance. A recent study demonstrated increased mortality for patients with severe traumatic brain injury who arrive to the hospital intubated and with $PaCO_2$ values either below 30 mmHg or above 36 mmHg, while patients with severe hypercapnia ($PaCO_2$ above 45 mmHg) have the worst outcomes. These findings suggest that brain-injured patients warrant fastidious attention to ventilation strategy. Finally, there is recent evidence that intrahospital transport of intubated patients is associated with various complications including ventilator-associated pneumonia, pneumothorax, atelectasis and longer ICU stays.

For patients with traumatic brain injury (TBI), pre-hospital secondary injuries associated with hypotension and hypoxia have long been recognized to be associated with increased mortality and disability. For a brain-injured patient, even a single episode of hypotension (SBP <90 mmHg) is associated with increased morbidity and a doubling of mortality. In addition, the duration of arterial hypotension or intracranial hypertension is significantly correlated with poor outcomes for these patients. Extrapolation suggests that patients with brain injuries are particularly vulnerable to transport mishaps and special care must be taken to prevent even brief episodes of hypoxia, hypotension, and increased ICP.

In the studies looking specifically at the intrahospital transport of neurosurgical patients, secondary insults are common. In one such study, secondary insults were seen in 51% of transports with the most common insults being arterial hypertension (28%) and intracranial hypertension (44%). Hypoxia (17%) and hypotension (17%) were also common complications of transport. In another study, ICP increased an average of 27% during transport despite carbon dioxide levels that trended downward. Increases in ICP during transport may be sustained after return to the ICU, which may contribute to worsened outcomes. One very small study ($n = 4$) used microdialysis catheters to continuously monitor cerebral glycolytic activity during transport of head-injured patients and found evidence of impaired oxygen delivery and increased metabolic demand, while concurrent conventional

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monitors showed no significant changes. Finally, a study investigating brain tissue oxygen partial pressure ($PbtO_2$) in comatose patients found decreases in $PbtO_2$ occurred during and in the 3 h following transport to and from a head CT scan in 80% of comatose patients. $PbtO_2$ decreased most in patients for whom $PbtO_2$ was compromised prior to transport from ICU to head CT.

Weighing the Risks Associated with the Transport of Neurosurgical Patients

Prior to undertaking transport of a neurosurgical patient, the question must be asked: "Is the potential benefit worth the risk?" Vigilance is required to avoid unnecessary transport of our most vulnerable neurosurgical patients. A study looking at the risk/benefit ratio for the transport of general ICU patients demonstrated that information gained from studies resulted in changes in management in only 24% of critically ill patients, while 68% of patients had potentially significant physiologic complications during transport. A recent literature review to delineate the risks and benefits of cervical spine MRI for TBI patients found that the risk of secondary injury from the transport to MRI and prolonged supine position for the MRI was much greater than the incidence of cervical injury unrecognized by CT and clinical exam alone. On a related note, it is worthwhile to consider whether the study can be performed without transport. One study compared complications during CT scans before and after their institution's use of a portable head CT for neurosurgical patients. They found an increase in patient safety and reduction in staff workload when CT scans were performed within the NICU and without patient transport. Specifically, 25% of high-risk patients transported for CT suffered complications during the transport, while only 4.3% of similar patients who received CT scan without a transport had complications during the scan. Even in moderate-risk patients, the results were impressive with a 20% complication rate completely eradicated when portable CT scan was performed in the NICU. Not surprisingly, bedside head CT scans are gaining in popularity, especially in NICUs.

Prevention

Neurosurgical ICU patients require more intrahospital transports than any other group of critically ill patients. Given the risks associated with transport of these patients, it is imperative that a transport protocol be developed for the safe and consistent transport of neurosurgical patients. A protocol for the routine transport of critically ill patients allows staff to function smoothly during nonroutine transports, specifically for emergent transports or the transport of acutely unstable patients. The American College of Critical Care Medicine developed guidelines for inter- and intrahospital transport of critically ill patients in 2004. These have been adapted for the specific needs of neurosurgical patients in this chapter. The "checklist," a simple summary of safety guidelines, has been shown to significantly reduce medical errors and improve outcomes. An abbreviated summary of what follows (a transport checklist) can be found in Table 83.1. For this chapter, an attempt has been made to keep the recommended transport supplies practical. The following is a list of considerations to be made prior to the transport of critically ill patients.

Table 83.1 Transport checklist

Consider physician accompaniment for unstable patients
Signed consent on chart with patient
Oxygen cylinder checked and confirmed to have adequate supply (consider backup for prolonged transports)
Monitor fully charged and capable of monitoring ECG, pulse oximetry, noninvasive blood pressure, and at least two pressure channels (e.g., for arterial blood pressure and ICP)
Airway kit to include various sizes of laryngoscopes, LMAs, endotracheal tubes with stylets, bougie, and oral/nasal airways
Emergency medications including sedatives (see Table 83.2), with other medications appropriate to the clinical context
Mask and Ambu bag or transport ventilator with PEEP valve as necessary
$ETCO_2$ monitor or CO_2 detection kit
Injection port identified and immediately accessible with flushes available
Destination contacted and confirmed ready to receive

1. Equipment
   A. Monitors
      - All ICU patients should continue to receive the same monitoring during transport that they receive in the ICU with the reasonable exception of pulmonary artery or central venous pressure monitoring. At a minimum electrocardiogram, blood pressure (either invasive or noninvasive), respiratory rate, and pulse oximetry should be monitored (and documented) continuously for all transports. Continuous end-tidal carbon dioxide ($ETCO_2$) monitoring is ideal, although not all transport monitors have this capability. Disposable $ETCO_2$ devices should be available on all transports if continuous $ETCO_2$ monitoring is not available. Patients with abnormal intracranial compliance should continue to have ICP monitored throughout the transport and diagnostic study, particularly given the frequency of ICP elevation during "road trips." Related to this, patients requiring ICP monitoring should remain with the head of bed elevated at 30° and with the head in neutral position if at all possible. Although certain procedures such as CT studies or angiography require the patient to be supine, periods requiring a supine (and flat) position

should be minimized whenever possible. Brain tissue oxygenation monitoring should be continued if it is being used in the ICU. Finally, monitors with memory capability are ideal for continuous data collection and recovery, and monitor battery should be confirmed to be fully charged (or have a backup immediately available) prior to initiating transport. Many monitors have combined monitoring/defibrillation capability, but when a patient monitor does not have defibrillation capability, the presence of a defibrillator should be confirmed at the destination site.

B. Airway equipment

(i) Oxygen – it is essential to ensure adequate O_2 delivery during transport. To determine whether an oxygen tank will be adequate for a transport, the calculation is fairly straightforward. The pressure of a full E cylinder of oxygen is 2200 psi, and the tank contains 660 l of oxygen. As an ideal gas, the volume of oxygen is proportional to the psi as measured by the pressure gauge. Therefore, if 1200 psi remains in an oxygen tank, the tank contains:

$$1200 / 2200 = X / 660;$$
$$X = 360 \text{ liter of oxygen remaining}$$

If oxygen flow to the patient is 10 l/min, then there is oxygen available for 36 min of flow. It is reasonable to have oxygen adequate for the anticipated transport plus an additional 15–30 min of flow in case of a transport delay. For prolonged transports, a second tank of oxygen is advisable, and adequacy of oxygen supply should be confirmed prior to the return transport to the ICU. Oxygen cylinders should be attached to the patient bed with designated tank holders for the safety of the patient and accompanying staff.

(ii) A suggested list of airway equipment for transport can be found in Table 83.2. Laryngoscopes and portable $ETCO_2$ monitors should be checked for proper function on a regular basis. It should be noted that the use of a transport ventilator or self-inflating bag (e.g., Ambu bag) has a significant advantage over the use of a modified Jackson-Rees or Mapleson circuit, as the latter does not allow for any ventilation of the patient in the event that there are problems with oxygen tank supply (e.g., accidental discharge of the tank).

C. Medications

- A list of recommended drugs for the transport of NICU patients is included in Table 83.2. This list has been tailored for neurosurgical patients. It should be adjusted as necessary for patients with additional co-morbidities such as significant cardiac disease. Sedation "kits" including scheduled medications such as fentanyl, midazolam, and ketamine can be made in advance and stored with other controlled medications until required for urgent transportations. Induction agents such as propofol, ketamine, or etomidate should be included on every transport in case of urgent airway management or treatment of increased ICP. Both succinylcholine and a non-depolarizing muscle relaxant should also be immediately available for airway management.

2. Accompanying personnel

- The incidence of transport complications is related to the experience of the personnel accompanying the critically ill patient. Two to three staff should accompany all critically ill patients – at least one with intensive care training (RN and/or MD). Because of critical incidents associated with patient transport, hospitals are increasingly moving toward ICU nurses with additional training in patient transport and sedation who are responsible for the transport of ICU patients. There are currently no data to conclude whether the recent development of these "transport specialists" will reduce the incidence of transport complications in adult ICU patients, but there is evidence in pediatric patients to support this practice. Patient vital signs and clinical care should be documented throughout transport and the procedure or diagnostic study.

3. Patient preparation

- The final element in preparing for an ICU transport is getting the patient ready to travel. Although this component of preparation seems self-evident, there are a few considerations that must be taken into account with neurosurgical patients.

A. Airway

- Intubated patients on PEEP are at increased risk for transport-related complications. High-grade subarachnoid or severe TBI patients frequently have widened alveolar-arterial gradients for reasons commonly grouped as "neurogenic pulmonary edema," a subject beyond the scope of this chapter. Equipment for providing positive pressure ventilation (e.g., transport ventilator or Ambu bag) with PEEP capability is mandatory for these patients. For patients requiring high levels of PEEP and FIO_2 prior to

Table 83.2 Recommended emergency adult transport medications

Emergency transport medications (prefilled syringes when possible and practical)
Atropine
Epinephrine
Labetalol/esmolol
Phenylephrine
Propofol
Rocuronium
Succinylcholine

transport, it may be prudent to hand bag the patient in the ICU for several minutes prior to departure to see how the patient tolerates being removed from the ventilator. Transport ventilators available at some institutions vary in technical sophistication. Simple transport ventilators allow patients to receive a constant (high) level of PEEP and defined tidal volumes at constant rates, while more advanced models can deliver respiratory patterns similar to those provided by current ICU ventilators.

A critical consideration specific to deteriorating neurosurgical patients is whether to intubate prior to transport. Current CT scanners can complete a non-contrast CT in mere seconds, and thus it is understandable why caretakers frequently argue that airway management can be deferred until CT results are available. This assumption can be quite dangerous. The decision to intubate under controlled circumstances in the ICU must be determined by the status of the patient and the rate of decline. Unresponsive patients clearly require intubation, not only for airway protection but to allow for the institution of hyperventilation for management of presumed intracranial hypertension. It is the slowly declining marginally responsive patient who may present a dilemma. If the ICU team feels the patient will require sedation to undergo the diagnostic study, it is critical that the airway be controlled to avoid hypercapnia and resultant increases in ICP. Airway management under controlled conditions in the ICU is always preferable to emergent intubation during transport.

B. Volume status

- Hypotension (and resultant decreases in CPP) is a common complication of the intrahospital transport of ICU patients. Many deteriorating patients receive acute diuretic therapy (e.g., mannitol or furosemide) and are being actively dehydrated. However, poor cerebral perfusion pressure is clearly detrimental for patients with intracranial pathology, and if appropriate, small fluid boluses in addition to pressor administration should be considered prior to and during the transport of hypotensive patients. A discussion of fluid therapy for neurosurgical patients is beyond the scope of this chapter, but hypertonic saline or colloids may be considered under these circumstances.

C. Sedation

- Because of their deteriorating neurologic status, neurosurgical patients requiring transport for diagnostic or interventional studies may be unable to cooperate for completion of the procedure. Furthermore, the transport of agitated patients risks complications such as arterial hypertension, inadvertent extubation, or other patient injury. It is therefore recommended that sedation be initiated prior to transport for these patients to allow for assessment of effects. Infusions of relatively short-acting sedatives such as propofol or dexmedetomidine are ideal, if the patient's hemodynamic response allows. If the patient is hemodynamically unstable, small doses of opiate (fentanyl) and/or benzodiazepines (midazolam) plus paralysis, if necessary, will facilitate completion of the transport and study.

D. ICP monitoring

- Anecdotal experience suggests that complications related to ventricular catheters are common during transport. This is related to both displacement of the catheter during patient transfers and inexperience managing externalized ventricular drains. It is imperative that personnel transporting patients with externalized ventricular drainage systems familiarize themselves with the system and recognize when the patient's drain is closed ("to monitor," with no cerebrospinal fluid [CSF] drainage) or open ("to drain"). It is suggested that the catheter be closed to drain but ICP continuously monitored during transport. This is to prevent accidental changes in the "pop-off" height (level above tragus at which drainage occurs) and unintended over drainage of CSF. This can be devastating in subarachnoid hemorrhage patients with an unsecured cerebral aneurysm. Conversely, should ICP increase while the system is closed to drain it should be opened at the original pop-off level and CSF allowed to drain, again with particular caution in patients with an unsecured aneurysm. The drainage chamber must always be maintained in an upright position to avoid contamination of the internal filter and any retrograde flow of CSF. Discussion of the ICP monitoring and documentation of pop-off level should occur prior to transport of any patient with these devices in place.

E. General preparation

- Finally, prior to departing the ICU, all lines and the endotracheal tube should be checked to ensure that they are well secured. A functioning IV line and port for the administration of medications should be identified and immediately accessible with flushes available. Adequate volumes of infused medications (such as pressors or sedatives) should also be confirmed. In the case of unstable patients, a call to the receiving end should be made to ensure readiness for the patient.

Crisis Management

The goal of this chapter is the *prevention* of transport emergencies and subsequent secondary injuries in neurosurgical patients. Recognition and management of the conditions for which patients are being transported are discussed elsewhere in this textbook. Transport is not the time for clinical intervention, and any patient management issues that can be handled in the ICU prior to transport, e.g., airway management, should be managed under controlled conditions whenever possible. Having said this, a mechanism for contacting immediate help and a knowledge of the location of emergency equipment (e.g., arrest carts) along the transport route is critical in the case of a transport catastrophe.

Key Points

- Complications are common during the transport of critically ill patients.
- NICU patients require more transports than other ICU patients.
- The benefits of any proposed study must be carefully weighed against the significant risks associated with transporting critically ill patients.
- Secondary insults to brain-injured patients are associated with increased morbidity and mortality.
- Standardized preparation for transport may reduce the risk of complications.
- Continuation of mechanical ventilation using adequate transport ventilators should be considered in all NICU patients requiring PEEP or at risk for ICP increase; $ETCO_2$ measurements should be continued during transport.
- Risk of complications is related to the experience of accompanying personnel.
- In deteriorating neurosurgical patients, consider securing the airway prior to transport.
- ICP elevation is common during the transport of patients with brain injuries.

Suggested Reading

Andrews PJ, Piper IR, Dearden NM, Miller JD. Secondary insults during intrahospital transport of head-injured patients. Lancet. 1990;335:327–30.

Bekar A, Ipekoglu Z, Tureyen K, Bilgin H, Korfali G, Korfali E. Secondary insults during intrahospital transport of neurosurgical intensive care patients. Neurosurg Rev. 1998;21:98–101.

Bercault N, Wolf M, Runge I, Fleury JC, Boulain T. Intrahospital transport of critically ill ventilated patients: a risk factor for ventilator-associated pneumonia – a matched cohort study. Crit Care Med. 2005;33:2471–8.

Chesnut RM, Marshall LF, Klauber MR, et al. The role of secondary brain injury in determining outcome from severe head injury. J Trauma. 1993;34(2):216–22.

Dunham CM, Brocker BP, Collier BD, Gemmel DJ. Risks associated with magnetic resonance imaging and cervical collar in comatose, blunt trauma patients with negative comprehensive cervical spine computed tomography and no apparent spinal deficit. Crit Care. 2008;12:R89.

Gunnarsson T, Theodorsson A, Karlsson P, Fridriksson S, Boström S, Persliden J, Johansson I, Hillman J. Mobile computerized tomography scanning in the neurosurgery intensive care unit: increase in patient safety and reduction of staff workload. J Neurosurg. 2000;93:432–6.

Papson J, Russel KL, Taylor DM. Unexpected events during the intrahospital transport of critically ill patients. Acad Emerg Med. 2007;14:574–7.

Peerdeman SM, Girbes AR, Vandertop WP. Changes in cerebral glycolytic activity during transport of critically ill neurotrauma patients measured with microdialysis. J Neurol. 2002;249:676–9.

Sarrafzadeh AS, Peltonen EE, Kaisers U, Küchler I, Lanksch WR, Unterberg AW. Secondary insults in severe head injury—do multiply injured patients do worse? Crit Care Med. 2001;29(6):1116–23.

Schwebel C, Clec'h C, Magne S, Minet C, Garrouste-Orgeas M, Bonadona A. Safety of intrahospital transport in ventilated critically ill patients: a multicenter cohort study. Crit Care Med. 2013;41:1919–28.

Swanson EW, Mascitelli J, Stiefel M, MacMurtrie E, Levine J, Kofke WA, Yang W, Le Roux PD. Patient transport and brain oxygen in comatose patients. Neurosurgery. 2010;66:925–32.

Warner KJ, Cuschieri J, Copass MK, Jurkovich GJ, Bulger EM. The impact of prehospital ventilation on outcome after severe traumatic brain injury. J Trauma. 2007;62:1330–6.

Warren J, Fromm RE Jr, Orr RA, Rotello LC, Horst HM. Guidelines for the inter- and intrahospital transport of critically ill patients. Crit Care Med. 2004;32:256–62.

Part XIV

Challenges in Neurocritical Care of Neurosurgical Patients

Altered Mental Status in Neurosurgical Critical Care

84

Christoph S. Burkhart and Luzius A. Steiner

Overview

Altered mental status or altered level of consciousness is a nonspecific symptom of many complications in neurosurgical patients and may be caused by conditions such as rebleeding of cerebral aneurysms, decompensating brain edema, postoperative hematoma, or seizures. Consciousness can be divided into wakefulness and awareness. The former includes arousal, alertness, and vigilance, while the latter is the sum of cognitive and emotional functions. The anatomical structures, upon which wakefulness and awareness depend, and the signs of dysfunction are shown in Table 84.1. Disorders of wakefulness are always accompanied by impaired awareness. Although the distinction between wakefulness and awareness is important for the understanding of the pathophysiology of altered consciousness, in our experience, the distinction between the two is of limited clinical importance as far as timing and manner of the clinical evaluation of patients with altered levels of consciousness are concerned. However, treatment may differ considerably.

Table 84.1 Anatomy and signs of altered consciousness

	Wakefulness	Awareness
Components	Arousal, alertness, vigilance	Sum of cognitive and emotional functions
Anatomical structures	Ascending reticular activating system (ARAS), descending corticoreticular pathways	Cerebral cortex of both hemispheres, associated white matter tracts, subcortical nuclei, and descending corticofugal systems
Dysfunction	Quantitative disturbance of consciousness Hypervigilance Somnolence Stupor Coma	Qualitative disturbance of consciousness Delirium Persistent vegetative state

Incidence

Overall, neurological complications are reported with an incidence of 3–7% after intracranial procedures, a rate which depends on the investigated patient population. After resection of intra-axial brain tumors, neurological complications have been reported in more than 25% of patients and commonly include motor and sensory deficits as well as coma (2%). Postoperative hematoma occurs in approximately 1% of patients after intracranial surgery, with decreased level of consciousness being the most common clinical symptom (61% of patients with postoperative hematoma).

Elderly patients are particularly at increased risk for postoperative delirium and postoperative cognitive dysfunction after neurosurgical procedures, especially when preexisting mild cognitive impairment or dementia is present.

Epidemiology

Certain patients have an elevated risk for developing neurological complications postoperatively (Table 84.2). Up to 18% of patients have been reported to have postoperatively sustained ICP elevation after brain surgery. The incidence of retraction injuries varies considerably depending on the surgical technique and the duration of retraction.

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Table 84.2 Most important complications in specific groups of patients; incidence is indicated where available

Operative interventions	Increased risk for
Resection of gliomas	Postoperative seizures, postoperative ICP elevation brain edema
Resection of meningioma	Postoperative hematoma, postoperative seizures, postoperative ICP elevation, brain edema
Surgical abscess drainage	Postoperative seizures, septic shock, brain edema
Evacuation of chronic subdural hematoma	Postoperative seizures, reaccumulation of blood, tension pneumocephalus
Evacuation of intracerebral hematoma	Postoperative seizures, reaccumulation of blood
Surgery for arteriovenous malformations	Postoperative seizures
	Retraction injury
	Perforator stroke
	Normal pressure breakthrough edema
Aneurysmal subarachnoid hemorrhage	Postoperative seizures
	Retraction injury
	Perforator stroke
Stenting of symptomatic intracranial stenosis	Perforator stroke (3%), reperfusion injury
Skull base surgery	Retraction injuries (10%)
Carotid endarterectomy	Hyperperfusion syndrome (3%), carotid dissection
Repeat surgery	Postoperative ICP elevation
Duration of intracranial surgery >6 h	Postoperative ICP elevation
Large intraoperative blood loss	Postoperative hematoma
Coagulopathy, current use of antiplatelet agents or anticoagulants	Postoperative hematoma

Table 84.3 Etiology of altered level of consciousness

Focal brain lesions	Diffuse or toxic/metabolic encephalopathies
Postoperative bleeding	Hypo/Hyperglycemia
Raised ICP	Seizures
Ischemic, embolic, perforator stroke	Electrolyte and osmolality abnormalities
Vasospasm	Hypercapnia
Retraction injury	Hypoxia
Tension pneumocephalus	Drugs/toxins and withdrawal
CSF hypotension	Delirium
Hyperperfusion syndrome	Hypotension
Delayed ischemic neurological deficits	Renal and hepatic failure
	Myxedema, M. Addison

Etiology (Table 84.3)

Clinical Implications

Rapid diagnosis and treatment of an abnormal level of consciousness are essential. Irreversible brain damage will develop rapidly, within minutes, if the cerebral cortex or other brain areas are not perfused. Generally, patients who are admitted to the hospital in coma (not postoperative neurosurgical patients) and who do not spontaneously open their eyes within the following 6 h have only a 10% chance of making a good or moderate long-term recovery. After 1 week of coma, the likelihood of a good or moderate recovery is 3%. Such data are not available for the chance of recovery from coma postoperatively following neurosurgical procedures. However, it is reasonable to assume that the chance of making a good recovery decreases with the duration of coma in this group of patients as well.

Anticipated Problems

Delayed diagnosis and treatment of the causes of the altered level of consciousness may lead to significant morbidity or mortality, including irreversible neurological sequelae, increased cost, prolonged length of stay in the intensive care unit, and extended overall hospital stay.

Prevention

Clinical management should aim to prevent conditions favoring the development of complications and avoid strategies that interfere with the early detection of changes in the mental status. For example, the use of short-acting anesthetics, early extubation, and prevention of unintended hypothermia allows for an early and a more detailed neurological examination. Stable hemodynamics should be achieved. Both, hypo- and hypertension are detrimental. In fact, arterial hypertension during emergence from brain surgery is associated with a higher incidence of postoperative intracranial hemorrhage. Electrolyte, fluid, and metabolic imbalances should be rapidly corrected. In addition, post-craniotomy pain may be significant and should be treated. There is no reason not to use opiates, provided they are carefully titrated and the patient is carefully monitored.

To further reduce the incidence of delirium, risk factors such as sleep deprivation, immobility, dehydration, and visual, auditory, and cognitive impairments should be considered and adequately addressed if necessary. Risk factors such as anticholinergic drugs should be eliminated. Drug withdrawal (e.g., benzodiazepines) should be anticipated and avoided if possible by providing adequate substitution.

No pharmacological prophylaxis for delirium can be recommended at this time, but avoidance of benzodiazepines for premedication in elderly patients might be an option because benzodiazepines themselves may cause delirium.

Crisis Management

Efficient crisis management of patients presenting with an altered level of consciousness in the intensive care environment aims to identify and treat reversible causes before irreversible brain damage ensues. Thus, even prior to a rapid neurological assessment, measures should be initiated to secure adequate oxygenation and stable hemodynamics (ABCs).

Pathophysiology and Clinical Presentation

Two groups of pathophysiological processes impair consciousness: diffuse or toxic encephalopathies and focal lesions. Diffuse or toxic/metabolic encephalopathies decrease the function of both hemispheres via hypoxia, ATP depletion, impaired glucose utilization, or accumulation of cytotoxic metabolites. Focal lesions have a direct or an indirect effect on critical areas of the diencephalon or brain stem that are involved in the maintenance of consciousness. Infratentorial focal lesions directly compromise the ascending reticular activating system (ARAS). Tables 84.4 and 84.5 provide an overview of the clinical findings of focal lesions

Table 84.4 Differential diagnosis of altered level of consciousness by clinical presentation of focal lesions

Clinical signs	Differential diagnosis	Further steps to consider
Lateralizing signs	Postoperative bleeding	CT/CT angiography, MRI, TCD, angiography, surgical intervention, ICP decreasing/lowering treatment, treat vasospasm
	Ischemic stroke	
	Perforator stroke	
	Raised ICP	
	Vasospasm	
	Retraction injury	
	Hyperperfusion syndrome	
Pupillary abnormalities; unilateral vs. bilateral	Postoperative bleeding	CT/CT angiography, MRI, TCD, angiography, surgical intervention, medically lower ICP, treat vasospasm
	Ischemic stroke	
	Raised ICP	
	Vasospasm	
	Retraction injury	
	Central anticholinergic syndrome	
Hypersomnia	Residual anesthetic	CT, MRI, surgical intervention, EEG
	Hypercarbia	
	Hypoglycemia	
	Delirium	
	Central anticholinergic syndrome	
	Postoperative intracranial bleeding	
	Ischemic (perforator) stroke	
Visual abnormalities	Postoperative bleeding	CT, MRI, TCD, angiography, surgical intervention, medically lower ICP, treat vasospasm
	Ischemic stroke	
	Perforator stroke	
	Raised ICP	
	Vasospasm	
	Retraction injury	
Postural headache	CSF hypotension	Rehydration, surgical intervention
Seizures, convulsions	Postoperative bleeding	CT, MRI, surgical intervention, EEG, medically lower ICP
	Ischemic stroke	
	Perforator stroke	
	Raised ICP	
	Retraction injury	
	Tension pneumocephalus	
	Hyperperfusion syndrome	
Arterial hypertension	Postoperative bleeding	CT, surgical intervention, lower ICP, analgesics, antihypertensive drugs
	Ischemic stroke	
	Perforator stroke	
	Raised ICP	
	Tension pneumocephalus	
	Hyperperfusion syndrome	
	Pain	
Cheyne-Stokes respiration	Raised ICP, brainstem involvement	CT, medically lower ICP, surgical intervention
Respiratory depression	Intracranial bleeding	CT, MRI
	Stroke	
	Cerebral edema, general or regional	

Precise knowledge of the procedure performed and the associated pathophysiology is essential to identify the underlying complications and guide further diagnosis and treatment

Table 84.5 Differential diagnosis of altered level of consciousness by clinical presentation of toxic/metabolic encephalopathies

Clinical signs	Differential diagnosis	Further steps to consider
Persistent coma	Nonconvulsive epileptic state	EEG, anticonvulsants, correct hypoglycemia, laboratory analysis, correct electrolytes
	Hypoglycemia	
	Hypercapnia	
	Hyper-/hyponatremia	
	Residual anesthetic effect	
	Hypothermia	
Small reactive pupils	Opiate overdose	Ventilation, opioid antagonists
Respiratory depression	Opiate overdose	Ventilation, opioid antagonists
Inattention, disorganized thinking	Delirium	Reassurance, neuroleptic drugs, correct hypoglycemia, physostigmine
	Hypoglycemia	
	Central anticholinergic syndrome	
Hypersomnia	Hypoglycemia	Correct hypoglycemia, treat delirium, physostigmine
	Delirium	
	Central anticholinergic syndrome	
	Hypercarbia	
	Residual anesthetic effect	
Tachycardia	Hypoglycemia	Correct hypoglycemia or hypovolemia, analgesics, physostigmine
	Pain	
	Hypovolemia	
	Inadequate brain perfusion (shock)	
	Hypercarbia	
	Withdrawal symptoms	
	Central anticholinergic syndrome	
ECG changes	Electrolyte and osmolality abnormalities	Laboratory analysis, correct electrolytes, treat ischemia, CT
	Myocardial ischemia/infarction	
	Subarachnoid hemorrhage	
Tachypnea	Hypercapnia	Correct hypercapnia and hypoxia, laboratory analysis
	Hypoxia	
	Systemic inflammatory response syndrome	
Sympathetic hyperactivity	Hypercapnia	Correct hypercapnia, laboratory analysis
	Systemic inflammatory response syndrome	
	Alcohol withdrawal	

and toxic/metabolic encephalopathies. The history of the patient and the type of surgery performed will provide crucial insight into the problems that may occur. Unspecific signs include headache, vomiting, restlessness, lethargy, stupor, and tremor.

We suggest that standardization and predefined timing of assessments are crucial to obtain an early diagnosis and allow rapid interventions. Early consultation with neurosurgeons and neurologists is essential.

Patient Assessment (Fig. 84.1)

In patients without focal signs, the decision to perform a CT scan must be based on the patient's history and clinical presentation and on the judgment of the treating physician. Consider MRI for suspected posterior fossa lesions and early detection of ischemia (diffusion-weighted imaging; DWI). Do not delay imaging while waiting for laboratory results.

Perform EEG in patients with inconspicuous imaging results who remain comatose or with altered levels of consciousness not otherwise explained. Nonconvulsive seizures and nonconvulsive status epilepticus may be clinically undetectable. If delirium is suspected, use delirium assessment instruments such as the Confusion Assessment Method for the ICU (CAM-ICU) or the Intensive Care Delirium Screening Checklist (ICDSC). Screening for delirium should be performed regularly as part of routine care.

Intervention/Treatment

- Airway management.
  - Ensure adequate oxygen supply.
  - Intubation and mechanical ventilation if necessary.
- Treat unstable hemodynamics.
  - Correct hypovolemia with crystalloids, colloids, or blood as appropriate.
  - Hypotension: vasopressors (e.g., phenylephrine boluses of 50–100 μg i.v. or a norepinephrine infusion).
  - Consider treatment of hypertension (e.g., labetalol boluses of 5–15 mg i.v., esmolol boluses of 10–50 mg i.v., or urapidil boluses of 5–10 mg i.v.).
- Perform surgery if indicated.
  - Early consultation with neurosurgeon
  - CT if appropriate
- Consider antagonists if opioid or benzodiazepine overdose is suspected (naloxone 40–200–400 μg i.v., flumazenil 0.2–0.5 mg i.v., respectively).
- Consider physostigmine if central anticholinergic syndrome is suspected (physostigmine 0.01–0.03 mg/kg initially).
- Use specific instruments such as the CAM-ICU or the Intensive Care Delirium Screening Checklist (ICDSC) at regular intervals, i.e., once every shift, to screen for delirium. Consider haloperidol or an atypical antipsychotic drug (off-label use) if delirium is suspected. Elderly

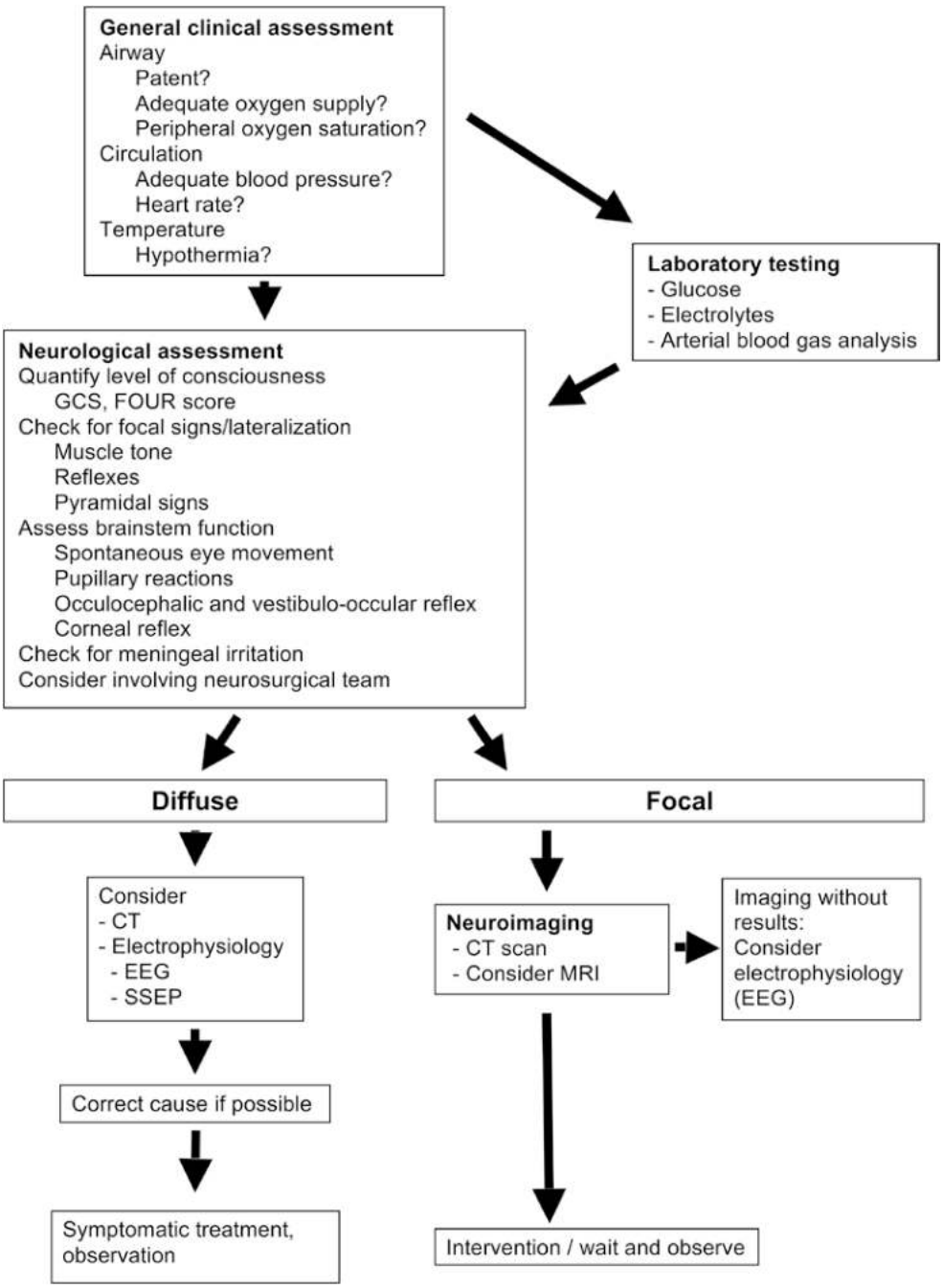

Fig. 84.1 Suggested sequence for the evaluation of patients with a decreasing level of consciousness. *EEG* electroencephalography, *SSEP* somatosensory evoked potentials. Hypothermia will influence neurological assessment. Scoring systems: *GCS* widely used, may not detect subtle neurological changes, and does not consider brainstem reflexes. *F*ull *O*utline of *UnR*esponsiveness (FOUR score) includes brain stem reflexes and respiratory patterns, thus, allowing further evaluation of patients with a low GCS. (For further information see Wijdicks et al. 2005)

patients may be very susceptible to the effects of these drugs. Therefore, treatment is typically started with oral haloperidol at 0.5–1.0 mg every 8 h. Doses may be increased or given intravenously if necessary. Beware: hypotension and prolongation of QT interval. Atypical antipsychotics (off-label use), e.g., oral quetiapine, is typically started at 12.5–25 mg every 12 h. Alternatively, olanzapine (5 mg every 12 h) or risperidone (0.5 mg every 12 h) could be considered.

Key Points

Any change in the level of consciousness may be the first sign of a life-threatening complication.

- Perform regular clinical assessment.
- Perform frequent neurological scoring.
- Careful documentation of observations and scores is crucial.
- If scores are deteriorating (e.g., GCS score is 2 points less than that assessed during the previous

scoring), initiate immediate careful examination. Depending on the results, perform further diagnostic tests (e.g., CT scan).
- Develop unit-specific standard operating procedures for patients with an altered or deteriorating level of consciousness.

Suggested Reading

Bassetti C, Aldrich MS. Consciousness, delirium, and coma. In: Albin MS, editor. Textbook of neuroanesthesia: with neurosurgical and neuroscience perspectives. New York: McGraw-Hill Professional; 1996. p. 369–408.

Claassen J, et al. Recommendations on the use of EEG monitoring in critically ill patients: consensus statement from the neurointensive care section of the ESICM. Intensive Care Med. 2013;39:1337–51.

Le Roux P, et al. Consensus summary statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care: a statement for healthcare professionals from the Neurocritical Care Society and the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40:1189–209.

Pfister D, Strebel SP, Steiner LA. Postoperative management of adult central neurosurgical patients: systemic and neuro-monitoring. Best Pract Res Clin Anaesthesiol. 2007;21:449–63.

Stevens RD, Shoykhet M, Cadena R. Emergency neurological life support: intracranial hypertension and herniation. Neurocrit Care. 2015;23(Suppl 2):S76–82.

Wijdicks EF, Bamlet WR, Maramattom BV, Manno EM, McClelland RL. Validation of a new coma scale: the FOUR score. Ann Neurol. 2005;58:585–93.

85

Cerebrovascular Vasospasm, Normal Perfusion Pressure Breakthrough Edema, and Posterior Reversible Encephalopathy Syndrome (PRES) in Neurosurgical Critical Care

Sanjeev Sivakumar and José I. Suarez

Abbreviations

aSAH	Aneurysmal subarachnoid hemorrhage
AVM	Arteriovenous malformation
CSF	Cerebrospinal fluid
CTA	CT angiography
CTP	CT perfusion
DCI	Delayed cerebral ischemia
DSA	Digital subtraction angiography
EEG	Electroencephalography
EVD	External ventriculostomy drain
HIT	Heparin-induced thrombocytopenia
NPPB	Normal perfusion pressure breakthrough
PRES	Posterior reversible encephalopathy syndrome
RCT	Randomized control trial
SIADH	Syndrome of inappropriate secretion of antidiuretic hormone
SIRS	Systemic inflammatory response syndrome
TCD	Transcranial Doppler
WFNS	World Federal of Neurological Societies

Cerebral Vasospasm

Overview

Cerebrovascular vasospasm is a major implication in the pathogenesis of delayed cerebral ischemia (DCI), one of the most dreaded complications after aneurysmal subarachnoid hemorrhage (aSAH) and the most important factor impacting functional outcome. Vasospasm is defined by radiographic or sonographic evidence of arterial narrowing, whereas DCI is defined as the occurrence of focal neurological impairment (hemiparesis, aphasia, apraxia, hemianopia, etc.) or a decrease of at least 2 points on the Glasgow Coma Scale, lasting at least 1 h, not immediately following aneurysm occlusion and not attributed to other causes. Approximately 30% of all patients with SAH develop DCI within 2 weeks after aSAH (Suarez 2015).

Predictors of vasospasm and DCI after aSAH

- Thickness, density, location, and persistence of subarachnoid blood
- Poor clinical grade
- Loss of consciousness at ictus
- Cigarette smoking
- Cocaine use
- Systemic inflammatory response syndrome (SIRS)
- Hyperglycemia
- Hydrocephalus

Prevention

Of the available interventions aimed at preventing DCI, calcium channel blockers and intravascular volume status are the ones most studied.

- Data from meta-analyses of RCTs supports the early use of calcium channel blocker nimodipine for improving neurological outcomes following SAH, by preventing processes other than large-vessel narrowing (Dorhout et al. 2007).
- Oral nimodipine at a dose of 60 mg Q4H (dose at 30 mg Q2H if hypotensive) should be administered in all patients for a period of 21 days after SAH [Class I, Level A].

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- Maintain euvolemia [Class I, Level B].
- Prophylactic hypervolemia or balloon angioplasty before development of angiographic spasm is not recommended [Class III, Level B].
- A promising phase 2 study of albumin in SAH (ALISAH) showed improved clinical outcomes in patients treated with 1.25 g/kg/day for 7 days.
- Meta-analyses and phase 3 trials failed to demonstrate evidence of improvement in short- or long-term outcomes following SAH, with magnesium sulfate and statins.

Other strategies for the medical management of SAH aimed at neuroprotection are summarized in Table 85.1.

Crisis Management

The risk for vasospasm and DCI are highest between days 3 and 14 after aSAH. A clinical diagnosis is made when the patient experiences a new focal neurological deficit or deterioration in level of consciousness. Large artery narrowing seen in angiographically visible vessels only results in ischemic

Table 85.1 Summary of key recommendations for management of patients with subarachnoid hemorrhage

Modality	Recommendations	Level of evidence
Prevention of re-bleeding	Early aneurysm repair whenever possible[a, b]	Class I, Level B
	Short-course antifibrinolytic therapy prior to aneurysm repair (begun at diagnosis and continued until securing aneurysm or at 72 h post ictus, whichever shorter) should be considered[a, b]	Class IIa, Level B
	Avoid delayed (more than 48 h after ictus) or prolonged (more than 3 days) antifibrinolytic therapy[b]	
Hydrocephalus	Acute symptomatic hydrocephalus should be managed by CSF diversion (EVD or lumbar drainage)[a]	Class I, Level B
	Gradual weaning (>24 h) of EVD does not appear effective in reducing need for ventricular shunting[a]	Class III, Level B
	Chronic symptomatic hydrocephalus should be treated with permanent CSF diversion[a]	Class I, Level C
Seizures	Routine use of anticonvulsant prophylaxis with phenytoin not recommended[a, b]	Class III, Level B
	Short term prophylaxis (3–7 days) may be considered in immediate post hemorrhagic period[a, b]	Class IIb, Level B
	Consider continuous EEG in patients with poor grade SAH with neurologic deterioration of undetermined etiology[b]	
Blood pressure management	Premorbid baseline blood pressures should be used to refine targets[b]	Class IIa, Level C
	Decrease in systolic blood pressure less than 160 mmHg is reasonable until aneurysm is secured[a]	
Aneurysm treatment	Surgical clipping or endovascular coiling as early as feasible, and when amenable to both, endovascular coiling should be considered[a, b]	Class I, Level B
	Consider coiling in elderly (>70 years), poor grade SAH and basilar apex aneurysms[a]	Class IIb, Level C
	Consider clipping if associated (>50 ml) intraparenchymal hematoma and middle cerebral artery aneurysm[a]	Class IIb, Level C
	Complete obliteration of aneurysm recommended[a]	Class I, Level B
	Stenting is associated with increased morbidity and mortality[a]	Class III, Level C
Cardiopulmonary complications	Baseline cardiac assessment with enzymes, ECG, ECHO, especially if evidence of myocardial dysfunction[b]	
	Cardiac output monitoring if evidence of hemodynamic instability[b]	
Anemia	Reasonable to transfuse patients at risk for cerebral ischemia[a]	Class IIb, Level B
	Transfusion to maintain hemoglobin of 8–10 g/dL[b]	
Intravascular volume status	Maintain euvolemia and avoid prophylactic hypervolemia[a, b]	Class I, Level B
Hyponatremia	SIADH and salt wasting are common causes	Class IIa, Level B
	Fluid restriction should not be used to treat hyponatremia[b]	
	Fludrocortisone or hydrocortisone and hypertonic saline can be used to correct hyponatremia[a,b]	
Glycemic control	Hypoglycemia (less than 80 mg/dL) should be avoided[a, b]	Class IIb, Level B
	Serum glucose should be maintained below 200 mg/dL[b]	
Pyrexia	Aggressive control of fever to target normothermia[a, b]	Class IIa, Level B
	Surface cooling or intravascular devices when antipyretics fail[b]	
Coagulopathy	Early identification and targeted treatment of HIT and DVT[a]	Class I, Level B
	Measures to prevent DVT should be used in all patients and unfractionated heparin should be started 24 h after securing aneurysm[b]	

[a]Guidelines from American Heart Association/American Stroke Association (Connolly Jr. et al. 2012)
[b]Recommendations from Neurocritical Care Society's multidisciplinary consensus (Diringer et al. 2011)

Table 85.2 Pathophysiology, diagnosis, and management of cerebrovascular vasospasm and DCI

Pathophysiology	The release of oxyhemoglobin and erythrocyte contents through hemolysis stimulates secretion of endothelin-1, decreases production of nitric oxide, and produces activated oxygen species. These free radicals are believed to play a role in lipid peroxidation and mediate structural changes in vessel wall that promote a contracted state
	Other mechanisms implicated in pathogenesis of DCI:
	Microcirculatory dysfunction
	Microthrombosis
	Cortical spreading depression
	Delayed cellular apoptosis
Clinical presentation	Symptoms present between days 4 and 12 and range from excessive sleepiness, lethargic, and stupor to focal neurological deficits such as hemiparesis, aphasia, visual field deficits, gaze impairment, and cranial nerve palsies
	Evaluate for and rule out hydrocephalus, seizures, and electrolyte dysfunction
Monitoring and diagnostic tests for vasospasm and DCI	I. Digital subtraction angiography (DSA) is gold standard for detection of large artery vasospasm
	II. Transcranial Doppler (TCD): [Class IIa, Level B]
	TCD has adequate sensitivity and specificity to detect delayed cerebral ischemia secondary to cerebral vasospasm in large arteries compared to DSA
	TCD thresholds for vasospasm
	Absence: Mean cerebral blood flow velocities of less than 120 cm/s or Lindegaard ratio (MCA mean cerebral blood flow velocity/extracranial internal carotid artery mean blood flow velocity) <3
	Presence: Mean cerebral blood flow velocity >200 cm/s or Lindegaard ratio >6
	Increase in mean cerebral blood flow velocity by more than 50 cm/s within 24–48 h also associated with DCI
	III. CT angiogram in conjunction with CT perfusion (CTP) is accurate in predicting the need for endovascular intervention. CTP finding of mean transit time (MTT) greater than 6.4 s predicts DCI [Class IIa, Level B]
	IV. Other modalities include EEG, brain tissue oxygenation, and cerebral blood flow determination
Treatment	Noninvasive measures
	Hypervolemia does not appear to offer any benefit over euvolemia: goal should be to maintain euvolemia [Class I, Level B]
	Hemodynamic augmentation: [Class I, Level B]: IV fluid bolus (1–2 l of 0.9% saline) followed by induced hypertension with norepinephrine, phenylephrine, or dopamine in a stepwise fashion with frequent assessment of neurologic function at each 10 mm Hg change in systolic blood pressure (up to 200 mm Hg)
	Invasive measures
	Endovascular treatment using cerebral angioplasty and/or intra-arterial vasodilator therapy (verapamil, papaverine, nicardipine, etc.) is reasonable for patients refractory to hypertensive therapy and with symptomatic vasospasm and DCI [Class IIa, Level B]
	While transluminal balloon angioplasty produces sustained reversal of arterial narrowing, there is a 5% complication rate of vessel rupture, occlusion, dissection, and hemorrhagic infarct
	Intrathecal thrombolytic therapy is associated with reduction in angiographic vasospasm; however this needs further evaluation

neurological symptoms in 50% of cases. The pathophysiology, clinical presentation, monitoring strategies, and interventions for vasospasm and DCI are summarized in Table 85.2.

The timing and frequency of monitoring techniques can be based on risk stratification (Macdonald 2014).

- All patients with aSAH undergo daily or every other day TCD and CT/CTA/CTP on admission and days 3–5 and days 7–10 to screen for vasospasm and DCI.
- DSA can be obtained instead of CTA; high-risk patients undergo additional studies such as brain tissue oxygenation, CBF monitoring, and EEG.
- Low risk: Older age, WFNS score 1 or 2, modified Fisher score less than 3. If neurologically stable and absence of vasospasm or hypoperfusion on TCD and CTA/CTP: consider transition to lower level of care, 5 days post ictus.
- High risk: Poor neurological status, WFNS score 3–5, modified Fisher scale score of 4. If neurologically stable and no spasm on diagnostic tests: consider transition 7 days post ictus.
- If low- or high-risk patients develop clinical or radiographic spasm, intensity and frequency of neurologic monitoring are escalated along with interventions as outlined in Table 85.2.

Key Points

- Cerebrovascular vasospasm and DCI are major complications of aSAH and associated with high morbidity and mortality.
- Risk for vasospasm is highest between days 3 and 14 after SAH.
- TCD ultrasonography should be performed every day or every other day to monitor for spasm; along with serial neurological exam, CTA/CTP and DSA can guide interventions for vasospasm.
- Clinical or diagnostic suspicion for vasospasm should prompt immediate therapy with hemodynamic augmentation and endovascular therapy.

Posterior Reversible Encephalopathy Syndrome (PRES)

Overview

PRES is a clinico-neuroradiological condition characterized by generally reversible, acute neurological symptoms of encephalopathy, headache, seizures, and visual disturbances with radiographic findings of subcortical vasogenic edema characteristically involving bilateral parieto-occipital regions. The literal meaning of term "PRES" is inaccurate, as brain edema is often not isolated posteriorly, and not always reversible. Brain regions commonly involved are summarized below. PRES is associated with conditions summarized in Table 85.3.

Brain regions involved (McKinney et al. 2007; Fugate and Rabinstein 2015):

- Parieto-occipital (>90% of cases)
- Posterior frontal (up to 75%)
- Temporal (up to 75%)
- Cerebellum (up to 50%)
- Thalamus (one-third of cases)
- Brain stem (one-third of cases)
- Basal ganglia (one-third of cases)

Pathophysiology

A leading theory proposes that acute severe hypertension exceeds the upper limit of cerebral autoregulation, leading to breakdown of blood-brain barrier and interstitial extravasation of plasma and macromolecules resulting in cerebral edema. Paucity of sympathetic innervation to posterior brain regions makes them more susceptible. In addition to hypertension, endothelial dysfunction could arise from direct effects of excessive cytokines (Fugate and Rabinstein 2015).

Table 85.3 Causes of PRES

Hypertensive syndromes	Hypertensive encephalopathy, preeclampsia, and eclampsia
Autoimmune disorders	Systemic lupus erythematosus, Sjögren syndrome, scleroderma, granulomatosis with polyangiitis, Crohn's disease, ulcerative colitis, rheumatoid arthritis, polyarteritis nodosa, and others
Immune suppression	Tacrolimus, cyclosporine, interferon alpha, antiretroviral therapy
Chemotherapy	Cytarabine, cisplatin, gemcitabine, anti-VEGF (bevacizumab, sunitinib, sorafenib)
Hepatic and endocrine	Liver failure, primary aldosteronism, pheochromocytoma, hyperparathyroidism
Renal and electrolyte dysfunction	Renal failure, dialysis disequilibrium syndrome, hypomagnesaemia, hypercalcemia
Hematological and infectious	Thrombotic thrombocytopenic purpura, hemolytic uremic syndrome, blood transfusion, erythropoietin therapy, systemic inflammatory response syndrome
Miscellaneous associations	Contrast media exposure, intravenous immune globin therapy, ephedra overdose, scorpion poison, digoxin intoxication, tumor lysis syndrome

Symptoms associated with PRES in their order of decreasing frequency

- Encephalopathy
- Seizure
- Headache
- Visual disturbances
- Focal neurological deficits
- Status epilepticus

Crisis Management

It is important to consider and work up for potential disorders that can mimic the radiological description of PRES, as summarized below.

Differential Diagnoses for PRES

1. Infective encephalitis
   - Fever
   - Peripheral leukocytosis
   - Unilateral or bilateral on brain imaging
   - CSF pleocytosis
   - Positive CSF gram stain or culture
   - Positive CSF microbial PCR or serology
2. Central nervous system vasculitis
   - Subacute presentation
   - CSF pleocytosis

- Cytotoxic edema
- Non-PRES-like pattern

3. Stroke and vascular disorders
   - Ischemic stroke
   - Cerebral venous thrombosis
   - Cerebral autosomal dominant arteriopathy with subcortical infarcts and leukoencephalopathy (CADASIL)
4. Primary malignancy (lymphoma, gliomatosis cerebri), paraneoplastic or autoimmune encephalitis, and metastatic disease
   - Subacute to chronic clinical presentation
   - History of systemic malignancy
   - Unintentional weight loss
   - Abnormal CSF cytology
   - Antigen-specific antibody in serum or CSF
   - Absence of clinical and radiological resolution
   - Unilateral or bilateral on brain imaging
5. Demyelinating disorders
   - Acute disseminated encephalomyelitis (ADEM)
   – Usually affects children
   – Preceded by infection and fever
   – Asymmetrical supratentorial lesions which can enhance with contrast
   - Progressive multifocal leukoencephalopathy (PML)
   – Subacute to chronic clinical presentation
   - Osmotic demyelination syndrome
   – Rapid correction of sodium or glucose abnormality
   – Characteristic central pontine signal changes on imaging
6. Toxic leukoencephalopathy
   - History of illicit drug use with positive drug screen
   - Magnetic resonance spectroscopy findings of abnormally raised lactate and decreased N-acetylaspartate (NAA)

Treatment of PRES

- No RCTs assessing therapeutic interventions.
- No specific treatment for PRES; disorder is reversible when precipitating cause is treated or eliminated.
- Monitor airway ventilation and volume status.
- Antihypertensive therapy with a goal of 25% reduction in blood pressure within first few hours. Titratable intravenous drip (e.g., nicardipine 5–15 mg/h) is preferable to avoid fluctuations in blood pressure.
- Antiepileptic drugs for treatment of seizures.
- When a specific medication is identified as the cause, it needs to be discontinued, at least temporarily in the acute setting to avoid perpetuation of PRES.
- Delivery or cesarean section for eclampsia.
- Underlying disorders like sepsis, autoimmune disorders should have their recommended treatments.

Key Points

- PRES is a well-recognized clinico-neuroradiological condition.
- Although PRES is generally reversible and most commonly involves parieto-occipital region, it can involve other brain regions. Delay in diagnosis and treatment can result in irreversible neurological sequela.
- Early recognition and prompt control of blood pressure or removal of precipitating factor is essential to avoid perpetuation of PRES.

Normal Perfusion Pressure Breakthrough Edema

Overview and Pathophysiology

Cerebral edema or hemorrhage in the ipsilateral cerebral hemisphere can sometimes complicate arteriovenous malformation (AVM) treatment by endovascular obliteration or neurosurgical resection. Evidence points to relative hypotension due to loss of autoregulation in the arteries supplying the normal brain tissue adjacent to AVM, which then remain maximally dilated to maintain flow to normal brain. Following AVM resection, the redirection of blood flow to chronically dilated low-resistance vessels and failure of autoregulatory mechanisms to increase resistance to the new perfusion pressure in order to protect capillaries result in edema or hemorrhage (Spetzler et al. 1978). The term "normal perfusion pressure breakthrough (NPPB)" was coined to describe this phenomenon, which can happen in less than 10% of cases. Occlusive hyperemia (also called "venous overload") has been described as the alternate theory, in which obstruction of draining veins, in addition to stagnation of arterial flow in AVM feeders and their branches to adjacent normal brain, results in their engorgement, hyperemia, edema, and hemorrhage (Al-Rodhan et al. 1993). Clinical and radiological predictors of NPPB are summarized below.

Clinical and Radiological Predictors of NPPB

- Presence of preoperative ischemic symptoms
- Pre-existing "steal syndrome" (decrease in regional cerebral blood flow to viable adjacent parenchyma)
- Spetzler-Martin grade III or higher AVM
- Intraoperative increase in local cerebral blood flow around the nidus after temporary clipping of the feeder
- Progressive postoperative neurological deficit suggesting hemisphere ischemia
- Post procedural/postoperative CT showing cerebral swelling and contrast medium leakage

Intraoperative Prevention

There are no randomized studies that have looked into intraoperative prevention of NPPB. However, following strategies have been useful.

- Gradual increase in perfusion to ischemic hemisphere by staged ligation/embolization of feeding arteries
- Nidus embolization
- Intraoperative bleeding control

Diagnosis

TCD ultrasound in conjunction with acetazolamide to challenge vasoreactivity can be used preoperatively to identify patients with vasomotor paralysis and risk for NPPB. Intraoperative indocyanine green angiography, while quick and safe for mapping angioarchitecture of superficial AVMs, is of less value for deep-seated AVMs. Intraoperative and/or immediate postoperative angiography is therefore recommended.

Crisis Management

There are no specific guidelines or algorithm for management of this complication. When hemorrhage does occur, residual AVM as a potential cause should be ruled out first. Intra- and postoperative hypotension, barbiturate coma, and steroid use, which were based on limited evidence, are no longer used and are contraindicated. Avoidance of postoperative hypertension and maintenance of normal blood pressure are recommended (Rangel-Castilla et al. 2015). Hyperosmolar therapy can be used for the medical management of raised intracranial pressure. The role of hyperventilation, hyperoxia, and administration of L-arginine, a nitric oxide precursor which has been tried for restoration of impaired cerebral autoregulation in patients with traumatic brain injury, needs further evaluation in the setting of AVMs.

Key Points

- Cerebral AVM resection can be complicated by massive edema and hemorrhage in the ipsilateral hemisphere secondary to NPPB.
- High-grade AVMs with pre-existing steal syndrome and ischemic symptoms are at higher risk for NPPB.
- Diamox TCD can be used to predict preoperative risk for NPPB. Staged ligation/embolization of feeding arteries and maintenance of normal blood pressure while avoiding precipitous elevations in blood pressure are implicated in its management.

References

Al-Rodhan NR, Sundt TM Jr, Piepgras DG, Nichols DA, Rufenacht D, Stevens LN. Occlusive hyperemia: a theory for the hemodynamic complications following resection of intracerebral arteriovenous malformations. J Neurosurg. 1993;78(2):167–75.

Connolly ES Jr, Rabinstein AA, Carhuapoma JR, Derdeyn CP, Dion J, Higashida RT, et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. Stroke. 2012;43(6):1711–37.

Diringer MN, Bleck TP, Claude Hemphill J 3rd, Menon D, Shutter L, Vespa P, et al. Critical care management of patients following aneurysmal subarachnoid hemorrhage: recommendations from the Neurocritical Care Society's Multidisciplinary Consensus Conference. Neurocrit Care. 2011;15(2):211–40.

Dorhout Mees SM, Rinkel GJ, Feigin VL, Algra A, van den Bergh WM, Vermeulen M, et al. Calcium antagonists for aneurysmal subarachnoid haemorrhage. Cochrane Database Syst Rev. 2007;3:CD000277.

Fugate JE, Rabinstein AA. Posterior reversible encephalopathy syndrome: clinical and radiological manifestations, pathophysiology, and outstanding questions. Lancet Neurol. 2015;14(9):914–25.

Macdonald RL. Delayed neurological deterioration after subarachnoid haemorrhage. Nat Rev Neurol. 2014;10(1):44–58.

McKinney AM, Short J, Truwit CL, McKinney ZJ, Kozak OS, SantaCruz KS, et al. Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. AJR Am J Roentgenol. 2007;189(4):904–12. PubMed PMID: 17885064.

Rangel-Castilla L, Spetzler RF, Nakaji P. Normal perfusion pressure breakthrough theory: a reappraisal after 35 years. Neurosurg Rev. 2015;38(3):399–404; discussion -5. PubMed PMID: 25483235.

Spetzler RF, Wilson CB, Weinstein P, Mehdorn M, Townsend J, Telles D. Normal perfusion pressure breakthrough theory. Clin Neurosurg. 1978;25:651–72.

Suarez JI. Diagnosis and management of subarachnoid hemorrhage. Continuum. 2015;21(5 Neurocritical Care):1263–87.

Sedation, Analgesia, and Neuromuscular Blockade in Neurosurgical Critical Care

86

Travis Melin and Miko Enomoto

Overview

The essence of this chapter can perhaps be best summarized as follows: Don't contribute to delirium in the ICU. In the neurosurgical critical care setting, therapeutic goals include control of pain, relief of anxiety, and facilitation of necessary medical therapies. Ideally, the ability to follow an accurate neurological examination is preserved. Sedative-hypnotic, analgesic, and occasionally neuromuscular-blocking agents are often used to achieve these goals, but their use can be fraught with difficulty and complications. The most common and serious complications are listed in Table 86.1.

Neurosurgical patients, and critically ill patients in general, often have pain associated with their disease and/or treatment and often experience altered consciousness. Untreated pain can lead to increased anxiety and a hyperadrenergic state with resulting hemodynamic, immunologic, and neuropsychiatric effects.

Agitation can represent a significant danger to patients and staff. It may contribute to events such as falls, traumatic removal of catheters, patient-ventilator dyssynchrony, and cardiovascular instability. There may be long-term mental health consequences, as well, with the reported incidence of posttraumatic stress disorder (PTSD) in critically ill patients being between 15% and 30%.

PTSD has historically been cited as a reason to utilize sedatives in the ICU. Frequent phlebotomy, invasive procedures, indwelling catheters, and mechanical ventilation provoke anxiety in patients. Clinical studies have shown the use of benzodiazepines to be harmful, rather than helpful, in the prevention of PTSD in this setting. In fact, recall of pain and prolonged administration of GABAergic sedatives are the only factors associated with the development of PTSD after ICU admission. Indeed, trials comparing light sedation to deep sedation do not demonstrate significant difference in PTSD incidence, and patients report fewer disturbing memories when less GABAergic sedation is utilized.

Table 86.1 Complications associated with the use of sedation, analgesia, and neuromuscular blockade in neurocritical care patients

Complications
Respiratory
Respiratory depression, hypercapnia, increased ICP
Prolonged mechanical ventilation
Cardiovascular
Hypotension
Hypertension
Neurological
Over sedation
Delayed diagnosis secondary to obscured exam
Possible worsening of pathophysiology by medications
Delirium
Others
Poor pain control due to inadequate analgesia
Anxiety and agitation with inadequate sedation
Posttraumatic stress disorder (PTSD)
Increased hospital length of stay
Possible increase in organ failure
Increased mortality associated with delirium
Increased infection rate associated with prolonged mechanical ventilation
Medication-related adverse reactions
Unnecessary imaging

When treating pain, anxiety, and agitation or when inducing temporary muscle relaxation, it is important to remember that there are critical differences between the three main categories of medications discussed here. Each needs to be used appropriately:

1. Analgesics should be used for pain control, sedatives for sedation, and neuromuscular-blocking agents for paralysis. Some analgesic agents, especially opioids, do have sedative properties, but use of these agents to sedate a

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patient who does not have pain will require high doses, which is associated with respiratory depression and cognitive dysfunction. On the other hand, analgesics may be more helpful than sedatives for the treatment of agitation due to pain. Useful analgesic agents and advantages and disadvantages to their use in the neurocritical care patient are listed in Table 86.2.

2. Most sedative-hypnotic agents (notable exceptions include ketamine and alpha-2 adrenergic agonists) completely lack analgesic properties and require high doses when used as monotherapy, which often results in a comatose patient. By combining a sedative-hypnotic agent with an analgesic agent for patients who experience pain, it is usually possible to achieve a

Table 86.2 Analgesic classes of drugs, advantages, and disadvantages in the critically ill neurosurgical patient

Analgesic class	Advantages	Disadvantages
NSAIDs First-generation: (nonsteroidal anti-inflammatory drugs): ibuprofen, naproxen, flurbiprofen, ketoprofen, indomethacin, etodolac, diclofenac, ketorolac, piroxicam, and phenylbutazone	Analgesia without cognitive impairment, respiratory depression, or nausea; opioid sparing	Risk of bleeding (less with COX-2 inhibitors)
	COX-2 inhibitors are associated with less risk of bleeding, but have not been extensively studied in the postoperative neurosurgical patient	Risk of renal dysfunction (increased in elderly and decreased GFR)
		Risk of gastric ulcers (less with COX-2 inhibitors)
COX-2: rofecoxib, celecoxib, meloxicam, nimesulide		Risk of cardiovascular events (with long-term use of COX-2 inhibitors, unclear if risk increases with short-term use)
Paracetamol (acetaminophen)	Effective for control of mild pain	Inadequate relief for moderate to severe pain, as a single agent
	Opioid-sparing effect	
	No increased risk of bleeding or gastric ulcers	Risk of hepatic toxicity at high doses
	No cognitive dysfunction	
Opioids	Effective for moderate to severe pain	Respiratory depression
		Cognitive dysfunction/over sedation
		Itching
		Nausea
		Decreased GI motility
		Delirium
		Muscle weakness
		Increased pulmonary resistance and decreased chest wall compliance
NMDA antagonists: ketamine	Effective for moderate to severe pain; analgesic dose substantially lower than amnestic dose	Increase ICP in spontaneously ventilating patients (not seen in patients with controlled ventilation and eucapnea)
	Antinociceptive action (more than analgesic), effective in preemptive analgesia	Animal studies indicate neurotoxicity at high doses in neonatal and elderly brains
	Opioid-sparing effect	
	Less hypotension, decreased need for vasopressor support	Higher doses associated with hallucinations/night terrors
	Hemodynamic stimulation may be associated with improved cerebral perfusion	Cardiovascular stimulant, leads to increased myocardial oxygen consumption (can potentially be avoided with concomitant benzodiazepine use)
	Minimal respiratory depression	
	Experimental studies suggest neuroprotective effects (racemic ketamine) and regenerative effects (*S*(+)-ketamine)	
Alpha-2 adrenergic agonists: clonidine, dexmedetomidine	Minimal effect on respiratory drive	Can be associated with hypotension and bradycardia with continuous infusions
	Opioid-sparing effects	
	Provide analgesia, sedation, and anxiolysis while facilitating neurological examination	Can be associated with hypotension or hypertension with loading dose
	Suggested to have cardioprotective effects	
	Less deleriogenic compared to benzodiazepines	
Anticonvulsants (gabapentin)	Helpful in the acute treatment of neuropathic pain	Generally not effective as sole agent
	Opioid sparing	Potentially sedating
	Have a role in the treatment of alcohol withdrawal	

calm, comfortable patient with lower doses than would be required with either class alone. Useful sedative-hypnotic agents, including advantages and disadvantages for the neurocritical care patient, are listed in Table 86.3.

3. Without exception, neuromuscular-blocking drugs have no sedative or analgesic properties. It is rarely appropriate to treat with a neuromuscular-blocking drug without also giving a sedative-hypnotic agent, with the possible exception of the moribund patient. Useful neuromuscular-

Table 86.3 Sedative-hypnotic classes of drugs, advantages, and disadvantages in the critically ill neurosurgical patient

Sedative-hypnotic class	Advantages	Disadvantages
Benzodiazepines: diazepam, lorazepam, midazolam, and others	Anxiolytic, amnestic, sedative-hypnotic, and anticonvulsant properties	Diazepam and lorazepam have very long context-sensitive half-lives
	Decrease both, $CMRO_2$ and CBF, but unable to achieve burst suppression	Dose-dependent respiratory depression, synergistic with opioids
	Generally associated with less hemodynamic instability than propofol or barbiturates	Hyperosmolar acidosis with lorazepam (due to propylene glycol diluent)
		Hepatic metabolism
	Antagonist available (flumazenil)	Clearance significantly decreases with age
		Delirium
Propofol	Relatively short context-sensitive half-life; minimally effected by hepatic or renal dysfunction	Hypotension can lead to reduced CPP
	Decreases equally $CMRO_2$ and CBF, thereby decreasing ICP, putative neuroprotective agent	Dose-dependent myocardial depression, decreased systemic vascular resistance
		Dose-dependent respiratory depression
	Does not affect cerebrovascular autoregulation	Risk for life-threatening propofol infusion syndrome at very high doses (increased in neurocritical care patients)
	Effective anticonvulsant	
	Antiemetic effect	
Barbiturates: thiopental, methohexital, thiamylal	Neuroprotective by decreasing $CMRO_2$ and CBF, thereby decreasing ICP	Long elimination half-life and long context-sensitive half-time
	Thiopental is a potent anticonvulsant at high doses, but methohexital, at therapeutic doses, and thiopental, at low-doses, are epileptogenic	Rely on hepatic and renal metabolism
		Decreases CO, BP, and peripheral vascular resistance
		Dose-dependent respiratory depression
Alpha-2 adrenergic agonists: clonidine, dexmedetomidine	Provide sedation, anxiolysis, and analgesia without inducing unresponsiveness or coma	Can be associated with hypotension and bradycardia with continuous infusions
	Associated with lower rates of delirium than benzodiazepines	Can be associated with hypotension or hypertension with loading dose
	Mitigates symptoms of EtOH withdrawal	No amnestic properties when used as single agent
	Minimal effect on respiratory drive	
	Opioid-sparing effects	
	Facilitate neurological examination	
	Potentially cardioprotective	
NMDA antagonist: ketamine	Effective for moderate to severe pain; analgesic dose substantially lower than amnestic dose	Increase ICP in spontaneously ventilating patients (not seen in patients with controlled ventilation and eucapnea)
	Antinociceptive action (more than analgesic), effective in preemptive analgesia	Animal studies indicate neurotoxicity at high doses in neonatal and elderly brains
	Opioid-sparing effect	
	Less hypotension, decreased need for vasopressor support	Higher doses associated with hallucinations/night terrors
	Hemodynamic stimulation may be associated with improved cerebral perfusion	Cardiovascular stimulant, leads to increased myocardial oxygen consumption (can potentially be avoided with concomitant benzodiazepine use)
	Minimal respiratory depression	
	Experimental studies suggest neuroprotective effects (racemic ketamine) and regenerative effects (*S*(+)-ketamine)	
Inhalational anesthetics	May be associated with less severe delusional memories and hallucinations (compared to, e.g., midazolam)	Not commonly used outside the operating room in the USA
		Require special equipment
		Risk for malignant hyperthermia
		Risk for nausea

Table 86.4 Neuromuscular-blocking classes of drugs, advantages, and disadvantages in the critically ill neurosurgical patient

Neuromuscular-blocking drug class	Advantages	Disadvantages
Depolarizing NMB: succinylcholine	Short acting	Increases ICP, IOP
	Fast onset	Mandates airway management
	Facilitate tracheal intubation	Infusions can be associated with phase II block
		Hyperkalemia; particularly concerning in patients with renal failure, immobile patients, patients with preexisting neuromuscular disease, or paralysis
		Risk for malignant hyperthermia
Non-depolarizing NMB: Intermediate-duration agents are the most commonly used for maintenance of NMB in the ICU: atracurium, cisatracurium, rocuronium, vecuronium	Facilitate tracheal intubation and mechanical ventilation and can be helpful in cases of refractory elevated ICP	Use mandates airway management and mechanical ventilation
		Risk of critical illness myopathy and polyneuropathy with prolonged use
	Cisatracurium clearance is independent of end-organ function (Hofmann degradation)	Increased risk of nosocomial pneumonia
	Rocuronium is available for rapid sequence induction (RSI) at adequate doses (1.2 mg/kg)	Associated with longer mechanical ventilation, hospital stay
		Increased risk of polyneuropathy and increased duration of action in the setting of renal failure make pancuronium a less attractive neuromuscular blocker in the ICU setting

blocking agents, including advantages and disadvantages for the neurocritical care patient, are listed in Table 86.4.

Delirium

Delirium is defined in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-IV as a disturbance of consciousness and cognition which develops over a short period of time (hours to days) and fluctuates over time. Delirium can be categorized into hyperactive, hypoactive, and mixed delirium. Pure hypoactive delirium is the most common in critically ill patients, as well as the most difficult to diagnose. Mixed delirium is also relatively common. Pure hyperactive delirium is relatively rare in this population, an often triggered by withdrawal from regular use of drugs or alcohol.

Delirium is now recognized as an adverse event that carries significant morbidity and mortality. It is estimated to occur in up to 80% of patients admitted to the ICU. There is strong evidence that delirium is associated with increased length of hospital stay and ICU stay, longer duration of mechanical ventilation, decreased cognitive function, and increased mortality. Although the pathophysiology is complex, many commonly used pharmacological agents and factors common to the ICU environment are thought to contribute.

Identified risk factors for delirium include preexisting dementia, hypertension, history of alcoholism or use of recreational drugs, high severity of illness, coma, and benzodiazepine use. Additional contributing factors include sleep deprivation, hypoxia, anoxia, hypercarbia, metabolic abnormalities, and numerous medications (predominantly those with anticholinergic activity) including opioids. The American Geriatrics Society updated the Beers Criteria in 2015 (a list of inappropriate medications for elderly patients, initially created by Mark H. Beers M.D.), which contain a full list of medications believed to contribute to delirium.

Delirium is also frequently seen in postoperative patients in the ICU. This population is often exposed to additional risk factors including long duration of surgery, deeper levels of intraoperative sedation, poor vision/hearing, electrolyte derangement, and poor postoperative pain control.

Pathophysiology

Undoubtedly, the unwanted psychoactive effects of drugs used for sedation and analgesia in the intensive care environment play a major role in the etiology of delirium. There are multiple hypotheses for the pathogenesis of delirium: neurotransmitter imbalance (with the greatest focus being on an excess of dopamine and deficient acetylcholine), CNS inflammation, and impaired oxidative metabolism. In all likelihood, these and other mechanisms contribute.

Because of the serious sequelae (increased length of stay and increased morbidity and mortality), onset of delirium must be seen as a crisis, akin to failure of another organ system (i.e., kidneys).

Patient Assessment

Diagnosis of delirium in critically ill patients requires assessing every patient's level of consciousness on a regular basis.

There are two important components in this evaluation: (1) arousal (sedation) assessment and (2) content (delirium) assessment. Level of consciousness can be assessed using any one of a number of ICU-validated sedation scales [Ramsay scale, SAS, RASS, and motor activity assessment scale (MAAS)]. Patients who are deeply sedated or comatose (RASS≤ -4) cannot be evaluated for content. Validated instruments for assessing thought content in critically ill, even ventilated, patients include the Intensive Care Delirium Screening Checklist (ICSDC) and the CAM-ICU.

In the neurocritical care patient, it is imperative to first rule out treatable and life-threatening causes of altered mental status (e.g., intracranial hemorrhage, cerebral edema, hydrocephalus, cerebral vasospasm, ischemia, seizures, intoxication, infection [e.g., urinary tract infection; meningitis], etc.). Vigilance is necessary to identify typical symptoms, which should then trigger systematic evaluation for potentially treatable causes. In addition to physical examination, appropriate imaging studies, EEG, and screening for infections should always be included in the initial diagnostic workup in these patients.

Intervention/Treatment

There are no FDA-approved treatments for delirium. The best treatment is prevention. Treatment of acute agitation/hyperactive delirium involves the use of non-pharmacologic and pharmacologic methods to maintain patient safety. In addition to the use of sedative hypnotics (to reduce the immediate danger the patient poses to self or others) and analgesics, the selective use of antipsychotic medications may be an important therapeutic strategy.

Haloperidol (Haldol), a D2 receptor antagonist and typical antipsychotic, is frequently used to treat acute agitation/hyperactive delirium in the critical care setting. However, several significant risks need to be considered, including the risk for extrapyramidal effects, QT prolongation, and malignant neuroleptic syndrome, all of which may occur even with moderate doses. In addition, some experimental data suggest that dopamine and norepinephrine antagonists may delay neuronal recovery and impair neuronal plasticity. Among persons with traumatic brain injury, typical antipsychotics appear to exacerbate cognitive impairments and may prolong the period of posttraumatic amnesia.

Atypical antipsychotics such as quetiapine (Seroquel), olanzapine (Zyprexa), and risperidone (Risperdal) are being increasingly used in the critical care setting. Quetiapine may be effective in decreasing the duration of delirium in patients who are critically ill (including mechanically ventilated), but tends not to interfere strongly with cerebral dopaminergic function and produces fewer adverse motor effects than haloperidol. These agents may facilitate, or at least not adversely affect, cognition when used for the treatment of posttraumatic delirium.

Table 86.5 Antipsychotic drugs, advantages, and disadvantages in the critically ill neurosurgical patient

Antipsychotic class	Advantages	Disadvantages
Typical antipsychotics: haloperidol	Useful as a chemical restrain in patients who present danger to self of others	Risk of extrapyramidal effects, QT prolongation, torsades, and malignant neuroleptic syndrome
	May be beneficial to prevent postoperative delirium	Black box warning, increased mortality when used for dementia-related psychosis
		Sedating
		No evidence to suggest effectiveness in delirium in ICU setting
Atypical antipsychotics: olanzapine, quetiapine, risperidone	May reduce duration of delirium	Sedating
		Similar risk profile to typical antipsychotic

Treatment of hypoactive delirium, the most common and most difficult to diagnose type of delirium, is difficult. Today's treatments center on the predominate theory that hypoactive delirium is due to excess central serotonin. Atypical antipsychotics, especially risperidone which is less sedating, are the most studied therapies so far.

Ultimately, the diagnosis of delirium in the neurosurgical patient population remains a challenge and requires a high index of suspicion and an awareness of the harmful effects of common medications. Antipsychotics used in the management of delirium are listed in Table 86.5.

Prevention

The lack of effective therapies for treating existing delirium places a greater focus on the need for preventative measures. Historically, management of mechanically ventilated patients in the ICU involved infusions of both opioid and sedative medications and was likely necessary with the mechanical ventilator technology at the time. However, it is now well understood that this approach is associated with increased incidence of delirium, mortality, PTSD, prolonged intubation, and various length of stay measures. Additionally, modern ventilators have a variety of synchronous modes that decrease the need for sedation. Ideal practice today would include treating pain with intermittent dosing of multimodal analgesic agents and using sedatives only when additional sedation is absolutely required for patient safety. Indeed, one trial has even shown positive outcome differences when using a no-sedation strategy in mechanically ventilated patients.

Patients in the neurosurgical ICU are frequently admitted for postoperative surveillance and treatment. Several strategies have been shown to be of benefit in this unique population. Utilization of preoperative non-opioid analgesia (ketamine, acetaminophen, etc.) and regional anesthesia and intraoperative use of higher BIS/lighter sedation are useful as delirium prevention strategies.

Additional preventative measures include ensuring patients with hearing aids or visual devices have them on or available as appropriate. Utilization of devices that limit mobility such as Foley catheters, chest tubes, and especially physical restraints should be limited as much as possible.

Whenever possible, patients should follow a regular day-night cycle. Waking patients frequently overnight should be avoided in favor of bundled and coordinated care times. Melatonin receptor antagonists have recently been used successfully to prevent delirium by pharmacologically mimicking day-night cycling.

Additional measures may be helpful, including:

- Frequent orientation
- Maintenance of a calm and quiet environment
- Minimizing distracting stimuli (televisions)
- Exposure to natural light
- Prompt treatment of infections and metabolic disturbances and frequent screening for subclinical infections (UTI)
- Promoting regular daytime voiding

Guidelines

Several groups, including the Society of Critical Care Medicine, have published guidelines for the treatment and management of pain, agitation, and delirium (PAD) in the ICU. There is a large body of evidence to suggest that certain interventions can minimize the impact and incidence of delirium. The PAD guidelines suggest the implementation of care bundles such as the awakening and breathing coordination, delirium monitoring/management, early exercise/mobility, and family engagement (ABCDEF) bundle. Bundle implementation has been shown to prevent and minimize the impact of delirium in both ventilated and non-ventilated patients.

Awakening and Breathing Coordination

- Maintain an analgesia-first strategy, bolus dosing preferred to infusion.
- Aim for light levels of sedation.
- Use non-benzodiazepine sedatives when sedation is necessary.
- Use non-opioid analgesia/regional anesthesia when possible to minimize opioid used.

Delirium Monitoring and Management

- Routinely monitor for delirium using a validated tool such as the Confusion Assessment Method for the ICU (CAM-ICU).
- There are no well-established pharmacological methods for preventing/treating delirium, though small studies suggest atypical antipsychotics may decrease duration of delirium.
- Maintenance of normal sleep-wake and day-night cycles by grouping patient care activities, reducing noise, light, and awakenings.
- Rivastigmine (acetylcholinesterase inhibitor) is not effective.

Early Exercise and Mobility

- Initiate prompt physical therapy and early mobilization.

Family Engagement

- Utilization of family members to provide a calming and familiar environment

Key Points

- Delirium in the critically ill patient is associated with increased morbidity and mortality and needs to be rigorously monitored.
- Minimize sedation using an analgesia-first approach to decrease ventilator days and ICU length of stay.
- Minimize the use of psychoactive medications when possible.
- Most sedatives (with the exception of ketamine, dexmedetomidine, and clonidine) lack analgesic properties.
- With the exception of the treatment of alcohol withdrawal, GABA agonists, especially benzodiazepines, increase the risk of delirium and PTSD.
- Prolonged neuromuscular blockade conveys significant risk to the patient and is indicated only when other means of treating patient-ventilator dyssynchrony or elevated ICP have failed, or in other rare instances.

Suggested Reading

American Geriatrics Society 2015 Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2015;63(11):2227–46.

Arciniegas DB, McAllister TW. Neurobehavioral management of traumatic brain injury in the critical care setting. Crit Care Clin. 2008;24(4):737–65, viii.

Balas MC, Vasilevskis EE, Olsen KM, Schmid KK, Shostrom V, Cohen MZ, et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. Crit Care Med. 2014;42(5):1024–36.

Baron R, Binder A, Biniek R, Braune S, Buerkle H, Dall P, et al. Evidence and consensus based guideline for the management of delirium, analgesia, and sedation in intensive care medicine. Revision 2015 (DAS-Guideline 2015) – short version. Ger Med Sci GMS e-J. 2015;13:Doc19.

Barr J, Fraser GL, Puntillo K, Ely EW, Gelinas C, Dasta JF, et al. Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Crit Care Med. 2013;41(1):263–306.

Bergeron N, Dubois MJ, Dumont M, Dial S, Skrobik Y. Intensive Care Delirium Screening Checklist: evaluation of a new screening tool. Intensive Care Med. 2001;27(5):859–64.

Chan MT, Cheng BC, Lee TM, Gin T. BIS-guided anesthesia decreases postoperative delirium and cognitive decline. J Neurosurg Anesthesiol. 2013;25(1):33–42.

de Wit M, Gennings C, Jenvey WI, Epstein SK. Randomized trial comparing daily interruption of sedation and nursing-implemented sedation algorithm in medical intensive care unit patients. Crit Care (London, England). 2008;12(3):R70.

Friedman JI, Soleimani L, McGonigle DP, Egol C, Silverstein JH. Pharmacological treatments of non-substance-withdrawal delirium: a systematic review of prospective trials. Am J Psychiatry. 2014;171(2):151–9.

Girard TD, Pandharipande PP, Ely EW. Delirium in the intensive care unit. Crit Care (London, England). 2008;12(Suppl 3):S3.

Hatta K, Kishi Y, Wada K, Takeuchi T, Odawara T, Usui C, et al. Preventive effects of ramelteon on delirium: a randomized placebo-controlled trial. JAMA Psychiat. 2014;71(4):397–403.

Himmelseher S, Durieux ME. Revising a dogma: ketamine for patients with neurological injury? Anesth Analg. 2005;101(2):524–34, table of contents.

Lai LT, Ortiz-Cardona JR, Bendo AA. Perioperative pain management in the neurosurgical patient. Anesthesiol Clin. 2012;30(2):347–67.

Maldonado JR. Pathoetiological model of delirium: a comprehensive understanding of the neurobiology of delirium and an evidence-based approach to prevention and treatment. Crit Care Clin. 2008;24(4):789–856, ix.

Riker RR, Shehabi Y, Bokesch PM, Ceraso D, Wisemandle W, Koura F, et al. Dexmedetomidine vs midazolam for sedation of critically ill patients: a randomized trial. JAMA. 2009;301(5):489–99.

Sackey PV, Martling CR, Carlsward C, Sundin O, Radell PJ. Short- and long-term follow-up of intensive care unit patients after sedation with isoflurane and midazolam – a pilot study. Crit Care Med. 2008;36(3):801–6.

Strom T, Martinussen T, Toft P. A protocol of no sedation for critically ill patients receiving mechanical ventilation: a randomised trial. Lancet (London, England). 2010;375(9713):475–80.

The Confusion Assessment Method for the ICU (CAM-ICU) training manual. http://wwwicudelirium.org/delirium/CAM-ICU-Training.html. SCCM; 2013.

Trogrlic Z, van der Jagt M, Bakker J, Balas MC, Ely EW, van der Voort PH, et al. A systematic review of implementation strategies for assessment, prevention, and management of ICU delirium and their effect on clinical outcomes. Crit Care. 2015;19:157.

Airway and Pulmonary Management in Neurosurgical Critical Care

87

Edward M. Manno

Airway Management

Overview

Management of airways in patients with intracranial hypertension secondary to trauma, intracerebral hemorrhage, subarachnoid hemorrhage, or other space-occupying lesions requires a special set of knowledge and skills. The physician managing acute airway emergencies in critically ill patients needs to be familiar with cerebrovascular physiology and the management of intracranial hypertension.

Patients with a Glasgow Coma score of ≤8 are generally intubated for airway protection. With progressive deterioration in levels of consciousness, there will be a loss of pharyngeal reflexes and muscular tone. Under these circumstances, the tongue will fall posteriorly, and the pharyngeal muscles will relax leading to the obstruction of the upper airway. The purpose of elective intubation in this population is to secure the airway to prevent aspiration, maintain adequate oxygenation, and prevent hypercapnia. The practice of electively intubating patients with a GCS ≤8 was supported by a retrospective analysis of the national traumatic coma data base which reported an increase in aspiration rates and worse outcomes in comatose patients that were not immediately intubated.

Prevention of Complications

Aspiration Pneumonia

The risk of aspiration is high in patients with significant alteration in level of consciousness. Almost all urgent endotracheal intubations will require rapid sequence intubation with little opportunity to empty the stomach prior to intubation. Cricoid pressure is generally used to prevent regurgitation and aspiration of gastric contents during endotracheal intubation. However, cervical neck injuries may limit the amount of cricoid pressure that can be applied. The cricoid is located at approximately C_4–C_5. If possible, evaluation for the level of injury with a focused neurological exam and neck images should precede endotracheal intubation in patients with a stable airway and good oxygenation (pulse oximetry of greater than 95% on less than 40% inspired oxygen). Although far from ideal, a Combitube can be placed to facilitate ventilation (and help to prevent aspiration), until a clinician with appropriate expertise can secure the airway (either with endotracheal intubation or tracheostomy).

Hypoxia

Hypoxia has been reported in >50% of severe head trauma patients who are not immediately intubated. Hypoxia and hypercapnia will cause cerebral vasodilation and increases in intracranial pressure. The morbidity and mortality of prolonged hypoxia defined as a PaO_2 of <60 mmHg is almost 50%. A functional airway needs to be obtained immediately.

- Clearing the mouth of foreign objects, suctioning, and providing a chin lift and jaw thrust to avoid cervical injury can be performed quickly.
- Bag-mask ventilation with high-flow oxygen should be applied as soon as safely possible. In the setting of hypoxia and hypercapnia, bag-mask ventilation may be necessary, even in patients at risk of regurgitation and aspiration.
- All patients with a depressed level of consciousness and the loss of protective airway reflexes should be intubated. The nature and type of neurological injury will dictate the exact approach for safe and efficient intubation.

In general, nasal tracheal intubation is avoided in head trauma due to the possibility of basilar skull fractures. Also

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nasal tracheal intubations may be associated with a higher incidence of sinus infection, and patient discomfort may lead to excessive agitation with head and neck movement with possible worsening of hypoxia.

Cervical Neck Injury

Cervical neck injury occurs in about 10% of all severe head trauma and should be assumed in most accidents. Prophylactic spinal immobilization and careful airway management may prevent secondary spinal cord injury. Most injuries occur at C_5–C_6 and C_6–C_7; however, higher lesions may occur. Patients with cervical lesions above C_3 will lose phrenic nerve innervation to the diaphragm and will need immediate intubation. Patients with lesions below C_5 retain diaphragmatic function but will lose the use of their thoracic intercostal muscles. This leads to a form of paradoxical respiration where the abdomen protrudes and the thorax involutes with inspiration. Patients with these injuries will ventilate better in the supine position since this position will push the abdominal contents upward, thus maximizing diaphragmatic muscle length and optimizing muscle contraction with subsequent air movement. Many, if not most, of these patients will also require intubation since the patient's functional residual capacity will decrease as atelectasis progresses. Under these circumstances, an ineffective cough, inadequate chest wall expansion, and incomplete emptying of the lungs can lead to inadequate clearance of secretions and poor gas exchange.

Endotracheal intubation should occur with the technique that maximizes the likelihood of first chance success and minimizes cervical spine motion. In an emergency, in-line stabilization with direct laryngoscopy is appropriate, whereas under more elective situations, fiberoptic bronchoscopy may be appropriate. In-line stabilization can be performed by an assistant holding the head and neck in alignment from below. Traction from above does not need to be applied and can interfere with the individual performing laryngoscopy. Nasal intubation can be considered but holds the same drawbacks as listed above.

Intracranial Hypertension

Increased intracranial pressure is common in many forms of acute neurological injury. In addition, endotracheal intubation can lead to increased intracranial pressure and subsequent decreases in cerebral perfusion. This response can be attenuated by premedication with intravenous lidocaine or local application of topical anesthesia to airway structures. The use of succinylcholine (1–2 mg/kg) as a paralytic agent to facilitate rapid airway management is common practice. The clinical importance of increased intracranial pressure occurring with the use of succinylcholine appears small. In the balance, the risk of increased intracranial pressure with hypoxia is far greater than the risk of increased intracranial pressure with succinylcholine. Thus succinylcholine should be used for rapid airway management in patients with head injury unless the patient also presents with crush injuries, seizures, prolonged bed rest, or under any circumstance where there may be direct muscle damage due to concerns of the development of life-threatening hyperkalemia. Under these circumstances, rocuronium may be a better choice as a quick-onset paralytic. Rocuronium or vecuronium however will limit the neurological assessment of the patient for an extended period of time. A new reversal agent, Sugammadex, has been developed for these agents and can be used judiciously to rapidly reverse the duration of their paralytic effects.

Once the airway is secured, hyperventilation can occur to decrease intracranial hypertension through vasoconstriction of cerebral arterioles and veins and a reflex decrease in cerebral blood volume. This effect, however, is relatively short lived, on the order of a few hours, and thus other methods of decreasing intracranial hypertension should be initiated as soon as they become available.

Crisis Management

Many issues in airway management in the neurological patient will occur under emergency conditions. Following airway management, many patients will need emergent surgery or transfer to an intensive care unit.

Head trauma provides several possible problems. For example, patients with significant facial trauma may not be able to be safely bag-mask ventilated. In these circumstances, placement of a Combitube or laryngeal mask airway may be needed prior to endotracheal intubation, despite the risk that these patients are at significant risk for regurgitation and aspiration. Fiber-optic intubation after placement of an oral airway is preferred if possible. Cricothyroidotomy may need to be performed, if severe facial trauma precludes any form of endotracheal intubation. This, however, is a technique of last resort since the complication rate is as high as 30% when placed under emergency situations.

Multiple medical issues may also complicate the neurological patient in need of acute airway management. Cardiac or pulmonary contusion, tension pneumothorax, cardiac tamponade, and other chest wall injuries are common in trauma patients. Many patients will be hypovolemic on presentation and will need active fluid resuscitation. Several induction agents administered at the time of intubation may compromise cardiac output and blood pressure. Etomidate may cause less cardiovascular depression than propofol or thiopental and does not compromise cerebral blood flow. However, myoclonus that is often observed after injection of etomidate can be mistaken for seizure activity and confuse the clinical assessment. Furthermore, the full clinical impact

of the adrenal suppression effects of etomidate is unknown. Vasopressors and atropine need to be available at the time of induction, to facilitate rapid treatment of induction-/intubation-induced alteration in hemodynamics. Long-acting paralytic agents are ideally avoided in the neurological patient to allow for serial neurological examinations.

Key Points

- Neurological emergencies present with some of the most difficult airway management issues.
- Patients with a Glasgow Coma score ≤8 are intubated for airway protection.
- Outcome after head trauma is directly related to the length of time a patient is hypoxic.
- Cervical neck and facial injuries provide specific challenges to airway management.
- Intracranial hypertension is assumed in most patients with neurological emergencies and needs to be addressed during airway management.
- Sugammadex may be used to reverse deep neuromuscular blockade if an assessment of neurological status is needed quickly.

Pulmonary Management

Overview

Pulmonary complications are common after neurological injury. Aspiration can occur at the time of trauma, hemorrhage, or after seizures. Patients treated in intensive care units are at risk for nosocomial pneumonia. Prolonged immobilization in patients with spinal cord injury is associated with increased risk for pulmonary emboli and pneumonia. One study of pulmonary complications in patients with intracerebral hemorrhage reported pneumonia in 20%, pulmonary edema in 8%, and rare cases of pulmonary emboli and acute respiratory disease states. Pulmonary complications were related to a Glasgow Coma score ≤8 and endotracheal intubation. Patients with pulmonary complications had longer length of stays and worse outcomes. Patients with ischemic stroke that require mechanical ventilation have a mortality >60%.

Prevention of Complications

Nosocomial Pneumonia

Nosocomial pneumonias are prevented by thorough application of pulmonary hygiene and respiratory therapy. The ventilator bundle, a series of maneuvers designed to decrease medical complications, should be employed when feasible. Obviously, certain populations (i.e., cervical injuries) may not be immediately amenable to head of bed elevation. Rotation beds for immobilized patients are useful for decreasing pneumonia. Compulsive oral care with chlorhexidine has been shown to decrease the incidence of nosocomial pneumonias in a medical intensive care unit population but has not been studied directly in a neurological population.

Extubation should occur as soon as feasible. Many patients in a neurological intensive care unit are intubated for airway management (level of consciousness) issues and not for primary pulmonary difficulties. Traditional teaching has required that a patient have a Glasgow Coma score >8 prior to extubation. A large retrospective study, however, suggested that maintaining endotracheal intubation based on mental status alone led to an increase in nosocomial pneumonia and worse outcome. A safety and feasibility trial has recently been completed testing the hypothesis that comatose patients with pulmonary and airway control can be extubated.

Pulmonary Emboli

Prevention of pulmonary emboli in a neurological population can be challenging. Neurological injured patients are at high risk for the development of deep venous thrombosis. Patients with spinal cord injury and the neurosurgical population are at particular risk.

Available evidence suggests that the early implementation of subcutaneous heparin is useful for the prevention of deep venous thrombosis and can be used safely in a neurosurgical population. Despite this many neurosurgeons have reservations and will not administer anticoagulants to patients who have recently had surgery (or who are planned to have surgery). Sequential compression devices should be used in all patients. When used properly, sequential compression devices decrease the incidence of deep venous thrombosis formation. In high-risk populations (e.g., neurosurgery patients), when possible, both heparin (low dose and low molecular weight) should be used in combination with sequential compression device stockings. In patients who are at a great risk for administering heparin, consideration should be given to sequential screening for deep venous thrombosis (Doppler ultrasound) and with confirmation to placement of an inferior vena cava filter, to prevent the consequences of devastating pulmonary emboli.

Crisis Management

Neurogenic pulmonary edema is common after severe neurological injury. The proposed mechanisms involved include massive sympathetic discharge directly to the contractile elements of the pulmonary endothelium. This leads to the devel-

opment of a pulmonary exudate. Concurrently, sympathetically mediated cardiac stunning and pulmonary venoconstriction lead to congestive heart failure. The pulmonary edema can be abrupt, severe, and present with significant hypoxia. Treatment is largely supportive. Diuresis may improve oxygenation. Inotropic or vasopressor support is common. A Swan-Ganz catheter or transesophageal echo evaluation can be useful for directing management. Most neurogenic pulmonary edema will resolve or improve within a few days to a week.

Standard diagnostic methods and treatments of pneumonia and acute respiratory disease states are used in the neurological population. Fluid management may be complicated in acute respiratory disease states since volume depletion is avoided in most neurological disease states. Maintaining euvolemia with hypertonic solutions could be one possible solution.

Key Points

- Pulmonary complications are common after neurological injury and increase length of stay and worsen outcomes.
- Prolonged immobilization places many patients at high risk for deep venous thrombosis and pulmonary emboli. Treatment includes the use of compression stocking and sequential compression devices. Early institution of subcutaneous heparin can be beneficial.
- Aggressive diuresis and support are needed for the management of neurogenic pulmonary edema. Neurogenic pulmonary edema is usually self-limited.

Suggested Reading

Airway References

Albin MS. Textbook of neuroanesthesia. New York: McGraw Hill; 1997.

Luce JM. Cardiopulmonary physiology and management in neurosurgical intensive care. In: Andrews BT, editor. Neurosurgical intensive care. New York: McGraw-Hill; 1993. p. 1–43.

Pulmonary References

Coplin WP, Pierson DJ, Cooley KD, Newell DW, Rubenfeld GD. Implication of extubation delay in brain injured patients meeting extubation criteria. Am J Respir Crit Care Med. 2000;161:1530–6.

Maramattom BV, Weigand S, Reinalda M, Manno EM, Wijdicks EFM. Pulmonary complications after acute intracerebral hemorrhage. Neurocrit Care. 2006;5:1–5.

Smith WS, Matthay MA. Evidence for a hydrostatic mechanism for neurogenic pulmonary edema. Chest. 1997;111:1326–33.

Myocardial and Vascular Management in Neurosurgical Critical Care

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Neurogenic Stunned Myocardium

Overview

The most likely etiology of cardiac injury after SAH is the increased release and decreased reuptake of catecholamines, specifically circulating norepinephrine. Neurogenic cardiac injury following SAH is characterized by electrocardiographic abnormalities (ECG), arrhythmias, myocardial infarction (both non-ST elevation and ST elevation), left ventricular dysfunction, elevation of troponin, and cardiac arrest. Stress-induced cardiomyopathy, also called "neurogenic stunned myocardium," "transient left ventricular apical ballooning," "Takotsubo cardiomyopathy," and "broken heart syndrome," is an increasingly reported phenomenon. It is a transient condition and is typically precipitated by intense physiologic stress including that precipitated by brain injury and has even been described in the context of a profound emotional crisis. Typically stress-induced cardiomyopathy is reversible after several weeks.

Prevention

Prevention is by avoiding the physiologic stress itself. All patients presenting with intracranial pathology should have a 12-lead ECG and cardiac enzyme measurements (e.g., troponin) on admission and telemetry until their neurologic condition has stabilized. A thorough history and physical examination is necessary to identify patients at risk for primary cardiac disease. Awareness of the potential for neurogenic stunned myocardium, especially in those patients presenting with severe neurologic injury, will aid in the prompt search and diagnosis if myocardial stunning occurs.

Diagnosis

The clinical presentation is identical to that of an acute MI; however, coronary arteriography shows no critical lesions. It is important to differentiate the two; stunned myocardium is a reversible condition that will resolve completely in about 80% of the patients within days-weeks after the initial event, whereas a primary ischemic injury may cause irreversible cardiac dysfunction. Other diagnostic characteristics of neurogenic myocardial stunning include:

- Abnormal wall motion involving the cardiac apex and midportion with relative sparing of the base, termed "apical ballooning"
- ST segment elevation or depression or T-wave changes
- A prolonged QT interval
- Increased cardiac enzymes
- More common in elderly or postmenopausal females
- Precipitated by acute physiologic or emotional stress

Characteristics that are commonly associated with neurogenic myocardial stunning and not with ischemic acute coronary syndrome (ACS) are no history of cardiac problems, new onset left ventricular dysfunction, cardiac wall motion abnormalities on echo that do not correlate with the coronary vascular distribution, and cardiac troponin levels <2.8 ng/ml. If there is doubt, then coronary angiography should be performed if feasible.

Proposed mechanisms include catecholamine excess, coronary artery spasm, and microcirculatory dysfunction. Postmortem examinations of hearts that displayed characteristics of stress-induced cardiomyopathy do not show overt pathology in the majority of cases. However, microscopic analysis reveals myofibrillar degeneration, myocytolysis, and inflammatory cell infiltration unevenly distributed

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throughout the heart, but most dense at the apex and ventricular subendocardial areas.

Crisis Management

Treatment of the underlying neurologic insult will aid in the resolution of myocardial stunning. Patients with significant heart failure and hemodynamic compromise will need inotropic and vasopressive support for a period of time. Early involvement of a cardiologist is recommended.

Key Points

- Onset subsequent to an acute emotional or physiologic stress such as brain injury.
- Similar presentation to acute MI, therefore, must differentiate between the two.
- Typical echocardiographic appearance of apical ballooning without angiographic critical lesions.
- Inotropic and vasopressive support may be necessary.
- Complete resolution of the apical wall motion abnormality and depressed cardiac function typically within 48 h after the initial insult and with successful treatment of neurologic crisis.

Cardiac Arrhythmias

Many cardiac arrhythmias can occur in neurologically injured patients with known cardiac disease as well as in those without. Some arrhythmias are attributable to coronary artery insufficiency or ischemia, but others are due to conduction disturbances that result from the neurological illness itself. The most frequent arrhythmias following brain injury are premature ventricular complexes, sinus arrhythmia, and atrial fibrillation. Other arrhythmias including atrial flutter, ventricular tachycardia, torsades de pointes, ventricular fibrillation, and asystole have been documented as well. SAH patients have arrhythmias about 35–85% of the time. Life-threatening arrhythmias occur in <5% of patients with SAH. As with neurogenic myocardial stunning, resolution of the acute intracranial pathology, e.g., normalization of the ICP, injury generally leads to improvement or resolution of arrhythmias.

Supraventricular Tachycardia/Arrhythmia

Overview

Supraventricular tachycardia (SVT) such as sinus tachycardia, atrial fibrillation, and paroxysmal supraventricular tachycardia (PSVT) is common in all critical care settings. Sinus tachycardia (HR >100/min) usually represents a physiologic response to pain, stress, hypotension, heart failure, or excessive catecholamine drive.

Atrial fibrillation (A-fib) with or without a rapid ventricular response (RVR) is commonly seen with acute neurologic insults particularly in the elderly. A fair number of patients manifest atrial arrhythmias, mainly atrial fibrillation, within the first few days after stroke. Occasionally, a cardiac arrhythmia will actually be the initial event that provokes brain injury because of clot formation in the heart that embolizes into the brain (ischemic stroke). However, in other cases, the original injury is in the brain, which then is associated with cardiac rhythm disturbances. RVR is often an urgent issue as it can precipitate a demand ischemia of the myocardium or may compromise cardiac function. PSVT is related to a reentry or similar mechanism at the AV node. See Table 88.1 for management.

Table 88.1 Supraventricular arrhythmia crisis management

Sinus tachycardia	Analgesia and sedation as appropriate, fluid and electrolyte replacement, resolution of the precipitant
Atrial fibrillation	Determine chronicity – if new onset is less than 48 h old, then chemical or electrical cardioversion can be instituted. If more than 48 h since onset or undetermined delay cardioversion until anticoagulation can be instituted. Echocardiography to evaluate for clot formation prior to cardioversion. Beta-adrenergic blockers first line – labetalol or esmolol
	Diltiazem and digoxin, if hypotension is a problem
PSVT	Vagal stimulation maneuvers – carotid sinus massage. Adenosine, amiodarone, diltiazem, and beta-blockade can all be effective

Prevention

Cardiac monitoring for all ICU patients, adequate pain control, assessment of volume status, adequate sedation, careful assessment of electrolyte balance, and treatment of precipitating cause is paramount to prevention (Table 88.1).

Ventricular Arrhythmias

Overview

Ventricular tachycardia, ventricular fibrillation, and torsades de pointes are less common than atrial tachycardias in the neurocritical care unit. These particular arrhythmias are likely a cause for sudden death in patients with a significant neurologic insult. Isolated premature ventricular contractions (PVCs) are common and do not require treatment, but if they occur with increasing frequency, they may signify elevated ICP and the risk for serious ventricular arrhythmias.

Table 88.2 Ventricular arrhythmia crisis management

Ventricular tachycardia (VT)	For significant hemodynamic compromise cardioversion and ACLS guidelines as appropriate
	If hemodynamically stable – amiodarone, then cardioversion
	Polymorphic VT gives magnesium sulfate IV and cardioversion
Ventricular fibrillation (VF)	Early defibrillation according to ACLS guidelines
Torsades de pointes	Stop all QT-prolonging medications, magnesium sulfate IV, and cardioversion

Ventricular flutter and fibrillation are more commonly seen in patients with underlying ischemic heart disease. See Table 88.2 for management.

Prevention

All patients with a neurologic injury or insult need cardiac monitoring until the acute phase of the illness has resolved, as prompt treatment will be necessary for ventricular arrhythmias. Monitoring of QT intervals is important as a prolonged QT places a patient at risk for ventricular ectopy.

Bradycardia

Overview

A HR below 60 bpm is usually the result of sinus node dysfunction or an atrioventricular conduction disturbance. Acute cerebral insults can also produce a vasovagal response. Bradycardia can be seen after carotid angioplasty and stenting procedures from direct and prolonged carotid sinus stimulation as well. Bradycardia in a neurocritical care patient is a red flag for increased intracranial pressure. The triad of bradycardia, hypertension, and respiratory depression is, of course, termed the "Cushing reflex" and results from acutely increased intracranial pressure. Always consider increased ICP as one of the differential diagnoses for bradycardia and hypertension in the context of neurologic injury. This is of particularly concern, if the disease process is suspected in the posterior fossa.

Crisis Management

Cardiac monitoring and careful assessment of a patient's neurologic exam and ICP monitoring as appropriate is paramount to identify the precipitating causes. Consider anticholinergic drugs such as atropine and glycopyrrolate and transcutaneous or transvenous pacing in the presence of significant hemodynamic compromise.

Key Points

- Arrhythmias occur in the neurologically injured with and without intrinsic cardiac disease.
- All brain-injured patients need cardiac monitoring until the acute phase of illness has passed.
- SAH patients have arrhythmias about 35% of the time. Life-threatening arrhythmias occur in <5% of patients with SAH.
- Ventricular arrhythmias are less common than supraventricular arrhythmias.
- For life-threatening arrhythmias institute cardioversion and ACLS early.
- Chronicity of atrial fibrillation should be determined before cardioversion because of the possibility of mural thrombus and the risk for embolic stroke.
- Bradycardia may be a sign of increased ICP as part of Cushing's triad.

Blood Pressure Disturbances in the Neurocritical Care Unit

The central nervous system (CNS) is susceptible to extremes in blood pressure (BP) fluctuations. Hypertension can be associated with increased risk of bleeding and cerebral edema. Hypotension can be associated with infarcts or global ischemia. Cerebral blood flow (CBF) is relatively constant over a wide range of systemic blood pressures in a healthy brain.

The autoregulation curve is shifted rightward in chronically hypertensive patients (CBF remains stable at higher mean arterial blood pressures (MAP) but becomes flow passive that is prone to ischemia already at low-normal MAP). This section focuses on blood pressure management in the setting of subarachnoid hemorrhage, intracranial hemorrhage, and ischemic stroke.

Hypertension in SAH

Overview

Blood pressure management in SAH differs according to the presence of an aneurysm, if that aneurysm has been surgically secured, and the presence of additional/residual aneurysms. Hypertension is common immediately following aneurysmal rupture and often reflecting a hyperadrenergic state and/or increased ICP with a Cushing's response. For hypertension in ruptured and unsecured aneurysms, maintaining systolic BPs in a range for adequate perfusion while avoiding rapid and extreme changes in BP is paramount to avoid shear stress on an aneurysm. Shear stress places the patient at risk for rebleeding. Generally systolic BP goals should be between 120 and 160 mmHg while keeping a cerebral perfusion pressure (CPP)

>70 mmHg to avoid exacerbation of cerebral ischemia. CPP is calculated as MAP – ICP or CVP, whichever is greater – and it ranges normally between 70 and 100 mmHg. After an aneurysm has been secured, BP goals should shift in an upward direction due to lessened risk of bleeding and the increased risk of vasospasm. Permissive hypertension is a strategy after an aneurysm is secured to obtain higher perfusion pressures with the goal to prevent further brain ischemia. Arterial hypertension is frequently even induced therapeutically for the treatment of cerebral vasospasm. The technique involves the use of vasopressors and IV fluids to achieve a higher than normal MAP and thus augment the CPP. These therapies have the goal of preventing or ameliorating brain ischemia, which is created by cerebral vasospasm.

Prevention

All patients with SAH should have beat to beat blood pressure monitoring via an arterial line in addition to cardiac monitoring. Initial prevention of hypertension in SAH includes initiation of sedation, analgesia, antiepileptic therapy, and nimodipine (a calcium channel blocker shown to improve outcome in SAH) all of which lower blood pressure.

Crisis Management

Blood pressure management (see Table 88.3) is used in conjunction with ICP control as appropriate (hyperventilation, head of bed elevation >30°, anti-edema therapies, CSF drainage), as well as surgical evaluation for clipping and coiling of aneurysms as determined by a neurosurgeon to prevent further injury.

Hypertension in Intracerebral Hemorrhage

Overview

Intracerebral hemorrhage (ICH) includes nontraumatic brain injuries with bleeding into the epidural, subdural, subarachnoid, intraventricular, and intraparenchymal spaces. There are many causes for nontraumatic ICH. Hypertension is an important cause for ICH, and it is of utmost importance to control for the prevention of further bleeding leading to hematoma expansion and poor outcomes. Management of BP is individualized depending on the cause of the ICH. Patient factors such as chronic hypertension (which shifts the CBF autoregulation curve to the right), age, and time from the hemorrhage are all important factors to consider.

Table 88.3 Therapeutic hypertension goals in SAH with vasospasm

Secured aneurysm	Titrate vasopressors to SBP 180–200, DBP 100–120, MAP 120–140
Unsecured aneurysm	Titrate vasopressors to SBP 160–170, DBP 90–100, MAP 100–120

Table 88.4 Commonly used antihypertensive medications

Drug	Dose
Labetalol	5–10 mg IV q10′ as needed
Enalaprilat	
Hydralazine	0.625–1.250 mg IV q6h as needed
Esmolol	2.5–10 mg (up to 40 mg/dose) IV q4–6 h as needed
Nicardipine	0.25–0.5 mcg/kg load; 50–200 μg/kg/min

Prevention

All patients, who are at risk for rebleeding after ICH, should remain under intensive care surveillance and have beat to beat blood pressure monitoring via an arterial line in addition to cardiac monitoring. Initiation of analgesia and sedation (with close monitoring of neurologic function) as appropriate are initial steps for blood pressure management.

According to the American Heart Association (AHA) guidelines treat for:

- SBP >230 mmHg or DBP >140 × 2 readings 5 min apart – sodium nitroprusside
- SBP 180–230 mmHg or DBP 105–140 mmHg or MAP >130 mmHg × 2 readings 20 min apart – IV labetalol, esmolol, enalaprilat, or nicardipine

Crisis Management

Goal CPP with ICP monitoring is >70 mmHg.

Blood pressure management is used in conjunction with ICP control (hyperventilation, head of bed elevation >30°, anti-edema therapies) as well as surgical evacuation to prevent further injury. See Table 88.4 for suggestions of antihypertensive medications.

Hypotension in ICH

Overview

Determination of hypotension depends on the patient's history and clinical picture, the presence of elevated ICP, and the cause of an ICH. Hypotension is relatively uncommon in ICH.

Prevention

Close monitoring of BP and assessment of a patient's volume status are paramount to the prevention of hypotension, which can place a patient at risk for or exacerbation of brain ischemia.

Crisis Management

Treatment with volume replacement is usually first line avoiding hypotonic and glucose-containing solutions. Normal saline and hypertonic saline are the fluids of choice as appropriate. Vasopressors may be indicated.

Hypertension in Ischemic Stroke

Overview

Most ischemic stroke patients become hypertensive after the onset of symptoms. In addition, many affected patients are hypertensive at baseline as one of the risk factors for the disease. Hypertension during the acute poststroke time period is usually thought of as beneficial, to improve perfusion to the ischemic penumbra via collateral circulation. Balancing the potential benefits of hypertension with the risk of hemorrhagic transformation of a large stroke is an important consideration.

Prevention

All patients with ischemic stroke, who are critically ill, should have beat to beat blood pressure monitoring via an arterial line in addition to cardiac monitoring. Consider careful sedation and analgesia, if appropriate with close monitoring of neurologic function.

Crisis Management

The specific blood pressure targets established by the American Heart Association depend on whether the patient has received IV tissue plasminogen activator (tPA). The rationale for this is that patients who have received IV tPA are at higher risk of bleeding complications. For patients after ischemic stroke who have not received tPA, permissive hypertension should be allowed to a SBP up to 220 mm Hg. For patients who have received tPA or thrombectomy, SBP should be lowered only when it rises above SBP 180 mm Hg. Any patient who suffers a hemorrhagic transformation of their stroke should have blood pressure maintained below SBP 140 mm Hg.

Key Points

- Hypertension is common following SAH, ICH, and ischemic stroke and is secondary to the underlying pathophysiology, a hyperadrenergic state, and increased ICP and need for elevated CPPs.
- Blood pressure management is crucial in SAH to prevent further ischemic damage secondary to rebleeding, increased ICP, and vasospasm.
- Hypertension is an important cause for ICH blood pressure control which is paramount to prevent hematoma expansion and poorer outcomes.
- Treatment of hypertension in ischemic stroke should be avoided unless BP is profoundly elevated SBP >220 mmHg or MAP >130 mmHg, or IV thrombolytics were given (tight control for 24 h).

Suggested Reading

Banki N. Acute neurocardiogenic injury after subarachnoid hemorrhage. Circulation. 2005;112:3314–9.

Bhardwaj A, Mirski M, Ulatowski JA. Handbook of neurocritical care. Totowa: New Jersey: Humana Press Copyright; 2004.

Bybee KA, et al. Systematic review: transient left ventricular apical ballooning: a syndrome that mimics ST –segment elevation myocardial infarction. Ann Intern Med. 2007;141(11):858–65.

Chen S, Li Q, Wu H, Krafft PR, Wang Z, Zhang JH. The harmful effects of subarachnoid hemorrhageon extracerebral organs. Biomed Res Int. 2014;858496:2014.

Grunsfeld A, Fletcher JJ, Branett RN. Cardiopulmonary complications of brain injury. Curr Neurol Neurosci Rep. 2005a;5:488–93.

Grunsfeld A, Fletcher JJ, Barnett RN. Cardiopulmonary complications of brain injury. Curr Neurol Neurosci Rep. 2005b;5(6):488–93.

Macmillan CSA, Grant IS, Andrews PJD. Pulmonary and cardiac sequelae of subarachnoid hemorrhage: time for active management? Intensive Care Med. 2002;28(8):1012–23.

Naval NS, Stevens RD, Mirski MA, Bhardwaj S. Controversies in the management of aneurysmal subarachnoid hemorrhage. Crit Care Med. 2006;34(2):511–24.

Ropper AH. Neurological and neurosurgical intensive care. 4th ed. Philadelphia: Lippincott Williams and Wilkins; 2004. Copyright.

Virani SS, Khan AN, Mendoza CE, Ferreira AC, de Marchena E. Takotsubo cardiomyopathy, or broken heart syndrome. Houston: Division of Cardiology Texas Heart Institute at St. Lukes Episcopal Hospital, Baylor College of Medicine. Tex Heart Inst J. 2007;34(1):76–9.

Wybraniec MT, Mizia-Stec K, Krzych L. Cardiol J. 2014;21(3):220–8.

Wybraniec MT, Mizia-Stec K, Krzych L. Neurocardiogenic injury in subarachnoid hemorrhage: a wide spectrum of catecholamin-mediated brain-heart interactions. Cardiol J. 2014;21(3):220–8.

Nutrition and Glucose Management

89

Michael J. Souter and Arthur M. Lam

Overview

Nausea, anorexia, vomiting, and feeding intolerance after brain insult and injury can significantly compromise nutritional status, compounded by cognitive and behavioral deficits. Over 60% of patients requiring rehabilitation for brain injury demonstrate problems with swallowing, with an aspiration incidence of over 40%.

Feeding intolerance may be compounded by iatrogenic gastric stasis, ileus, and constipation induced by concurrent pharmacotherapy, in addition to any coincident abdominal injury from primary trauma.

Not surprisingly, acute injury to the brain is associated with significant weight loss (averaging 13 kg), from the time of injury to the start of rehabilitation, with 60% of such patients at less than 90% of their ideal body weight.

Aggressive enteral feeding protocols have been adopted to compensate, but even in these circumstances, brain injury is associated with nutritional feeding intolerance in up to 55% of cases. The incidence is decreased by the use of continuous enteral feeding as opposed to bolus feeding. Risk factors associated with feeding intolerance in the brain injured and general ICU populations are listed in Table 89.1.

Subsequent nutritional deficit and hypoproteinemia may further affect fluid and electrolyte balance, as well as complicating healing, protein binding, and pharmacokinetics. The resulting intestinal edema will diminish absorption, in conjunction with an enteropathy of malnutrition.

Table 89.1 Risk factors associated with feeding intolerance

General ICU population	Brain injury
Traumatic brain injury (TBI)	TBI
Diabetes mellitus/hyperglycemia	Mechanical ventilation
Sepsis	Paralytics
Narcotics	Increasing age
Sedatives	Ischemic stroke
Catecholamine infusions	Intracerebral hemorrhage
Gastric residual volumes >100 ml	
Recumbent position	

Erosive stress ulceration (Cushing ulcers) is a very real risk – protocolized gastric acid prophylaxis is recommended until feeding is established. Prophylaxis itself is associated with increased frequency of aspiration pneumonia related to gastric pH changes and bacterial colonization.

Any primary deficiency in intake is complicated by the observed hypermetabolic response after brain injury, with a resting metabolic expenditure of up to 240% of patients without neurotrauma (Table 89.2).

This hypermetabolism results in an induced catabolism of protein, fat, and glycogen stores. Protein breakdown may in turn affect availability of drug binding sites and plasma kinetics, oncotic forces determining water distribution, and hormonal binding proteins with consequent endocrine effects – all magnified by the effects of feeding deficiency.

Any other increases in metabolic requirements (e.g., fever, seizures) may further aggravate the relative nutritional insufficiency.

Systematic review of feeding within 24 h of trauma has demonstrated a significant reduction in mortality (OR 0.2), albeit with limited study numbers.

Conversely, failure to establish feeding by 5 days has been associated with a two- to fourfold increase in the risk of death, with a dose-effect relationship between caloric inadequacy and mortality rate, even when controlling for age, hypotension, and intracranial hypertension.

While some studies suggest that enteral feeding is associated with fewer complications than parenteral feeding, meta-

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Table 89.2 Metabolic responses to brain injury

Increases	Decreases
Increased cortisol	Albumin
Glucagon	Thyroxine binding protein
Catecholamines	Thyroxine retinol binding prealbumin
O_2 consumption	Serum zinc
CO_2 production	
Acute phase proteins – including fibrinogen and CRP	
Release of calcium from bone	
Urinary calcium excretion	
Urinary zinc excretion	

analysis suggests more equivalence. Both are superior to delayed feeding. Jejunal tubes are associated with less pulmonary infection than gastric tubes and offer more security in quality and volume of feeding, being less susceptible to ileus and/or obstruction. They are however more demanding of time and expertise in placement – frequently requiring radiologic guidance.

In either circumstance facial injuries and/or basal skull fracture may compromise the ability to pass the tube safely, in which case a percutaneous gastrostomy may be required.

This is a largely inevitable requirement for intermediate and long-term feeding, given the reduced incidence of feeding intolerance, sinusitis, oral infection, aspiration, and pneumonia. There are however significant complications of misplacement that are not infrequent – including hemorrhage and peritonitis. Assiduous care should be taken to secure the tube once in place.

A common frustration of all tube placement is the patients' disinhibition and/or inability to comprehend and obey commands after brain injury, resulting in the compromise of feeding routes.

Glucose intolerance and hyperglycemia are frequently observed, with strong associations to worse outcomes within all etiologies of brain injury. The benefit of intervention to restore systemic normoglycemia remains unproven however, with some concerns for associated increased cerebral metabolic stress.

Electrolyte derangements may occur as a consequence of injury stress response to systemic trauma, with retention of sodium and water, but increased losses of potassium.

Overfeeding can occur in long-term patients with hepatic steatosis, centripetal obesity, and ventilatory dysfunction as a consequence of diaphragmatic embarrassment.

Prevention

Avoidance of nutritional difficulties is best accomplished by attention to the risk factors above. However, there is an obligate catabolism after brain injury that cannot be avoided by any current therapies.

Multidisciplinary team rounding together with the presence of protocols to initiate feeding and monitor nutritional progress has been demonstrated to protect against tissue breakdown. Regular monitoring and surveillance of both intake and nutritional screen results is a necessary component of daily review to limit and avoid the complications of inadequate, mismatched, or excessive feeding.

Crisis Management

Pathophysiology and Clinical Presentation

- Hypercatabolism and malnutrition are unlikely to present as acute crises but can acutely complicate the presentation of other problems.
- Hyperglycemia above 170 mg/dl has been associated with a poor outcome in brain-injured patients, while levels above 140 mg/dl had a worse mortality in a series of critically ill postsurgical patients.
- Conversely both cerebral glycopenia and systemic hypoglycemia have been reported with the introduction of aggressive insulin regimens. However, several recent studies suggest that these systemic hypoglycemic episodes may not be associated with significant effects on longer-term outcome. The significance of reduction in cerebral glucose, however, remains uncertain. There is evidence of associated cerebral metabolic stress but little in the way of outcome data. Moderate targets of 100–140 remain reasonable at this time.
- Even with conservative insulin regimens, particular care must be taken to maintain continuity of the supply of energy substrate, especially when feeding intolerance develops.
- Refeeding syndrome – some populations with preexisting nutritional compromise are more likely to suffer brain injury, e.g., preceding alcohol or drug abusers, as well as the elderly and indigent populations. Their protracted malnourishment reduces body stores of potassium, magnesium, and phosphorous while preserving serum concentrations. Energy demands are supplied from fat stores with relative protein sparing and reduction in insulin secretion. Abrupt restitution of carbohydrate supply induces anabolic restoration of normal intracellular stores. The consequent ionic shift results in an acute reduction of serum phosphate, magnesium, and calcium with a deficit of adenosine triphosphate and 2,3 DPG. Thiamine is frequently depleted contributing a superimposed encephalopathy. The hypophosphatemia also inhibits sodium and water excretion. The end result is impaired diaphragmatic/respiratory power, myocardial contractility, oxygen dissociation, and neuromuscular function, the combination of which can be fatal. This can be avoided by careful monitoring and staged institution of feeding to patients with known risk factors.

- Abdominal stasis is a frequent complication seen in patients with brain injury – arising from associated autonomic dysfunction and associated abdominal injuries or complicating the use of narcotics and sedatives. Inauspicious presentation may be followed by progressive abdominal hypertension, diaphragmatic embarrassment, post-renal obstruction, and if particularly severe, abdominal compartment syndrome. Attention to the use of prokinetics, stool softeners and aperients as well as the early recognition of presenting signs and symptoms are key components of care.
- Stress gastric erosion arises commonly within 24 h of brain injury, correlating with the severity of insult, and related etiologically to hypothalamic autonomic activation. It presents with hemorrhage in 17% of cases, with an associated mortality of 50% after bleeding. The incidence in ischemic stroke is relatively low (although aspirin usage increases risk), while spinal cord injury demonstrates an incidence of up to 20%, supporting the concept of vagally mediated hypersecretion. The prophylactic use of H2-antagonists, proton pump inhibitors, and sucralfate has significantly reduced the development of serious hemorrhage. This is at the expense of associated changes in gastric pH, consequent colonization by enteric bacterial flora (including increased risk of *C. difficile*), and an increased incidence of pneumonia associated with aspiration of infected gastric content. Ventilator-associated pneumonia is seen in over 50% of patients with TBI. Prophylactic agents should be removed as soon as feeding is established, while the head of the bed should be elevated to at least 30°.
- Diarrhea is a frequent complication of enteric feeding. Possible etiologies include *C. difficile* superinfection, hyperosmolarity of feed, and excess fiber. Hyperosmolarity of feed is relatively easily prevented with regular appraisal of needs, as is the control of fiber content.

  Sixteen percent of patients admitted to rehabilitation after brain injury are already colonized by *C. difficile*, associated chiefly with antibiotic-induced changes in intestinal flora. Typical clinical manifestations of symptomatic infection include diarrhea, abdominal pain, low-grade fever, and leukocytosis. The possible exacerbations include colitis, liver abscess, bacteremia, sepsis, splenic and pancreatic abscesses, peritonitis, small bowel enteritis, and bone and prosthetic joint infection. Treatment is with oral metronidazole and thereafter intravenous vancomycin in resistant cases.

Patient Assessment

A nutritional screen on admission should include physical exam and the assessment of basal metabolic rate. While albumin and prealbumin can be useful trend monitors, they tend to reflect catabolic activity of inflammation rather than nutritional reserve and protein depletion. Trace elements and phosphate levels can be measured on admission and at regular intervals with the caveat that serum levels may not reflect total body stores as mentioned above.

Indirect calorimetry remains the gold standard of energy requirement assessments. Normal adult requirements are of the order of 2500 kCal/day. The Harris-Benedict equation has been employed for many years to determine energy requirements but has been shown to underestimate those of brain injured patients. A conversion factor of 1.4 improves the accuracy of calculation.

The Mifflin St Jeor equation is currently recommended by the American Dietetic Association as providing the most accurate energy calculation in the care of the critically ill, although it remains unproven in the context of brain injury.

Intervention/Treatment

Suggested nutritional goals are listed in Table 89.3.

"Immune-enhancing" formulas (containing arginine, glutamine, probiotics, omega-3 fatty acids, etc.) have demonstrated reduced infection risks when compared to standard formulas, and there has been no evidence to support theoretical concerns of excitatory side effects arising from conversion of glutamine to glutamate. Obviously coexisting renal compromise will require the use of low protein feed. There is significant interest currently in polydrug regimes of vitamins, flavonoids, and trace elements.

The use of anabolic agents such as growth hormone has been shown to reduce nitrogen loss and catabolic activity but at the expense of increased mortality in the critically ill – their use is not recommended.

Key Points

- Nutrition is frequently compromised after brain injury and insult by limited opportunity of intake and significant obligatory catabolism.
- Outcome is adversely affected by nutritional dysfunction.
- Iatrogenic exacerbation of feeding intolerance is common.
- Good nutritional control is best achieved by multidisciplinary input, protocolized care and systematic appraisal.
- Normoglycemia is associated with better outcomes, and while moderate glucose ranges appear a reasonable strategy for the brain, the effects of intervention upon cerebral metabolism and outcome remain uncertain.

Table 89.3 Suggested nutritional targets for patients after brain injury

Protein	1.5–2.2 g/kg/day
Calories: Harris Benedict	Women: BMR = 655 + (4.35 × weight in lbs) + (4.7 × height in inches) − (4.7 × age) Men: BMR = 66 + (6.23 × weight in lbs) + (12.7 × height in inches) − (6.8 × age)
Calories: Mifflin St Jeor	Male: BMR = (10 × weight in kg) + (6.25 × height in cm) − (5 × age) + 5 Female: BMR = (10 × weight in kg) + (6.25 × height in cm) − (5 × age) − 161
Lipids	30–40% of calculated caloric requirements
Omega 3:6 ratio	1:2 to 1:4

Suggested Reading

Chapple LS, Deane AM, Heyland DK, Lange K, Kranz AJ, Williams LT, Chapman MJ. Energy and protein deficits throughout hospitalization in patients admitted with a traumatic brain injury. Clin Nutr. 2016;35(6):1315–22. https://doi.org/10.1016/j.clnu.2016.02.009. [Epub ahead of print].

Cook AM, Peppard A, Magnuson B. Nutrition considerations in traumatic brain injury. Nutr Clin Pract. 2008;23:608–20.

Doig GS, Heighes PT, Simpson F, Sweetman EA. Early enteral nutrition reduces mortality in trauma patients requiring intensive care: a meta-analysis of randomised controlled trials. Injury. 2011;42(1):50–6.

Finfer S, Chittock D, Li Y, Foster D, Dhingra V, Bellomo R, Cook D, Dodek P, Hebert P, Henderson W, Heyland D, Higgins A, McArthur C, Mitchell I, Myburgh J, Robinson B, Ronco J. Intensive versus conventional glucose control in critically ill patients with traumatic brain injury: long-term follow-up of a subgroup of patients from the NICE-SUGAR study. Intensive Care Med. 2015;41(6):1037–47.

Horn SD, Kinikini M, Moore LW, Hammond FM, Brandstater ME, Smout RJ, Barrett RS. Enteral nutrition for TBI patients in the rehabilitation setting: associations with patient pre-injury and injury characteristics and outcomes. Arch Phys Med Rehabil. 2015;96(Supp):S245–55.

Kerner A, Schlenk F, Sakowitz O, Haux D, Sarrafzadeh A. Impact of hyperglycemia on neurological deficits and extracellular glucose levels in aneurysmal subarachnoid hemorrhage patients. Neurol Res. 2007;29(7):647–53.

Vespa P, McArthur DL, Stein N, Huang SC, Shao W, Filippou M, Etchepare M, Glenn T, Hovda DA. Tight glycemic control increases metabolic distress in traumatic brain injury: a randomized controlled within-subjects trial. Crit Care Med. 2012;40(6):1923–9.

Vonder Haar C, Peterson TC, Martens KM, Hoane MR. Vitamins and nutrients as primary treatments in experimental brain injury: clinical implications for nutraceutical therapies. Brain Res. 2016;1640(Pt A):114–29.

Wang X, Dong Y, Han X, Qi XQ, Huang CG, Hou LJ. Nutritional support for patients sustaining traumatic brain injury: a systemic review and meta-analysis of prospective studies. PLoS One. 2013;8(3):1–14.

Wang D, Zheng SQ, Chen XC, Jiang SW, Chen HB. Comparisons between small intestinal and gastric feeding in severe traumatic brain injury: a systematic review and meta-analysis of randomized controlled trials. J Neurosurg. 2015;123(5):1194–201.

Fluid and Electrolyte Management in Neurosurgical Critical Care

90

Guillermo Bugedo and Maria Magdalena Vera

Overview

Imbalance and dysregulation of the fluid and electrolyte homeostasis are common and of great concern in patients after insults to the central nervous system. Disturbances may occur as a part of the disease process or they may be iatrogenic. The consequences of fluid and electrolyte derangements are frequently life-threatening and are recognized to determine outcome, particularly if unrecognized or persistently severe.

Fluid Management

Prevention

Traumatic Brain Injury (TBI)

Outcome after TBI depends on the magnitude of the initial insult and upon the extent of secondary injuries to the brain that may result if the insult is survived. Systemic hypotension is a major cause of secondary brain injury and should be prevented and treated aggressively. Restoration of normovolemia with isotonic or hypertonic fluids is one essential component of the therapeutic strategy aimed at restoration of adequate blood pressure, thus ameliorating ischemia and further brain damage.

Fluid management in patients with TBI and brain edema presents many challenges, including preserving adequate cerebral perfusion pressure (CPP), avoiding hypervolemia, and maintaining osmolality.

Some decades ago, hypovolemia and dehydration were widely accepted in order to decrease brain edema ("keep them dry"), inadvertently producing hypotension and jeopardizing brain perfusion.

Rosner et al., in the mid-1990s, challenged this concept by directing treatment at preserving CPP. Fluid management was aimed at maintaining euvolemia or mild hypervolemia. Isotonic crystalloids, albumin, and packed red blood cells (RBC) were used for the first 24–48 h, to obtain pulmonary artery wedge pressures (PAWP) above 12 mm Hg and central venous pressure (CVP) above 8 mm Hg and to mobilize extravascular water into the vascular space, with the objective of decreasing brain edema.

At a similar time, the Lund concept, introduced in Sweden, focused on improving perfusion and oxygenation around contusions (perfusion-targeted goal) but also in reducing intracranial pressure (ICP-targeted goal). For this approach, normovolemia is mandatory, which is accomplished by RBC transfusions to normal hemoglobin (12.5–14.0 g/dl) and albumin to normalize plasma oncotic pressure. This fluid therapy was intended to decrease brain edema and improve microcirculation. Diuretics (but not mannitol) were used to avoid hypervolemia and promote hypernatremia.

Both the Rosner and the Lund approach require maintenance of normovolemia to avoid hypotension and assure brain perfusion. Careful fluid balance is mostly important to reduce the progressive accumulation of fluids in the extracellular matrix, which can worsen brain edema and increase ICP.

Subarachnoid Hemorrhage (SAH) and Vasospasm

Cerebral vasospasm is a leading cause of morbidity and mortality aneurismal SAH. Hypertensive, hypervolemic, and hemodilution ("triple-H") therapy was introduced more than 20 years ago to improve cerebral blood flow in these patients. Several studies described the effectiveness of triple-H therapy for preventing neurologic deficits due to cerebral vasospasm. However, its efficacy has not been proven in randomized controlled clinical trials. Furthermore, triple-H therapy has severe side effects, such as pulmonary edema or arrhythmias, and caution must be taken in older patients or those with cardiovascular diseases. Pulmonary artery catheter, continuous cardiac output monitoring

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(e.g., PiCCO (Pulse index Continuous Cardiac Output)), or repeat echocardiography may help orient fluid loading in these patients.

Crisis Management

Crystalloids Versus Colloids?

In patients with TBI, both isotonic crystalloids (lactated Ringer's solution and 0.9% NaCl) and colloids can be used to achieve normovolemia. However, there is uncertainty about the best choice of fluids due to the lack of adequately powered randomized, controlled trials. Crystalloid-based fluid strategies are favored in trauma resuscitation protocols, although the clinical evidence is limited. In the SAFE study, which compared saline versus albumin for fluid resuscitation, in 460 patients with TBI, use of albumin was associated with higher mortality rates than was resuscitation with saline (33.2% vs 20.4%, $P = 0.003$). Lactated Ringer's solution and 0.9% NaCl can be safely in patients with TBI. Hypertonic solutions can also be used to increase plasma osmolality and decrease cerebral edema. Most of these fluid loading protocols are based on physiologic endpoints, assuming that prompt restoration of the blood volume will prevent hypotension and improve the outcome of patients with brain injury.

In patients after SAH, colloids are suggested along isotonic crystalloids to adequate fluid loading (see above). If the patient remains hypotensive and/or neurologic impairment does not improve despite fluid loading, blood pressure support may be achieved with noradrenaline (0.05–0.3 μg/kg/min) to a goal mean arterial pressure (MAP) of 100–130 mmHg.

Optimal Hematocrit?

Anemia is common in neurocritical care patients and is thought to be associated with worse outcomes by a number of specialists. Although hemoglobin (Hb) concentrations as low as 7 g/dL are well tolerated by most critically ill patients, data from animal and human studies suggest that such a severe degree of anemia may jeopardize cerebral and systemic perfusion, being harmful in the brain-injured patient. Beneficial physiologic effects of transfusion have been shown in patients with severe TBI. However, in a recent clinical trial in 200 patients with closed head injury, neither the administration of erythropoietin nor maintaining a hemoglobin concentration of greater than 10 g/dL resulted in improved neurological outcome.

The importance of ischemia in causing secondary brain injury appears to vary for different neurocritical care conditions. For example, cerebral vasospasm and delayed infarction are major causes of morbidity after a ruptured aneurysm. In contrast, the relevance of cerebral ischemia in the pathophysiology of TBI or intracerebral hemorrhage (ICH) is more debated.

Electrolyte Disturbances and Management

Hyponatremia

Hyponatremia is the most important and frequently encountered electrolyte disturbance in the neurocritical care setting. Plasma sodium concentration is the main determinant of plasma osmolality, which regulates the movement of water inside and outside the cells. Thus, hyponatremia (Na <135 mmol/L) is particularly deleterious in the neurologic population, as it will produce or increase brain edema.

Crisis Management

Pathophysiology

Hypothalamic-pituitary-adrenal axis dysfunction can occur at any time during TBI and is more common with severe injuries. There can be multiple hormonal disturbances in TBI, but not all are associated with clinically significant sequelae. Among the most important are the syndrome of inappropriate antidiuretic hormone secretion (SIADH) and the cerebral salt-wasting syndrome (CSWS). However, hyponatremia may also occur secondary to multiple other conditions (Table 90.1 and Fig. 90.1), as, for example, the iatrogenic excess free water and hypotonic fluid administration. Frequently, hypovolemia may contribute to or perpetuate a hyponatremic state.

Table 90.1 Common causes of hyponatremia in the neurosurgical patient

Decreased ECF Volume
Extrarenal sodium loss
Diarrhea
Vomiting
Blood loss
Excessive sweating
Renal sodium loss
Cerebral salt-wasting syndrome
Diuretics
Osmotic diuresis
Adrenal insufficiency
Normal ECF Volume
Syndrome of inappropriate ADH secretion
Central nervous system diseases
Drugs (carbamazepine)
Pulmonary conditions
Thiazide diuretics
Adrenal insufficiency
Hypothyroidism
Primary polydipsia
Increased ECF Volume
Congestive cardiac failure
Renal failure
Cirrhosis

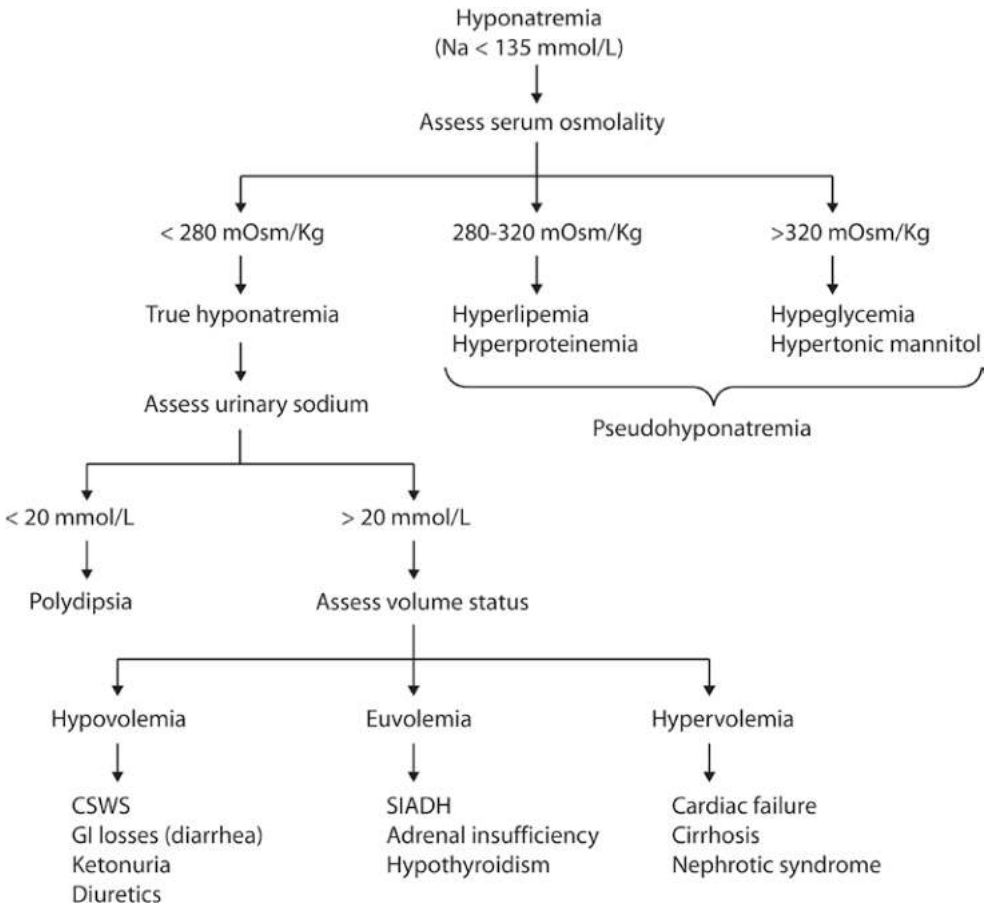

Fig. 90.1 Algorithm for the diagnosis of hyponatremia. *CSWS* cerebral salt-wasting syndrome, *GI* gastrointestinal, *SIADH* syndrome of inappropriate secretion of antidiuretic hormone

Syndrome of Inappropriate Antidiuretic Hormone Secretion

The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is associated with many clinical conditions: neoplasia, nonmalignant lung diseases, drugs, and neurologic diseases, including brain tumors, stroke, aneurysmal subarachnoid hemorrhage (SAH), traumatic brain injury (TBI), meningitis, and encephalitis. Carbamazepine-related hyponatremia might also be relevant in these patients. Clinical features are nonspecific and depend upon the absolute serum sodium level and rate of development.

Diagnostic criteria for SIADH require:

- Serum sodium <135 mmol/L
- Serum osmolality <280 mmol/kg
- Urine sodium >40 mmol/L
- Urine osmolality > serum osmolality (usually >100 mOsm/kg)
- Normal thyroid, adrenal and renal function
- The absence of peripheral edema or dehydration
- The absence of potassium and acid-base abnormalities
- The absence of use of diuretic agents

Cerebral Salt-Wasting Syndrome

CSWS is characterized by polyuria and marked natriuresis, leading to hyponatremia and hypovolemia. High levels of brain natriuretic peptide (BNP) have been described in patients with SAH and vasospasm. It usually occurs during the first 2 weeks after brain injury and resolves spontaneously after 2–4 weeks.

Biochemical and clinical criteria for CSWS include:

- Serum sodium <135 mmol/L
- Low or normal serum osmolality
- High urine sodium (>50–100 mmol/L)
- Clinical hypovolemia

The key clinical diagnostic factor in CSWS is the presence of volume depletion and hyponatremia. However, CSWS and SIADH are often difficult to differentiate in the clinical setting, and response to treatment may help determine the diagnosis (Table 90.2).

Clinical Presentation and Assessment

Symptoms due to acute hyponatremia are secondary to its effects on the brain and include headache, anorexia, lethargy,

Table 90.2 Clinical features of syndrome of inappropriate antidiuretic hormone (SIADH) and cerebral salt-wasting syndrome (CSWS)

	SIADH	CSWS
Extracellular fluid volume	Increased	Normal/decreased
Plasma volume	Increased/normal	Decreased
Salt balance	Positive/equal	Negative
Water balance	Positive/normal	Negative
Preload	Normal/increased	Decreased
Serum sodium	Low	Low
Serum potassium	Normal	Normal/increased
Serum uric acid	Decreased	Normal/decreased
Serum BUN/creatinine	Decreased	Increased
Serum osmolality	Decreased	Decreased
Urine sodium	High	High/very high
Urine osmolality	High	Normal/high
Urine volume	Normal/variable	High

nausea, and vomiting. Left untreated and as plasmatic sodium drops below 115 mmol/L, hyponatremia may result in seizures, coma, respiratory arrest, and death. Noncardiogenic pulmonary edema has also been described.

Hyponatremia is an important comorbidity in the neurosurgical population and may adversely affect outcome. It may be a cause of refractory intracranial hypertension in patients with TBI. In patients with SAH and vasospasm, hyponatremia may increase the frequency and fatality of brain infarction.

Treatment of Hyponatremia

Two basic principles involve the correction of hyponatremia: raising the plasma Na+ at a safe rate and to a safe level and diagnose and treat the underlying cause.

In patients with severe TBI and increased ICP, reaching a Na+ concentration of 150–155 mmol/L is a common therapeutic goal to decrease brain edema. In these patients, mild hyponatremia (130–135 mmol/L) could be disastrous and should be treated vigorously.

A differentiation must be made if hyponatremia is associated with hypervolemia (suggesting SIADH) or hypovolemia (suggesting CSWS) as treatments are opposed: SIADH is best treated by fluid restriction, while CSWS requires sodium (and fluid) loading. If diagnostic uncertainty exists, sodium administration may be attempted before fluid restriction, as hypovolemia may jeopardize brain perfusion and worsen outcome. Isotonic fluids, such as normal saline, often in excess of 5 l, may be necessary to restore normal Na and promote volume expansion in patients with CSWS.

Fluid restriction alone or isotonic fluids have no role in the immediate management of severe hyponatremic encephalopathy, and hypertonic solutions, such as 3% sodium chloride/acetate, have been safely used in patients with SAH and in the immediate management of severe hyponatremic encephalopathy.

Exogenous mineralocorticoids, such as fludrocortisone (0.1–0.6 mg daily), which induce a positive salt balance, can be safely used in patients with CSWS. Recently, ADH receptor antagonists ("aquaretics") have been tested and shown effective in SIADH.

Correction of hyponatremia requires frequent measurement of serum sodium levels, and the rate of correction should not exceed 0.5 mEq/L/h to avoid adverse effects associated with rapid serum sodium correction (e.g., pontine myelinolysis). When hypertonic solutions are used in patients with brain edema, sodium levels should be closely monitored, i.e., every 6–8 h.

Hypernatremia and Hyperosmolar Syndromes

Hypernatremia (Na >145 mmol/L) is less frequent but not rare in the neurocritical care patient population in the ICU, both as a result of hypothalamic dysfunction or secondary to treatment with hypertonic saline in patients with brain edema (induced or therapeutic hypernatremia).

Crisis Management

Pathophysiology

Most commonly, hypernatremia may occur due to water loss, inadequate fluid intake, and/or exogenous administration of sodium. Non-induced hypernatremia usually implies a deficit of total body water and denotes a state of hypertonic hyperosmolality causing cellular dehydration.

Hypernatremia-associated mortality has been reported in excess of 50% and often results not from the disorder itself but by inappropriate treatment. Rapid correction of hypernatremia with hypotonic fluids may thus induce osmotic brain edema.

Thirst is the main defense against development of hypernatremia. The hyperosmolar state can be maintained only when access to water or thirst mechanism is impaired, as in patients with altered mental status, intubated patients, and those at extremes of age.

Diabetes insipidus (DI) is characterized by complete or partial failure of ADH secretion (central DI) or of renal response to ADH (nephrogenic). Most patients with DI do not develop hypernatremia as their thirst mechanism is intact.

In the context of brain injury, the diagnosis of DI should be suspected in the presence of high urine output associated with hypernatremia:

- High urine volume (>200 ml/h)
- High serum sodium (>145 mmol/L)
- High serum osmolality (>305 mmol/kg)
- Low urine osmolality (<350 mmol/kg)

The diagnosis of DI is confirmed by response to exogenous ADH.

In neurocritical care patients with brain edema, hypertonic saline (3–7%) is frequently used to induce hypernatremia (Na 145–155 mmol/L) and hyperosmolality and decrease intracranial pressure. In these patients, hypernatremia is associated with an excess of sodium and water. Mannitol can also be used to induce a hyperosmolar state, but plasma sodium concentration will move in the opposite direction (Fig. 90.1).

Clinical Presentation and Assessment

Symptoms associated with hypernatremia are nonspecific and secondary to brain involvement and cardiovascular compromise. Anorexia, restlessness, and nausea and vomiting occur early and may progress to altered mental status, lethargy, or coma. Musculoskeletal symptoms may include twitching, hyperreflexia, ataxia, or tremor.

Treatment of Hypernatremia

Proper treatment of hypernatremia requires a two-pronged approach: addressing the underlying cause and correcting the prevailing hypertonicity. In patients with acute hypernatremia, developed on the course of hours, rapid correction of plasma sodium (±1 mmol/L per hour) improves the prognosis without increasing the risk of brain edema because accumulated electrolytes are rapidly extruded from brain cells. However, rapid correction of chronic hypernatremia may induce the entrance of water into the cells and induce convulsions and brain edema.

Extreme care must be taken also in the critically ill patient who is at risk for brain edema formation or exacerbation when correcting hypernatremia. A correction rate of no more than 0.5 mmol/L/h or 10–12 mmol/L/24 h is recommended.

Free water administration by mouth or feeding tube is the preferred route for correcting hypernatremia. If not available, hypotonic fluids, as 5% dextrose or 0.45% sodium chloride, can be safely used intravenously.

Diabetes insipidus is best treated with desmopressin, especially when the urinary output is greater than 200–250 ml/h and maintained for 6 h or more. Parenteral desmopressin (0.4–1 μg intravenously or subcutaneously) formulations are preferred in the acute intensive care setting, but there are no guidelines on the optimal protocol. The usual duration of action is 12 h, but significant inter-individual variability occurs in the duration and the amplitude of the effect and treatment with additional doses should be dictated by careful assessment of the fluid and electrolyte balance.

Hyperkalemia

Potassium is the most abundant cation in the body, being preferentially intracellular. Only 2% of total body potassium is found in the extracellular space, and serum potassium concentration is tightly regulated between 3.5 and 5.0 mmol/L. The large potassium gradient across cell membranes contributes to the excitability of nerve and muscle cells, including myocardium. Thus, disorders of potassium are one of the most common causes of life-threatening arrhythmias.

Crisis Management

Pathophysiology

Potassium is excreted mainly by the kidney, so hyperkalemia ($K > 5.5$ mmol/L) is most commonly the result of impaired excretion by the kidney but also can result from increased release from the cells (Table 90.3). Hyperkalemia is a relatively uncommon electrolyte abnormality in neurocritical patients; however, it may occur particularly in those who have coexisting acute or chronic renal failure.

Clinical Presentation and Assessment

The first indicator of hyperkalemia may be the presence of electrocardiographic (ECG) abnormalities or arrhythmias. Progressive ECG changes with potassium levels include peaked T waves, prolonged PR interval and flattened P waves. Widened QRS appears when potassium levels are

Table 90.3 Common causes of hyperkalemia

Drugs
ACE inhibitors (e.g., captopril)
NSAIDs (e.g., ibuprofen, diclofenac)
Beta-blockers (e.g., atenolol)
K+ supplements—e.g., oral or IV replacement
K+ sparing diuretics (e.g., spironolactone)
Renal diseases
Acute and chronic renal failure
Type 4 renal tubular acidosis
Metabolic acidosis
Diet
Foods with high potassium content
Endocrine disorders
Addison's Disease
Hyporeninemia
Insulin deficiency/hyperglycemia
Hematological disorder/Massive Cell Death
Tumor lysis syndrome
Rhabdomyolysis
Massive blood transfusion
Massive hemolysis—mechanical cell damage
Others
Hyperkalemic periodic paralysis
Pseudo-hyperkalemia
Abnormal erythrocytes
Thrombocytosis
Leukocytosis

ACE angiotensin-converting enzyme, K^+ potassium, *NSAIDs* nonsteroidal anti-inflammatory drugs, *IV* intravenous
Modified from Alfonzo et al. (Alfonzo et al., 2006)

Table 90.4 Therapeutic agents for the management of hyperkalemia

Therapy	Dose	Onset (min)	Duration (h)
Calcium chloride	10 ml of 10% IV	1–3	0.5–1
Sodium bicarbonate	1 mmol/kg IV	15–30	Several
Insulin/50% glucose	10 units in 25 g IV	15–30	4–6
Salbutamol	0.5 mg IV/20 mg Neb	15–30	4–6

IV intravenous, *Neb* nebulized
Modified from Alfonzo et al. (Alfonzo et al., 2006)

above 8.0 mmol/L, and at this point the patient is at very high risk of cardiac arrest if not treated immediately.

Treatment of Hyperkalemia

There is no standardized treatment for hyperkalemia, and it depends on severity and ECG abnormalities (Table 90.4). Emergency treatment is directed to protect the heart from malignant arrhythmias (calcium, bicarbonate) or shifting potassium into the cells (e.g., hyperventilation [alkalosis], insulin, beta-agonists).

Removal potassium from the body is the definitive treatment of hyperkalemia, and it will often depend on renal function. Loop diuretics (e.g., furosemide) will increase diuresis and potassium excretion and are extensively used along 0.9% saline. If the patient is oligoanuric, dialysis is the indicated treatment. Potassium may also be removed from the body through the GI track following the administration of kayexalate.

Hypokalemia

Crisis Management

Pathophysiology

Hypokalemia ($K < 3.5$ mmol/L) is one of the most common electrolyte abnormalities in ICU patients. It occurs most frequently because of renal and gastrointestinal losses (Table 90.5). Unfortunately, several common therapies in the neurocritical care patient may cause hypokalemia. For example, mannitol, frequently used to treat elevated ICP, has potassium-wasting properties. Fludrocortisone is employed in the treatment of hyponatremia in the context of CSWS and results in renal potassium leakage. Other therapies, such as hyperventilation (alkalosis), steroids, insulin, and salbutamol, may also cause hypokalemia by their effect to move potassium from the intravascular to intracellular compartment.

Clinical Presentation and Assessment

Moderate to severe hypokalemia induces EKG changes including U waves, T-wave flattening, and ST segment alterations. Cardiac arrhythmias are more frequent when combined with other pro-arrhythmic conditions such as ischemia, digitalis toxicity, or magnesium depletion.

Table 90.5 Common causes of hypokalemia

Increase potassium loss
Drugs: diuretics, mannitol, laxative abuse, liquorice, steroids, fludrocortisone
GI losses: diarrhea, vomiting, ileostomy, intestinal fistula, villous adenoma
Renal: renal tubular disorders, Bartter's syndrome, Liddle's syndrome, Gitelman's syndrome, nephrogenic diabetes insipidus
Endocrine: hyperaldosteronism, Cushing's syndrome, Conn's syndrome
Dialysis: hemodialysis on low potassium dialysate, peritoneal dialysis
Transcellular shift
Insulin/glucose therapy
Beta-adrenergic stimulation (e.g., salbutamol)
Alkalosis
Hypothermia
Hypokalemic periodic paralysis
Decreased potassium intake
Poor dietary intake (less than 1 g/day)
Magnesium depletion (increases renal potassium loss)
Poor dietary intake
Increased magnesium loss

Modified from Alfonzo et al. (Alfonzo et al., 2006)

In patients with high risk of arrhythmias, such as those with SAH or ischemic stroke, who frequently have coexisting cardiac disease, potassium levels should be closely monitored and replaced as needed.

Treatment of Hypokalemia

Intravenous potassium should be given by continuous infusion at a rate not faster than 10–40 mEq/h. Because of the risk of hyperkalemia, patients should be under continuous ECG monitoring and with serial sampling of potassium levels.

Because of the role of magnesium in transmembrane potassium transport, simultaneous correction of hypomagnesemia is required to correct hypokalemia. Hypokalemia and hypocalcemia can be refractory to replacement therapy in the setting of hypomagnesemia. Therefore it is common administer magnesium salts (e.g., magnesium sulfate) along with potassium infusion.

Hypomagnesemia

Magnesium is the second most abundant intracellular cation, after potassium. Magnesium acts as a cofactor for many enzymatic reactions involving ATP and regulates the movement of calcium into smooth muscle cells rendering it important for cardiac contractility and vascular tone. Magnesium sulfate has neuroprotective properties in diverse animal models of stroke. However, the use of magnesium sulfate has showed no benefit in clinical trials involving patients with stroke or to prevent vasospasm in patients with SAH.

Neuroprotection may be rendered via several mechanisms: Magnesium

- Acts as an endogenous calcium channel antagonist
- Inhibits of excitatory neurotransmitter release (e.g., glutamate)
- Acts as a NMDA receptor antagonism
- Mediates directly vascular smooth muscle relaxation

Magnesium is frequently used as a pharmacological agent for a variety of conditions, usually as an intravenous continuous infusion of 0.5–1 g/h of magnesium sulfate. Magnesium is also a first-line treatment for "torsade de pointes" and other cardiac arrhythmias induced by supratherapeutic digitalis.

Crisis Management

Pathophysiology of Hypomagnesemia

Hypomagnesemia (Mg <1.3 mEq/L) occurs mainly because of renal losses (e.g., after administration of loop diuretics) or during CSWS. Clinically, hypomagnesemia is often associated with hypokalemia and hypocalcemia.

Clinical Presentation and Assessment

Hypomagnesemia symptoms include neuromuscular irritability and weakness, muscle spasms, seizures and coma, as well as cardiac arrhythmias.

Approximately 30% of patients presenting with SAH have coexisting hypomagnesemia upon admission. The relationship between low magnesium levels, SAH, and cardiac arrhythmias remains unclear. Magnesium depletion results in prolonged cardiac cell repolarization and prolonged QT intervals on ECG. "Torsade de pointes" is frequently associated with hypomagnesemia.

Low magnesium levels reduce the seizure threshold, and magnesium currently is the primary agent used to prevent seizures during preeclampsia.

Treatment of Hypomagnesemia

Magnesium sulfate is usually administered as a slow intravenous infusion up to 10 g/day to correct a magnesium deficit. For an emergency situation, 8–12 mmol (2–3 g) magnesium sulfate can be infused over 1–2 min, followed by 40 mmol (10 g) over the next 5 h. Rapid intravenous administration of magnesium sulfate is often associated with significant nausea and vomiting.

Hypermagnesemia (Mg >2.0 mEq/L) occurs rarely after therapeutic magnesium infusion and usually in patients with renal failure. Hypermagnesemia becomes symptomatic at levels >4 mEq/L. Symptoms progress from hyporeflexia to complete AV heart block, respiratory failure, and cardiac arrest. While not a common problem in neurocritical care patients, hypermagnesemia should be on the differential diagnosis of patients with hyporeflexia.

Hypocalcemia

Calcium is a critical intracellular messenger and regulator of cell function. Calcium is of primary importance in neurocritical care patients due to its central role in neuronal death after central nervous system injury. Cytotoxic intracellular calcium accumulation is mediated via glutamate receptors, voltage-gated calcium channels, and pH-dependent calcium channels. In the context of intensive care management in general, it is important to remember that calcium is also the primary mediator of muscle contraction.

The calcium channel antagonist nimodipine has been shown to reduce the incidence of delayed cerebral ischemia following SAH and is now routinely initiated at hospital admission in affected patients and continued for 21 days. A similar benefit has not been seen in patients after ischemic stroke.

Crisis Management

Pathophysiology

Hypocalcemia (ionized Ca <1.1 mmol/L) is one of the most frequent electrolyte abnormality in intensive care therapy. Frequent causes include hypoparathyroidism after neck surgery, phenytoin and phenobarbital therapy, renal failure, and blood transfusion (citrate anticoagulant in packed red blood cells binds calcium).

Respiratory alkalosis as a result of hyperventilation (i.e., for treatment of elevated ICP) results in an increase in protein binding of calcium.

Clinical Presentation and Assessment

Clinical manifestations are related to cardiac and neuromuscular conduction as well as depressed myocardial contractility. Cardiac findings include prolonged QT and ST intervals, decreased cardiac output, hypotension, and bradycardia and can progress to ventricular arrhythmias. Neurologic symptoms include paresthesias, overall muscular weakness, tetany, and seizures.

Treatment of Hypocalcemia

In symptomatic patients and those with low serum concentrations, calcium may be administered by slow injection of 1 g of calcium chloride. There is no clear evidence that parenteral calcium supplementation impacts the outcome of critically ill patients.

Key Points

- Hypotension is a major cause of preventable secondary brain injury and should be aggressively prevented and treated.
- Fluid substitution to achieve normovolemia with isotonic or hypertonic fluids is essential to restore blood pressure, thus preventing ischemia and further brain damage.
- Isotonic crystalloids are favored in fluid resuscitation protocols, although the clinical evidence is limited.
- Red blood cell transfusions are recommended in patients with increased ICP or those who are at risk for brain ischemia when serum hemoglobin concentrations fall below 8–9 g/dl.
- Sodium is the main determinant of plasma osmolality, which regulates the movement of water inside and outside the cells.
- Sodium disturbances are common and highly detrimental in patients with head injury and should be avoided or, if present, promptly treated.
- Hyponatremia is associated with water shifts into the cells and therefore may increase brain edema and intracranial pressure.
- When hyponatremia or hypernatremia develops, measurement of urinary sodium, serum and urine osmolarity, and intravascular volume status may help to identify the cause and the appropriate treatment strategy.
- Hypernatremia causes hypertonic hyperosmolality and may occur when hypertonic solutions are used to treat patients with brain edema and intracranial hypertension.
- Close monitoring of plasmatic sodium is required to tailor the desired sodium plasma levels and osmolar state in neurocritical care patients.
- Potassium is excreted mainly by the kidney, and hyperkalemia is most commonly associated with renal failure.
- Therapeutic stimulation of diuresis or dialysis is definitive treatments for hyperkalemia.
- Hypokalemia is one of the most common electrolyte abnormalities in ICU patients and occurs frequently because of renal and gastrointestinal losses, frequently secondary to other therapeutic interventions.
- Because of the risk for hyperkalemia, intravenous potassium substitution requires continuous ECG monitoring and serial controls of potassium serum levels.

Suggested Reading

Alfonzo AV, Isles C, Geddes C, Deighan C. Potassium disorders – clinical spectrum and emergency management. Resuscitation. 2006;70(1):10–25.

Ellison DH, Berl T. Clinical practice. The syndrome of inappropriate antidiuresis. N Engl J Med. 2007;356(20):2064–72.

Fraser JF, Stieg PE. Hyponatremia in the neurosurgical patient: epidemiology, pathophysiology, diagnosis, and management. Neurosurgery. 2006;59(2):222–9; discussion 222–229

Investigators SS, Australian, New Zealand Intensive Care Society Clinical Trials G, Australian Red Cross Blood S, George Institute for International H, Myburgh J, Cooper DJ, Finfer S, Bellomo R, Norton R, et al. Saline or albumin for fluid resuscitation in patients with traumatic brain injury. N Engl J Med. 2007;357(9):874–84.

Kramer AH, Zygun DA. Anemia and red blood cell transfusion in neurocritical care. Crit Care. 2009;13(3):R89.

Moritz ML, Ayus JC. Maintenance intravenous fluids in acutely ill patients. N Engl J Med. 2015;373(14):1350–60.

Noronha JL, Matuschak GM. Magnesium in critical illness: metabolism, assessment, and treatment. Intensive Care Med. 2002;28(6):667–79.

Robertson CS, Hannay HJ, Yamal JM, Gopinath S, Goodman JC, Tilley BC, Epo Severe TBITI, Baldwin A, Rivera Lara L, Saucedo-Crespo H, et al. Effect of erythropoietin and transfusion threshold on neurological recovery after traumatic brain injury: a randomized clinical trial. JAMA. 2014;312(1):36–47.

Singh S, Bohn D, Carlotti AP, Cusimano M, Rutka JT, Halperin ML. Cerebral salt wasting: truths, fallacies, theories, and challenges. Crit Care Med. 2002;30(11):2575–9.

Temperature Management in Neurosurgical Critical Care

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Martin H. Dauber

Overview

Experimental evidence and clinical experience demonstrate that there are multiple mechanisms involved in cellular damage following neurological insult. Laboratory experiments since the 1950s demonstrated that there are benefits of mild hypothermia. Since that time hypothermia has been proposed as a valid clinical modality for several neurologic conditions.

Based on experimental and clinical evidence, this overview explores some of the current indications including prevention of elevation of intracranial pressure in the postsurgical and the cerebral hemorrhage patient, as well as use for stroke and central nervous system injury (brain and spinal cord) patients. Brief mention is to be made of the postcardiac arrest scenario.

Experimental Evidence

During Napoleon's reign Baron de Larrey employed hypothermia both to preserve amputated limbs and to provide numbing effects during battlefield surgery. In 1950, it was demonstrated that mild cerebral hypothermia during and after cardiac arrest improved neurologic outcomes in dog and primate models. Several years later it was shown by Rosomoff and Gilbert that there was a direct relationship between body temperature and both intracranial pressure and brain volume. Several studies proposed that hypothermia afforded beneficial effects in brain tissue because it caused reduced cerebral metabolic rate ($CMRO_2$) and blood flow. These findings were quickly adopted by cardiovascular specialists who employed hypothermia during cardiopulmonary bypass in their efforts to prevent insults to the central nervous system.

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As cerebral metabolism is dependant on temperature, hypothermia reduces oxygen consumption, glucose utilization, and lactate production. It is accepted that every 1°C decrease in temperature from 37° decreases $CMRO_2$ by 6–7%. An increase in brain pH of 0.0161 per degree of temperature decrease also results as presumably due to the reduction in metabolism. Excitotoxicity, the pathological process by which neurons are damaged and killed, by the neurotransmitters glutamate, dopamine, and serotonin is decreased. The calcium-dependent protein kinase C (PKC) translocates to the nerve cell membranes in ischemia, and this destructive process is inhibited by hypothermia.

Cerebral blood flow is also reduced by cold-induced vasoconstriction. This mechanism decreases intracranial volume and, therefore, intracranial pressure, especially in traumatic brain injury (TBI). On a microscopic level, the blood–brain barrier (BBB) permeability may be favorably altered by hypothermia. The mechanism is likely due to a decrease in effect of extracellular enzymes that can disrupt the BBB. The effect of hypothermia on the cerebral vasculature, therefore, is an important mechanism for neuroprotection from the increased BBB permeability, vasogenic edema formation, and extravasation of circulating inflammatory mediators seen in ischemic injuries.

Clinical Evidence

Although the experimental evidence for the benefits of hypothermia is convincing, there is considerable controversy in the clinical literature regarding the evidence-based medicine indications for the application of therapeutic hypothermia.

Traumatic Brain Injury

For TBI, many randomized controlled studies have demonstrated widely varying overall mortality yet have failed to

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demonstrate statistically significant benefit from hypothermia. A recent meta-analysis of hypothermia treatment for TBI, including 8 trials with 800 patients, revealed a 20% decrease in mortality and a 25% increase in "good neurologic outcome" relative to the conventional therapy, though these effects were not statistically significant. Patients cooled more than 48 h showed reductions in risk of mortality and more favorable neurologic outcomes. In part, on the basis of this review, the Brain Trauma Foundation (BTF)/American Association of Neurological Surgeons (AANS) guidelines' task force has issued a (Level III) recommendation for optional and cautious use of hypothermia for adults with TBI.

Spinal Cord Injury

Although the physiology and anatomy of the spinal cord is in many ways thought of as analogous to the brain, there are subtle differences that have impact on our subject. Whereas the brain is rarely exposed to the physician to directly impose hypothermia, during spine and spinal cord surgery, direct application of hypothermia upon the damaged or at-risk spinal cord is possible. Spinal cord injury (SCI) can be a devastating injury and most commonly affects young males. Many treatment modalities including pharmacologic interventions such as steroids, NMDA antagonists, and barbiturates as well as hypothermia have been advocated.

Experimental animal studies done in the 1960s produced promising results supporting hypothermia. Local cooling of the spinal cord was performed with iced saline during surgical decompression. The mechanisms were elucidated in the 1990s when studies demonstrated that early cooling strategies (relative to the timing of the insult) lessened the deleterious effects on the microvasculature and reduce local swelling. Further studies showed better preservation of gray and white matter and locomotor function in rats when systemic hypothermia was induced 30 min postinjury and maintained for 4 h. Histological studies confirm that these findings of the locomotor benefit to hypothermia in animals.

Clinically spinal cord ischemia can result from trauma or medical procedures such as aortic cross-clamping. Initial experiments used cool irrigation applied locally during spinal cord exposure but yielded inconclusive results. More recent attempts at systemic hypothermia have failed to conclusively demonstrate efficacy for hypothermia, due to side effects, primarily shivering. As these consequences can be controlled by medications that lower the shivering threshold, definitive randomized, controlled studies should be available. Case reports in the literature include the 2010 report of a National Football League player who sustained a C3/C4 fracture dislocation and was found to have an ASIA type A injury (i.e., complete sensorimotor loss) from which he has recovered nearly fully. The mild hypothermia was immediately induced while the player was in transport to the hospital, and the passive and active efforts to achieve hypothermia during the first several days are credited with his dramatic improvement.

Postcardiac Arrest

In 2002, an advisory statement about therapeutic hypothermia was issued by the Advanced Life Support Task Force of the International Liaison Committee on Resuscitation. Cooling to 32–34 °C for 12–24 h was recommended for unconscious adult patients who had return of spontaneous circulation (ROSC) after out-of-hospital cardiac arrest when the initial rhythm is ventricular fibrillation. Two years later the panel stated that hypothermia may also be beneficial for other rhythms as well as in-hospital cardiac arrest. (This author's institution, The University of Chicago, is currently conducting a study of hypothermia for in-hospital cardiac arrest patients with ROSC.) A recent clinical practice article highlighted the application of these principals and the clinical difficulties therein. Cardiac arrest outside the hospital is a poorly defined entity in clinical medicine, and though the utilization of hypothermia may improve outcome, it can also confound prognostication.

There is ongoing investigation regarding therapeutic hypothermia for other conditions such as near-drowning, traumatic cardiac arrest, neonatal hypoxia-ischemic encephalopathy, hepatic encephalopathy, ARDS, and a variety of pediatric situations. In each of these scenarios, there is evidence to support the use of hypothermia of a varying degree and for variable durations. Due to the substantial interest in the modality and its potential for benefit in many disease states, it is likely to be an area of great research interest in the future.

Ischemic and Hemorrhagic Stroke

As noted earlier the beneficial effects of hypothermia seen in experimental models of ischemia are the result of many biological effects. There is essentially no effect on infracted tissue; rather, any benefits are probably in the penumbra. The imperatives for mechanical ventilation via a secure airway and shivering control have limited the use of hypothermia in stroke patients, though some early reports in spontaneously breathing patients have demonstrated small and statistically insignificant improvement in mortality. Similar results were obtained when hypothermia was compared with medical management (tissue plasminogen activator). In a prospective study of massive ischemic infarction (>2/3 of one hemisphere), hemicraniectomy with hypothermia showed a ten-

dency toward improved 6 month outcome as compared to hemicraniectomy alone. Many clinical questions currently remain unanswered and are the focus of ongoing trials.

After poor-grade subarachnoid hemorrhage, the addition of hypothermic therapy to barbiturates had no positive long-term effect. The multicenter IHAST (intraoperative hypothermia for aneurysm surgery trial) study failed to show a benefit of intraoperative hypothermia during aneurysm surgery in good-grade subarachnoid hemorrhage patients. Few animal studies and little useful clinical research exist to support the use of hypothermia in intracranial hemorrhage.

Complications of Therapeutic Hypothermia

Any therapeutic intervention including deliberate hypothermia is associated with its potential complications. The clinician needs to be aware of the ways to prevent, recognize, and treat those complications in a timely manner. Patient comfort and tolerance of this intervention are necessary to address during institution of this modality. Several means are available to lower body temperature in a safe and efficient way that may help to prevent or reduce the risk for major complications. "Preventions" present some of the most common techniques that are in use in neurointensive care units. "Crisis management" discusses adverse effects hypothermia has on cardiovascular function, coagulation and metabolic function, and infectious risk. The section concludes with a protocolized suggestion for achieving therapeutic hypothermia in the neurointensive care unit.

Prevention

There are three basic methods to cool patients in the ICU:

1. Conventional surface cooling and cold fluids
2. Commercial surface cooling devices
3. Intravascular cooling devices
4. Body cavity lavage, extracorporeal circulation, whole-body ice submersion, cooling helmets

Conventional cooling can begin after neurologic assessment, sedation, and placement of a core temperature monitor. Subsequently, to maintain hypothermia ice packs can be placed over the groins, neck, and axillae. Water-cooled rubber mattresses can be placed over the patient as placement under patients has caused skin breakdown. Though these relatively simple means are often effective, drawbacks include lack of a feedback loop resulting in a high incidence of overcooling and the concomitant nursing vigilance required to maintain the goal temperature. The rate of cooling is unpredictable with these conventional and widely available methods.

Commercial surface cooling devices such as the Arctic Sun device (Medivance, Louisville, CO) controls the temperature of the water circulating through the ArcticGel Pads via a patient/temperature feedback loop. The patient can be cooled or kept normothermic as the pads which cover approximately 40% of the surface transfer heat from patient. Disadvantages include the purchase cost of the unit and the disposable pads. CoolBlue (Innercool Therapies, San Diego, CA) and ThermoWrap (MTRE, Rehovot, Israel) are recently introduced, less-expensive garment-type devices without the gel of the Arctic Sun. As with the Arctic Sun, they both have servo units to enhance ease of use and safety. Other similar devices that may cool faster are being tested in animals.

Intravascular cooling devices have the complications associated with placement of very large bore central lines including placement risks, infection, and thrombosis. However, once placed, these catheters can serve the additional functions of a central line. The Celsius Control System (Innercool Therapies) is a servo-controlled system in which water circulates through a (10.7 or 14 Fr) metallic catheter with a textured surface that is placed in the inferior vena cava via a femoral vein. Patients must be immobile during its use to prevent migration of the catheter. There is no infusion or monitoring port on the device, so additional central venous access may be necessary.

There has been no direct comparison of the devices or techniques, so each institution needs to compare efficacy and safety in its environment.

Crisis Management

Shivering

Shivering is disturbing to awake patients. It also induces *unfavorable increases* in:

1. Overall metabolic rate
2. Oxygen consumption
3. Work of breathing
4. Heart rate
5. Myocardial oxygen demand and consumption

In perioperative patients, hypothermia may lead to additional cardiac morbidity especially in those patients with preexisting cardiac disease. These consequences may be from the hemodynamic and central nervous system responses rather than from the shivering itself. They may be controlled by pharmacologic means including sedatives, opiates, and sympatholytics. Magnesium (2 g intravenously over 1 h) and nondepolarizing relaxants (in patients with controlled ventilation) may also be helpful upon the initiation of hypothermia. Midazolam and meperidine may then be added as needed.

Cardiovascular Effects

Hypothermia causes cardiovascular effects that are complex; opposing effects on myocardium and contractility depend upon patient's volume status and presence/degree of sedation. In patients treated to prevent shivering, mild hypothermia will decrease heart rate and increase contractility, but cardiac output will fall as blood pressure increases slightly. The supply–demand balance for myocardial oxygen will thus improve. Deep hypothermia (<30 °C), however, will cause a decrease in contractility. Also, diuresis often results with hypothermia and causes hypovolemia through an increase in venous return, increase in atrial natriuretic peptide, and decreased antidiuretic hormone. Nonetheless, with attention to the prevention and treatment of the volume loss, normotension can be maintained.

The increase in venous return will cause mild sinus tachycardia especially in unsedated patients. When temperatures drop below 35.5 °C, sinus bradycardia results from decreased repolarization of pacemaker cells and gives the ECG findings of prolonged PR and QT intervals and widened QRS complexes. As temperature drops below 28–30 °C, atrial fibrillation, ventricular tachycardia, or ventricular fibrillation may result. Therefore, temperature below 30 °C should be strenuously avoided in the ICU.

Coagulopathy

In the operating room, it is well known that even mild hypothermia can induce coagulopathy from decreased platelet numbers and dysfunction. At temperatures less than 33 °C, the synthesis and function of clotting factors in the cascade are affected, at least in vitro. This has not been demonstrated clinically in therapeutic cooling for TBI, cardiac arrest, or stroke patients.

Immunosuppression

The proinflammatory response is inhibited by hypothermia via inhibition of leukocyte migration and phagocytosis and decreased production of cytokines. The risk for nosocomial infection in hypothermic patients is linked to the duration of the therapy (>24 h is at higher risk) as well as the indication (low risk in cardiac arrest, high risk in stroke patients) for the therapy. Hypothermia may mask the signs of infection, such as fever, C-reactive protein, and WBC counts. An increased workload of the cooling device may be the only clue.

Miscellaneous Problems

Other effects of hypothermia include decrease in bowel function and delayed gastric emptying. Serum amylase may increase, but pancreatitis is rare. Other laboratory values changed in hypothermia include:

1. Hyperglycemia
2. Low electrolyte levels
3. Thrombocytopenia
4. Low WBC counts
5. Elevated LFTS (SGOT and SGPT)
6. Elevated stress hormones (cortisol, epinephrine, and norepinephrine)

Though there is potential for disruption of many systems throughout the body during therapeutic hypothermia, attention to each of the areas leads to a manageable clinical situation and should rarely be a cause of discontinuation of the intervention.

After identification of a clinical indication for therapeutic hypothermia, a complete neurologic exam must be performed (Fig. 91.1), as it results will be suspect after initiation of therapy. The goal is typically to cool the core to 33 °C for 12–24 h.

Thirty to forty milliliter per kilogram of isotonic intravenous fluid at 4 °C is administered. This can rapidly decrease core temperature by 3–4 °C. Administer sedative agents as tolerated by hemodynamics. Midazolam and meperidine are especially helpful for titratable sedation and decreasing shivering. Maintain serum potassium levels greater than 3.8 mEq/dL. Nondepolarizing neuromuscular blockade can be instituted with vecuronium 0.1 mg/kg or rocuronium 1.0 mg/kg, which are both devoid of cardiovascular side effects or cisatracurium 0.15 mg/kg in patients with renal impairment. Full ventilatory support to normalize oxygen and pH levels is almost always required. Blood gases should be managed with the pH stat method during the period of hypotension, as this approach allows the brain to more consistently respond normally to physiologic perturbations.

The serum glucose levels should be tightly controlled in the desired range (<150 mg/dL). The systemic blood pressure should be supported to provide the desired cerebral perfusion pressure (depending upon the indication for hypothermia). Early administration of broad-spectrum antibiotics as indicated for suspected infection (e.g., aspiration pneumonia during event/initial resuscitation) should be considered. Attention to the skin to prevent breakdown from the cooling device should be given.

When the decision to begin warming to normothermia has been made, either as a result of presumed success or failure or due to intolerance to the procedures, it should be realized that "decooling" should be done at 0.25–0.33 °C/h to prevent problems. Hemodynamic instability is common as cutaneous vasodilation occurs, and an inflammatory response may begin especially after arrest. The paralytics should be discontinued, and their residual effect can be monitored with a peripheral nerve stimulator. Sedation should be weaned slowly during warming. When the patient is ready, he/she

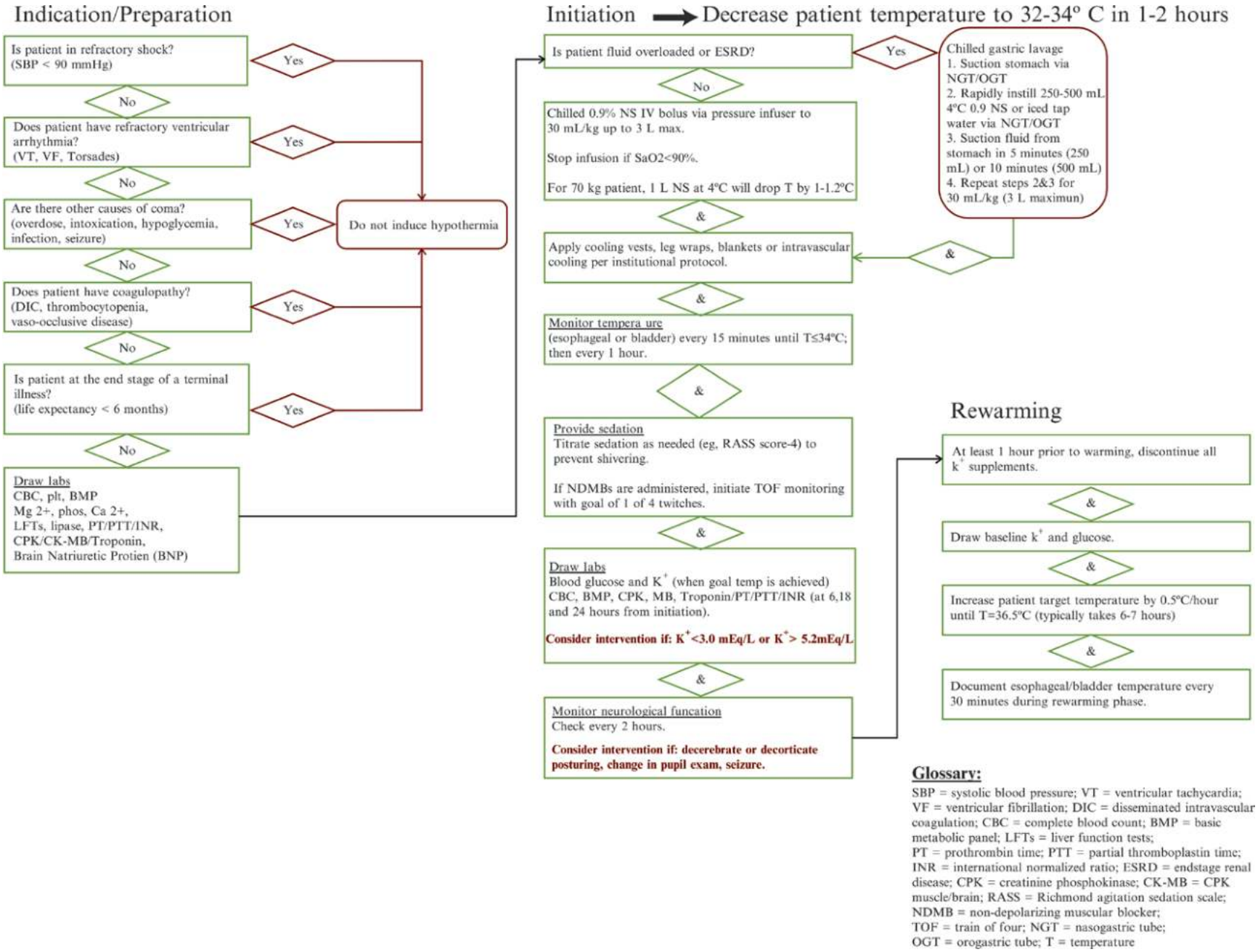

Fig. 91.1 Protocol for therapeutic hypothermia

can be separated from ventilatory support and extubated if appropriate. Shivering can be treated with meperidine or acetaminophen 650 mg. The temperature should not be allowed to increase above 37.5 °C for 72 h. At this time, neuroprognostication can be undertaken again.

Key Points

- Significant experimental and clinical data suggest a potential value of therapeutic hypothermia in neurocritical care patients aimed to protect the CNS or prevent deterioration in certain situations including:
  - Postoperative elevated ICP
  - Cerebral hemorrhage complicated by elevated ICP
  - Ischemic stroke
  - Brain and spinal cord injury
- There are theoretical advantages to the CNS outcomes, and these are clinically substantiated in small studies. It is likely that through expanding application of deliberate hypothermia, our understanding will be increased, and our patients will thereby experience less CNS damage from their underlying diseases.
- Several methods are readily available to cool patients including surface cooling, cool intravenous fluids, body cavity lavage, and extracorporeal circulation. There are also several proprietary devices that can be employed.
- Complications of systemic cooling primarily are related to shivering, which is readily prevented by pharmacologic means. Cardiac, infectious, metabolic, and other systems may be affected but are rarely reasons to reverse therapeutic hypothermia.

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Suggested Reading

Peterson K, Carson S, Carney N. Hypothermia treatment for traumatic brain injury: a systematic review and meta-analysis. J Neurotrauma. 2008;25:62–71.

Seder DB, Van der Kloot TE. Methods of cooling: practical aspects of therapeutic temperature management. Crit Care Med. 2009;37(7):S211–22.

Varon J, Pilar A. Therapeutic hypothermia: past present, and future. Chest. 2008;133(5):1267–74.

Coagulation Management in Neurosurgical Critical Care

92

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Thromboembolic Disease

Overview

Incidence

- Highest risk for DVT is in patients with brain tumors (28–43%) followed by those undergoing craniotomy (25%) followed by those with head injury (20%) (Hamilton).
- Risk of PE is as high as 5% with mortality ranging from 9% to 50% (Hamilton).

Risk Factors

- Paresis
- Immobility
- Prolonged surgery
- Combined anterior/posterior spinal surgery
- Brain tumor
- Traumatic brain injury
- Central venous catheters
- Long bone fractures
- Spine trauma

Clinical Implications

- Pain
- Limb swelling
- Chronic venous stasis
- Pulmonary embolism
- Postthrombotic syndrome

Prevention

Despite the known benefits of pharmacological prophylaxis, concern for bleeding complications and iatrogenic neurologic injury often limits their use in neurosurgery patients. Chemical prophylaxis initiated prior to surgery may be associated with a higher rate of hemorrhagic complications. Studies have shown that chemical prophylaxis is relatively safe for most neurosurgical patients when started 24–72 h after surgery (Norwood; Kim). A randomized trial compared low-dose heparin with low molecular weight heparin (LMWH) prophylaxis and showed LMWH was more effective than low-dose heparin in preventing VTE after major trauma and both therapies were safe (Geerts). Timing of chemical prophylaxis must be individualized. Mechanical prophylaxis [graduated compression stockings (GCS) and sequential compression devices] should be started preoperatively or immediately upon entering the operating room to decrease the incidence of DVT. GCS when used along with another form of DVT prophylaxis is more effective than GCS alone (Sachdeva). A multicenter, randomized, double-blind trial showed that enoxaparin combined with compression stockings is more effective than compression stockings alone for the prevention of venous thromboembolism after elective neurosurgery and does not cause excessive bleeding (Agnelli). The incidence of catheter-related DVT correlates with the size of the catheter (rates are higher with larger caliber catheters) (Grove). Therefore, practitioners should place the smallest caliber central venous catheter necessary.

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Table 92.1 Prevention of thromboembolic disease

Prophylactic measure	Mechanism	Dose	Potential adverse effects/CI
Early and frequent Ambulation	Venous stasis prevention	–	Discomfort
GCS	Venous stasis prevention	Wear daily	Discomfort
Sequential compression device	Venous stasis prevention; several theories proposed	Use when in bed	Discomfort
Unfractionated heparin	Activates antithrombin; inhibits thrombin and other clotting factors	5000 U SQ q12 h or q8 h	Bleeding; HIT
LMWH	Activates antithrombin; Inhibits mostly factor Xa	Enoxaparin 40 mg SQ daily or 30 mg bid Dalteparin 2500–5000 units SQ daily	HIT; may require dose adjustment/use with caution in patients with impaired CrCl, pregnant, obese, elderly
Fondaparinux	Binds to antithrombin; Inhibits factor Xa	2.5 mg SQ daily	Safe to use in HIT; May require dose adjustment/use with caution in patients with impaired CrCl, underweight, elderly
IVC filter	Blocks clot from embolizing to the pulmonary vasculature	Retrievable (preferred over permanent)	Postthrombotic syndrome; thrombosis of device

GCS graduated compression stockings, *LMWH* low molecular weight heparin, *HIT* heparin-induced thrombocytopenia, *SQ* subcutaneous, *CrCl* creatinine clearance

Special attention must be paid to patients when epidural/spinal anesthesia or spinal puncture is employed. These patients are at increased risk of developing an epidural or spinal hematoma, which may result in permanent neurologic impairment. Chemical anticoagulation should be used with caution in these patients with doses appropriately timed with respect to placement and removal of epidural catheters. Risk versus benefit analysis must be fully considered in this patient population.

Options for the prevention of thromboembolic disease are summarized below (Table 92.1).

Crisis Management

DVT may be detected after extremity pain and swelling are noted. Anticoagulation is the first-line treatment to prevent propagation of clot and PE. If anticoagulation is contraindicated, inferior vena cava (IVC) filter may be considered. However, anticoagulation should be resumed in patients with IVC filters when pharmacologic treatment is safe.

Upper extremity DVT should be treated the same as lower extremity DVT. If an upper extremity DVT is associated with an indwelling central venous catheter (CVC), in most patients, the CVC should not be removed if it is functional and there is an ongoing need for the catheter (ACCP guidelines).

PE refers to the obstruction of a pulmonary vessel by material that comes from elsewhere in the body. This chapter refers to obstruction due to thrombus. PE is associated with a mortality rate of 30% without treatment; however, accurate diagnosis followed by anticoagulation therapy can significantly reduce the recurrence of PE and, therefore, decrease mortality.

Clinical Presentation: Pulmonary Embolism (Stein)

- Dyspnea
- Pleuritic chest pain
- Cough
- Hemoptysis
- Tachypnea
- Tachycardia
- Hypotension
- Acute right ventricular heart failure

Patient Assessment (Table 92.2)

Intervention/Treatment

- Resuscitation
  - Intravenous fluid administration – use with caution in patients with evidence of right heart failure
  - Supplemental oxygen and/or intubation
  - Vasopressors and/or inotropes
- Anticoagulation
  - Should be given after thorough evaluation of bleeding risk
  - Prevents further clot formation, but does not lyse existing clot
- Thrombolysis
  - Persistent hypotension is primary indication (Kearon).
  - Associated with increased risk of hemorrhage, particularly in patients after surgery and intracranial hemorrhage.

Table 92.2 Assessment of the patient with possible pulmonary embolism

Assessment	Findings	Notes
Electrocardiography	S1Q3T3 Right ventricular strain Atrial arrhythmias Right bundle branch block	Often nonspecific changes Nondiagnostic
Computed tomographic pulmonary angiography (CTPA)	Evaluate for filling defects in pulmonary vasculature; Sensitive and specific for diagnosing PE (van Belle); If negative for PE, CTPA may detect alternative pulmonary abnormalities that may explain the patient's clinical findings	Potential contrast reaction; renal injury
V/Q scan	Mismatch in ventilation and perfusion; Reserved for patients in whom CTPA is contraindicated	Most useful for patients with high probability of PE and high-probability V/Q scan; Low specificity; Test of choice in pregnant patients
Angiography	Historic gold standard; evaluate for filling defect or cutoff in pulmonary vasculature	Invasive study Potential contrast reaction; renal injury
D-Dimer	Level <500 ng/mL by ELISA excludes PE unless the pretest probability is high (Stein D-dimer)	Baseline elevation in acute/chronic illness, pregnancy, elderly (Crowther, Rathbun) Less sensitive in patients with subsegmental PE (De Monyé)
Ultrasound	Upper or lower extremity Doppler showing filling defect in appropriate clinical setting	Not definitively diagnostic of PE; Not appropriate as initial diagnostic test for PE; Reserve for patients in whom definitive testing is indeterminate or contraindicated (van Rossum, Righini)

  - Recombinant tissue plasminogen activator (rt-PA) is most commonly used. Administer 100 mg intravenously over 2 h.
  - Heparin resumed when the aPTT is less than twice its upper limit of normal and titrated to therapeutic aPTT.
- Embolectomy
  - Indicated for persistent hypotension, if thrombolysis fails or is contraindicated (Aklog, Stein)
- IVC filter
  - Prevents migration of thrombus from lower extremities to pulmonary vasculature; not effective for upper extremity DVT.
  - Indicated for PE when anticoagulation is contraindicated (i.e., bleeding risk) (Guyatt).
  - Anticoagulation should be started even in patients with IVC filters once bleeding risk deemed acceptable.

Anticoagulation and thrombolysis even in the setting of a hemodynamically significant PE may be contraindicated in patients with intracranial hemorrhage. Various medical organizations provide guidelines as to the timing of initiation or resumption of anticoagulation. The European Stroke Initiative recommends that patients with a strong indication for anticoagulation, such as a history of embolic stroke with atrial fibrillation, should be restarted on warfarin after 10–14 days, depending on the risk of thromboembolism and ICH (intracerebral hemorrhage) recurrence (Goldstein). The American Heart Association suggests that, in patients with a very high risk of thromboembolism for whom restarting warfarin is considered, warfarin may be restarted 7–10 days after ICH onset. The American College of Chest Physicians recommends starting prophylactic-dose heparin the day after an ICH, with no clear guidance on restarting warfarin.

Coagulopathy

Overview

Anticoagulants and antiplatelet drugs are used with increasing frequency for the treatment of a variety of disorders including atrial fibrillation, thromboembolic disease, and stroke. In addition, bleeding dyscrasias may be seen in primary coagulopathies such as hemophilia or secondary to liver disease, disseminated intravascular coagulation, or sepsis. Coagulopathic patients who are suffering from bleeding complications such as intracranial hemorrhage or need surgical intervention may require acute reversal of coagulopathy.

Incidence

- Warfarin use is associated with a two- to fivefold increase in the rate of intracerebral hemorrhage (ICH).
- Risk of ICH associated with warfarin use increases with elderly population, hypertension, history of cerebrovascular disease, and intensity of anticoagulation

- Dual antiplatelet therapy with aspirin and clopidogrel increases the risk of ICH twofold compared with aspirin alone (0.4% versus 0.2%) (Connolly)
- Symptomatic ICH occurs in 6.4% of acute stroke patients treated with rt-PA at 3 h and 7.9% of those treated up to 4.5 h
- Target specific oral anticoagulants including rivaroxaban, dabigatran, apixaban, and edoxaban are associated with lower rates of ICH than warfarin (Schaefer, Chatterjee)

Risk Factors

- Pharmacologic platelet inhibition
- Anticoagulation
- Disseminated intravascular coagulation
- Uremia
- Liver failure
- Sepsis
- Massive blood loss
- Bleeding disorders

Crisis Management

Indications for platelet transfusion

- Neurosurgical procedure and platelet count less than 100×10^9/L (Liumbruno)
- Platelet count greater than 100×10^9/L with platelet dysfunction not responsive to DDAVP or cryoprecipitate
- Massive blood transfusion (expect platelets to fall below 50×10^3/μl following two times blood volume replacement) (Stainsby)

One six-pack of pooled platelets (derived from six units of whole blood) contains at least 3×10^{11}/L platelets which should raise the peripheral blood platelet count by at least 20,000–30,000/μL (ASH-SAP). The role for platelet transfusion in patients with intracranial hemorrhage recently on antiplatelet therapy has become more defined. While bleeding in the setting of antiplatelet therapy is often treated with platelet transfusion in clinical practice, a prospective, randomized controlled trial showed that platelet transfusion after spontaneous cerebral hemorrhage associated with antiplatelet therapy seems to increase the risk of death or dependence as compared to patients who did not receive platelet transfusion (Baharoglu); see Table 92.4.

To correct a coagulopathy, a variety of hemostatic agents may be considered. The choice of hemostatic agent depends on the clinical scenario. Determining the cause of the coagulopathy is essential to determining the appropriate treatment plan. Table 92.3 outlines drugs available to treat coagulopathies. Table 92.4 provides an overview of blood products and clotting factor concentrates used to assist in hemostasis. Hemodialysis may be considered in patients with dabigatran-associated severe bleeding (Siegal).

Prothrombin complex concentrates and activated prothrombin complex concentrates for warfarin and target specific oral anticoagulants have not been directly compared. Per the Neurocritical Care Society 2016 guidelines for the reversal of warfarin in intracranial hemorrhage, more reliable INR correction occurs with four-factor PCC over three-factor PCC (Frontera). Recombinant factor VIIa is significantly more expensive, replaces only one coagulation factor as compared to the PCCs that replace more, and has a short half-life (De Oliveira Manoel). Recombinant factor VIIa is not recommended for VKA or direct thrombin inhibitor reversal. PCCs are recommended over recombinant factor VIIa for direct factor Xa inhibitor reversal.

After successful reversal of pharmacologically induced coagulopathy and further stabilization of the patient, practitioners need to initiate discussions regarding the need, the timing, and the dosing of anticoagulation if warranted. The current practice varies considerably between clinicians regarding the many patient groups due to the paucity of evidence-based guidelines.

Table 92.3 Drugs to treat coagulopathy

Drug	Mechanism	Administration	Clinical use	Notes
Protamine	Neutralizes heparin; Disrupts heparin-antithrombin complex	1 mg protamine neutralizes 100 units of heparin; Neutralizes heparin within 5 min; check aPTT to verify reversal 1 mg of protamine neutralizes 1 mg enoxaparin; 1 mg of protamine neutralizes 100 units dalteparin	Heparin reversal	Completely neutralizes UFH; Only partially reverses LMWH due to anti-factor Xa activity only 60% neutralized; Still consider if significant bleeding on LMWH
Vitamin K	Provides substrate for vitamin K-dependent factors II, VII, IX, and X	PO, IV, or SQ; 12–18 h onset (Hoffman)	Bleeding/supratherapeutic INR on warfarin; vitamin K deficiency	Anaphylaxis with IV; Erratic absorption with SQ (Raj) (Van Berkel)

Table 93.3 (continued)

Drug	Mechanism	Administration	Clinical use	Notes
Desmopressin (i.e., DDAVP)	Increases plasma concentrations of factor VIII and vWf as a result of their release from vascular endothelium (Mannucci desmopressin)	IV, SQ, or IN administration Peak levels (~2 to 4 times baseline) achieved 30–60 min after IV and 60–90 min after SQ or IN administration (Mannucci hemostatic drugs)	Hemophilia A and Type 1 vWD for low-risk procedures; congenital platelet disorders; Uremia; qualitative platelet defect	May repeat doses every 12–24 h, but tachyphylaxis may occur after three or four doses Associated with a 2.4-fold increase in the risk of perioperative MI in cardiac surgery patients (Levi)
Antifibrinolytics	Bind reversibly to plasminogen blocking plasminogen to fibrin and its activation and transformation to plasmin	ε-Aminocaproic acid PO, IV Tranexamic acid PO, IV	Mucosal hemorrhage (epistaxis, oral bleeding, menorrhagia, GIB); Bleeding from trauma (Shakur)	Case reports of thrombosis with these agents (Hoffman); Tranexamic acid is 10× more potent in vitro than ε-aminocaproic acid
Activated charcoal	Reduces dabigatran adsorption in the gut (Van Ryn)	PO	Dabigatran reversal if early ingestion of the drug (i.e., within 2 h) (Siegal)	No known role in reversal of factor Xa inhibitors (Siegal)
Idarucizumab	Antibody that directly neutralizes the effects of dabigatran	Immediate onset; Provides full reversal up to at least 24 h in most patients	Reversal of the anticoagulant effects of dabigatran for emergency surgery/urgent procedures or in life-threatening or uncontrolled bleeding	Thromboembolic risk; Hypersensitivity; Risks of serious adverse reactions in patients with hereditary fructose intolerance due to sorbitol excipient (Praxbind®)
Andexanet alfa	Binds and sequesters the FXa inhibitors rivaroxaban and apixaban; inhibits the activity of tissue factor pathway inhibitor, increasing tissue factor-initiated thrombin generation	IV Dosing regimen is based on specific factor Xa inhibitor given, its dose, and time last taken	Labeled indication: reversal of anticoagulation from apixaban or rivaroxaban in patients experiencing life-threatening or uncontrolled bleeding; off-label use: reversal from anticoagulation from direct and indirect factor Xa inhibitors	Associated with arterial and venous thromboembolic and ischemic events, cardiac arrest, and sudden deaths

UFH unfractionated heparin, *LMWH* low molecular weight heparin, *SQ* subcutaneous, *vWf* von Willebrand factor, *IN* intranasal, *vWD* von Willebrand disease, *MI* myocardial infarction, *GIB* gastrointestinal bleed

Table 92.4 Blood products and clotting factor concentrates used to assist in hemostasis

Product	Clinical use	Mechanism/dosing	Onset of action/dosing	Notes/risks
Platelets	Bleeding (other than intracranial hemorrhage) in the setting of thrombocytopenia, uremia, platelet antagonist drug use	One six-pack of pooled platelets should raise the peripheral blood platelet count by at least 20,000–30,000/μL (ASH-SAP)	Immediate/variable	Transfusion reaction; Viral transmission
Fresh frozen plasma	Liver disease, disseminated intravascular coagulation, on warfarin and/or vitamin K deficiency requiring urgent reversal, dilutional coagulopathy from massive transfusion, TTP	Fibrinogen; factor XIII; vWF; factor VIII primarily bound to its carrier protein vWF; and the vitamin K-dependent factors II, VII, IX, and X (Hoffman)	10–15 ml/kg (1 unit of plasma contains 200–280 ml); Variable onset for INR reduction may need to redose every 4–6 h	Volume overload; Viral transmission
Cryoprecipitate	Congenital or acquired hypofibrinogenemia, vWD, or hemophilia A (when factor concentrates are unavailable), uremia, life-threatening hemorrhage secondary to thrombolytic therapy (ASH-SAP)	Replaces fibrinogen, factors VII, XIII, and vWF	Adult dose is 1 unit/5 kg body weight, up to a total dose of 10 units (bags); Will raise fibrinogen by 0.5 g/L (Droubatchevskaia) Variable onset for fibrinogen replacement	Volume overload; Viral transmission
Activated PCC (FEIBA®)	Hemorrhage, perioperative bleeding or routine prophylaxis in hemophilias A and B; Off-label for acquired hemophilia and intracranial hemorrhage associated with non-VKA anticoagulants	Replaces Factors II, VII, IX, and X	Onset is within 15–30 min; Half-life is 4–7 h; variable dosing	Thrombosis; Infectious transmission (made from human blood)

(continued)

Table 93.4 (continued)

Product	Clinical use	Mechanism/dosing	Onset of action/dosing	Notes/risks
Recombinant factor VIIa (NovoSeven®)	Hemophilia patients with factor VIII or factor IX inhibitors, acquired hemophilia, congenital factor VII deficiency	Induces hemostasis at local sites of tissue injury through enhancement of thrombin generation on the surface of thrombin-activated platelets (Hoffman)	Half-life is 2–3 h; IV dosing; variable dosing	Thrombosis; Off-label use in acute intracranial hemorrhage lacks evidence (Mannucci ICH not so good news)
Nonactivated PCC (Kcentra®)	Urgent reversal of acquired coagulation factor deficiency induced by VKA therapy in adult patients with acute major bleeding or need for an urgent surgery/ invasive procedure	Replaces Factors II VII, IX, and X and proteins C and S	Normalizes INR in 30 min	Thrombosis, Infectious transmission, HIT (contains heparin); Hypersensitivity reaction

TTP thrombotic thrombocytopenic purpura, *PCC* prothrombin complex concentrate, *HIT* heparin-induced thrombocytopenia, *VKA* vitamin K antagonist

Key Points

- The neurosurgical population is at high risk for both thromboembolic disease and bleeding events.
- The benefit of chemical prophylaxis and treatment for thromboembolic disease must be weighed against the risk of hemorrhage into the brain or spinal canal.
- Multiple hemostatic agents are available for the treatment of coagulopathy in the setting of bleeding or urgent invasive procedure.

Suggested Reading

ACTIVE Investigators, Connolly SJ, Pogue J, Hart RG, et al. Effect of clopidogrel added to aspirin in patients with atrial fibrillation. N Engl J Med. 2009;360:2066–78.

Agnelli G, Piovella F, Buoncristiani P, et al. Enoxaparin plus compression stockings compared with compression stockings alone in the prevention of venous thromboembolism after elective neurosurgery. N Engl J Med. 1998;339:80–5.

Aklog L, Williams CS, Byrne JG, Goldhaber SZ. Acute pulmonary embolectomy: a contemporary approach. Circulation. 2002;105(12):1416–9.

Ansell J, Hirsh J, Hylek E, et al. Pharmacology and management of the vitamin K antagonist. Chest. 2008;133:160S–98.

Chatterjee S, Sardar P, Biondi-Zoccai G, Kumbhani DJ. New oral anticoagulants and the risk of intracranial hemorrhage: traditional and Bayesian meta-analysis and mixed treatment comparison of randomized trials of new oral anticoagulants in atrial fibrillation. JAMA Neurol. 2013;70:1486–90.

Crowther MA, Cook DJ, Griffith LE, et al. Neither baseline tests of molecular hypercoagulability nor D-dimer levels predict deep venous thrombosis in critically ill medical-surgical patients. Intensive Care Med. 2005;31:48–55.

De Manoel O, et al. The critical care management of spontaneous intracranial hemorrhage: a contemporary review. Crit Care. 2016;20:272.

De Monyé W, Sanson BJ, Mac Gillavry MR, et al. Embolus location affects the sensitivity of a rapid quantitative D-dimer assay in the diagnosis of pulmonary embolism. Am J Respir Crit Care Med. 2002;165:345–8.

Droubatchevskaia N, Wong WP, Chipperfield KM, Wadsworth LD, Ferguson DJ. Guidelines for cryoprecipitate transfusion.

Frontera, et al. Guideline for reversal of antithrombotics in intracranial hemorrhage; a statement for healthcare professionals from the Neurocritical Care Society and Society of Critical Care Medicine. Neurocrit Care. 2016;24:6–46.

Geerts WH, Jay RM, Code KI, et al. A comparison of low-dose heparin with low-molecular-weight heparin as prophylaxis against venous thromboembolism after major trauma. N Engl J Med. 1996;335:701–7.

Goldstein JN, Greenberg SM. Should anticoagulation be resumed after intracerebral hemorrhage? Cleve Clin J Med. 2010;77(11):791–9.

Grove JR, Pevec WC. Venous thrombosis related to peripherally inserted central catheters. J Vasc Interv Radiol. 2000;11:837–40.

Guyatt GH, Akl EA, Crowther M, et al. Executive summary: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):7S–47S.

Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. N Engl J Med. 2008;359:1317–29.

Hamilton MG, Hull RD, Pineo GF. Venous thromboembolism in neurosurgery and neurology patients: a review. Neurosurgery. 1994;34:280–96.

Hart RG, Tonarelli SB, Pearce LA. Avoiding central nervous system bleeding during antithrombotic therapy: recent data and ideas. Stroke. 2005;36:1588–93.

Irem Baharoglu M, Cordonnier C, Al-Shahi Salman R, de Gans K, Koopman MM, Brand A, Majoie CB, Beenen LF, Marquering HA, Vermeulen M, Nederkoorn PJ, de Haan RJ, Roos YB. Platelet transfusion versus standard care after acute stroke due to spontaneous cerebral haemorrhage associated with antiplatelet therapy (PATCH): a randomised, open-label, phase 3 trial. Lancet. 2016;387:2605–13.

Joffe HV, Kucher N, Tapson V, et al. Upper-extremity deep vein thrombosis a prospective registry of 592 patients. Circulation. 2004;110:1605–11.

Karafin MS, Hilyer CD, Shaz BH. Principles of plasma transfusion: plasma, cryoprecipitate, albumin, and immunoglobulins. In: Hoffman R, Benz EJ, Silberstein LE, Heslop H, Weltz J, Anstasi J, editors. Hematology: diagnosis and treatment. Philadelphia: Elsevier; 2012. p. 1683–94.

Kearon C, Akl EA, Comerota AJ, et al. Antithrombotic therapy for VTE disease: antithrombotic therapy and prevention of thrombosis, 9th

ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. Chest. 2012;141(2 Suppl):e419S–96S.
Kim J, Gearhart MM, Zurick A, et al. Preliminary report on the safety of heparin for deep venous thrombosis prophylaxis after severe head injury. J Trauma. 2002;53:38–43.
Levi M, Cromheecke ME, de Jonge E, et al. Pharmacological strategies to decrease excessive blood loss in cardiac surgery: a meta-analysis of clinically relevant endpoints. Lancet. 1999;354:1940–7.
Liumbruno GM, Bennardello F, Lattanzio A, et al. Recommendations for the transfusion management of patients in the peri-operative period. I. The pre-operative period. Blood Transfus. 2011;9:19–40.
Mahdy AM, Webster NR. Perioperative systemic haemostatic agents. Br J Anaesth. 2004;93:842–588.
Mannucci PM. Hemostatic drugs. N Engl J Med. 1998;339:245–53.
Mannucci PM. Intracerebral haemorrhage and recombinant factor VIIa: not so good news! Intern Emerg Med. 2007;2:235–6.
Mannucci PM, Ghirardini A. Desmopressin: twenty years after. Thromb Haemost. 1997;78:958.
Nelson MD, Maeder MA, Usner D, et al. Prevalence and incidence of intracranial hemorrhage in a population of children with haemophilia. The hemophilia growth and development study. Haemophilia. 1999;5:306–12.
Norwood SH, McAuley CE, Berne JD, et al. Prospective evaluation of the safety of enoxaparin prophylaxis for venous thromboembolism in patients with intracranial hemorrhagic injuries. Arch Surg. 2002;137:696–702.
Pantanowitz L, Kruskall MS, Uhl L. Cryoprecipitate patterns of use. Am J Clin Pathol. 2003;119:874–81.
Praxbind®. Ridgefield: Boehringer Ingelheim Pharmaceuticals; 2015. https://www.accessdata.fda.gov/drugsatfda_docs/label/2015/761025lbl.pdf.
Qureshi AI, Suri MFK. Acute reversal of clopidogrel-related platelet inhibition using methyl prednisolone in a patient with intracranial hemorrhage. Am J Neuroradiol. 2008;29:e97.
Raj G, Kumar R, McKinney WP. Time course of reversal of anticoagulant effect of warfarin by intravenous and subcutaneous phytonadione. Arch Intern Med. 1999;159:2721–4.
Rathbun SW, Whitsett TL, Vesely SK, Raskob GE. Clinical utility of D-dimer in patients with suspected pulmonary embolism and nondiagnostic lung scans or negative CT findings. Chest. 2004;125:851–5.
Righini M, Le Gal G, Aujesky D, et al. Diagnosis of pulmonary embolism by multidetector CT alone or combined with venous ultrasonography of the leg: a randomised non-inferiority trial. Lancet. 2008;371:1343–52.
Sachdeva A1, Dalton M, Amaragiri SV, Lees T. Elastic compression stockings for prevention of deep vein thrombosis. Cochrane Database Syst Rev. 2010;7:CD001484.
Schaefer JK, McBane RD, Wysokinski WE. How to choose appropriate direct oral anticoagulant for patient with nonvalvular atrial fibrillation. Ann Hematol. 2016;95:437–49.
Schroder WS, Gandhi PJ. Emergency management of hemorrhagic complications in the era of glycoprotein IIb/IIIa receptor antagonist, clopidogrel, low molecular weight heparin, and third-generation fibrinolytic agents. Curr Cardiol Rep. 2003;5:310–7.
Shakur H, Roberts I, Bautista R, et al. Effects of tranexamic acid on death, vascular occlusive events, and blood transfusion in trauma patients with significant haemorrhage (CRASH-2): a randomised, placebo-controlled trial. Lancet. 2010;376:23–32.
Siegal D, Cuker A. Reversal of novel oral anticoagulants in patients with major bleeding. J Thromb Thrombolysis. 2013;35:391–8.
Stainsby D, MacLennan S, Hamilton PJ. Management of massive blood loss: a template guideline. Br J Anaesth. 2000;85:487–91.
Stein PD, Hull RD, Patel KC, et al. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. Ann Intern Med. 2004;140:589–602.
Stein PD, Beemath A, Matta F, et al. Clinical characteristics of patients with acute pulmonary embolism: data from PIOPED II. Am J Med. 2007a;120:871–9.
Stein PD, Alnas M, Beemath A, Patel NR. Outcome of pulmonary embolectomy. Am J Cardiol. 2007b;99:421–3.
The National Institute of Neurological Disorders and Stroke rt-PA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. N Engl J Med. 1995;333:1581–7.
van Belle A, Büller HR, Huisman MV, et al. Effectiveness of managing suspected pulmonary embolism using an algorithm combining clinical probability, D-dimer testing, and computed tomography. JAMA. 2006;295:172–9.
Van Berkel MA, Crannage AJ, Murphy JA. Evaluation of education on the appropriate use of vitamin k in warfarin reversal in adult inpatients. Hosp Pharm. 2013;48(8):662–7.
van Rossum AB, van Houwelingen HC, Kieft GJ, Pattynama PM. Prevalence of deep vein thrombosis in suspected and proven pulmonary embolism: a meta-analysis. Br J Radiol. 1998;71:1260–5.
Van Ryn J, Stangier J, Haertter S, Liesenfeld KH, Wienen W, Feuring M, Clemens A. Dabigatran etexilate – a novel, reversible, oral direct thrombin inhibitor: interpretation of coagulation assays and reversal of anticoagulant activity. Thromb Haemost. 2010;103(6):1116–27.

Gastrointestinal Hemorrhage in Neurosurgical Critical Care

93

Corey R. White and Kamila Vagnerova

Overview

Upper gastrointestinal bleeding (UGIB) is a common medical condition that results in high morbidity and mortality. Peptic ulcer disease (PUD) is the most common related cause of UGIB in general population.

Attenuating risk factors for PUD, including prevention of *Helicobacter pylori* (*H. pylori*) infection, avoidance of nonsteroidal anti-inflammatory drugs (NSAID), and reduction of gastric acid and stress, help to minimize ulcer occurrence and bleeding/rebleeding rates. Stress-related ulcers are a common cause of acute UGIB in intensive care unit (ICU) patients. There is a paucity of data specific to neurosurgical and neurocritical care patients. Thus, much of the information provided in this chapter specific to ICU patients in particular is based on evidence from the general ICU patient population.

Two major risk factors for overt GI bleeding due to stress ulceration:

- Mechanical ventilation >48 h (odds ratio 15.6)
- Coagulopathy – international normalized ratio (INR) >1.5, platelet count <50,000, or partial thromboplastin time of more than two times the control value (odds ratio 4.3)

Among patients with one or both of these risk factors, almost 4% develop clinically important UGIB compared to 0.1% with neither risk factor.

Additional risk factors for stress ulceration:

- Advanced age
- Shock
- Sepsis
- Hepatic failure
- Acute renal failure
- Multiple trauma
- Burns >35% of total body surface area
- High-dose glucocorticoid therapy
- Traumatic brain injury
- Traumatic spinal cord injury
- History of PUD or UGIB

Most UGIB in critically ill is due to gastric or esophageal ulcerations. Stress ulceration can also cause perforation (<1% of surgical ICU patients). However, endoscopy (EGD) performed within 72 h of a major burn or cranial trauma reveals acute mucosal abnormalities in >75% of patients. In isolated head injury, GI tract dysfunction presents early and includes risk of GI bleed (see Table 93.1 for risk factors in postoperative patients).

Table 93.1 General and selected neurosurgical risk factors in postoperative patients

Risk factors in postoperative patients	Incidence of UGIB (%)
Male	6.64
Female	3.40
Age >50 years	9.88
Age <50 years	3.35
Adrenocortical hormone therapy	5.46
No adrenocortical hormone therapy	2.13
GCS <10	17.5
Intracerebral hematoma	15.7
Intraventricular hemorrhage	10.0
Subdural hematoma	6.00
Extradural hematoma	2.94
Tumor of fourth ventricle	15.79
Tumor of brainstem	7.89
Tumor of cerebral hemisphere	5.71
Tumor of sellar hypothalamus	3.74

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Prevention

Incidence of overt UGIB ranges from 1.5% to 8.5% of all ICU patients but may be as high as 15% if no prophylaxis is used. It is widely accepted that prophylaxis is indicated for ICU patients at risk; however, there is lack of consensus regarding which stress ulcer prophylaxis intervention should be used. Antisecretory agents such as histamine H2 receptor antagonists (H2RA) or proton pump inhibitors (PPI) decrease the risk of stress-related mucosal damage and UGIB in high-risk patients. H2RA blockers are often considered first-line agents; however, thrombocytopenia can develop in neurosurgical patients on H2RA. For patients who are at high risk, the number needed to treat with prophylaxis (H2RA or PPI) to prevent one GI bleed is 30. The Surviving Sepsis Campaign guidelines recommend stress ulcer prophylaxis in patients with severe sepsis/septic shock who have bleeding risk factors and suggest PPI use rather than H2RA for stress ulcer prophylaxis. Other studies also favor the use of PPI over H2AR due to the lower rates of GIB.

Recent meta-analysis of eight randomized controlled trials (RCT) evaluating the use of the stress ulcer prophylaxis in neurocritically ill patients concluded that prophylaxis with either PPI or H2RA reduced the incidence of UGIB as well as all-cause mortality when compared to placebo or no prophylaxis without increasing the risk of nosocomial pneumonia.

Although less commonly used, antacids and sucralfate are more effective than no prophylaxis in reducing overt bleeding (see Table 93.2 for recommendations). Enteral feeding has also proven beneficial due to its ability to improve splanchnic blood flow and alone may reduce the risk of overt GI bleeding due to stress ulceration.

The use of antisecretory agents may increase the incidence of *Clostridium difficile* infection and nosocomial and postoperative pneumonia. This risk should not prevent the use of GI prophylaxis, when indicated, in critically ill patients.

Prophylaxis is recommended for ICU patients with:

- Mechanical ventilation >48 h
- Coagulopathy (platelet count <50,000 per m^3, INR >1.5, or partial thromboplastin time (PTT) >2 times the control value)
- GI ulceration or bleeding within the past year
- Traumatic brain injury or spinal cord injury
- Severe burns >35% of the body surface area
- Two or more of the following: sepsis/septic shock, ICU >1 week, occult GIB >5 days, high-dose steroids

In 2016 Buendgens' review supported pharmacologic prophylaxis in patients with known peptic ulcer disease, craniocerebral injury, cardiogenic shock, post liver or renal transplant, acute renal failure, and NSAID use.

Crisis Management

Most patients with acute UGIB can be managed with fluid and blood resuscitation, medical therapy, and endoscopic intervention. *All patients with UGIB require urgent gastroenterology consultation*.

Table 93.2 Common medications used for prophylaxis of stress-related mucosal disease

Medication	Route	Standard dosing	Renal dosing
Histamine H2 receptor antagonists			
Cimetidine	IV	50 mg/h continuous infusion	If CrCl <30 mL/min: 25 mg/h
	PO; NG tube	300 mg every 6 h	If CrCl <30 mL/min: 300 mg every 12 h PO or IV
Ranitidine	IV	50 mg every 6–8 h	If CrCl <30 mL/min: 50 mg every 18–24 h
	PO	300 mg loading dose and then 150 mg every 12 h	If CrCl <30 mL/min: 150 mg daily
Famotidine	IV	1.7 mg/h continuous infusion	If CrCl <30 mL/min: 0.85 mg/h by continuous infusion
	PO; NG tube; IV	20 mg every 12 h	If CrCl <30 mL/min: 20 mg once daily
Sucrose–aluminum complex			
Sucralfate	PO; NG tube	1 g every 6 h	Use with caution in severe renal impairment
Proton pump inhibitors			
Esomeprazole	PO; NG tube; IV	40 mg every day	–
Lansoprazole	PO; NG tube	30 mg every day	–
Omeprazole	PO; NG tube; IV	40 mg on the first day and then 20–40 mg daily	–
Pantoprazole	PO; NG tube; IV	40 mg every day	–

IV intravenous, *CrCl* creatinine clearance, *PO* by mouth, *NG* nasogastric

Pathophysiology and Clinical Presentation

The upper GI tract is protected by mucosa. Disruption in this mucosal layer or a significant shift in pH begins the process of ulceration. Ulcerations usually occur in the acid-producing areas, the fundus, and body of the stomach but may also develop in the distal esophagus, antrum, or duodenum. Ulcerations are usually shallow and cause slow bleeding from the superficial capillary beds and rarely lead to hemodynamically significant bleeding. Deeper lesions, usually occurring between the third and seventh ICU day, may erode into the submucosa which can result in injury of larger vessels and massive hemorrhage or even organ perforation.

UGIB commonly presents with melena or hematemesis. Common reasons for UGIB in ICU patients include the following:

- Impaired mucosal protection – Under normal conditions the glycoprotein mucous layer forms a physical barrier to hydrogen ion diffusion and traps bicarbonate, but it may be denuded by increased concentrations of refluxed bile salts or uremic toxins common in critically ill patients. Alternatively, or in addition, mucosal integrity may be compromised due to poor perfusion associated with shock, sepsis, and trauma.
- Hypersecretion of acid – Excessive gastrin stimulation of parietal cells has been detected in patients with head trauma, whereas it is usually normal or subnormal in most other ICU patients. Gastric acid and pepsin are essential cofactors in the pathogenesis of peptic ulcers. Control of gastric acidity is an essential therapeutic maneuver in active UGIB.
- *Helicobacter pylori* infection – *H. pylori* is a spiral bacterium that infects the superficial gastric mucosa. It may contribute to stress ulceration, but the evidence is limited. It disrupts the mucosal layer, liberating pepsin and hydrogen ions, leaving underlying mucosa more vulnerable. The immune response to *H. pylori* incites an inflammatory reaction that promotes further tissue injury.
- NSAID-induced injury results from both systemic prostaglandin inhibition and local effects. The majority of NSAID-induced ulcers are clinically uncomplicated and asymptomatic. NSAIDs may play a role in nonhealing ulcers.
- Steroids – Systemic steroids frequently used in neurosurgical patient almost double the risk of a new episode of UGIB or perforation. Concomitant use with high doses of NSAIDs has been associated with a 12-fold increased risk for upper GI complications.
- Head injury – GI dysfunction manifests as gastroparesis, ileus, increased intestinal mucosal permeability, and UGIB due to stress ulceration and coagulopathy. Plasma levels of cortisol and advanced age are independent predictors of stress ulcers following acute head injury. There is a relationship between the severity of head injury and the incidence of gastroparesis. Significant gastric intramucosal acidosis occurs commonly in severe head injury. Primary insult to the central nervous system likely results in derangement of splanchnic blood flow secondary to neurohumoral mechanisms.

Patient Assessment

Clinical Assessment

The medical history, physical examination, and initial laboratory values are important for triage decisions, assessing resuscitation requirements, need for further treatment, consults, and prognosis (see Fig. 93.1).

- Medical history
  - Prior GI bleed, GI symptoms, alcohol use/abuse
  - Gastrotoxic medication, e.g., NSAIDs, anticoagulants, antiplatelet agents
  - Comorbidities (renal and coronary artery and peripheral vascular diseases)
  - Head injury
- Physical exam and monitoring
  - *Hemodynamic stability*
    (a) Tachycardia, thready pulse

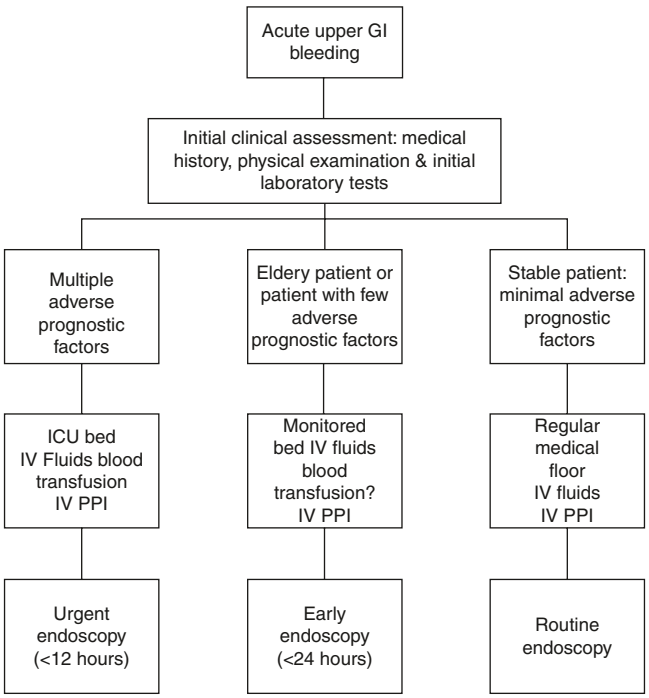

Fig. 93.1 Initial management and triage of patients with UGIB. (Adapted from Cappell and Friedel (Cappell & Friedel, 2008))

(b) Systolic pulse pressure variation (arterial line) of greater than 13 mmHg
(c) Hypotension, orthostatic hypotension
(d) Hypoxia
– *Abdominal examination*
(a) Bowel sounds, abdominal tenderness, ascites
– *Signs of chronic liver disease or portal hypertension*
(a) Hepatomegaly, splenomegaly
(b) Palmar erythema, spider angiomata, caput medusa
(c) Peripheral edema
– *Signs of shock (see vital signs listed above)*
(a) Cold clammy extremities
(b) Altered mental status
– *Rectal examination*
(a) Occult or gross blood
– *Laboratory work-up*
(a) Complete blood count (CBC), basic metabolic panel (BMP), coagulopathy work-up, type and screen

Nasogastric aspiration with saline lavage is useful in detecting intragastric blood. Care must be taken regarding the use of saline that is colder than normal body temperature, as this may cause hypothermia, shivering, and additional cardiovascular stress.

Surgical consultation is recommended for ongoing active or recurrent UGIB, massive bleeding, bleeding associated with significant abdominal pain, acute lower GIB, variceal bleeding, and suspicion for acute abdomen. Patients with severe symptoms, signs of shock, continuing hematochezia, and/or significant comorbidities are critically ill and require aggressive treatment/intervention.

Intervention/Treatment

First, stabilize the patient. Secure IV access (two large-bore (16 gauge or larger) IVs), and initiate resuscitation by warmed fluid administration. Start crystalloid infusion to maintain the blood pressure, and send for type and cross-match of several units of packed erythrocytes. Evaluate the patient for airway protection and secure the airway, if needed. Maintain cardiorespiratory support as needed, and treat associated conditions (e.g., sepsis, myocardial infarction, traumatic brain injury). Begin general supportive measures including supplemental oxygen by nasal cannula and cardiac monitoring (e.g., EKG, blood pressure, and pulse oximetry).

Patients with massive bleeding, active hematemesis, hypoxia, tachypnea, or altered mental status should have airway protection (i.e., endotracheal intubation). Keep the patient NPO for urgent EGD and potential surgery, and place a Foley catheter to monitor urine output. Transfuse packed erythrocytes for hemodynamic instability despite crystalloid resuscitation, hemoglobin <9 g/dL in high-risk patients or <7 g/dL in low-risk patients, and consider fresh frozen plasma for coagulopathy or platelets for thrombocytopenia (platelets <50,000). For massive transfusion protocols, most authorities now advocate administration of units of packed erythrocytes, plasma, and platelets in a ratio of 1 to 1 to 1.

Immediate gastroenterology consultation obtains surgical and interventional radiology consultation for any large-scale bleeding. Balloon tamponade may be performed as a temporizing measure for patients with uncontrollable variceal hemorrhage.

Empiric Pharmacotherapy

PPIs are the initial medical therapy. Currently pantoprazole and esomeprazole are the only intravenous formulations available in the United States; start with an IV bolus of 80 mg, and continue IV infusion at 8 mg/h for a total of 72 h. Alternatively, treatment with IV pantoprazole or esomeprazole at a dose of 40 mg twice daily can be used rather than a high-dose continuous infusion. Trials have failed to show superior outcomes with high-dose continuous IV PPI administration compared with intermittent dosing. Giving the PPI intermittently rather than as a continuous infusion could decrease resource utilization and cost.

If no signs of rebleeding after 24 h, switch to oral PPI.

Octreotide is used in esophagogastric variceal bleeding and/or cirrhosis. Start with an IV bolus of 50 mcg, and continue IV infusion at 25–50 mcg/h for 2–5 days.

Nonselective beta-blockers also help to reduce portal hypertension.

Antibiotic (e.g., ceftriaxone, amoxicillin–clavulanate, or quinolone) prophylaxis should be started in any patient with GI hemorrhage with esophagogastric variceal bleeding and/or cirrhosis.

Endoscopy

EGD is a primary diagnostic and therapeutic tool for UGIB. It helps to determine the cause and provides rationale for triage of patients. The most commonly used methods for control of the bleeding are injection and cautery/thermal techniques, as well as mechanical therapy including endoclips and banding.

Key Points

- Stress ulcer prophylaxis is indicated for ICU patients with:
  – Mechanical ventilation >48 h
  – Coagulopathy
  – GI ulceration or bleeding within the past year

  - Traumatic brain injury or spinal cord injury
  - Severe burns >35% of the body surface area
  - Two or more of the following: sepsis, ICU >1 week, occult GIB >5 days, high-dose steroids
- Stress ulcer prophylaxis can include the use of antisecretory agents (PPI, H2RA), sucralfate, antacids, and enteral nutrition. Either PPI or H2RA is most commonly used in high-risk patients as there remains a lack of consensus on which stress ulcer prophylaxis intervention should be used.
- The initial evaluation of UGIB involves an assessment of hemodynamic stability and the necessity for fluid and blood resuscitation.
- Use IV PPI, continuous or intermittent dosing, as first-line agent in acute UGIB.
- All patients with UGIB require urgent gastroenterology consultation.

References and Suggested Reading

Barkun AN, Bardou M, Pham CQ, Martel M. Proton pump inhibitors vs. histamine 2 receptor antagonists for stress-related mucosal bleeding prophylaxis in critically ill patients: a meta-analysis. Am J Gastroenterol. 2012;107:507–20.

Buendgens L, Koch A, Tacke F. Prevention of stress-related ulcer bleeding at the intensive care unit: risks and benefits of stress ulcer prophylaxis. World J Crit Care Med. 2016;5(1):57–64.

Cappell M, Friedel D. Initial management of acute upper gastrointestinal bleeding: from initial evaluation up to gastrointestinal endoscopy. Med Clin N Am. 2008;92:491–509.

Cook DJ, Fuller HD, Guyatt GH, et al. Risk factors for gastrointestinal bleeding in critically ill patients. Canadian Critical Care Trials Group. N Engl J Med. 1994;330(6):377–81.

Cook DJ, Griffith LE, Walter SD, et al. The attributable mortality and length of intensive care unit stay of clinically important gastrointestinal bleeding in critically ill patients. Crit Care. 2001;5(6):368–75.

Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. Intensive Care Med. 2013;39(2):165–228.

Kwok CS, Arthur AK, Anibueze CI, et al. Risk of *Clostridium difficile* infection with acid suppressing drugs and antibiotics: meta-analysis. Am J Gastroenterol. 2012;107:1011–9.

Liu B, Liu S, Yin A, et al. Risks and benefits of stress ulcer prophylaxis in adult neurocritical care patients: a systematic review and meta-analysis of randomized controlled trials. Crit Care. 2015;19:409.

Lu WY, Rhoney DH, Boling WB, et al. A review of stress ulcer prophylaxis in the neurosurgical intensive care unit. Neurosurgery. 1997;41:416–25.

MacLaren R, Reynolds PM, Allen RR. Histamine-2 receptor antagonists vs proton pump inhibitors on gastrointestinal tract hemorrhage and infectious complications in the intensive care unit. JAMA Intern Med. 2014;174:564–74.

Sachar H, Vaidya K, Laine L. Intermittent vs continuous proton pump inhibitor therapy for high-risk bleeding ulcers: a systematic review and meta-analysis. JAMA Intern Med. 2014;174:1755–62.

Sesler JM. Stress-related mucosal disease in the intensive care unit. AACN Adv Crit Care. 2007;18(2):119–28.

Venkatesh B, Towsend S, Boots R. Does splanchnic ischemia occur in isolated neurotrauma? A prospective observational study. Crit Care Med. 1999;27(6):1175–80.

Zheng K, Wu G, Cheng NN, Yao CJ, Zhou LF. High risk factors of upper gastrointestinal bleeding after neurosurgical procedures. Chung-Hua Hsueh Tsa Chih [Chin Med J]. 2005;85(48):3387–91.

Intracranial Monitors in Neurosurgical Critical Care

94

Matthew A. Kirkman

Introduction

While the clinical neurologic examination is the cornerstone of neuromonitoring, a complete clinical assessment is not possible in intubated or sedated/anesthetized patients. There are several devices available for monitoring a range of physiological variables and guiding decision-making in the critical care setting, and these are discussed in detail in Chap. 5. The most commonly used devices include external ventricular drains (EVDs), intraparenchymal intracranial pressure (ICP) monitors, brain tissue oxygen ($PbtO_2$) monitors, and cerebral microdialysis (CMD) probes. This chapter discusses the epidemiology, prevention, detection, and management of the commonest complications associated with these four devices. First, these monitoring devices and their indications are briefly described.

Overview

Intracranial Pressure Monitoring

ICP is the pressure inside the skull and thus in the brain tissue; it is synonymous with the cerebrospinal fluid (CSF) pressure in the lateral ventricles. ICP monitoring is performed widely in neurocritical care settings, as ICP is a therapeutic target for several conditions (Table 94.1), and it also facilitates the quantification of cerebral perfusion pressure (CPP; itself another therapeutic target, calculated as the difference between mean arterial pressure and ICP). The identification and analysis of pathological ICP waveforms and assessment of cerebrovascular pressure reactivity are also possible through ICP monitoring.

Table 94.1 Indications for intracranial pressure monitoring

Indication	Comments
Traumatic brain injury	The most evidence-based indication. Recommended in specific TBI patients in the Brain Trauma Foundation guidelines and in expert consensus recommendations from the 2013 Milan conference on ICP monitoring in TBI
Aneurysmal subarachnoid hemorrhage	
Intracerebral hemorrhage	
Hydrocephalus	A standard in hydrocephalus management, including chronic monitoring of normal pressure hydrocephalus
Hypoxic brain injury	
Central nervous system infections	
Fulminant hepatic failure	
Perioperative management of neoplastic lesions with associated mass effect	ICP monitoring is becoming increasingly common in this setting

Normal mean ICP is 5–10 mmHg in healthy, resting supine adults. Although thresholds for treatment of raised ICP vary both within and between specific conditions, in traumatic brain injury (TBI), a common indication for ICP monitoring, it is generally advised that ICP greater than 20–25 mmHg requires treatment due to an association with increased mortality; the latest (fourth edition) Brain Trauma Foundation (BTF) guidelines for severe TBI recommend treating ICP values >22 mmHg.

The most common methods of ICP monitoring include EVDs and intraparenchymal ICP monitors. EVDs measure CSF pressure in the lateral ventricles through either:

1. A standard ventricular catheter connected via a fluid-filled system to an external pressure transducer
2. A catheter incorporating microstrain gauge or fiber-optic technology

EVDs are the preferred method of ICP monitoring when prolonged monitoring and therapeutic drainage of CSF are necessary, but their insertion is more technically challenging than for intraparenchymal ICP monitors.

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Intraparenchymal ICP monitoring systems are of two broad types:

1. Solid-state piezoelectric strain gauge devices (Codman) that incorporate pressure-sensitive resistors which translate pressure-generated changes in resistance into ICP values.
2. Fiber-optic devices (Camino, InnerSpace) which transmit light toward a mirror at the catheter tip which becomes distorted by changes in ICP; differences in the intensity of reflected light resulting from mirror distortion are translated into ICP values.

Intraparenchymal ICP monitors are usually placed ~2 cm into brain parenchyma through a cranial access device or at craniotomy when they can also be sited subdurally. These devices measure localized pressure but provide equivalent pressure measurements to ventricular catheters in most circumstances. The main limitations of intraparenchymal ICP monitors include "zero drift," which can result in measurement error over several days, and the inability to perform in vivo recalibration.

Brain Tissue Oxygen Monitoring

Evidence that combining $PbtO_2$ and ICP monitoring can identify cerebral hypoperfusion more reliably than ICP monitoring alone has led to $PbtO_2$ monitoring being increasingly incorporated into neuromonitoring strategies wherever ICP monitoring is indicated (Table 94.2). $PbtO_2$ is a complex and dynamic variable that represents more than just a monitor of hypoxia/ischemia; values of $PbtO_2$ result from the interaction of all factors affecting cerebral oxygen delivery and demand (oxygen metabolism), the relative proportion of arterial or venous vessels in the region of interest, and tissue oxygen diffusion gradients.

Normal brain $PbtO_2$ is 20–35 mmHg (2.66–4.66 kPa). $PbtO_2$ monitoring is currently most commonly used in TBI, and many recommend commencing treatment measures in TBI when $PbtO_2$ <20 mmHg (2.66 kPa) since this value represents compromised brain oxygenation. The latest BTF guidelines for severe TBI make no recommendation about $PbtO_2$ targets due to inconsistencies in findings between studies evaluating outcomes following $PbtO_2$-directed therapy. Although a systematic review incorporating 491 patients from four studies found overall outcome benefits from $PbtO_2$-directed therapy compared to ICP-/CPP-guided therapy alone (odds ratio of favorable outcome = 2.1, 95% confidence interval = 1.4–3.1), all four studies were non-randomized, and only two were truly prospective.

Table 94.2 Indications for brain tissue oxygen monitoring

Indication	Comments
Traumatic brain injury	The most evidence-based indication. The recent prospective, phase II randomized controlled trial (BOOST-2) confirmed the safety and efficacy of $PbtO_2$-directed therapy in TBI. Further data from a larger phase III trial to clarify potential outcome benefits are awaited
Aneurysmal subarachnoid hemorrhage	Recommended in Neurocritical Care Society guidelines as a complement to transcranial Doppler and radiological monitoring for detecting vasospasm, although evidence to date is conflicting
Intracerebral hemorrhage	$PbtO_2$ monitoring may identify CPP targets for optimal cerebral oxygenation in comatose ICH patients
Neurocritical care patients – to allow titration of individual CPP targets, ventilator parameters, transfusion, and management of intracranial hypertension in combination with ICP monitoring	As recommended by the International Multidisciplinary Consensus Conference on Multimodality Monitoring
Intraoperatively for intracranial aneurysm and arteriovenous malformation surgery	Limited evidence supporting these indications at present

Preliminary results from the prospective, phase II randomized BOOST-2 trial, which evaluated the safety and efficacy of treatment based on ICP (target ICP <20 mmHg) and $PbtO_2$ monitoring (target $PbtO_2$ >20 mmHg) compared to ICP monitoring and management alone (same target ICP), have been recently released. In 110 adult patients with non-penetrating severe TBI, time spent with $PbtO_2$ <20 mmHg was significantly lower in those in the ICP/$PbtO_2$ group, with no difference in adverse events between the two treatment arms. There was a trend towards lower overall mortality and less poor outcome in the ICP/$PbtO_2$ group although these differences were not statistically significant ($p = 0.229$ and $p = 0.221$, respectively); this is perhaps unsurprising given the study was not powered for outcome. A larger phase III trial is now required to clarify and expand these findings.

$PbtO_2$ catheters are similar in size to intraparenchymal ICP monitors and are placed in subcortical white matter through single or multiple lumen bolts, via a burr hole, or at craniotomy. Commercially available $PbtO_2$ monitoring probes incorporate a Clark-type cell with reversible electrochemical electrodes. Oxygen diffusing from brain tissue crosses a semipermeable membrane and is reduced by a gold polarographic cathode which produces a flow of electrical current directly proportional to the tissue oxygen

Table 94.3 Indications for cerebral microdialysis

Indication	Comments
Traumatic brain injury	The most studied indication, along with SAH. Recommended in the consensus statement from the 2014 International Microdialysis Forum. Evidence supporting CMD use in TBI from studies on the subjects of outcome and prognostication, early warning system of secondary insults, monitoring and treatment of low cerebral glucose/guiding systemic glucose management and insulin use, monitoring during CPP augmentation/reduction, monitoring during neurological wake-up test, evaluating the effects of body temperature on cerebral chemistry, and monitoring after decompressive craniectomy
Aneurysmal subarachnoid hemorrhage	The most studied indication, along with TBI. Recommended in the Consensus Statement from the 2014 International Microdialysis Forum. Evidence supporting CMD use in SAH from studies on the same subjects as TBI (above), plus: deciding on transfusion thresholds
Intracerebral hemorrhage	Limited evidence supporting these indications at present
Acute ischemic stroke	
Hepatic encephalopathy	
Epilepsy	
Intraoperatively during neurosurgical procedures	Limited and low-quality evidence supporting the use of CMD for diagnostic purposes during neurosurgery. Furthermore, the temporal resolution of the only commercially available clinical system (hourly sampling rate) unlikely to be adequate for intraoperative monitoring

tension. Probes are often placed in tissue immediately surrounding a hematoma/contusion or in appropriate vascular territories in cases of aneurysmal subarachnoid hemorrhage (SAH); however, such precise placement can be technically challenging, and some prefer routine probe placement in normal-appearing frontal subcortical white matter on the non-dominant side.

Cerebral Microdialysis

CMD is a bedside monitor of brain tissue biochemistry that monitors cellular metabolism as well as substrate supply and is thus able to identify both ischemic and nonischemic causes of cellular energy dysfunction and the ensuing metabolic crisis. Each of the biochemical substances measured in the clinical setting is a marker of a particular cellular process associated with glucose metabolism, hypoxia/ischemia, or cellular energy failure. In clinical practice, glucose, lactate, pyruvate, glycerol, and glutamate are the variables most commonly measured, although the latter two are considered less useful in facilitating clinical decision-making. Glucose is the main substrate for brain metabolism, and periods of low cerebral glucose concentration, as well as elevated lactate-to-pyruvate ratio (LPR), are associated with unfavorable outcome after TBI. However, increased LPR may result from both ischemic and nonischemic causes, with an elevated LPR in the presence of low pyruvate (and brain tissue oxygen tension) indicating classic ischemia, whereas elevated LPR in the presence of normal or high pyruvate indicates a nonischemic cause, i.e., mitochondrial dysfunction.

CMD has been most widely used in the critical care management of TBI and SAH (Table 94.3), and although most evidence of its clinical use relates specifically to these two conditions, the use of CMD can be considered in all patients at risk of developing cerebral hypoxia/ischemia, cellular energy failure, and glucose deprivation.

CMD-derived values that are usually recommended to guide clinical intervention are glucose <0.8 mmol/L and LPR >40, although a lower LPR threshold is recommended by some. When interpreting an elevated LPR, lactate concentration >4 mmol/l is generally considered abnormal.

To perform CMD, a miniature microdialysis catheter is placed into brain tissue, and diffusion of molecules across the semipermeable dialysis membrane at its tip allows collection of substances that pass from the brain extracellular fluid into the dialysis fluid. Concentrations of glucose, lactate, pyruvate, glycerol, and glutamate can be measured in a semiautomated analyzer at the bedside. Placement of the catheter in "at-risk" tissue is generally advocated, to facilitate assessment of biochemical changes in the region most susceptible to secondary injury. In patients with diffuse injury, placement in the right (non-dominant) frontal lobe is advised.

Complications Associated with Intracranial Monitors

Of the four intracranial monitors discussed in this chapter, it is EVDs that pose the biggest challenge in the prevention and management of complications. The three most important complications are infection, hemorrhage, and malpositioning/malfunctioning. The epidemiology, prevention, diagnosis, and management of these complications are now each discussed in turn. Given that the insertion techniques and safety profiles of intraparenchymal ICP monitors, $PbtO_2$, and CMD probes are similar, for the remainder of this chapter, they are discussed collectively.

Infection

External Ventricular Drains

Epidemiology

CSF infection is a primary concern following EVD placement, as it is associated with increased mortality and morbidity. Ventriculostomy-related infection (VRI) is more likely in the presence of specific risk factors (Table 94.4). Variations in insertion and management practices, study design, and methodologies, as well as a lack of universal agreement on specific diagnostic criteria, likely contribute to the wide variation in VRI rates in the literature (0–32%). However, most commonly, rates of 10% or less are reported, and a recent meta-analysis of 33 studies including 9667 cases of EVD placement found a pooled infection incidence rate of 7.9% (95% confidence interval [CI] 6.3–9.4).

Prevention

There are several measures which can be taken to reduce the chance of VRI (Table 94.5). As shown in a recent meta-analysis of 7 randomized and 29 non-randomized studies including 16,796 ventriculostomies, use of an antimicrobial (antibiotic- or silver)-impregnated catheter reduces the overall incidence of VRI compared to plain catheters (relative risk [RR] 0.44, 95% CI 0.35–0.56), although no difference in all-cause mortality was found. Although only half of the included studies provided data on specific bacterial species and Gram-positive/Gram-negative status, in subgroup analyses antimicrobial-impregnated catheters did not appear to reduce infections associated with Gram-positive bacteria, all staphylococci, coagulase-negative *Streptococcus*, and *Staphylococcus aureus*. Interestingly, antimicrobial-impregnated catheters were associated with an increased risk of methicillin-resistant *Staphylococcus aureus* (MRSA; RR 2.64, 95% CI 1.26–5.51), nonstaphylococcal (RR 1.75, 95% CI 1.22–2.52), and Gram-negative (RR 2.13, 95% CI 1.33–3.43) infections. There is insufficient evidence to recommend one specific type of antimicrobial catheter over another or to evaluate the relative effectiveness of different antibiotics contained in the antibiotic-impregnated catheters.

Tunneling of the catheter subcutaneously has been shown in several studies to reduce the risk of VRI, and, although the optimal length of tunneling is unclear, extending tunneling to more than 10 cm away from the burr hole appears to offer no additional benefit. To prevent CSF leak, ensuring equivalence of the dural puncture hole and catheter width at the time of EVD insertion is important, as is meticulous suturing of the skin after EVD removal.

Use of an EVD management bundle to standardize care has been shown to reduce CSF infection rates, with importance placed on aseptic insertion techniques, avoidance of manipulation of the EVD collection system unless absolutely necessary, and the use of sterile dressings. No recommendations about specific dressings can be made, owing to the lack of evidence for the relative effectiveness of different types of dressing in reducing infection. It is recommended that routine CSF sampling should be avoided except where clinically indicated; the use of antimicrobial-impregnated catheters means routine sampling is less likely to produce clinically useful information. There is currently no strong evidence to suggest that the use of antibiotics for the duration of EVD placement is superior to periprocedural administration alone, and in fact the former may increase the risk of resistant organisms developing as well as *Clostridium difficile* colitis. As such it is recommended that only one dose is given, prior to EVD insertion. The choice of specific antibiotic should be dictated by local antibiograms. Routine antibiotic prophylaxis in the presence of CSF leak without any evidence of CSF infection is not recommended.

The decision about how long to keep a ventricular catheter in situ is particularly contentious. There is a recognized association between the duration of catheter placement and infection risk. However, the relationship is not necessarily linear, and studies performed to date have shown that, 1 week after catheter insertion, infection risk can either

Table 94.4 Some of the risk factors for CSF infection following EVD insertion

Subarachnoid hemorrhage
Intraventricular hemorrhage
Systemic infection
Craniotomy and other neurosurgical procedures
Repeated manipulations of the EVD system for flushing and/or CSF sampling
Cranial fracture with CSF leak
CSF leak around the EVD site
Duration of placement

Table 94.5 Advice to reduce infection risk during the management of external ventricular drains

Periprocedure
Adhere to a standardized EVD management bundle
Administer one dose of periprocedural intravenous antibiotics
Use antimicrobial-impregnated catheters
Cleanse the EVD catheter insertion site using an antimicrobial agent at the time of insertion
Couple the dural puncture hole and catheter width at the time of EVD insertion
Tunnel the catheter subcutaneously
Use antibiotic-impregnated sutures for wound closing
Use standardized sterile dressings
Post-insertion
Adhere to a standardized EVD management bundle
Avoid routine CSF sampling, obtaining CSF only when clinically indicated
Avoid routine changing of catheters and catheter sites
Remove the EVD as soon as the clinical situation allows
Suture the skin meticulously following EVD removal

increase, decrease, or plateau. Furthermore, the routine changing of catheters and catheter sites is not recommended, as there is no convincing evidence that routinely changing catheter sites reduces the risk of VRI, and there is evidence that catheter changes can increase the risk of infection. Taken together, it is therefore difficult to provide a recommendation on the maximum length of time a catheter should stay in prior to being replaced, but EVDs should definitely be removed as early as the clinical situation allows.

Diagnosis

Despite EVDs being commonly used in neurocritical care settings, there is no consensus on specific diagnostic criteria for VRI. Although positive CSF Gram stain and CSF culture are the gold standard for diagnosing VRI, false-negative Gram stains occur commonly (even in culture-positive CSF), and CSF cultures can be affected by concomitant antibiotic therapy. In addition, organisms can colonize the catheter or contaminate the CSF without resulting in an infection, and infection is not the only cause of CSF inflammation. Although timely treatment with appropriate antimicrobials is key to the successful treatment of VRI, it takes several days to receive a definitive CSF culture result. Nosocomial ventricular drainage-related infections are often difficult to diagnose because of nonspecific CSF findings, subtle signs of infection, and slow-growing and fastidious microorganisms delaying identification of pathogens and appropriate treatment.

Clinical signs of VRI include fever, tachycardia, tachypnea, meningismus, a reduced level of consciousness, and photophobia. Muscle rigidity and seizures may also be present. However, clinical signs may be subtle, particularly in the early stages. Three findings in the CSF can support the diagnosis of ventriculitis in susceptible patients: elevated (100–5000) polymorphonuclear leukocytes, decreased glucose (<40 mg/dL), and elevated protein. Serum white blood cell (WBC) count and C-reactive protein (CRP) do not appear to facilitate the diagnosis. The CSF cell index – calculated as the ratio of leukocytes to erythrocytes in CSF divided by the ratio of leukocytes to erythrocytes in peripheral blood – was developed to account for the dilution effect of CSF hemorrhage seen in intraventricular hemorrhage (IVH) on the increase in CSF white blood cells. The cell index should equal one at the time of IVH onset, as the CSF relationship of leukocytes to erythrocytes should be equal to that in peripheral blood.

A significant rise in the cell index has been shown to occur 3 days before the conventional diagnosis of catheter-related ventriculitis in one prospective study of 13 patients with EVDs placed for IVH. However, recent retrospective data from 39 patients with EVDs and proven CSF infection showed no significant increase in the cell index at the time of EVD insertion compared to 48 h before the occurrence of infection and the time culture-proven infection. Although these data cast doubt on the sensitivity of the cell index, it remains widely used; a stagnant cell index cannot rule out VRI, but an increased cell index does support a diagnosis of VRI.

Taken together, these findings support the notion that diagnosing VRI should primarily rely on the clinical picture of the patient and the results of CSF Gram stain and cultures. It is possible that in the future CSF cytokines and other inflammatory markers may allow a more accurate biochemical diagnosis of CSF infection, but at present data on these are limited.

Crisis Management

There is no consensus on what constitutes optimal treatment of VRI. Initial management of the febrile patient with an EVD in whom VRI is suspected should, as a minimum, include obtaining a CSF sample for Gram stain and culture, as well as peripheral blood cultures. There is no robust evidence to support a specific antimicrobial or duration of treatment, and decisions should be made using local guidelines with microbiology input. Ventriculitis most frequently involves Gram-positive organisms; however, if the CSF fluid sample is particularly purulent, treatment should be initiated immediately with a broad-spectrum antimicrobial agent that covers resistant Gram-positive and Gram-negative bacteria. Intraventricular antimicrobial therapy for VRI results in faster sterilization of CSF and normalization of CSF microscopy, and it is recommended as a treatment in those who fail to respond to intravenous antimicrobials alone or when organisms have a high minimum inhibitory concentration (MIC) to antimicrobials that do not achieve high CSF concentrations – particularly multidrug-resistant organisms.

For an optimal response to treatment of the infection, it is often necessary to remove any infected hardware, which should be replaced or externalized when necessary and appropriate. Some clinicians base their decision about catheter removal on the causative organism, particularly since Gram-negative bacterial infections are associated with a high frequency of relapse if the catheters are retained.

Intraparenchymal ICP, $PbtO_2$, and CMD Probes

Epidemiology

Infection rates associated with intraparenchymal ICP, $PbtO_2$, and CMD probes are lower than for EVDs. In a single-center series of 61 patients undergoing multimodality monitoring with various combinations of neuromonitoring devices (including ICP, $PbtO_2$, and CMD) for a

range of acute brain pathologies, an infection rate of 4% was reported when excluding patients with EVDs in situ. However, these data did not identify device- or monitoring modality-specific risks. Other (largely retrospective) data specifically focusing on intraparenchymal ICP probes suggest the infection rates following intraparenchymal ICP monitor insertion, including superficial infection and intracranial abscess, are low (0–2.9%). There are no robust data to suggest any significant variation in infection rates between specific intraparenchymal ICP devices. Most series of patients undergoing $PbtO_2$ monitoring report a 0% infection rate associated with $PbtO_2$ probe insertion although, relative to ICP monitoring, it is a new monitoring modality and data are limited. Similarly, relevant studies on CMD are limited, but data from a retrospective analysis of 174 consecutive patients from one center who underwent CMD reported a 0% infection rate.

Prevention

Unlike for EVDs, there is no robust evidence suggesting that duration of intraparenchymal probe placement influences infection risk, even in patients undergoing long-term ICP monitoring. Nevertheless, the infection risks of intraparenchymal monitoring can be minimized through following a strict aseptic insertion technique and, following insertion, avoiding handling of the monitor unless absolutely necessary. Routine prophylactic antibiotics are not recommended.

Diagnosis

Clinical features of an infected intraparenchymal monitor tend to be subtler than those associated with VRI. Nevertheless, the patient may present with clinical signs of infection (e.g., fever, tachycardia, tachypnea) and other features of cerebritis or abscess such as headaches, focal neurological deficits, seizures, behavioral changes, meningismus, and nausea/vomiting. Cutaneous involvement is often apparent through local erythema and/or pus. In cases of suspected infection, contrast imaging should be performed to look for a ring-enhancing lesion suggesting intracranial abscess. Ultimately, however, confirmation of an infection is only possible through microbiological analysis of a sample (which may include the device itself).

Crisis Management

Replacement or removal of the device is often recommended, as well as commencement of intravenous antibiotics in line with local guidelines and microbiology advice. Neurosurgical opinion should be sought, particularly in the presence of a deep-seated infection.

Key Points

Infection

- Infectious complications of intracranial monitors can be reduced by several means, including use of a standardized management bundle for EVDs.
- When an EVD is required, use of an antimicrobial-impregnated catheter is strongly recommended.
- Periprocedural antibiotics are recommended for EVD insertion, but otherwise prophylactic antibiotics are discouraged for any type of intracranial monitor.
- Routine changing of catheters and catheter sites is not recommended.
- Clinical signs of infection associated with intracranial monitoring devices may be subtle.
- CSF analysis and culture are crucial to confirming the diagnosis and optimizing the management of VRI.
- Early broad-spectrum treatment should be initiated in the presence of infection associated with intracranial monitoring.
- To minimize infection risks, intracranial monitoring devices should be removed as soon as the clinical situation allows.

Hemorrhage

External Ventricular Drains

Epidemiology

Owing in part to heterogeneity in study design, methodologies, and definitions, there is wide variation in the reported estimates of bleeding risk associated with EVD insertion (0–41%). Although it is important to recognize that subdural hematoma(s) may develop as a result of CSF overdrainage and that hemorrhage may be associated with removal of the ventricular catheter, studies evaluating bleeding risk associated with EVDs have tended to focus on bleeding resulting directly from insertion of the ventricular catheter – which is the focus of the remainder of this chapter. Detailed thromboprophylaxis management for patients with EVDs (and intraparenchymal monitors) is beyond the scope of this chapter, and the reader is referred to Chap. 83 of this book and also to Neurocritical Care Society guidelines on the insertion and management of EVDs (Fried et al. 2016 – see "Suggested Reading" below).

Many studies may underestimate the risk of hemorrhage following EVD insertion, as frequent or systematic imaging surveillance is not common. It is also important to note that not all placement-associated hemorrhages are symptomatic, and life-threatening hemorrhage is extremely uncommon. A recent meta-analysis of 18 studies including 2829 cases of EVD placement found a pooled hemorrhage incidence rate of 8.4% (95% CI 5.7–11.1) and pooled symptomatic hemorrhage incidence rate of 0.7% (95% CI 0.4–1.1).

Prevention

To date, there are no well-designed studies that address potentially modifiable risk factors for placement-associated hemorrhage such as blood pressure at the time of insertion, coagulopathy, and the number of attempts before successful cannulation. Reversal of coagulopathy according to local protocols prior to EVD insertion should be performed in all cases except dire emergencies, as it has been shown that hemorrhage rates are higher in patients with coagulopathy. To minimize the risk of bleeding in neurosurgical procedures, a platelet count of 100,000/mm^3 has been recommended as the appropriate threshold for transfusion.

Diagnosis

Whether or not a patient presents clinically with EVD, placement-associated hemorrhage is dependent on several factors, including whether the patient is fully awake or sedated/anesthetized and the size and location of the hemorrhage. Bleeding may occur within the ventricular system and/or anywhere along the tract of the ventricular catheter, including extra-axially. In asymptomatic patients, EVD placement-associated hemorrhages are often detected incidentally on postoperative imaging. Bleeding may present clinically with seizures or reduced consciousness and, if affecting critical brain anatomy, may lead to the patient developing neurological deficits; in such instances, immediate computed tomography (CT) imaging of the head is indicated. EVD placement-associated hemorrhage may be detected through darkening of the CSF passing into the EVD drainage system, even in the presence of pre-existing SAH/IVH.

Crisis Management

In many cases, hemorrhage associated with EVD insertion can be managed conservatively, with either close neurologic monitoring if the patient is awake and responsive or with serial CT imaging if not. In some instances, for example, large superficial hematomas with mass effect, surgical evacuation of the hematoma may be required. If there is a large blood load within the ventricular system associated with incipient hydrocephalus, contralateral EVD insertion may be indicated. Decisions regarding the appropriateness and timeliness of surgery in such instances should always involve local neurosurgical teams.

Intraparenchymal ICP, $PbtO_2$, and CMD Probes

Epidemiology

Hemorrhages associated with intraparenchymal devices are often located within the parenchyma adjacent to the monitoring device, but extra-axial hematomas can also occur. The bleeding risk associated with intraparenchymal monitoring devices is largely considered to be lower than that for EVDs, with no robust data to suggest any significant variation between specific devices. In a series of 61 patients undergoing different combinations of multimodality monitoring, including the three intraparenchymal probes discussed here, a hemorrhage rate of 3% was reported, but device- or monitoring modality-specific risks were not described. Reported rates of hemorrhage specifically associated with intraparenchymal ICP monitors vary between 0–10.7%, but rates in patients with known coagulopathies can be higher. Data from a prospective study of 1000 patients undergoing intraparenchymal ICP monitoring found a hemorrhage risk of 2.5%, with symptomatic hemorrhages occurring in 0.6%. Observational studies of patients undergoing $PbtO_2$ monitoring report hemorrhage rates of 1.7–2.9%, with very few cases of symptomatic hemorrhage reported in the literature. Data on CMD probe-related hemorrhage are limited, although a retrospective single-center study of 174 patients undergoing CMD reported a 0% hemorrhage risk.

Prevention

As for EVD insertion, coagulopathy should be corrected, and platelet count should be 100,000/mm^3 or higher prior to intraparenchymal probe insertion in all but the most urgent of cases, to minimize the risks of placement-related hemorrhage.

Diagnosis

Most hemorrhages associated with intraparenchymal monitors are asymptomatic, and most patients undergoing intraparenchymal ICP monitoring, $PbtO_2$ monitoring, *or CMD* are sedated, anesthetized, or otherwise neurologically impaired. Thus, many hemorrhages associated with intraparenchymal monitors are detected incidentally on postoperative imaging. However, placement-associated hemorrhages may present with seizures, reduced consciousness, or, if the hemorrhage affects critical brain anatomy, neurological deficits. Any patient suspected of having placement-related hemorrhage should undergo CT imaging of the head.

Crisis Management

As for EVDs, in many cases intraparenchymal probe placement-associated hemorrhage can be managed conservatively, with either close neurologic monitoring if the patient is awake and responsive or with serial CT imaging if not. It is extremely uncommon for a hemorrhage resulting from an intraparenchymal pressure monitor to require surgical

intervention, although potential cases should always be discussed with the local neurosurgical department.

Key Points

Hemorrhage

- To minimize bleeding risk, coagulation parameters should be normal, and the platelet count should be 100,000/mm^3 or higher before placement of an intracranial monitor, except in dire emergencies.
- Small hemorrhages are common, and most hemorrhages are asymptomatic, detected incidentally on post-insertion imaging.
- In the awake and responsive patient, serial neurologic examinations may help monitor for hemorrhage progression; in others, serial imaging is advised.
- Larger hematomas with mass effect may require neurosurgical intervention.

Malpositioning/Malfunctioning

External Ventricular Drains

Epidemiology

Malpositioning of EVD catheters can increase morbidity and mortality through several means, including increasing time with untreated hydrocephalus, damage caused by passing through critical brain structures, and increasing the risk of complications (including infection) associated with multiple passes of the catheter. Reported rates of EVD malpositioning vary widely in the literature. One single-center retrospective review of 183 post-EVD insertion scans covering a 2-year period found that over 60% of EVDs were not situated in the desired target and that 40% of these required revision/reinsertion procedures. It is not uncommon for ventricular catheters to become blocked, particularly after long-term use.

Prevention

There is no robust evidence to support a relationship between an individual's seniority or experience with inserting ventricular catheters and complication rates. Similarly, most evidence suggests that EVDs inserted in the neurocritical care unit, including by intensivists, are no more likely to result in complications such as malpositioning or infection relative to those inserted in the operating room. Although there are a range of solutions designed to improve the accuracy of EVD insertion, including the use of intraoperative neuronavigation, data evaluating the outcome effects of these interventions are generally of low quality and lack meaningful comparison groups.

Following successful insertion, ventricular catheters can be dislodged/inadvertently externalized through nursing procedures and other interventions. It is therefore important to ensure the external part of the catheter is securely attached to the patient's scalp at the time of insertion (e.g., through using a three-point suturing technique) and to avoid handling the EVD where possible.

Diagnosis

Catheter malpositioning can be detected in several ways (Table 94.6), but a malpositioned catheter whose tip is lying in the subarachnoid space may allow CSF drainage, and such instances may only be detected incidentally on post-insertion imaging. A loss of CSF output from a previously functioning EVD should raise suspicions of a dislodged/inadvertently externalized EVD, although other causes such as catheter blockage should also be ruled out (Fig. 94.1).

Crisis Management

EVDs that are suboptimally placed but still functioning do not usually require revision. However, a nonfunctioning EVD requires further evaluation (Fig. 94.1), including consideration of whether or not the EVD is still required.

Intraparenchymal ICP, $PbtO_2$, and CMD Probes

Epidemiology

Malpositioning of intraparenchymal ICP, $PbtO_2$, and CMD probes is less studied than malpositioning of EVD catheters, and, for $PbtO_2$ and CMD probes, it is generally

Table 94.6 Potential indicators of malpositioned or malfunctioning intracranial monitoring devices

External ventricular drain
Attenuated CSF output into the drainage system
Absent or unexpected ICP readings
Absent or unexpected ICP waveform
Inadequate responsiveness of ICP readings to stimulated increases in ICP (e.g. through applying abdominal pressure)
Neurological signs/symptoms (typically in the awake patient) if the catheter has passed through critical brain structures
Intraparenchymal ICP monitor
Absent or unexpected ICP readings
Absent or unexpected ICP waveform
Inadequate responsiveness of ICP readings to stimulated increases in ICP (e.g., through applying abdominal pressure)
Neurological signs/symptoms (typically in the awake patient) if the device has passed through critical brain structures
Brain tissue oxygen monitor
Absent $PbtO_2$ readings
Unexpected $PbtO_2$ readings (at least 1 h after insertion)
Inadequate responsiveness of $PbtO_2$ readings to an oxygen challenge
Neurological signs/symptoms (typically in the awake patient) if the device has passed through critical brain structures
Cerebral microdialysis
Unexpected results
Neurological signs/symptoms (typically in the awake patient) if the device has passed through critical brain structures

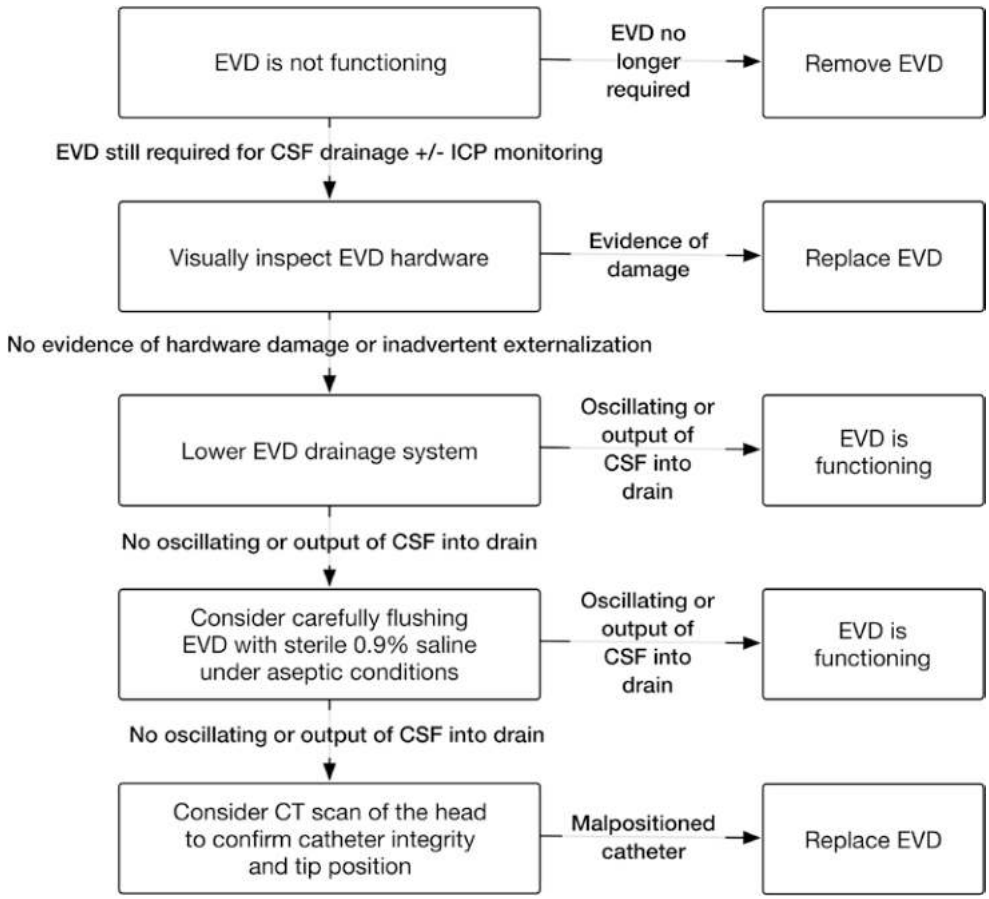

Fig. 94.1 Example of a management algorithm for an external ventricular drain (EVD) that is not functioning

recommended that correct probe placement is confirmed with a cranial CT scan. Many centers routinely place intraparenchymal ICP and $PbtO_2$ probes into frontal subcortical white matter, and malpositioned probes are a particular concern when more complex targets are chosen, such as the region surrounding a hemorrhage or contusion. Malfunctioning of intraparenchymal probes can result from probe and/or screw dislocation or defect and transducer/cable/fiber-optic damage. Rates of technical complications following intraparenchymal ICP monitor insertion vary widely from 0% to 25.4%. Reported rates of technical complications following $PbtO_2$ probe insertion vary from 5.9% to 17% and for CMD probes vary from 0% to 29%.

Prevention

As for EVD insertion, no robust evidence supports a relationship between an individual's seniority or experience with inserting intraparenchymal devices and complication rates. To prevent dislodgement/inadvertent externalization, the device should be securely attached to the patient's scalp at the time of insertion (e.g., through using a three-point suturing technique), and subsequent handling of the probe and its connections should be avoided where possible. Although malfunctioning of intraparenchymal monitors is difficult to prevent, to improve detection of technical problems with $PbtO_2$ probes, it is widely recommended that an "oxygen challenge" is performed post-insertion and thereafter on a daily basis to confirm probe function and responsiveness; a normal probe response is an increase of 200% or more from baseline $PbtO_2$ following an increase in FiO_2 to 1.0 for approximately 20 min, although impaired pulmonary function can affect responsiveness.

Diagnosis

Malfunctioning or malpositioned intraparenchymal monitors may be detected in several ways (Table 94.6), although many malpositioned intraparenchymal monitors are detected incidentally on post-insertion imaging. Suspicions of a malfunctioning or malpositioned intraparenchymal probe should prompt the clinician to perform a visual examination of the external hardware, and if this appears satisfactory, a CT of the head should be performed to check probe positioning and for any disconnection. It must be remembered that $PbtO_2$ readings are expected to be unreliable for approximately the first hour after insertion, due to the "run-in" period.

Crisis Management

If the positioning of the intraparenchymal monitoring device is suboptimal but continues to give reliable readings, revision

is not usually required. However, if the device is nonfunctioning and is still required for ongoing monitoring, it should be replaced under strict aseptic conditions.

Key Points

Malpositioning/malfunctioning

- Malpositioning of EVDs is common and revision is required more commonly than for other forms of intracranial monitors.
- Securely attaching intracranial monitors to the scalp is crucial in preventing dislodgement/inadvertent externalization of a previously well-sited intracranial monitor.
- If an EVD has stopped functioning, several steps should be followed (Fig. 94.1), including the exclusion of catheter blockage through gentle irrigation with sterile 0.9% saline under aseptic conditions.

Suggested Reading

Intracranial Pressure Monitoring

Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. Neurosurgery. 2017;80:6–15. https://doi.org/10.1227/NEU.0000000000001432.

Brain Tissue Oxygen Monitoring

Nangunoori R, Maloney-Wilensky E, Stiefel M, et al. Brain tissue oxygen-based therapy and outcome after severe traumatic brain injury: a systematic literature review. Neurocrit Care. 2012;17:131–8. https://doi.org/10.1007/s12028-011-9621-9.

Cerebral Microdialysis

Bossers SM, de Boer RD, Boer C, Peerdeman SM. The diagnostic accuracy of brain microdialysis during surgery: a qualitative systematic review. Acta Neurochir. 2013;155:345–53. https://doi.org/10.1007/s00701-012-1582-z.

Hutchinson PJ, Jalloh I, Helmy A, et al. Consensus statement from the 2014 International Microdialysis Forum. Intensive Care Med. 2015;41:1517–28. https://doi.org/10.1007/s00134-015-3930-y.

Infection

Chen JW, Rogers SL, Gombart ZJ, Adler DE, Cecil S. Implementation of cerebral microdialysis at a community-based hospital: a 5-year retrospective analysis. Surg Neurol Int. 2012a;3:57. https://doi.org/10.4103/2152-7806.96868.

Dey M, Stadnik A, Riad F, et al. Bleeding and infection with external ventricular drainage: a systematic review in comparison with adjudicated adverse events in the ongoing Clot Lysis Evaluating Accelerated Resolution of Intraventricular Hemorrhage Phase III (CLEAR-III IHV) trial. Neurosurgery. 2015a;76:291–300– discussion 301. https://doi.org/10.1227/NEU.0000000000000624.

Fried HI, Nathan BR, Rowe AS, et al. The insertion and management of external ventricular drains: an evidence-based consensus statement : a statement for healthcare professionals from the neurocritical care society. Neurocrit Care. 2016;24:61–81. https://doi.org/10.1007/s12028-015-0224-8.

Gelabert-González M, Ginesta-Galan V, Sernamito-García R, et al. The Camino intracranial pressure device in clinical practice. Assessment in a 1000 cases. Acta Neurochir. 2006a;148:435–41. https://doi.org/10.1007/s00701-005-0683-3.

Konstantelias AA, Vardakas KZ, Polyzos KA, et al. Antimicrobial-impregnated and -coated shunt catheters for prevention of infections in patients with hydrocephalus: a systematic review and meta-analysis. J Neurosurg. 2015;122:1096–112. https://doi.org/10.3171/2014.12.JNS14908.

Lozier AP, Sciacca RR, Romagnoli MF, Connolly ESJ. Ventriculostomy-related infections: a critical review of the literature. Neurosurgery. 2002;51:170–81. discussion 181–2

Stuart RM, Schmidt M, Kurtz P, et al. Intracranial multimodal monitoring for acute brain injury: a single institution review of current practices. Neurocrit Care. 2010a;12:188–98. https://doi.org/10.1007/s12028-010-9330-9.

Hemorrhage

Binz DD, Toussaint LG, Friedman JA. Hemorrhagic complications of ventriculostomy placement: a meta-analysis. Neurocrit Care. 2009;10:253–6. https://doi.org/10.1007/s12028-009-9193-0.

Chen JW, Rogers SL, Gombart ZJ, Adler DE, Cecil S. Implementation of cerebral microdialysis at a community-based hospital: a 5-year retrospective analysis. Surg Neurol Int. 2012b;3:57. https://doi.org/10.4103/2152-7806.96868.

Dey M, Stadnik A, Riad F, et al. Bleeding and infection with external ventricular drainage: a systematic review in comparison with adjudicated adverse events in the ongoing Clot Lysis Evaluating Accelerated Resolution of Intraventricular Hemorrhage Phase III (CLEAR-III IHV) trial. Neurosurgery. 2015b;76:291–300– discussion 301. https://doi.org/10.1227/NEU.0000000000000624.

Fried HI, Nathan BR, Rowe AS, et al. The insertion and management of external ventricular drains: an evidence-based consensus statement : a statement for healthcare professionals from the neurocritical care society. Neurocrit Care. 2016;24:61–81. https://doi.org/10.1007/s12028-015-0224-8.

Gelabert-González M, Ginesta-Galan V, Sernamito-García R, et al. The Camino intracranial pressure device in clinical practice. Assessment in a 1000 cases. Acta Neurochir. 2006b;148:435–41. https://doi.org/10.1007/s00701-005-0683-3.

Stuart RM, Schmidt M, Kurtz P, et al. Intracranial multimodal monitoring for acute brain injury: a single institution review of current practices. Neurocrit Care. 2010b;12:188–98. https://doi.org/10.1007/s12028-010-9330-9.

Malpositioning/Malfunctioning

Chen JW, Rogers SL, Gombart ZJ, Adler DE, Cecil S. Implementation of cerebral microdialysis at a community-based hospital: a 5-year retrospective analysis. Surg Neurol Int. 2012c;3:57. https://doi.org/10.4103/2152-7806.96868.

Fried HI, Nathan BR, Rowe AS, et al. The insertion and management of external ventricular drains: an evidence-based consensus statement: a statement for healthcare professionals from the neurocritical care

society. Neurocrit Care. 2016;24:61–81. https://doi.org/10.1007/s12028-015-0224-8.

Gelabert-González M, Ginesta-Galan V, Sernamito-García R, et al. The Camino intracranial pressure device in clinical practice. Assessment in a 1000 cases. Acta Neurochir. 2006c;148:435–41. https://doi.org/10.1007/s00701-005-0683-3.

Stuart RM, Schmidt M, Kurtz P, et al. Intracranial multimodal monitoring for acute brain injury: a single institution review of current practices. Neurocrit Care. 2010c;12:188–98. https://doi.org/10.1007/s12028-010-9330-9.

Toma AK, Camp S, Watkins LD, et al. External ventricular drain insertion accuracy: is there a need for change in practice? Neurosurgery. 2009;65:1197–200– discussion 1200–1. https://doi.org/10.1227/01.NEU.0000356973.39913.0B.

Central Nervous System Infection in Neurosurgical Critical Care

95

David W. Van Wyck and Michael L. James

Overview

Postoperative CNS infection following neurosurgical procedures has been reported to occur at rates ranging between 0.2% and 6% when perioperative prophylaxis is utilized. Older studies reported higher rates, but many did not include antibiotic prophylaxis. CNS infections are associated with prolonged hospitalizations, high readmission or reoperation rates, and increased risk of disability or death. The most common presentations of these infections include surgical site infections, meningitis, subdural empyema, and epidural, cerebral, or spinal abscess. Early infection can sometimes be difficult to detect clinically, as the symptoms often overlap with typical postoperative symptoms. Surgical site infections are often treated with a short course of antibiotics or wound debridement but can sometimes require more complex treatment if infections move to deeper tissues. Less commonly, intracranial infections, such as meningitis, subdural empyema, or brain abscess, must be identified as early as possible to prevent irreversible neurological injury through aggressive treatment courses. Finally, surgical infections after spine surgery may involve intervertebral disc space infection (diskitis), osteomyelitis, or spinal epidural abscess. Early identification of spinal epidural abscess is important since outcomes are related to the severity of neurological symptoms at presentation.

Cerebral angiography and neurointerventional therapies are being increasingly utilized by neurosurgeons in patient care. Scant data currently exist regarding the risk of CNS infection associated with these procedures. Despite this, risk of CNS infections with these procedures appears low, and no recommendations for prophylaxis with these procedures currently exist.

Risk factors associated with postoperative neurosurgical infections vary among studies and appear to be dependent on the study design. Risk factors which consistently recur in the literature with stronger associations include cerebrospinal fluid (CSF) leakage, preoperative traumatic injury, prolonged surgery, early reoperation, entry into the paranasal sinuses, and use of external ventricular drainage devices (EVDs), dural substitutes, and craniotomy as the surgical method. In spinal surgeries, surgery in the lumbar and sacral regions is associated with higher risk of infection than those in cervical or thoracic regions. Other risk factors reported in the literature include male sex, extremes of age, prior neurosurgery, the operating surgeon, a history of diabetes, use of perioperative steroids, immunocompromised states and malignancy, meningioma as the diagnosis, and wound closure with staples, though many of these are less well established. The use of prophylactic antibiotics has been shown to decrease the risk of infectious complications in high- and low-risk patients after neurosurgery and is now standard practice in most institutions.

Prevention

Perioperative antibiotic prophylaxis has been shown to lower the incidence of scalp and bone flap infections, subdural empyema, and abscess in neurosurgical patients, but does not reduce rates of postoperative meningitis. The routine use of prophylactic antibiotics is supported through retrospective, prospective, and meta-analysis showing a reduction in postoperative infections in patients at both low and high risks for complications. Prophylaxis extending beyond 24 h after surgery is associated with higher incidence of infection with resistant organisms and higher mortality in those who became infected. Thus, periprocedural prophylaxis is supported over extended antibiotic prophylaxis. For routine neurosurgical procedures, first-generation

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cephalosporins (i.e., cefazolin 2–3 g IV (depending on patient weight) given 60 min prior to incision; redose if surgery goes beyond 4 h) are often used to target common skin colonizers, gram-positive cocci (*Staphylococcus aureus* and *Staphylococcus epidermidis)*. Neurosurgical patients who have experienced prolonged hospitalization prior to surgery are at higher risk for infection with methicillin-resistant *S. aureus*, vancomycin-resistant *Enterococcus*, or gram-negative organisms. Thus, vancomycin IV 1 g q12h and ceftazidime IV 2 g q8h for 72 h post-operation are examples of commonly used regimen in such scenarios. Furthermore, trauma patients may require broad-spectrum coverage to include anaerobic coverage (i.e., metronidazole 500 mg IV q6h), particularly when penetrating injury is present. In any patient who is felt to be at high risk for infection from non-cutaneous or less commonly encountered organisms, consultation with an infectious disease specialist is advised.

Infection rates associated with the placement of EVDs are reported to be between 0% and 22%. However, the use of catheters impregnated with antibiotics or coated with silver nanoparticles is increasing in the hopes of reducing the risk of catheter-associated meningitis and ventriculitis. Results of randomized control trials and retrospective showing a reduction in positive CSF cultures with the use of such devices should be interpreted with caution. Antibiotic-impregnated catheters may suppress otherwise positive culture results when CSF is drawn through them. If antibiotic-impregnated catheters are not used, use of continuous prophylactic antibiotics after drain placement appears largely institution and physician dependent. Current evidence for this practice is conflicting and likely of no benefit beyond sterile insertion and handling. Likewise, data comparing infection rates between standard drainage catheters with prophylactic antibiotic use and antibiotic-impregnated catheters is scant. Another unsettled issue is the possible association between duration of catheter use and risk of infection. While a number of studies have reported increased risk of infection with catheters left in place for more than 5–9 days, several other studies have shown no relationship between duration and infection. Other monitoring devices, such as intracranial bolts for pressure monitoring and lumbar CSF drains, have a lower reported incidence of associated infections at 0–4% and 3–5%, respectively. Risk of infection with lumbar CSF drains may increase risk with puncture site CSF leaks and duration of use longer than 4 days. Additionally, continuous prophylactic antibiotic use for lumbar CSF drains does not appear to reduce the incidence of infection. In all cases, anti-infective protocols should involve sterile procedures at placement, minimal CSF sampling that occurs only under sterile conditions, and maintenance of insertion site cleanliness.

Systemic complications can also increase the risk for postoperative CNS infections. Maintaining perfusion, temperatures, metabolism, and nutrition within physiologic parameters is recommended. Hyperglycemia should be avoided to reduce the risk of systemic infections and possible seeding from remote infection sites.

Table 95.1 Prevention of postsurgical infections

Specific indication	Efficacy of prophylactic antibiotics/ recommendations
Craniotomy	Efficacy established. Reduces rates of scalp and bone flap infections, empyema, and abscess
	Recommended dose: cefazolin 1–3 g IV 60 min prior to incision (depending on patient size)
	Alternative dosing: vancomycin 1–2 g IV (depending on patient size) 2 h prior to incision (beta-lactam allergies, high risk for MRSA)
	No benefit in reducing rate of postoperative meningitis
Spinal surgery	Efficacy established; reduces superficial and deep complications
	Recommended dose: cefazolin 1–3 g IV 60 min prior to incision (depending on patient size)
Placement of CSF shunt	Efficacy established; ~50% reduction in infection rate
	Recommended dose: cefazolin 1–3 g IV 60 min prior to procedure (depending on patient size)
Basilar skull fractures with or without CSF leak	No evidence for routine use of prophylactic antibiotic
EVD	Controversial – studies suggesting beneficial effect but no definitive evidence
	Single dose at time of insertion more common than continued coverage (avoid resistant microorganisms)
	Recommended dose: cefuroxime 1.5 g IV q8h × 24 h periprocedurally
	Other preventative measures
	No difference in infection rate for ICU vs. operating room insertion
	Technique – strict aseptic technique, tunneling of catheter away from insertion site and minimal entry into system (i.e., CSF sampling only when clinically indicated) associated with decreased infection rates
	Use of drug-impregnated catheters appears to reduce the risk of EVD-associated infections
	Routine catheter exchanges do not decrease the risk of infection
Lumbar drain	Efficacy not established; infection risk may increase after 4 days
Intracranial pressure monitors	No consensus. Low overall risk for infectious complications

A summary of the efficacy of antibiotic prophylaxis in several common neurosurgical procedures is summarized in Table 95.1.

Evaluation and Management of Postoperative CNS Infections

Surgical Site and Bone Flap Infections

Pathophysiology and Clinical Presentation

- Involves superficial complications or those that occur outside the cranial vault such as wound necrosis and/or impaired wound healing and subgaleal infection.

- Most studies report an overall surgical site infection rate of 5–7%, generally higher after traumatic injury (up to 10.1%).
- Bone flap infections make up 15–35% of all surgical site infections.
- Most commonly caused by gram-positive cocci: *Staphylococcus aureus* (75%) and *Staphylococcus epidermidis* (11%). The most common gram-negative organism is *Acinetobacter baumannii* (14%). According to some studies, there may be a higher incidence of gram-negative infections in lumbar and sacral spinal surgery. This may reflect the predominant skin flora in that region, intraoperative inoculation, or postoperative contamination with organisms contained in fecal matter and urine.
- Risk factors: long-duration surgeries (>4 h), craniotomy as surgical method, lumbar or sacral region surgery, prolonged hospitalization, reoperation, prior irradiation, immunosuppressive medical conditions, use of drains/foreign body, dural substitutes, wound closure with staples, diagnosis of meningioma.
- Can result in cranial osteomyelitis or meningitis if unrecognized and/or untreated.

Patient Assessment

- Fever, local erythema, tenderness, wound dehiscence, ± purulent discharge.
- Symptoms typically manifest after 48 h, but can take days or weeks to develop.

Intervention

- Skull films or computed tomography (CT) with bony windows if there is concern for osteomyelitis.
- Fluctuance deep to the wound requires surgical drainage and debridement of tissue.
- Obtain wound culture to determine etiologic organism and to determine specific antibiotic regimen.
- Treat empirically for gram-positive organisms with first-generation cephalosporins (e.g., cefazolin 2 g IV q8h).
- Await cultures if patient is not toxic appearing before starting antibiotics. Tailor antibiotic regimen to culture and sensitivity results.
- Bone flap is devascularized and consequently more at risk for infection therefore warranting aggressive therapy: removal of bone flap, prolonged systemic antibiotics (4–6 weeks), and delayed cranioplasty after infection eradicated.
- There has been some renewed interest in recent years in antibiotic irrigation, such as a wash-in-wash-out irrigation systems to continuously infuse an antibiotic (e.g., vancomycin 500 mg/L infused at 10 mL/h per drain for 5 days) through the epidural and subgaleal spaces, constantly bathing infected material in antibiotic solution in hopes of salvaging bone flaps.

Postoperative Meningitis and Ventriculitis

Pathophysiology and Clinical Presentation

- Inflammation of the meninges or ventricular lining, respectively.
- Overall incidence of postoperative bacterial meningitis or ventriculitis is 0.3–8%. Most studies report a rate <5%.
- Mortality rate: approx. 20%.
- Risk factors: device-related communication between the CSF and external environment (CSF shunts, ventricular drainage catheters), posterior fossa surgery, CSF leaks, perioperative steroid use.
- Common organisms in healthy patients reflect skin flora: *S. aureus* (90%), *S. epidermidis*, and *Proprionibacteria* seen with ventriculoperitoneal shunts.
- Consider gram-negative organisms in patients with extended hospital stays and organisms prevalent to hospital environment.
- Clinical manifestations are nonspecific and may overlap with neurological abnormalities expected in the postoperative period.
- The most common symptoms are fever and an altered level of consciousness +/− meningismus.
- Approximately 10% of patients with bacterial meningitis will present with seizures.
- Between 10% and 20% of patients may also have cranial nerve deficits, particularly cranial nerves III, VI, and VII.

Patient Assessment

- CNS imaging prior to lumbar puncture in patients who have undergone recent craniotomy.
- CT – expected postsurgical changes in most patients may show leptomeningeal enhancement if contrasted study is performed.
- Magnetic resonance imaging (MRI) – meningeal enhancement especially apparent in coronal sections. Also sensitive for discovering potential sources of bacterial invasions, such as osteomyelitis or sinusitis. In the case of ventriculitis, there is often abnormal periventricular or subependymal signal intensity and enhancement of the ventricular lining.
- CSF analysis
  - Polymorphonuclear leukocytosis (WBC >1000 cells/mm^3; 90% polymorphic neutrophils) is suggestive of a bacterial etiology. In blood contaminated CSF (e.g., traumatic puncture, subarachnoid hemorrhage, etc.), the ratio of leukocytes to erythrocytes in CSF versus whole blood (cell index) should be considered. A cell

ratio of WBC/RBC ≤1:100 is unlikely in bacterial meningitis. A CSF WBC/RBC ratio ≥1:100 should raise concern for underlying infection).
  - Increased protein (>150 mg/dL; nonspecific, present with disruption of blood–brain barrier).
  - Decreased glucose (<40 mg/dL; CSF/serum glucose ratio <0.4 has a sensitivity of 77% and specificity of 87% for bacterial meningitis).
  - Gram stain and culture for diagnosis (60% and 80% yield drops, respectively, with perioperative prophylaxis).
  - Increased CSF lactate (>4 mmol/L; high specificity and sensitivity for bacterial meningitis). The CSF concentration of lactate is independent of serum lactate and is believed to be elevated due to anaerobic glycolysis occurring in brain tissue secondary to decreased cerebral blood flow and oxygen uptake. This rapid, inexpensive assay may help identify bacterial causes of meningitis.
- Antibiotics can be initiated prior to obtaining CSF sample. A short course of antibiotics prior to CSF sampling does not alter CSF WBC count, glucose, or protein, and cultures remain positive.
- Routine surveillance of CSF to help identify infection has not been shown to be more helpful in predicting infection than monitoring for clinical evidence of infection or following systemic white blood cell counts (WBCs).

Aseptic meningitis is a chemical irritation of the meninges from blood or tumor antigens introduced into the subarachnoid space at time of surgery and may account for up to 70% of postoperative meningitic symptoms. Aseptic meningitis has also been associated with longer operating times. CSF findings may be similar to those seen with postoperative bacterial meningitis. Antibiotics are unhelpful, but patients show clinical improvement with corticosteroids. If CSF cultures are repeatedly negative and aseptic meningitis is the diagnosis, antibiotics can be discontinued.

Intervention

- Removal of hardware (e.g., shunts) and other suspicious material (bone flap).
- Empiric antibiotic coverage: gram-positive (vancomycin 1 g IV q12h) and gram-negative (third- or fourth-generation cephalosporin, e.g., ceftazidime 2 g IV q8h or cefepime 2 g IV q8h). Metronidazole 500 mg IV q6h can be added for anaerobic coverage.
- IV vancomycin at usual dosages can achieve therapeutic concentration in CNS for at least 72 h postoperatively (possibly due to damage to blood–brain barrier that occurs during neurosurgical procedures and lasts for days). Due to limited CSF penetration, some advocate the administration of intraventricular vancomycin for EVD-associated staphylococcal ventriculitis given these patients may have less blood–brain barrier disruption compared to postoperatively. Others argue the intraventricular inflammatory reaction in response to the local application is counterproductive.
- Watch for neurologic complications: seizures from focal areas of cortical irritability (e.g., subdural effusion/parenchymal abscess, septic thrombophlebitis) and hydrocephalus secondary to inflammatory exudates.

Cranial Epidural Abscess and Subdural Empyema

Pathophysiology and Clinical Presentation

- Involves a collection of pus between the dura and the skull (epidural abscess) or the dura and arachnoid mater (subdural empyema).
- Associated with craniotomy wound site infection, suppuration of paranasal sinuses, or foreign body from trauma.
- Epidural abscesses alone may not cause neurologic symptoms, but 10% of epidural abscesses are associated with subdural empyema.
- Subdural empyema is a surgical emergency potentially progressing to death if untreated (70% of patients die or were disabled when treatment is delayed beyond 72 h).

Patient Assessment

- Fever, headaches, seizures, periorbital edema, papilledema, mental status change, and focal neurological deficits.
- Classic triad for subdural empyema: sinusitis, fever, and neurologic deficits.
- Postoperative cases are typically subtle and insidious.
- Lab data are nondiagnostic.
- Epidural abscess seen as lentiform (biconvex) and subdural empyema seen as crescentic on imaging.
- MRI is preferred over CT scan for diagnosis. Enhanced MRI can usually differentiate from other subdural collections (effusion, hematoma) – increased signal adjacent to

cerebral cortex due to inflammatory edema suggests empyema; MRI may demonstrate complications such as cortical/dural vein thrombosis.

Intervention

- Seizure prophylaxis for subdural empyema.
- Initial empiric IV antibiotic therapy should be broad spectrum (e.g., vancomycin 1 g IV q12h plus cefepime 2 g IV q8h or meropenem IV 2 g q8h). Add metronidazole 500 mg IV q6h if anaerobes are suspected. Subsequent consultation with infectious disease specialists is recommended.
- Craniotomy with surgical debridement is the preferred intervention. Stereotactic burr holes are less commonly utilized due to poor exposure and inability to completely drain purulent material. Antibiotic therapy alone can be used for a small subdural empyema (diameter <1.5 cm) or in those with contraindications to surgery.
- Operative cultures positive in 90%; adjust empiric therapy to culture and sensitivity results, and extend IV antibiotics out to 4–6 weeks.
- Serial imaging following evacuation to monitor for re-accumulation of purulent material.

Cerebral Abscess

Pathophysiology and Clinical Presentation

- Incidence between 0.2% and 0.6%.
- Mixed infections with multiple organisms are common.
- Etiologic agents in postoperative patients with cerebral abscess most often include aerobic *Streptococci* species, *Staphylococcus aureus*, *Clostridium* species, and *Enterobacteriaceae* (i.e., *Proteus mirabilis* or *Escherichia coli)*.
- Solitary lesion from bacteria introduced intracranially at the time of surgery and trauma or via contiguous spread from a parameningeal focus.
- Multiple lesions associated with systemic infection and hematogenous spread (gray–white junction, often in MCA artery distribution).

Patient Assessment

- Most common symptoms: headache and altered mental status.
- Laboratory findings are generally nondiagnostic.
- Ring-enhancing lesion – CT/MRI has 95–99% sensitivity in detecting brain abscess; steroids may decrease enhancement in early stages. MRI diffusion-weighted imaging can help confirm a suspected abscess.

Intervention

- Non-operative management can be considered with a small abscess (<2.5 cm), the absence of mass effect, with a known etiologic organism, in cases with multiple small abscesses or when the abscess is located in eloquent brain.
- Most cases require surgical intervention in addition to long-term antibiotic course of 6–8 weeks.
- Aspiration (stereotactic, ultrasound guidance) is best for deep abscesses or in cases involving multiple abscesses.
- Excision is a more definitive treatment but is most often performed in later, encapsulated stages when the abscess can be removed intact.
- Initial antibiotic coverage includes vancomycin 1 g IV q12h, a third- or fourth-generation cephalosporin (e.g., ceftazidime 2 g IV q8h or cefepime 2 g IV q8h), or meropenem 2 g IV q8h and metronidazole 500 mg IV q6h for anaerobic coverage.
- Steroids are used in cases with severe edema.
- Anticonvulsants are appropriate for prophylaxis if the abscess is adjacent to the cortex and are necessary in any patient presenting with seizures.

Table 95.2 summarizes the evaluation and treatment of postoperative infections of the head and brain

Postoperative Spinal Infections (Table 95.3)

Pathophysiology

- Incidence of postoperative spinal infection is related to the type of procedure: decompressive laminectomy, discectomy, and spinal fusion <3%; increases to as much as 12% with use of instrumentation.
- Primary pathogens: *S. aureus*, *S. epidermidis,* and β-hemolytic *streptococci*. Gram negatives are less common but include *Klebsiella pneumoniae*, *Escherichia coli*, *Pseudomonas aeruginosa*, and *Proteus* species. Gram-negative infections also tend to have the shortest time to onset of infection (median days to infection: 15). Delayed infections caused by *Propionibacterium acnes* and *diphtheroids* can occur out to 37 days after surgery.
- Patient risk factors include advanced age, obesity and diabetes, prolonged hospital bed rest, and remote infection.

Table 95.2 Postoperative infections of the head and brain

CNS infection	Clinical presentation	Assessment	Intervention
Wound Site Infections/Bone Flap Infections	Fever, local erythema, tenderness, wound dehiscence, ± purulent discharge Presentation can be delayed by days to weeks	Gram stain, culture Plain films, CT, or MRI to assess for bone flap infection	Await culture results if patient is nontoxic in appearance Cefazolin 2 g IV q8h or vancomycin 1 g IV q12h if MRSA suspected; adjust pending culture results, and continue for 4–6 weeks Wound debridement and irrigation for deep tissue or persistent infection despite antibiotic therapy For bone flap infection, consider flap removal vs. wash-in, wash-out antibiotic irrigation
Meningitis/ ventriculitis	Fever, altered mental status +/− meningeal signs Fever, headache, seizures, and cranial nerve III, VI, and VII abnormalities are less common May be difficult to distinguish from normal postoperative symptoms	Imaging: MRI or CT with contrast showing enhancement of meninges or ventricular lining Labs: CSF with PMN leukocytosis, ↑ protein, ↓ glucose, ↑ lactate CSG gram stain and culture	Remove any infected materials (drains, bone flap, etc.) Broad spectrum, empiric antibiotic coverage: vancomycin 1 g IV q12h PLUS third- or fourth-generation cephalosporin (e.g., ceftazidime 2 g IV q8h or cefepime 2 g IV q8h) OR meropenem 2 g IV q8h; for PCN allergy, use ciprofloxacin 400 mg IV q8h Metronidazole 500 mg IV q6h for anaerobic coverage if indicated Infectious diseases consult
Cranial Epidural Abscess or Subdural Empyema	Fever, headaches, periorbital edema, mental status changes, focal neurological deficits Typically has an insidious onset	CT or MRI with contrast (MRI preferred) Epidural abscess is lentiform in appearance; subdural empyema has crescenteric shape Obtain operative cultures	Emergent surgical debridement and removal of bone flap Empiric antibiotic therapy: vancomycin 1 g IV q12h PLUS a third- or fourth-generation cephalosporin (ceftazidime 2 g IV q8h or cefepime 2 g IV q8h) OR meropenem 2 g IV q8h; for PCN allergy, ciprofloxacin 400 mg IV q8h. Adjust pending culture results Metronidazole 500 mg IV q6h for anaerobic coverage Continue IV therapy for 4–6 weeks followed by oral therapy Infectious disease consult
Cerebral Abscess	Most common symptoms: fever and altered mental status Less common sx: headache, seizures, focal neurologic deficits	Labs are nondiagnostic CT or MRI with contrast – shows ring-enhancing lesion Centrally located diffusion restriction on diffusion-weighted imaging can help confirm abscess	Anticonvulsant therapy Empiric antibiotic coverage: vancomycin 1 g IV q12h PLUS a third- or fourth-generation cephalosporin (ceftazidime 2 g IV q8h or cefepime 2 g IV q8h) OR meropenem 2 g IV q8h; for PCN allergy, use ciprofloxacin 400 mg IV q8h Metronidazole 500 mg IV q6h can be added for anaerobic coverage if indicated Infectious disease consult Steroids when severe edema present Surgical aspiration or excision

WBC white blood cell count, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein

Table 95.3 Postoperative spinal infection

Spinal infection	Clinical presentation	Assessment	Intervention
Wound Infection	Persistent temperature elevation several days post-op Tenderness, erythema, swelling, drainage	Gram stain, culture	Antibiotic therapy tailored to culture results Wound debridement and irrigation for deep tissue or persistent infection despite antibiotic therapy
Diskitis	Acute cases occur 1–2 weeks after surgery Typically asymptomatic immediately after surgery Excruciating back pain or spasms with or without radiation to legs within 2 weeks Extreme local tenderness and fever	Spine XR Labs: ↑ESR ↑CRP (nonspecific). WBC usually normal CT sensitive early MRI with gadolinium can differentiate diskitis from expected post-op changes	Early recognition and treatment to prevent chronic infection Disc space aspiration (CT-guided) often negative 4–6 weeks of antibiotics until normalization of ESR/CRP Spinal immobilization Uncomplicated diskitis rarely requires surgery (vs. osteomyelitis requiring surgical intervention)
Spinal epidural abscess	Fever (uncommon), spinal tenderness, weakness, sensory abnormalities, paralysis, reflex abnormalities (early hyperreflexia; late hypo- or hyperreflexia) *Progression and time course of symptoms uniform*: radicular symptoms within 3 days, followed by weakness within 36 h and paralysis over the next 24 h Cervical epidural abscesses develop more rapidly and with severe neurologic deficits and possibly respiratory compromise	MRI (greatest diagnostic accuracy and the primary diagnostic evaluation) Labs: ↑WBC (absent in half of cases); ↑ESR (>75 mm/h) common, nonspecific Check blood cultures (positive in 50–60% of cases) Gram stain and culture of aspirated or surgically obtained fluid	Emergent spinal decompression Empiric antibiotic therapy: vancomycin 1 g IV q12h PLUS cefepime 2 g IV q8h or meropenem 2 g IV q8h; for PCN allergy, ciprofloxacin 400 mg IV q8h. Adjust pending culture results Continue IV therapy for 4–6 weeks followed by oral therapy

WBC white blood cell count, *ESR* erythrocyte sedimentation rate, *CRP* C-reactive protein

- Surgical risk factors include prolonged surgery, hardware, and use of microscope.
- Spinal epidural abscess after decompression is rare, but rapid neurologic deterioration to paralysis occurs; associated with osteomyelitis; mortality for cervical spinal epidural abscess approaches 18%.

Cerebral Angiography and Neurointerventional Procedures

- Despite the increasing prevalence of cerebral angiography and other neurointerventional therapies, little data currently exist on incidence of CNS infections following these procedures.
- The overall risk of infection with these procedures appears low (approximately 0.1%) with most cases occurring at the femoral artery puncture site.
- Several case reports of intracranial infections associated with neurointerventional procedures have been reported, most of which involve intracranial embolization.
- Reported pathogens have included *Staphylococcus aureus*, *Burkohleria caeca*, and *Salmonella.*
- The use of prophylactic antibiotics in these procedures has not been formally assessed. Given the low incidence of infection associated with these procedures, routine use of prophylactic antibiotics is discouraged and should only be considered in patients felt to have an elevated risk of infection for other reasons.

Key Points

- Postoperative CNS infections, while uncommon, are serious complications with life-threatening potential and high economic burden. Patients at increased risk for postoperative infection should be identified and signs/symptoms concerning for infection should be aggressively evaluated and treated.
- Prophylactic antibiotics are standard practice in most patients undergoing neurosurgical procedures and reduce surgical site infections, subdural empyema, and abscesses. They are less established in lowering the risk for meningitis, EVD-related infections, and lumbar drain-related infections. Gram-positive coverage is sufficient in most cases, but prophylaxis should be tailored to the individual patient after considering their clinical history and situation as well as institutional flora.
- EVDs may be left in place until clear evidence of infection develops. Catheter exchange and routine CSF sampling to monitor for infection are not recommended. Intraventricular antibiotics may be indicated in certain EVD-related infections.
- Postoperative meningitis or ventriculitis may present subtly and be overlooked as normal postoperative symptoms. When suspected, empiric antibiotics are warranted while awaiting CSF culture results and should be started as soon as possible to minimize potential complications.
- Intracranial subdural empyema is a life-threatening condition requiring prompt recognition and surgical intervention; extradural empyema is typically a more subacute condition requiring removal of bone plate.
- Cerebral abscess is a rare neurosurgical complication. If identified early, it can be managed solely with IV antibiotics; otherwise it often requires surgical aspiration or excision.
- The overall risk of CNS infection with cerebral angiography and other neurointerventional procedures appears extremely low, and routine prophylactic antibiotics are not recommended in these patients.
- There should be a low threshold for infectious disease consultation to assist in the medical management of patients with postoperative CNS infections.

Suggested Reading

Abdul-Jabbar A, Berven SH, Hu SS, Chou D, Mummaneni PV, Takemoto S, Ames C, Deviren V, Tay B, Weinstein P, Burch S, Liu C. Surgical site infections in spine surgery: identification of microbiologic and surgical characteristics in 230 cases. Spine. 2013;38(22):E1425–31.

Auguste KI, McDermott MW. Salvage of infected craniotomy bone flaps with the wash-in, wash-out indwelling antibiotic irrigation system. J Neurosurg. 2006;105(4):640–4.

Buchanan CC, Hernandez EA, Anderson JM, Dye JA, Leung M, Buxey F, Bergsneider M, Afsar-Manesh N, Pouratian N, Martin NA. Analysis of 30-day readmissions among neurosurgical patients: surgical complication avoidance as key to quality improvement. J Neurosurg. 2014;121(1):170–5.

French H, Schaefer N, Keijzers G, Barison D, Olson S. Intracranial subdural empyema: a 10-year case series. Ochsner J. 2014;14(2):188–94.

Greenlee JE. Subdural empyema. In: Mandell GL, editor. Principles and practice of infectious diseases, vol. 1. 4th ed. New York: Churchill; 1994. p. 900–3.

Hamdeh SA, Lytsy B, Ronne-Engström E. Surgical site infections in standard neurosurgery procedures-a study of incidence, impact and potential risk factors. Br J Neurosurg. 2014;28(2):270–5.

Haque R, Wojtasiewicz TJ, Hwang BY, Connolly ES. Postcraniotomy complication management. In: Lee K, editor. The NeuroICU book. New York: McGraw Hill; 2012. p. 445–9.

Howard AE, Yegge J, Recktenwald A, Jadwisiak L, Kieffer P, Hohrein M, Hopkins-Broyles D, Woeltje KF. Risk factors for craniotomy or spinal fusion surgical site infection. Pediatr Infect Dis J. 2015;34(12):1323–8.

Hsiu-Yin C, Kamath AS, Pottinger JM, Grenlee JDW, Howard MA III, Cavanaugh JE, Herwaldt LA. Risk factors and outcomes associated with surgical site infections after craniotomy or craniectomy. J Neurosurg. 2014;120(2):509–21.

Huy NT, Thao N, Diep D, Kikuchi M, Zamora J, Hirayama K. Cerebrospinal fluid lactate concentration to distinguish bacterial from aseptic meningitis: a systematic review and meta-analysis. Crit Care. 2010;14(6):R240.

Kelkar P, Fleming JB, Walters BC, Harrigan MR. Infection risk in neurointervention and cerebral angiography. Neurosurgery. 2013;72(3):327–31.

Kourbeti IS, Valkis AF, Ziakas P, Karabetsos D, Potolidis E, Christous S, Samonis G. Infections in patients undergoing craniotomy: risk factors associated with post-craniotomy meningitis. J Neurosurg. 2015;122:1113–9.

Kubilay Z, Amini S, Fauerbach LL, Archibald L, Friedman WA, Layon AJ. Decreasing ventricular infections through the use of a ventriculostomy placement bundle: experience at a single institution. J Neurosurg. 2013;118:514–20.

Kurland DB, Khaladj-Ghom A, Stokum JA, Carusillo B, Karimy JK, Gerzanich V, Sahuquillo J, Simard JM. Complications associated with decompressive craniectomy: a systematic review. Neurocrit Care. 2015;23(2):292–304.

McClelland S III, Hall WA. Postoperative central nervous system infection: incidence and associated factors in 2111 neurosurgical procedures. Clin Infect Dis. 2007;45:55–9.

Ratilal BO, Costa J, Sampaio C. Antibiotic prophylaxis for preventing meningitis in patients with basilar skull fractures (review). Cochrane Collab. 2009;1:1–17.

Rosenthal E, Nathan B. Neuroinfectious diseases. In: Hemphill III JC, Rabinstein AA, Samuels OB, editors. The practice of neurocritical care. Kindle ed. Minneapolis: Neurocritical Care Society; 2015. p. 2644–712.

Zhan R, Zhu Y, Shen Y, Shen J, Tong Y, Yu H, Wen L. Post-operative central nervous system infections after cranial surgery in China: incidence, causative agents, and risk factors in 1,470 patients. Eur J Clin Microbiol Infect Dis. 2014;33:861–6.

Antiepileptic Drug Therapy in Neurosurgical Critical Care

96

Panayiotis N. Varelas and Denise H. Rhoney

Overview

The prevalence of epilepsy is estimated worldwide at 0.5–2% of the total population. One-fourth to one-third of these epileptic patients may have more than one seizure per month, and one-fifth may have medically uncontrolled seizures. On the other hand, many neurosurgical conditions increase the risk for seizures (Table 96.1).

Although the incidence of immediate seizures (within 24 h) after craniotomy is estimated at 3% and 77.5% of those that occur within 6 h after aneurysm surgery, the incidence of perioperative AED use is unknown. Many of these patients receive AEDs on admission prophylactically and some therapeutically (if they present with a seizure or have a history of seizures). The AEDs used in this situation are often those available in an intravenous form. If seizures were diagnosed before the index admission or surgery, the majority of these patients will also be on chronic oral AED management, with various rates of compliance.

Table 96.1 Risk for seizures after common neurosurgical interventions

	Incidence of post-op seizures (%)		Incidence of post-op seizures (%)
Arteriovenous malformation	50	Glioma	Biopsy 9
		Metastasis	Resection 20
Intracerebral hematoma	10–20	Suprasellar tumor	5
Cerebral aneurysm	7.5–38	Shunt	22
Meningioma	36	Abscess	92

Modified from Manaka et al. (2003)

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Prevention

Medications that have epileptogenic potential should be avoided during the perioperative period in neurosurgical patients. Seizure activity has been reported with both volatile and nonvolatile agents. For example, atracurium may decrease the threshold for seizures via accumulation of its metabolite laudanosine, and meperidine can also provoke seizures via its metabolite normeperidine and should be used with caution, if at all. The most widely reported volatile anesthetic agent associated with seizures is enflurane; however, there are also reports of seizure activity with the use of sevoflurane especially in patients with a history of epilepsy. Other drugs that are associated with seizures in supratherapeutic concentrations (i.e., antibiotics) should have the dosage adjusted for the patient's hepatic or renal impairment in order to minimize the occurrence of seizures. Literature has suggested that 45% of seizures in the hospital or ICU are the result of alcohol or drug toxicity and drug withdrawal. For example, one-third of new onset seizures in critically ill patients has been attributed opioid withdrawal.

On the other hand, chronic AED administration may interfere with anesthetic agents during surgery. For example, liver enzyme inducers, like phenytoin, carbamazepine, or phenobarbital reduce the paralytic effect of nondepolarizing neuromuscular blockers. Higher doses of fentanyl may also be required in epileptic patients on AEDs to maintain comparable analgesia.

Epileptic patients undergoing surgery may not have received their morning AEDs, and if those have a short half-life (e.g., valproate, gabapentin, carbamazepine), their levels may drop precipitously, and seizures may emerge during the postoperative period. Therefore, a clear list of the home AEDs and the last time that the patient received them is imperative. In patients undergoing intracranial electrode placement, the goal is to allow seizures to emerge in order to be recorded. These patients usually are left with fewer AEDs

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or at decreased doses in the postoperative period intentionally. The neuroanesthesiologist should have a clear understanding of the postoperative plan after discussion with the attending epileptologist or neurosurgeon.

If a serum concentration of the drug is routinely measurable, one should test a trough concentration. For most of AEDs, this corresponds to a level drawn 6–8 h after the most recent dose or a level before the scheduled next dose. Frequently, a mistake is made by not confirming the timing of the last dose and measuring the concentration at its peak phase: it will be artificially high (which may erroneously lead to withholding the next dose or reducing the amount). Seizures may also occur later if this drug drops to subtherapeutic concentrations.

Another cause for confusion is the presence of low albumin in many critically ill or malnourished patients. AEDs highly bound to albumin (phenytoin, valproate) may have low total concentrations in this case, but the free concentration may be adequate. Therefore, free and total AED concentrations should always be measured before adding or withholding an AED that is highly protein bound.

Prophylactic administration of AEDs in patients undergoing craniotomy without previous seizures is not advocated. Despite the presence of cerebral lesions, such as tumors or ischemic stroke, the most recent guidelines do not support prophylactic AED treatment. For head trauma, the guidelines support treatment for up to 1 week to prevent early posttraumatic seizures. For hemorrhagic stroke, the current trend is that they should not be continued for more than 1 week in patients with subarachnoid hemorrhage after securing the cerebral aneurysm and for a brief period (e.g., up to 1 month) after ICH, especially lobar. The physician should, however, individualize the treatment, since specific subgroups of patients may benefit from prophylactic AEDs for longer periods. The selection of AED agent for prophylactic administration is less clear with older AED agents (i.e., phenytoin, valproate, etc.) associated with significant drug interactions and adverse effects including negative cognitive outcomes. The newer agents (levetiracetam and lacosamide) have fewer adverse effects but limited amount of data to support their prophylactic administration.

If seizures had occurred before or during surgery, however, AEDs should be administered as in any other nonneurosurgical patient presenting with seizures.

Crisis Management

Pathophysiology and Clinical Presentation

Presurgical brain pathology is the most common reason for having preoperative seizures. Two major mechanisms, however, play a role in the development of seizures after craniotomy:

- Free radical generation, mainly due to iron and thrombin from blood components that have leaked in the tissue during surgery
- Disturbance of ion balance across the cell membranes due to local ischemia or hypoxia

Additionally, one should not forget that systemic etiologies may also play a role:

- Severe hypoxia–ischemia
- Drug/substance toxicity or withdrawal
- Metabolic derangements
- Systemic infection, including meningitis, ventriculitis, or encephalitis

The majority of postoperative patients will present with partial seizures, either simple partial (focal motor or sensory phenomena without alteration of consciousness), complex partial (with alteration of consciousness), or partial with secondary generalization (bilateral tonic–clonic convulsions with loss of consciousness). Primary generalized seizures may also occur in an epileptic patient carrying this diagnosis, but pseudoseizures should be considered as low probability in the postoperative period.

The definition of status epilepticus (SE) has evolved over the years, and now many experts define it as either a prolonged seizure or multiple seizures in sequence lasting for >5–10 min (without regaining consciousness in between). A more ominous condition is refractory status epilepticus (RSE), defined as status not controlled after the initial parenteral therapy with the first 2–3 standard "front-line" AEDs or lasting >1–2 h.

Patient Assessment

- Basic ABCs (establishing a patent airway; assist ventilation as needed; assess and control cardiovascular function). Avoid hyperventilation (unless mandated for other reasons).
- Secure more than one intravenous catheter (peripheral catheters can be easily dislodged or veins blown during convulsions).
- Draw labs for electrolytes, glucose, AED concentrations, ammonia and liver enzymes, toxicology screen, and blood gases. Derangements such as hypoglycemia, hyponatremia, hypocalcemia, hypomagnesemia, hypoxia, or hyper- or hypocarbia should be corrected.
- (Initial management of patient is discussed below). After discussion with the attending neurosurgeon or epileptologist, consider a STAT CT of the head to exclude hemorrhage or ischemia.
- Electroencephalogram (EEG), either emergent or continuous, based on the continuation of seizures and the mental status of patient (to exclude ongoing nonconvulsive seizures or SE).

Intervention/Treatment

Patients Already Taking AEDs Before Surgery

The home AEDs should be administered orally at the usual doses in epileptic patients as soon as they are awake enough to swallow or as soon as a bedside swallowing evaluation is completed (because many neurosurgical patients may emerge from surgery with significant new deficits precluding safe oral administration of food and drugs). An alternative, placement of a naso- or orogastric tube and administration of the AEDs, is also feasible in the majority of cases.

It is preferable, however, to use AEDs available in parenteral forms in the postoperative period because of potential erratic enteral absorption. Currently, seven major AEDs are available in an intravenous form in the USA (Table 96.2), with three additional general anesthetics frequently used for refractory status epilepticus (pentobarbital, propofol, and midazolam). These medications should be used in the IV form to substitute the oral form of the same medication (until the enteral route and absorption is confirmed) or if an extra dose is required to reach therapeutic concentrations rapidly. Additionally, they can be used as a temporary alternative to different home AEDs not available parenterally, if an oral/gastric administration is not feasible or enteral absorption is questionable. As a rule of thumb, total IV doses are similar to the total daily oral dose of the same medication but may be administered at different frequencies. It is important to remember the following:

- Phenytoin can be administered at a maximum rate of 50 mg/min (in nonemergent situations in 30–60 min for 1 g IV) and is mixed only with normal saline. Since the cardiovascular suppression effects are synergistic with anesthetics, rate of administration should be much slower in the anesthetized patient. Phenytoin also exhibits nonlinear pharmacokinetics, which may lead to supratherapeutic or subtherapeutic concentrations, so a free level (target 1–2 μg/ml) should also be measured. In the absence of IV access, fosphenytoin can be administered IM as phenytoin equivalents (PE, i.e., 1 mg of PE is the same as 1 mg of phenytoin).
- Phenobarbital's sedative effect is minimized after a few weeks and, therefore, in chronic users, may not be a problem in the postoperative period.
- The two benzodiazepines, lorazepam and diazepam, are rarely used in chronic AED regimens, and their use is limited to management of seizures or SE (vide infra).

Table 96.2 Intravenously available AEDs

IV AED	Mechanism of action	Protein binding (%)	$T_{1/2}$ (hours)	Metabolism; elimination	Therapeutic level	Dose
Phenytoin or fosphenytoin	Na + channel block	90–96	24 ± 12	Hepatic	10–20 μg/ml	L: 18–20 mg/kg IV M: 3–5 mg/kg/day IV[a]
Phenobarbital	Prolongs Cl− channel conductance	20–45	96 ± 12	Hepatic; renal 25%	10–40 μg/ml	L: 20 mg/kg IV M: 2–4 mg/kg/day IV
Pentobarbital	Prolongs Cl− channel conductance	35–40	15–50	Hepatic; renal	10–50 μg/ml	L: 10–15 mg/kg IV M: 0.5–10 mg/kg/h IV to induce burst suppression on EEG
Propofol	Inhibits GABA receptors; activates Cl conductance	95–99	3–12 depending on the duration of gtts	Hepatic; renal	–	L: 1–2 mg/kg IV M: 2–10 mg/kg/h IV
Lorazepam	Increases Cl− channel conductance	90	8–25	Hepatic	–	L: 0.07–0.1 mg/kg IV
Diazepam	Increases Cl− channel conductance	90	24–57	Hepatic	–	L: 0.15–0.25 mg/kg IV
Midazolam	Increases Cl− channel conductance	94–97	1–5	Hepatic; renal	–	L: 0.1 mg/kg IV M: 0.1–1 mg/kg/h IV
Valproate	Slow Ca++ channel block; Na + channel block	90	8 ± 2	Hepatic	50–120 μg/ml	L: 10–25 mg/kg IV M: 15–50 mg/kg/day IV
Levetiracetam	Binding to synaptic vesicle protein 2A	<10	7 ± 1	Renal	Not recommended by manufacturer	<65 year old: 500–1000 mg q12 h IV >65-year old: 250–500 mg q 12 h IV
Lacosamide	Na + channel block; binds to collapsin response mediator protein-2 (CRMP-2)	<15	13	Renal	Not recommended by manufacturer	L: 200 mg IV M:100–200 mg q12 h IV

L Loading dose, *M* maintenance dose

[a]Doses are phenytoin equivalents for fosphenytoin dosing (e.g., fosphenytoin IV: give 18 mg/kg phenytoin equivalents)

- Valproate is an excellent drug for primary generalized epilepsies, but one should be careful using it in patients with hepatic failure, thrombocytopenia, and pancreatitis, if at all. Its administration can lead to hyperammonemia.
- From the newer AEDs, only levetiracetam and lacosamide are available in an IV formulation. These agents are renally eliminated, have minimal interactions with other common medications, and offer advantages in the ease of their use. However, patients with renal impairment will require dosage adjustment. Both agents have complete bioequivalence to the oral dose.

Patients Experiencing a Single Postoperative Generalized Seizure

In this situation, there is usually no time to administer an AED while the patient is convulsing, and close observation for a second seizure is required. During this period of time, three important diagnostic and therapeutic steps should be undertaken:

1. Prophylaxis for a second seizure is usually achieved by administering the home AEDs in patients with presurgical epilepsy. If the patient has never experienced seizures before, phenytoin IV (load and continue with the maintenance dose, Table 96.2) or valproate (in phenytoin allergy) or levetiracetam (if allergy to the other two AEDs is suspected or hepatic dysfunction is present) should be administered. Thiamine (100 mg IV) and lorazepam (1–2 mg IV over 3–5 min) are reasonable alternatives for patients with a history of heavy alcohol abuse. These patients are usually not at risk for loss of airway reflexes or catastrophic cardiovascular sequelae. However, the use of supplemental oxygen and padding of the bed are recommended.
2. The diagnostic workup (see above).
3. If the patients remain encephalopathic or with new unexplained focality in their neurological exam for more than 20–30 min (which is the usual postictal confusional period), an emergent EEG is also reasonable, to exclude subclinical seizures or interictal activity accounting for the mental status change. Such situation should also result in a careful consideration of the need for an urgent head CT as the seizures could have precipitated postoperative hemorrhage or edema.

Patients Experiencing Multiple Generalized Seizures or SE

This is an emergency and treatment should proceed at a fast pace. The management steps in this situation are similar to those for a single uncomplicated seizure (see above) as far as the diagnostic part (continuous video-EEG monitoring is advocated by many experts; consider STAT head CT). The treatment part is different with focus on ABCs and with benzodiazepines (lorazepam, see Table 96.3) as first-line AEDs.

Table 96.3 Management of multiple seizures or status epilepticus

Initial measures
ABC. Preserve airway and oxygenation by intubation
Check blood glucose. If less than 40–60 mg/dL, give 1 amp DW 50%, and recheck in 30–60 min. Give 100 mg thiamine IV
Check blood count, electrolytes, liver enzymes, toxicology screen, arterial blood gases, and antiepileptic drug concentrations
Immediately and in parallel with above steps: IV lorazepam 5–10 mg (0.1 mg/kg), diazepam 20–40 mg, or midazolam 5–20 mg over 5 min
Phenytoin loading dose 20 mg/kg at a maximum rate of 50 mg/min or fosphenytoin 20 mg/kg PE at a maximum rate of 50 mg/min (slower rate when under general anesthesia). Consider valproic acid IV load 15–20 mg/kg, maintenance 400–600 mg q6 h in phenytoin-intolerant patients. Consider IV levetiracetam 1500 mg bid, if patients are intolerant to phenytoin or valproic
Continuous video-EEG monitoring, if available; consider STAT head CT
Seizures continue clinically or electrographically
Additional phenytoin or fosphenytoin (IV 5–10 mg/kg or 5–10 mg/kg PE) or valproic acid IV load 15–20 mg/kg
Refractory status (seizures >60 min)
Mechanical ventilation. Avoid hyperventilation (PaCO2 38–45, if intracranial pressure normal)
Institute 10–20 s burst-suppression pattern on EEG: propofol 2 mg/kg bolus IV and 100–150 mcg/kg/min infusion. Alternatively, or if burst suppression not achieved, use pentobarbital boluses (6–12 mg/kg IV at 0.2–0.4 mg/kg/min) and titrate infusion at 0.25–4.0 mg/kg/h
Hemodynamic support – fluids, pressors, inotropes
Consider STAT CT of the head, if not done; the EEG leads must be removed before the CT (to avoid artifacts) and replaced after
Transfer to the neuro-ICU
Once EEG suppressed, continue for 12–24 h and start weaning from general anesthetics

Modified from Varelas et al. (2013a, b)

- Lorazepam is preferable to diazepam, because of the lack of active metabolites and redistribution to extracerebral tissues. If these lines of defense fail and seizures continue, the algorithm uses midazolam or general anesthetics.
- Midazolam may convey an advantage compared to propofol for seizure control, but if burst suppression becomes the goal (as in RSE), propofol and, especially, barbiturates are stronger choices.
- Pentobarbital is preferable to phenobarbital because of shorter elimination ($T_{1/2}$ around 24 h vs. 96 h) and in a meta-analysis was more efficacious than midazolam or propofol (albeit with higher risk for hypotension). Blood concentration monitoring is not very helpful in this situation, since there is inconsistent relationship between serum concentration and seizure control.

Key Points

- Home antiepileptics should be administered as earliest as possible in the postoperative period.
- If the patient is unable to swallow or is vomiting, the intravenous form of the home drug should be used. If no IV form is available, load with one of the IV antiepileptics (phenytoin, valproate, levetiracetam, or lacosamide), if the patient had seizures before.
- Craniotomy per se is not a reason for prophylactic antiepileptics.
- If patient has one post-op seizure, check trough antiepileptic drug concentrations, and, if low, supplement with the IV form. Check STAT glucose and electrolytes. Consider STAT CT of the head and EEG.
- If patient has multiple seizures or enters SE, use the ABC algorithm in parallel with lorazepam up to 0.1 mg/kg IV, load with phenytoin or fosphenytoin up to 20 mg/kg IV, do a fast diagnostic workup, and, if seizures continue, consider general anesthetics with continuous EEG monitoring.

Suggested Reading

Kofke AW, Tempelhoff R, Dasheiff RM. Anesthetic implications of epilepsy, status epilepticus and epilepsy surgery. J Neurosurg Anesthesiol. 1997;9(4):349–72.

Manaka S, Ishijima B, Mayanagi Y. Postoperative seizures: epidemiology, pathology and prophylaxis. Neurol Med Chir (Tokyo). 2003;43:589–600.

Rowe AS, Goodwin H, Bushwitz J, Brophy G, Castle A, Dean D, Johnson D, LaPointe M, Lesch C, Liang N, Potter E, Roels C, Samaan K, Rhoney DH, For the Neurocritical Care Society Pharmacy Work Group. Seizure prophylaxis in neurocritical care: a statement from the neurocritical care society pharmacy work group. Pharmacotherapy. 2014;34:396–409.

Varelas P, Spanaki M, Mirski M. Seizures and the neurosurgical intensive care unit. Neurosurg Clin N Am. 2013a;24(3):393–406.

Varelas PN, Spanaki MV, Mirski MA. Status epilepticus: an update. Curr Neurol Neurosci Rep. 2013b;13(7):357.

Withdrawal of Mechanical Ventilation in Neurosurgical Critical Care

97

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Overview

Patients arrive in the Neuro ICU in crisis, often the result of a sudden catastrophic injury to the brain. Sometimes, an irreversible injury is immediately apparent. In such cases, after urgent discussion with family, a decision is quickly made to forgo life-sustaining measures, allowing natural death. More often, the prognosis is uncertain at first. The Neuro ICU team therefore initiates emergency measures to sustain life. Typically, this means placement of an endotracheal tube and initiation of mechanical ventilation.

In the days, weeks, or months that follow, an understanding of a poor prognosis may emerge. This should prompt a discussion with family members about whether to continue life-sustaining measures. A separate chapter of this book provides guidance on how to conduct these essential conversations with families. Such conversations frequently conclude with a decision to withdraw life-sustaining measures, including mechanical ventilation, thus allowing natural death. Ethical principles hold that there is no meaningful difference between withholding life-sustaining measures and withdrawing them.

Once this difficult decision is made, some Neuro ICU clinicians choose to play a very limited role in the subsequent process of withdrawal of mechanical ventilation. A typical set of orders might read: "Extubate when family ready, initiate morphine infusion, titrate to comfort." The actual process of withdrawing mechanical ventilation is delegated to the bedside nurse and respiratory therapist. This approach can lead to poor symptom control for the patient; increased stress on staff, particularly those who may not be experienced in withdrawal of mechanical ventilation; and insufficient support for the family outcomes.

Implications for the Neurosurgical Patient

A poorly planned withdrawal of mechanical ventilation in the Neuro ICU can result in uncontrolled dyspnea, tachypnea, and, in the worst cases, severe stridor. The trajectory of Neuro ICU patients after withdrawal of mechanical ventilation can be variable. Some patients with catastrophic neurological insults will be comatose and nearly apneic. Such patients will generate minimal respiratory effort upon extubation. They will exhibit no outward distress, though there is lively debate about whether these individuals nevertheless can experience suffering. Some patients will have some retained consciousness and certainly will experience visible suffering if respiratory distress occurs. Families suffer as well as they witness uncontrolled respiratory distress in their loved one, even if the patient is deeply comatose. A skillful, coordinated, and compassionate withdrawal of life support may help families' transition to productive grieving with a sense of gratitude for a painless and comfortable dying.

Concerns and Risks

Patients in the Neuro ICU may develop severe respiratory distress when mechanical ventilation is withdrawn. Specific characteristics of Neuro ICU patients may account for this higher risk. Medical and surgical ICU patients typically have multiorgan failure by the time a decision is reached to withdraw life-sustaining measures. Withdrawal of mechanical ventilation is often accompanied by discontinuation of supplemental oxygen and vasopressor medications. This usually leads to prompt hypoxia and circulatory collapse. Death arrives within minutes, occasionally hours. Respiratory distress is blunted by brain hypo-perfusion and respiratory muscle weakness.

In contrast, many patients with catastrophic but isolated neurological conditions will have substantial, and even excellent, cardiopulmonary function. This means that the trajectory toward dying in these patients can be quite variable. A 1999 study reported a wide range of time to death after withdrawal

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of mechanical ventilation; 25% died within 1 hour and 69% within 24 hours, while 31% lingered near death for more than 24 hours. One patient took 11 days to die.

In general, four broad trajectories can be expected, depending on underlying ventilatory function:

1. Minimal ventilatory function with near-complete apnea. These patients will die quickly with minimal respiratory distress.
2. Preserved ventilatory function and no upper airway obstruction. These patients will have minimal respiratory distress and may have enough ventilatory function for long-term survival without mechanical ventilation. In such cases, difficult conversations will be needed regarding the provision of artificial hydration and nutrition to sustain life.
3. Impaired ventilatory function. These patients will likely experience respiratory distress upon withdrawal of mechanical ventilation. They will have enough ventilatory reserve to sustain life in the short term and to generate respiratory effort. However, ventilatory function will be insufficient to prevent hypercarbia and hypoxia, thus triggering respiratory distress. These patients will require a slower, stepwise reduction in ventilatory support. Reassessments occur with each reduction, with opioids administered to palliate tachypnea and dyspnea prior to subsequent reductions.
4. Preserved ventilatory function with severe upper airway obstruction. This is the most challenging patient. Withdrawal of mechanical ventilation will be uncomplicated. However, removal of the endotracheal tube may lead to stridor and severe respiratory distress.

Coordinated Process of Withdrawal of Mechanical Ventilation

The following are specific recommendations for a coordinated stepwise process for withdrawal of mechanical ventilation:

- Remain present. The draw of competing clinical obligations and the inherent discomfort in confronting mortality means that it will always be easier to depart from the bedside once a decision to withdraw mechanical ventilation is made. Remaining present will allow the provider to witness and receive the gratitude of the family for their loved one's safe and peaceful dying.
- Involve the family in the formulation of the plan for withdrawal of mechanical ventilation.
  Family preferences can and should influence the pace and timing of a withdrawal. It may also be helpful to discuss the family's expectations for administration of hydration and nutrition, if prolonged survival without mechanical ventilation is expected. Withdrawal may be delayed so that families can gather at the bedside for the death. Families with specific religious beliefs or practices may wish to incorporate those rituals into their time at the bedside. Some family members will prefer to remain at the bedside throughout the process. Others will prefer to remain in the waiting room until stable breathing and symptom control are achieved. Others will choose to leave the building and ask to be notified by phone when the death occurs. Such preferences should be solicited and respected. Family perception of their loved one's distress should be sought, as perhaps the "gold standard" assessment of suffering.
- Attend to the family's needs.
  Create a setting conducive to family presence in the room. Encourage families to bring in photos, music, or other mementos of their loved one. Extraneous medical devices should be removed from the patient's room. Families will benefit from specific guidance about what to expect as the withdrawal proceeds. Provide frequent updates as new information emerges. A clinician's calm presence in the room as extubation proceeds will help reassure families that symptoms will be promptly assessed and alleviated.
- Perform a spontaneous breathing test (SBT) to calculate the rapid shallow breathing index (RSBI).
  The SBT helps anticipate the patient's likely trajectory after withdrawal of mechanical ventilation providing valuable information for both families and for the care team. The RSBI is calculated by placing the patient on CPAP 5/5 without a backup rate and observing the patient's underlying respiratory rate and tidal volume. The RSBI is defined as respiratory rate divided by tidal volume, measured in liters. RSBI = RR ÷ TV.

  A patient with intact respiratory function will have a RSBI of approximately 20 (RR = 10. TV = 0.5 l RSBI 20 = 10 ÷ 0.5). When the SBT reveals excellent respiratory function, families can be advised well in advance that dying may be prolonged. The team can begin the process of discharge planning. The bedside nurse will not need to aggressively medicate with morphine. The respiratory therapist can proceed directly the withdrawal in a single-step process.

  Patients with near apnea will have an only modestly elevated RSBI of around 50, despite profound impairment in ventilatory capacity, owing to lack of respiratory drive and low respiratory rate (RR = 5, TV = 0.1 RSBI 50 = 5 ÷ 0.1. When the SBT reveals minimal respiratory function, families can be advised that the death will occur quickly. The bedside nurse will know that premedicating with opioids may not be necessary. The respiratory therapist can proceed directly with single-step withdrawal, without a stepwise downward titration in ventilatory support, as is needed when respiratory distress is anticipated.

Patients with impaired ventilatory function (TV = 250 ml, 0.25 l) but intact respiratory drive (RR = 25) will have an elevated RSBI of 100 (25 ÷ 0.25 = 100). This result alerts the teams that a stepwise withdrawal of ventilator support will be required, with opioids given to blunt respiratory distress.

- Use opioids, usually morphine, to palliate respiratory distress.

  Opioids have a specific palliative effect on dyspnea. Morphine, a natural opiate extracted directly from the opium poppy, was first discovered more than 200 years ago and has traditionally been the drug of choice in palliative care. The semisynthetic opiates, such as hydromorphone and oxycodone, and the synthetic opioid fentanyl are more similar to morphine than different. Nevertheless some clinicians prefer these to morphine, based on subtle differences in pharmacokinetics or side effect profile. Effective symptom control is probably more dependent on timely reassessment, and dose escalation when indicated, than on the selection of a specific opioid.

  Opioids help blunt the sensation of dyspnea. Of course, when given in excessive doses, morphine will cause respiratory depression, even death. However, when given in therapeutic doses, opiates may paradoxically prolong life. Opioids can blunt tachypnea, which leads to respiratory fatigue and premature death. Opioids are the preferred drug when mechanical ventilation is withdrawn. Benzodiazepines are useful as general sedatives, but have no specific effect of respiratory distress. They can be a useful adjunct to opiates, but should not be used as alone during withdrawal of mechanical ventilation.
- Use small, frequent, bolus doses of morphine, not continuous infusions

  Opioids should be administered as a bolus. Refer to the order in the back of this chapter for usual doses. Doses can be doubled and repeated as often as every 5–10 minutes when symptoms remain uncontrolled. Continuous infusion is not indicated for withdrawal of mechanical ventilation. Time to steady state after initiation of a continuous infusion is 3–4 half lives, or 6–12 hours. Serum levels of opioids will keep rising for 6–12 hours after the initiation of a continuous infusion, risking overdose. Continuous infusions are useful to maintain steady-state opioid levels, once symptom control has been achieved. A continuous rate can be started at a rate about 25% of the bolus dose required to achieve symptom control.
- Wean ventilator support in a stepwise method, when distress is predicted by SBT.

  Those patients with elevated RSBI and dyspnea noted on SBT require gradual stepwise decrease in ventilator support over 10–30 minutes. The first step is to administer an initial bolus of an opioid and then switch the ventilator to pressure support (PS) mode without mandatory rate or backup breaths. This allows the patient's underlying respiratory drive to emerge. Subsequently decrease PS by 25 or 30%, allowing the demand on the respiratory system to increase. Further opioid doses are given based on the presence of respiratory distress. Once respiratory drive and effort are controlled (RR < 20 and calm) at PS of 5, then extubation can proceed. Those patients whose SBT revealed little risk of distress, either near-complete apnea or excellent ventilatory capacity, can proceed directly to extubation without this stepwise weaning.
- Remove the endotracheal tube, when possible.

  Removal allows a family to see their loved one's last moments free of medical devices. In addition, leaving the endotracheal tube in place may prolong the dying process unnecessarily. In some circumstances, the endotracheal tube serves to keep the upper airway open sufficiently to allow a weakened respiratory system to sustain life. Removal of the endotracheal tube can produce an increase in upper airway resistance significant enough to cause those patients with impaired respiratory drive to decline much more quickly than had been predicted by the SBT.

  Removal of the endotracheal tube is usually well tolerated. A few patients with intact or heightened respiratory drive at the time of extubation will risk stridor and severe respiratory distress upon extubation, if airway resistance is increased. This risk for dyspnea may not be apparent from the SBT. Deflating the cuff to ensure that air can pass unobstructed through the upper airway prior to extubation will help identify those select patients in whom stridor may occur, requiring very aggressive use of opioids and sedatives. In rare cases, nebulized racemic epinephrine for tracheal edema or an oral airway upper airway obstruction can be an effective short-term palliation for stridor should opioids be insufficient to palliate dyspnea and stridor.

  Noisy breathing without dyspnea is common and probably more distressing to the family and care team than to the patient. Noisy breathing often resolves with changes in body position. Anticholinergics such as atropine or glycopyrrolate are routinely given for noisy breathing, though there is no evidence that they are effective.
- Create a plan for coordinated care outside the ICU, when necessary.

  Some patients will survive days after extubation. These patients can be transferred from the ICU to a hospital ward, hospice unit, or even the patient's home, in certain circumstances. Transfers of care must be well coordinated to insure continuity of symptom control and complete understanding of goals of care and family needs by the accepting medical team. Careful and ongoing assessments of prognosis will ensure that transfers happen only when justified by expected duration of life. Update the family as soon as new information emerges that alters the patient's expected trajectory. When survival after extubation was unexpected, a separate, explicit discussion with family members about discontinuation of artificial nutrition and hydration will be required. Ideally, some discussion of the

possibility of transfer out of the ICU, and the need for a decision about artificial hydration and nutrition, will occur ahead of time, along with the discussion about proceeding with withdrawal of mechanical ventilation.

- Maintain communication with family and staff throughout the process.

  Kind and empathetic words, such as "You all have demonstrated how much you care for your loved one in making this difficult decision," "He (or she) must have been a remarkable person," or "This is such as sad time for all of you," will be help families feel supported as they enter their time of grief. This can be a time also for the team to gather with family together and share memories they have of the patient, to express gratitude for the opportunity to care for patients and families in such an emotional and difficult time (Table 97.1).

Table 97.1 Sample order set to guide withdrawal of mechanical ventilation

Do not resuscitate, do not intubate (if not already noted in chart)
Attending signature_____
Note written in chart documenting discussions with family leading to change in goals of care to comfort.
Nursing interventions
1. Implement standards of nursing care for end of life/comfort care.
2. Remove NG tube, extra IV sites.
3. Continue monitoring as often as needed to assess patient comfort/prognosis.
Respiratory therapy interventions
1. Perform Spontaneous Breathing Trial (CPAP 5/5, room air).
2. Record symptoms and measure respiratory rate and tidal volume to calculate the Rapid Shallow Breathing Index (Tobin) score.
3. Resume prior ventilator settings if patient becomes symptomatic or unstable.
MD orders
Discontinue all medications, IV fluids, and tube feeds. The only exceptions are medication such as vasopressors that sustain life moment to moment, which should be continued until family indicates they are ready.
Medication principles for vent withdrawal
1. Provide frequent boluses as necessary to control symptoms.
2. If already on analgesics and sedatives, maintain continuous infusion at current level.
3. No change or initiation of in continuous infusion until patient stable and extubated.
Opioid (choose one only)
Morphine 2–10 mg IV q 5-15" as needed for prn pain/dyspnea RR >20
Hydromorphone 0.5–2 mg IV q 5-15" prn pain/dyspnea RR >20
Fentanyl 25–100 mcg IV q 5-15" prn pain/dyspnea RR >20
Sedative (choose one only)
Lorazepam 1–2 mg q 15" IV prn distress
Midazolam 1–2 mg q 15" IV prn distress
Propofol 20–40 mg q 5" IV prn distress
Begin upon confirmation from family that ready to proceed
1. Discontinue pressors – if indicated. If death likely upon discontinuation of pressors, await imminent cardiac death before ventilator withdrawal.
2. Wean mechanical ventilation to CPAP and room air
(a) If earlier SBT uneventful proceed directly to withdrawal of mechanical ventilation.
(b) If symptomatic for respiratory distress during SBT, then wean pressure support and oxygen to CPAP and room air over 20–30 minutes, administering bolus opiate +/− sedative with each decrease in ventilator support to maintain calm respirations.
3. Discontinue ventilator and extubate (unless patient has tracheostomy)
(a) Proceed only if symptoms controlled.
(b) Perform cuff leak test to ensure patency of upper airway.
(c) Monitor carefully for upper airway obstruction.
(d) Administer nebulized racemic epinephrine prn stridor uncontrolled by opioids.

Key Points

- Remain present.
- Involve the family in the formulation of the plan for withdrawal of mechanical ventilation.
- Attend to the family's needs.
- Perform a spontaneous breathing trial (SBT) to calculate the rapid shallow breathing index (RSBI).
- Use an opioid, usually morphine, to palliate respiratory distress.
- Use small, frequent, bolus doses of opioids, not continuous infusions.
- Wean ventilator support in a stepwise method, when distress is predicted by SBT.
- Remove the endotracheal tube, except when severe dyspnea and stridor are anticipated.
- Create a plan for coordinated care outside the ICU, when necessary.
- Maintain communication with family and staff throughout the process.

Suggested Reading

Bascom PB. Dyspnea can be, and should be, palliated with opioids. J Palliat Med. 2013;16:465.

Campbell MJ, Yarandi HY, Mendez M. A Two-Group Trial of a terminal ventilator withdrawal algorithm: pilot testing. J Palliat Med. 2015;18:781–5.

Chan JD, Treece PD, Engelberg RA, Crowley L, Rubenfeld GD, Steinberg KP, Curtis JR. Narcotic and benzodiazepine use after withdrawal of life support: association with time to death? Chest. 2004;126:286–93.

Kompanje EJ, van der Hoven B, Bakker J. Anticipation of distress after discontinuation of mechanical ventilation in the ICU at the end of life. Intensive Care Med. 2008;34:1593–9.

Mayer AM, Kossoff SB. Withdrawal of life support in the neurological intensive care unit. Neurology. 1999;52:1602–9.

Brain Death in Neurosurgical Critical Care

98

Amit Prakash and Basil Matta

Overview

Brain death is best defined as absence of clinical brain functions when the primary etiology is known and demonstrably irreversible. The key findings in brain death are coma, absence of brain stem reflexes, and apnea. Irreversible loss of higher brain functions of consciousness and cognition is classified as persistent vegetative state and should not be confused with brain death.

Whole brain death formulation codified as "an individual who has sustained irreversible cessation of all functions of the entire brain, including the brain stem, is dead," by the Uniform Determination of Death Act 1993 is the accepted norm in the USA, Canada, and most parts of the European Union (EU). It mandates ancillary testing to confirm the diagnosis.

The brain stem formulation of brain death was formally adopted in the UK in 1995. In 2008, the Academy of Medical Royal Colleges published a code of practice, which builds upon the earlier code published in 1998. It provides rigorous criteria for confirming death in clinical settings where confirmation of death by brain stem testing is appropriate (Table 98.1).

Table 98.1 Potential complications associated with brain stem death

Complication	Physiological cause	Manifestation
Neurological	Hypothalamic and pituitary failure	Hypothermia, neurogenic diabetes insipidus (DI)
Cardiovascular	Sympathetic storm secondary to medullary ischemia followed by autonomic dysfunction	Myocardial dysfunction, dysrhythmias followed by decreased cardiac output, systemic vascular resistance, and asystole
Pulmonary	Sympathetic storm with resultant pulmonary edema and interstitial hemorrhage	Hypoxemia and impaired gas exchange
Renal	Hypotension and hypovolemia secondary to cardiovascular dysfunction	Renal failure and parenchymal damage
Endocrine	HPA axis failure along with sympathetic surge	DI (polyuria > 200 mL/h with S. osmolarity > 300, U osmolarity < 200)
		Hypothyroid state and decreased intrinsic ADH contributing to autonomic instability
Metabolic	Sympathetic surge, DI, hypothalamic-pituitary axis failure	Hyperglycemia, insulin resistance, $\uparrow Na^+$,$\downarrow K^+$, $\downarrow Mg^+$,$\downarrow Ca^+$, $\downarrow PO_4$
Coagulation (rare)	Release of tPA and fibrinolytics from affected brain tissue	Bleeding diathesis including DIC

Diagnosis of Brain Stem Death

In the UK, clinical testing must be undertaken by two physicians who have been fully registered for more than 5 years and are competent in the procedure and independent of the transplant team. At least one should be a consultant. Testing should be undertaken by the doctors together and must be successful on two occasions in total. The legal time of death for documentation is when the first set of tests, which finds the irreversible cessation of all functions of the entire brain, including the brain stem, was completed.

Preconditions

All of the following conditions must be fulfilled before clinical testing is undertaken:

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- The etiology of irreversible brain damage must be known. In most cases this is obvious, but when the primary event was prolonged circulatory insufficiency or cerebral hypoxia, it may take longer to establish the diagnosis and to be confident of the prognosis.
- The patient must be irreversibly comatose, unresponsive and apneic, and artificially ventilated.
- There should be no consideration that the state is due to depressant drugs. The action of narcotics, tranquilizers, and hypnotic agents can be prolonged due to hypothermia or renal/ hepatic failure. If drug assays are available, it is recommended that testing should not be undertaken if thiopentone level is >5 mg/L or midazolam level is >10 μg/L. If opioids or benzodiazepines are thought to be contributing to the coma, specific antagonists such as naloxone or flumazenil should be used. In other circumstances, residual sedative effects must be predicted according to pharmacokinetic principles.
- There is diversity of regulatory requirements for core temperature depending upon region, which should be adhered to. At the time of testing, core temperature should be greater than 34 °C in the UK and greater than 36 °C in the USA.
- Potentially reversible circulatory, metabolic, and endocrine disturbances must have been excluded as the cause of the continuation of unconsciousness.
  - The mean arterial pressure should be consistently >60 mmHg with maintenance of normocarbia and avoidance of hypoxia, acidemia, or alkalemia ($PaCO_2$ < 6.0 KPa, PaO_2 > 10 KPa, and pH 7.35–7.45).
  - Sodium levels above 160 mmol/L and below 115 mmol/L are associated with unresponsiveness.
  - Serum potassium concentration above 2 mmol/L and significant weakness are unlikely unless levels of magnesium and phosphate are <0.5 and >3.0 mmol/L, respectively.
  - Severe hypoglycemia with glucose levels below 3.0 mmol/L and significant hyperglycemia with levels above 20 mmol/L can itself be associated with coma and stupor and should be corrected.
  - Thyroid storm, myxedema, and Addisonian crisis may be associated with severe neuromuscular weakness or coma. These conditions are extremely rare; however, if there is any clinical reason to expect these disturbances, then appropriate hormonal assays should be undertaken.
- Neuromuscular blocking agents and other drugs must have been excluded as the cause of respiratory inadequacy or failure.
- An underlying high cervical spine injury and associated cord injury can rarely cause apnea and invalidates the apnea test.

Brain Stem Testing

The brain stem often fails from the rostral to caudal direction, and therefore, it is logical to undertake testing in the same manner (Table 98.2).

Ancillary Testing

Confirmatory tests are essential when doubt exists about the clinical findings, conditions preclude an apnea challenge, or suspicion of confounding conditions exists. These are routinely undertaken in parts of the world where the whole brain death concept is applicable.

EEG A result of no activity greater than 2 μV at a sensitivity of 2 μV/mm with the filter set at 0.1 or 0.3 second and 70 Hz over a 30-minute time span supports the diagnosis of

Table 98.2 Brain stem testing

Reflex	Cranial nerves tested	Procedure	BSD criteria	Remarks
Pupillary reflex	II and III, localizes to midbrain	Direct and consensual reflex	No response to either	Pupil size indicates the site of brain stem involvement
Oculocephalic reflex (doll's eye reflex)	III, VI, and VIII localizes to midbrain and pons	Move head to right or left while noting eye movement	Eyes move with the head and are *not* fixed to a point	Cervical fracture or instability must be ruled out
Corneal reflex	V, VII, and III localizes to pons	Touch the cornea with cotton to elicit eyelid closure	No response	Normal response is "Bell's phenomenon" (upward rotation of eye)
Oculovestibular reflex	III, VI, VIII, and IV localizes to midbrain and pons	Elevate the head 30°, irrigate tympanic membrane with 50 cc iced water	Eyes tonically deviate toward the side of the stimulus	Ensure intact tympanic membrane
Gag and cough reflexes	IX and X, both localize to medulla	Cough-tested by stimulation of carina by suction catheter, gag by stimulating the posterior pharynx with a tongue depressor	Both reflexes should be absent	
Apnea test	Demonstrates the failure of medullary drive for ventilation	Pre-oxygenate at saturation greater than 95%, induce apnea to achieve $EtCO_2$ > 6 kPa	No spontaneous breathing	Oxygen insufflation at 2–5 L/min or CPAP may be used to maintain oxygenation

brain death. Reversible causes such as barbiturate poisoning may result in an isoelectric EEG in a living patient.

Cerebral angiography is the gold standard for diagnosis of brain death and conclusively proves the absence of cerebral perfusion. The absence of intracerebral filling detected above the entry level of the carotid or vertebral artery in the skull confirms the diagnosis of brain death. The study needs transportation to neuroradiology suite and can take several hours.

Technetium nuclear medicine scan As with the cerebral angiogram, it is a positive test that confirms the diagnosis of brain death by demonstrating failure of uptake in the brain consistent with absent cerebral perfusion.

Other techniques include CT and MR angiography and transcranial Doppler studies.

Legal Status

The legally acceptable definition of death varies in different parts of the world. Brain stem death is lawfully accepted in Australia and New Zealand. Few states in the USA accept this, and most require additional confirmatory testing. While in South Africa neither form of testing is legally acceptable as death.

The following table depicts the situation in the EU (Table 98.3):

Controversies

Despite numerous publications there is a paucity of evidence-based literature to support many current practices related to brain death determination. Definitions of brain death vary around the world and so does physician expertise specified to be qualified for testing. Many guidelines explicitly exclude transplant physicians from brain death determination process.

Table 98.3 Legal status in EU

Country in EU	BSD[a] legally accepted	Confirmatory tests needed
Belgium	Yes	No
Denmark	Yes	Yes
France	Yes	Yes
Germany	No	Yes
Italy	Yes	Yes
Netherlands	No	Yes
Spain	Yes	Yes
UK	No	No

[a]*BSD* Brain stem death

Clinical assessment criteria however are similar in all guidelines except for subtle differences notably:

- North American guidelines recommend an apneic threshold $PaCO_2 \geq 60$ mm of Hg and some also require an acidemic pH <7.28.
- Oculocephalic or doll's eye reflex is not required by the UK code for brain death determination.
- Many guidelines (including the UK) incorporate specific core temperature thresholds for clinical determination of brain death, but recommended thresholds range from 32.2 °C to 36.0 °C without clear evidence base for any of these limits.

Where full examination is restricted by the nature of the injuries, it is generally, but not uniformly, recommended that ancillary diagnostic testing be performed.

Brain Death and Family

It is imperative that clear communication exists between the relatives and the caring team. The information given must be honest, clear, concise, consistent, and communicated in a sensitive manner. In most cases the nursing staff are the primary point of contact and should be included in all discussions with the family. The pace of the process that should be individualized to the family would generally be determined by their level of understanding.

Care of the brain stem dead patient is subsequently dictated by the presence and wishes of the next of kin and the potential for donation. If donation is not an option, ventilatory support can be withdrawn at a time acceptable to all parties.

Key Points

- The definition of brain death varies in different parts of the world with whole brain death requiring ancillary testing being the norm in the USA, Canada, and most of Europe with the exception of the UK where brain stem death is legally and medically accepted.
- Strict adherence to the criteria for brain death diagnosis should be followed according to the region and institution.
- The diagnosis of brain death is primarily clinical. However, ancillary tests are performed when the clinical criteria cannot be applied reliably or are legally applicable.
- Attentive care of the brain dead organ donor should be undertaken to preserve organ viability.

Suggested Reading

Academy of Medical Royal Colleges (70 Wimpole Street, London, W1G 8AX). A Code of Practice for the Diagnosis and Confirmation of Death, October 2008.

Baron L, Shemie SD, et al. Brief review: history, concept and controversies in the neurological determination of death. Can J Anesth. 2006;53(6):602–8.

Department of Health. A code of practice for the diagnosis of brain stem death. London: Department of Health; 1998.

Lang CJG, Heckmann JG. Apnea testing for the diagnosis of brain death. Acta Neurol Scand. 2005;112:358–69.

McKenzie CA, McKinnon, et al. Differentiating midazolam oversedation from neurological damage in the intensive care unit. Crit Care. 2005;9:R32–6.

Morenski JD, Oro JJ, et al. Determination of death by neurological criteria. J Intensive Care Med. 2003;18(4):211–21.

Pratt OW, Bowles B, et al. Brain stem death testing after thiopental use. A survey of UK neuro critical care practice. Anaesthesia. 2006;61:1075–8.

Smith M. Physiologic changes during brain stem death—lessons for management of the organ donor. J Heart Lung Transplant. 2004;23:S217–22.

Uniform Determination of Death Act, 12 Uniform Laws Annotated (U.L.A.) 589 (West 1993 and West Supp.1997).

Wijdicks EFM. Determining brain death in adults. Neurology. 1995;45:1003–11.

Young GB, Shemie SD, et al. Brief review: the role of ancillary tests in the neurological determination of death. Can J Anesth. 2006;53(6):620–7.

Organ Donation

99

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Introduction

Advances in the science of immunology and transplantation have made organ donation a culturally and socially accepted practice. However, in spite of advances in patient selection and pretransplantation management, the imbalance between the number of patients on the waiting lists for organ donation and the number of available organs for transplantation continues to widen. According to the United Network for Organ Sharing (UNOS), as of January 2016, over 133,0353 patients are on the waiting list for organ donation, with 7592 deceased donors having given the gift of life to 20,845 transplanted patients in 2015. Every 10 min it is estimated that someone is added to the waiting list, and an estimated 22 people on the waiting list die each day. This chapter will discuss the current possibilities for organ donation and the ICU care of the potential organ donor, as well as a systems based approach to the development of institutional protocols for organ donation.

Incidence and Epidemiology

In the United States and Canada, the majority of organ donation involves patients after neurologic determination of death (previously termed "brain death"), while living related and unrelated donors account for nearly 40%, and donation after cardiac death (DCD) accounts for about 7% of all donors [1]. With improved donor management, the percentage of donors over age 50 years accounts for nearly 35% of all deceased donors. Currently, up to one fourth of all deaths occur in intensive care units (ICUs) with patients dying according to either cardiac or neurological criteria. While many of the ICU deaths are related to respiratory failure or pneumonia, many patients die after withdrawal of life-sustaining measures. Up to 61% of deaths that occur in a neurological ICU may be related to withdrawal of support due to predicted poor prognosis for recovery and patient wishes. Given that many deaths occur in hospital intensive care units, strategies for improving the donation process have been focused in the ICU and have proven to be successful in facilitating organ donation. The strategies include aggressive donor management (ADM) and the use of an in-house coordinator for organ donation (IHC). Recently, two critical care societies have developed a consensus statement for the management of the donor in association with the organ procurement groups [2].

Today, the most common mechanism of death for those who die and donate their organs is divided between cerebral anoxia (37 percent (%), intracranial hemorrhage or stroke (30 percent (%)) and head trauma (30 percent (%)). The shift away from death due to traumatic brain injury in younger patients to older patients with cerebrovascular disease with ischemic stroke or anoxic injury has important implications for the ICU care team caring for the potential organ donor.

Pathophysiology of Brain Death and Medical Management of the Potential Donor

Alterations and instability in the virtually all organ systems can be expected as part of the physiological changes that occur as or after brain death occurs. In the early stages of brain death, there is a loss of blood pressure regulation and sympathetic tone. As cerebral ischemia progresses toward the brainstem, a "catecholamine storm" can arise, and a severe increase in systemic vascular resistance (SVR) and blood pressure occurs. This quickly subsides, and a decrease in systemic vascular resistance and vasodilatation and increase in capillary permeability and intravascular hypovolemia and hypotension result. The primary goal of management of the potential donor is to maintain adequate blood pressure through the use of volume expansion, either crys-

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talloids or colloids, often institution dependent (Table 99.1). More than 80% of patients will require some form of vasoactive support. During this time period, ongoing aggressive medical management of the patient is critical to maintain optimal conditions for organ procurement and transplantation and ensure good graft function and quality of life for the recipient. Standard patient monitoring includes blood pressure measurement, cardiac monitoring, and measurement of urine output and central venous pressures. While still controversial, some authors suggest that a pulmonary artery catheter (PAC) should be utilized to monitor hemodynamics and to guide and balance fluid administration. However there are inadequate data to support this suggestion definitively. The primary goal of management of the potential donor is to maintain adequate blood pressure through the use of volume expansion. Often additional vasoactive agents are needed. As these situations are often heterogeneous, clinical trial evidence cannot guide us firmly with respect to the best vasoactive or inotropic agents to use in patients with hypotension and/or depressed cardiac contractility. As noted above, first and foremost, the clinician must ensure that the patient is well hydrated, recognizing that maximal hydration is beneficial for renal transplantation, but worsens pulmonary transplantation. Dopamine has been typically a frontline agent for inotropic support, though it has not been shown to be superior to any alternative agent. The use of catecholamines has been shown to promote long-term graft survival and a lower incidence of kidney rejection; however, some clinicians find the vasoconstrictive properties of these drugs harmful in that they may lead to organ ischemia by increasing systemic vascular resistance (SVR) especially in a hypovolemic donor. Vasopressin has been suggested for its catecholamine-sparing effects as initial therapy for hemodynamic support and the treatment of diabetes insipidus. Echocardiography is performed both to assist in hemodynamic monitoring and adequacy of volume and later to assess potential cardiac donation and focal wall motion abnormalities. Transthoracic echocardiography should be attempted as a first step to assess appropriateness for cardiac donation, but transesophageal echocardiography may be required. Serial echocardiographic assessments should be performed as cardiac abnormalities may resolve over time and reduction or removal of exogenous catecholamine support. Coronary angiography is recommended in donors >40 years of age and in younger patients with risk factors for early cardiac disease.

Table 99.1 Goals of organ donor management

Overall goals of organ donor management		
Mean arterial pressure at least 60 mmHg		
Vasoactive agent requirement: ≤10 mcg/kg/min (dopamine, dobutamine)		
Urinary output ≥ 1.0 ml/kg/h		
Left ventricular ejection fraction >45%		
Volume goals		
Pulmonary capillary wedge pressure 8–12 mmHg,		
Central venous pressure 6–8 mm Hg		
Action: fluids (crystalloids or colloids) and/or diuretics		
Cardiac performance		
Cardiac index>2.4 l/min		
Left ventricular stroke work index ≥ 15 g∗m/cm^3/beat		
Urine output ≥ 1.0 ml/kg/h		
Action: ionotropic agents (dopamine, dobutamine, or epinephrine)		
Resistance		
Mean arterial pressure at least 60 mm Hg		
Systemic vascular resistance 800–1200 dynes∗s∗cm^{-3}		
Action: vasopressors (norepinephrine, epinephrine, vasopressin)		
Endocrine failure		
Hormonal replacement		
Drug	Bolus dose	Continuous infusion
Triiodothyronine	4.0 μg	3.0 μg/h
or		
Thyroxine	20 μg	10 μg/h
and		
Methylprednisolone	15 mg/kg, or 1000 mg IV, or 250 mg IV	100 mg/h
Vasopressin	1 U	0.5–4.0 U/h
Insulin	10 U (50% dextrose)	Maintain glucose at institutional standards

More than 90% of individuals will have abnormalities in the posterior pituitary function, with low or undetectable levels of vasopressin. Hormones controlled by the anterior pituitary are seen at variable levels (thyroxine, human growth hormone, adrenocorticotropic hormone, thyroid stimulating hormone). While the data supporting administration of a combination of hormones are mixed, current guidelines support the administration of intravenous vasopressin in the setting of hemodynamic instability. 1-desamino-8-D-arginine vasopressin (desmopressin; DDAVP) is highly selective for the V2 receptor which mediates renal medulla antidiuretic effects and has little vasopressor activity. It should be used in patients without hemodynamic instability but with signs of dilute urine and diabetes insipidus, while vasopressin in doses typically less than (<) 0.04 units/min can be used in patients with both diabetes insipidus and hemodynamic instability. Doses above these typical values may at times be utilized cautiously.

As might be expected by common management strategies and the pathophysiology of brain death, electrolyte abnormalities are common in the dying patient with neurological injury. Hypernatremia may be used as a therapeutic strategy to treat the patient with elevated intracranial pressure. However, the clinician must be able to recognize and treat the patient who transitions to diabetes insipidus. Diabetes insipidus causes polyuria (>1–2 l/h), dehydration, hypernatremia, and other electrolyte abnormalities (hypokalemia,

hypomagnesemia, hyopcalcemia, and hypophosphatemia). Careful monitoring of urine output is essential and routine electrolyte monitoring is important. Monitoring donor sodium levels and correcting hypernatremia are critical for successful liver transplantation because high serum sodium levels (greater than 155 mEq/l) in the donor can lead to primary graft non-function.

While the absolute effectiveness of hormonal resuscitation (HR) remains to be established, in unstable patients (mean arterial pressure (MAP) < 45 mmHg), it is recommended (Table 99.1). Use of donor guidelines and meeting established goals of care results in an increase in the number of organs donated.

Identifying patients who are eligible for pulmonary donation is a significant challenge, with only 15–25% of patients being able to donate lungs. Strategies for pulmonary management are targeted at maximizing the PaO_2/FIO_2 ratio with a minimum of 300 mmHg. Patients who fail to meet this threshold should undergo a lung management protocol that includes judicious fluid administration, possible diuresis, chest physiotherapy, and therapeutic bronchoscopy and recruitment maneuvers. In some settings ex vivo perfusion strategies have been utilized to increase the potential donor pool. Bronchoscopy should be performed in all potential lung donors to assess for occult aspiration and infection and to perform therapeutic airway clearance. Steroid administration and maintaining of a central venous pressure of 4–6 mmHg is considered optimal for pulmonary donation.

The liver, as an allograft, is fairly resistant to the immune factors which can cause immediate posttransplantation problems. As noted above, serum sodium should be maintained at levels less than 155 mEq/l. In addition, outcomes appear best if the central venous pressure of the donor is in the range of 8–10 mmHg, PEEP is kept as low as possible, and nutrition is provided to restore glycogen in the liver. Bedside ultrasonography (US) has a limited role in guiding percutaneous biopsy when histologic results are needed to determine suitability of the organ. Bedside US has a high sensitivity (96%) but a marginal specificity (68%) in the evaluation of hepatic steatosis and other liver abnormalities.

Outcomes of Aggressive Donor Management

Aggressive donor management (ADM) protocols have been shown to reduce the incidence of cardiovascular death before consideration of organ donation and improve organ recovery and function in the recipient. In addition to the aggressive management noted above, identification of potential donors, and by using a clear facilitated process of the declaration of brain death, additional patients may be eligible for organ donation. The success of these programs is attributed to early aggressive management of the potential donor, education of the staff, a collaborative relationship with the Organ Procurement Organization (OPO), and guidelines of a standardized protocol.

Identification and Process Management for the Potential Organ Donor

The identification of potential donors in the ICU is a multidisciplinary effort that should originate from identifying a high-risk patient population from the admitting diagnosis (traumatic brain injury, respiratory arrest, cardiac arrest, stroke, drug overdose, intraventricular hemorrhage) (Fig. 99.1). Accurate documentation of the presence or absence of central nervous system reflexes is critical when brain death is imminent and when explaining poor prognoses to families. The critical care nurse and the respiratory therapist are often the first members of the ICU team to detect a change in the level of consciousness and loss of neurologic exam and notification of providers who can rapidly begin brain death testing should follow. Thus, timely initiation of brain death testing is imperative, as cardiac instability often follows.

While this chapter has focused on the clinical aspects of the medical management of the potential organ donor, communication and support of the family during the discussion of grave prognosis and brain death testing are essential. Consent for organ donation is the biggest impediment to organ donation, and the family's understanding of the death of the patient, and the initial interaction with the team requesting consent has been shown to influence the probability of consent. The time period between identification of a grave medical prognosis and ultimate death allows the family time to consider the imminent death of the patient, while the medical team maintains the dying patient in the best medical condition. Discussion of organ donation should be seen as a routine part of end-of-life process, and every patient and family must have the opportunity to consider organ donation.

In the United States, regulations state that the person requesting organ donation be specifically trained to perform this function and training and role delineation of the members of the multidisciplinary team help alleviate stress during the request for donation. A collaborative approach with the Organ Procurement Organization staff and hospital staff is considered best practice for informing the family of a patient's death. Effective requesting is a term maximized by the Organ Donation Breakthrough Collaborative and begins with the "huddle." The huddle is a short, timely, coordinated exchange between hospital and OPO staff which establishes an effective request process that meets the needs of the family. An

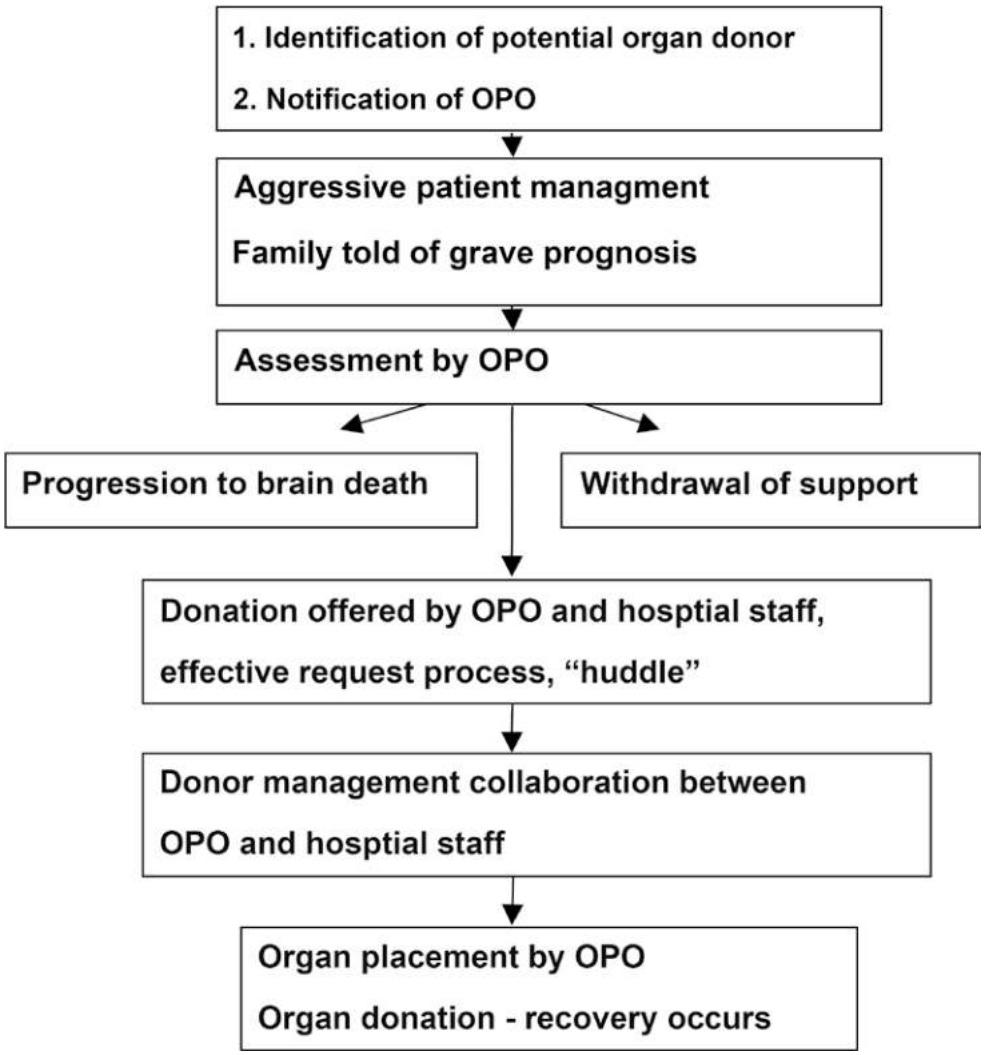

Fig. 99.1 Organ donation process

effective request includes the following components: the right person making the request, the right timing of the request, the right family and staff (including OPO) present for the request, and the right place for the request to occur. When death is imminent and the family understands the prognosis, the hospital and OPO staff, working collaboratively, can introduce organ donation as a possibility and provide information to assist the family in understanding what to expect.

One best practice is the implementation of the In-House Coordinator (IHC). The IHC typically assists and facilitates the donation process by donor surveillance, timely referral, education, family support and consent, donor management, and hospital/family follow-up. The IHC improves the donation process, consent rates, and conversion rates for donation through early and frequent interaction with families of potential donors and ICU staff. In most hospitals the ICU team provides ongoing medical care of the patient following brain death in collaboration with local procurement staff to ensure that the patient and family's goals of donation can occur.

Organ Donation After Circulatory Determination of Death

Organ donation after circulatory determination of death (DDCD) significantly contributes to the numbers of successful organ donations, and protocol development in appropriate hospitals is expected by the Joint Commission to further increase this opportunity for patients and families involved. A patient may be considered a candidate for DDCD when the patient does not meet the criteria for brain death and the decision has been made to withdraw active life-sustaining medical support. Other patients who could be considered for DDCD are patients with non-recoverable and irreversible neurologic injury resulting in ventilator dependency but not fulfilling brain death criteria, end stage musculoskeletal disease, high spinal cord injury, and some pulmonary diseases. In all cases, the patient or family should have made the decision to withdraw life-sustaining therapy. When this decision to withdraw support has been made, but before the therapies have been withdrawn, an assessment should be made in

conjunction with the local OPO and the ICU team, about whether the patient would be a candidate for organ donation after cardiac death. No predetermined assumptions about the candidacy of the patient should be made by the ICU team. The needs and respect of the patient and family at the time of withdrawal of life-sustaining therapy should be at the forefront of all decisions made about care, processes, and protocols. Importantly, the candidacy of the patient for organ donation will depend on an assessment of whether death would occur within a predefined period of time (usually 1 h). A UNOS DCDD Consensus Committee developed criteria predictive of death within 60 min after withdrawal of life support (Table 99.2). A study prospectively using these criteria identified a clear relationship between the number of criteria and whether death occurred within 60 min with a total of 29%, 52%, 65%, and 82% of patients with 0, 1, 2, and 3 of these criteria, respectively, dying within 60 min. Clinical staff must be prepared for potential DCDD scenarios in which death does not occur after withdrawal of life-sustaining therapies. Institutional protocols should be prepared for this outcome in establishing where a patient will receive care and ensure that families receive ongoing support. Authorization (formerly called consent) for donation of organs after cardiac death should include all donor-related procedures (placement of lines, administration of drugs such as heparin, withdrawal of the endotracheal tube, and termination of medication for blood pressure support). No donor-related procedures or medication administration should occur without authorization. In some cases, the medical examiner or coroner must provide clearance before the staff of the hospital and procurement agency can proceed with DCDD.

Hospital protocols will vary as to where withdrawal of support will occur. While it is ideal for a patient to be transferred to the operating room or near the operating room for withdrawal of support and DDCD, the needs of the family should be paramount in the development of protocols, and the family should have the option to be present (or not) with the patient at the time of withdrawal of support and death. If the family wants to be with the patient at time of death, the family support team must prepare them for what they will see and that they will need to leave the room shortly after death occurs so that organ donation procedures can occur. The psychosocial needs of the family must be addressed, and members skilled in providing this support should be available on site.

In DDCD, members of the transplant recovery team are not allowed to be present in the operating room with the potential donor at the time of withdrawal of support nor are these personnel allowed to participate in the guidance or administration of end-of-life care or declaration of death. The Ethics Committee of the Society of Critical Care Medicine (SCCM) recommends that physicians who are part of the transplant team or who will be responsible for care of an identified recipient may not determine cardiac death. In DDCD deaths, only one physician is required to certify death because objective data from an arterial line transducer can confirm the physical exam findings. Once cardiorespiratory function has ceased, the patient is pronounced dead based on cardiopulmonary criteria in the usual fashion by the attending physician or designee, and the time of death is established. If death does not occur within the established timeframe after withdrawal of life support (usually a 60 min time period), organ donation is not an option any longer, and protocols for continued end-of-life care and notification of the family need to be followed. The family must be aware of the fact that donation may not be possible and the hospital system should have a well-established process for aftercare in the event that death does not occur.

When cardiopulmonary function is absent, typically a predetermined time must elapse for the declaration of death and recovery of organs for donation. This time period is to ensure that reanimation cannot occur but keeps the needs of the transplanted organ and benefit of successful donation balanced. The Institute of Medicine guideline suggests 5 min but individual policies may vary from 2 to 5 min. The consensus of the Ethics Committee of SCCM states that no less than 2 min is acceptable and no more than 5 is necessary. As soon as declaration of death is determined by the declaring physician, the organ recovery team can begin. All OPOs and transplant centers must develop and comply with protocols for organ recovery according to the Organ Procurement and Transplantation Network for Organ Sharing (OPTN/UNOS) standards which were established in 2007.

Table 99.2 United Network for Organ Sharing Consensus Committee criteria for prediction of death within 60 min of withdrawal of life-sustaining treatment

Apnea
Respiratory rate <8 or >30 breaths/min
Dopamine >15 mcg/kg/min
Left or right ventricular assist device
Venoaterial or venovenous extracorporeal membrane oxygenation
Positive end-expiratory pressure > 10 and SaO_2 < 92%
FIO_2 > 0.6 and SaO_2 < 92%
Norepinephrine or phenylephrine > 0.2 mcg/kg/min
Pacemaker unassisted heart rate of < 30
IABP 1:1 or dobutamine or dopamine ≥ 10 mcg/kg/min and CI < 2.2 l/min/m^2
IABP 1:1 and CI < 1.5 l/min/m^2

SaO_2 Arterial oxygen saturation, *IABP* intra-aortic balloon pump, *CI* cardiac index

Designations and Advanced Directives

The Uniform Anatomical Gift Act created the power for individuals to donate organs, eyes, and tissues. In 2006, this was revised to enable OPO's access to the registries or Motor Vehicle Administration records to determine individuals' preferences. On occasion, the ICU team may be faced with

managing a situation where the patient has made the decision to be a donor by driver's license designation, donor registry, or advance directive, yet the family may wish to override this decision. Legally the first-person authorization provides sufficient grounds for organ procurement in all 50 states in the United States. ICU clinicians and OPO's are sensitive to the potential conflict between first-person authorization given at an earlier time period and the wishes of a grieving family. A patient's previously expressed preferences for organ donation are paramount, and as such the ICU clinicians and OPO's should inform the decedent's family of the legality of first-person authorization.

Summary

The development of clear protocols and aggressive clinical management of potential donors with the use of specialized personnel for identification and management of donors is key to successful organ donation. Best practices for organ donation have been identified by the consensus of two large critical care societies and OPOS's and should be employed in protocol development and in the verification of practice. Institutional commitment is critical to the success of organ donation protocols, and retention and recruitment of dedicated professionals to care for these potential donors. Ongoing training of the intensive care staff, the inclusion of donation as part of the end-of-life decision-making and commitment to the donation process with a multidisciplinary team approach to standardize donor management in the ICU will narrow the gap between the supply and demand for organ donation.

Key Points

- Aggressive protocolized clinical management of potential organ donors is recommended.
- Specialized personnel should identify and help manage the potential donor.
- A collaborative working relationship with the local OPO should be employed for protocol development.
- Organ donation is part of the end-of-life care, and a multidisciplinary investment is needed for the best outcomes.

References

1. United Network for Organ Sharing: Organ donation and transplantation. https://optn.transplant.hrsa.gov/converge/latestData/rptData.asp. Accessed 14 Jan 2016.
2. Kotloff RM, Blosser S, Fulda GJ, Malinoski D, Ahya VN, Angel L, Byrnes MC, DeVita MA, Grissom TE, Halpern SD, Nakagawa TA, Stock PG, Sudan DL, Wood KE, Anillo SJ, Bleck TP, Eidbo EE, Fowler RA, Glazier AK, Gries C, Hasz R, Herr D, Khan A, Landsberg D, Lebovitz DJ, Levine DJ, Mathur M, Naik P, Niemann CU, Nunley DR, O'Connor KJ, Pelletier SJ, Rahman O, Ranjan D, Salim A, Sawyer RG, Shafer T, Sonneti D, Spiro P, Valapour M, Vikraman-Sushama D, Whelan TP, Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations Donor Management Task Force. Management of the Potential Organ Donor in the ICU: Society of Critical Care Medicine/American College of Chest Physicians/Association of Organ Procurement Organizations consensus statement. Crit Care Med. 2015;43(6):1291–325.

Suggested Reading

Broderick AR, Manara A, Bramhall S, Cartmill M, Gardiner D, Neuberger J. A donation after circulatory death program has the potential to increase the number of donors after brain death. Crit Care Med. 2016;44(2):352–9.

Citerio G, Cypel M, Dobb GJ, Dominguez-Gil B, Frontera JA, Greer DM, Manara AR, Shemie SD, Smith M, Valenza F, Wijdicks EF. Organ donation in adults: a critical care perspective. Intensive Care Med. 2016;42:305–15.

DeVita MA, Brooks MM, Zawistowski C, et al. Donors after cardiac death: validation of identification criteria (DVIC) study for predictors of rapid death. Am J Transplant. 2008;8:432–41.

Escudero D, Valentín MO, Escalante JL, Sanmartín A, Perez-Basterrechea M, de Gea J, Martín M, Velasco J, Pont T, Masnou N, de la Calle B, Marcelo B, Lebrón M, Pérez JM, Burgos M, Gimeno R, Kot P, Yus S, Sancho I, Zabalegui A, Arroyo M, Miñambres E, Elizalde J, Montejo JC, Domínguez-Gil B, Matesanz R. Intensive care practices in brain death diagnosis and organ donation. Anaesthesia. 2015;70(10):1130–9.

Ortega-Deballon I, Hornby L, Shemie SD. Protocols for uncontrolled donation after circulatory death: a systematic review of international guidelines, practices and transplant outcomes. Crit Care. 2015;19:268.

Patel MS, Zatarain J, De La Cruz S, Sally MB, Ewing T, Crutchfield M, Enestvedt CK, Malinoski DJ. The impact of meeting donor management goals on the number of organs transplanted per expanded criteria donor: a prospective study from the UNOS Region 5 Donor Management Goals Workgroup. JAMA Surg. 2014;149(9):969–75.

Shah VR. Aggressive management of multiorgan donor. Transplant Proc. 2008;40(4):1087–90.

Wind J, van Mook WN, Dhanani S, van Heurn EW. Determination of death after circulatory arrest by intensive care physicians: a survey of current practice in the Netherlands. J Crit Care. 2016;31(1):2–6.

Interaction with Family and Friends in Neurosurgical Critical Care

100

Amy E. Guthrie, Robert Hugo Richardson, and Mary Denise Smith

Overview

In their clinical practice in the intensive care unit, clinicians constantly need to communicate with patients, families, and nonfamily members chosen as care partners. For the sake of inclusion, "care partner" will be used to refer to family and nonfamily members providing support and presence for the patient. Care partners are considered a unit of care and may consist of many people representing a variety of connections with the patient. Communication expertise is especially important when the patient is critically ill in an intensive care unit (ICU), where information exchange occurs more commonly with care partners. Communication challenges in the ICU are greater because critically ill patients frequently are unable to speak for themselves and the clinician is dependent on surrogate decision-makers to understand the patient's goals and values regarding life and health-care. Evidence shows that skillful communication with care partners contributes to higher patient satisfaction while also improving efficiency of the clinicians' time and efficacy of treatment.

Clinician communication is crucial in developing a care partnership to improve outcomes for patients and families in the ICU. Communication patterns in the ICU consist of two major processes:

1. Informal – day-to-day contact to answer questions and report changes in the patient's condition
2. Formal – planned conferences attended by care partners, medical specialties, and an interprofessional health-care team

Health-care providers can maximize information exchange and consensus building if a trusting relationship is built early in the patient's hospitalization and care partners feel supported and valued.

Implications for the Neurosurgical Patient

Building Rapport

There are many aspects to the care of the critically ill patient that can work to challenge the traditional clinician–patient relationship. Time pressures, lack of continuity, and technology all add to the difficulty of relationship building. Because the ICU team often meets the Care Partners for the first time as a result of the patient's severe illness, there is little time to establish the trust necessary to make major treatment decisions. Clinicians should work to initiate contact early in the hospitalization by making an effort to meet them on the day of admission and remaining available for daily informal contact. Providing a private meeting place can help the health-care team in building trust; however, many informal contacts occur at the bedside and are most effective using the five-step approach identified by the mnemonic VALUE.

- Value and seek the care partner's input.
- Acknowledge the care partner's emotional needs.
- Listen actively to what the care partner is saying.
- Understand by asking questions about the patient.
- Elicit questions from care partners.

Information can best be elicited by asking open-ended questions seeking what is important to the patient and how care partners have been affected by the current condition of their loved one.

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Initially, focus on common goals, and discuss routine aspects of care before introducing more emotionally charged information. Listen for the care partner's perspective on the patient's illness and goals of care, allowing them to do most of the talking during each meeting time. With each contact, continue to emphasize mutual goals and values.

As interaction increases, acknowledge the stress of having a loved one in the hospital, and assess their readiness to come to terms with the patient's illness. Utilize chaplains, social workers, and palliative care specialists to meet the additional needs of the care partners.

Finally, build consensus by identifying points of agreement with broad goals and specific therapies. Building consensus may require multiple touch points with care partners establishing continuous and open communication with easy access to the health-care team.

Communication

There is evidence that care partners of the critically ill patients who survive the ICU hospitalization are less satisfied with communication from ICU clinicians than care partners of patients who do not survive. Regardless of outcome, skillful communication can reduce emotional stress caused by the uncertainty of critical illness. In addition, care partners report clinician communication skills as being equally important as clinical expertise.

There are many opportunities for informal clinician–care partner contacts in the ICU. However, a more formal meeting known as a Care Partner Conference conducted within 72 h of admission has been associated with reduced length of ICU stay and a favorable experience. Improved patient and care partner outcomes have been associated with consistent communication by all health-care members and following Care Partner Conference guidelines listed in Table 100.1.

Table 100.1 Care Partner Conference

Preparation
Identify all members planning to attend the meeting
Capacity fluctuates, consider including the patient in the meeting when appropriate
"Preconference"/provider conference
Coordinate health-care team
Discuss goals of meeting with health-care team
Establish a unified medical opinion among health-care providers participating in the meeting to provide a consistent message
Identify a meeting leader among the health-care team
Arrange a private, quiet location with seating for all
Limit distractions: plan for enough time to reduce interruptions
Turn off pagers if possible
Open the meeting
Introduce all attendees
Establish and recognize appointed surrogate decision-maker or next of kin while addressing the importance of each member's input
Assess perception in the role of decision-maker along with influences affecting that role
Establish and communicate overall goal of the meeting
Allow for flexibility to change the original goal(s) for the meeting
Inform the care partners that the meeting will allow them to speak for the patient, as the patient would communicate for him/herself
Spend more time listening and less time talking
Elicit understanding
Inquire about the care partner's understanding of the patient's illness and current course of treatment
Review medical information
Diagnosis and prognosis
Current treatment plan
Recommended changes to treatment plan
Elicit values and goals
Multiple perspectives may be represented
Understand ethnic and cultural influences on communication styles, medical treatment decisions, and end-of-life care
Explore the care partner's knowledge of the patient's perspective on health and illness
What would be acceptable outcomes for the patient?
Explore the care partner's perspective on health and illness
Assist care partners to compare and contrast the perspectives if necessary
Discuss decisions that need to be made
Establish a common understanding of the medical issues and probable outcomes
Be clear that decisions rely on an exchange of medical information and their understanding of the patient's values and desires for medical care
Using substituted judgment by involving all individuals familiar with the patient's wishes
Seek consensus
Close the meeting
Offer a brief summary of what was discussed
Ask for final questions
Express appreciation for the team approach to provide a plan closest to what the patient would have requested
Acknowledge the difficulty of living with uncertainty
Make a clear follow-up plan, including plans for the next meeting and how to contact the health-care team
Follow-up
Document the meeting in the medical record. Record a summary of the information exchange, observations of all attendees, and plan
Follow up with care partners to reassess information processing and understanding
Arrange for emotional, spiritual, and social service team members to provide additional support opportunities

Concerns and Risks

Care Partners as Surrogate Decision-Makers

There are significant consequences that individuals may experience when they are in the role of surrogate decision-maker either through appointment or through recognized hierarchies. Surrogates can experience increased stress associated with decision-making, guilt about the decisions made, or doubting if they made the correct decision. The impact of these consequences can last for months and even years for at least a third of surrogates based on a systematic review of the literature.

Building consensus, while making treatment decisions for the incapacitated patient, represents an ethical challenge in clinical care. High-quality shared decision-making is a process with many important components and requires more than a simple agreement to allow care partners to be involved in the process.

In a truly shared decision, physicians and care partners mutually influence the other, each potentially ending up with a different perspective and a different understanding than either would have reached alone. Shared decision-making promotes establishment of an environment of mutual influence and helps to eliminate power imbalances.

Shared decision-making relies on the standard of substituted judgment to make treatment decisions that the patient would have made if he or she were capacitated. This standard extends autonomy allowing the patient's preferences and values to guide medical care during times of incapacity.

- Is there a recent advance directive document available? The written directives may have been completed at a time of health. It is important to share information regarding the patient's change in health, expected outcomes, and prognosis.
- Can the care partners recall previous conversations when the patient clearly stated treatment preferences in similar situations and similar expected outcomes?
- Did the patient ever express an opinion regarding life-sustaining medical treatment of other loved ones or controversial medical cases in the news?

When sufficient evidence is lacking to identify the patient's preferences and values, health-care providers can encourage care partners to use the "Best Interests" standard, which directs them to make decisions based on what they perceive to be in the patient's best interests. Questions to address when exploring Best Interest:

- Is there evidence the current treatment is causing the patient to suffer?
- Do the benefits of the treatment outweigh the burdens?

If consensus is not easily attained, points of conflict can be renegotiated by exploring the values and influences of the individuals in disagreement. If needed, discussions can be deferred to a later time; timed treatment trials can be offered; and if all else fails, it is acceptable to agree to disagree.

The stress, sorrow, and uncertainty that care partner's experience while caring for a loved one in a critical condition can cloud accurate accounts of previous conversations and influence their evaluation of the patient's best interests. Care partners of patients who are critically ill are at risk for developing multiple stress-related experiences or conditions. Awareness of this has increased the focus on support in the intensive care units. The society of critical care medicine describes the psychological conditions that care partners experience as post-intensive care syndrome. Conditions that care partners may experience include anxiety, depression, complicated grief, post-traumatic stress disorder, and acute stress disorder. Stress levels are at risk for being higher if the patient died, if care partners were present at the time of death, if care partners believed the patient was at risk for dying, and if illness was either unexpected or illness was greater than 5 years in duration.

For that reason, it is important to acknowledge the physical, emotional, spiritual, and financial support of the as complete care for the ICU patient. Since decision-making in the ICU is more frequently a process, and not an event, an interprofessional team is extremely helpful. Interprofessional team members should represent medicine, nursing, social services, chaplaincy, and ancillary therapies. Key domains of care for patient and care partners in the intensive care include management of physical, psychological, and spiritual distress patients, and care partners are experiencing communication and discussions with patient and/or care partners of goals of care taking into consideration the patient's medical condition, prognosis and values, aligning treatments with patient preferences, and planning for care transitions. Palliative Care specialists are clinicians representing multiple disciplines/professions with advanced training in communication skills and grief support that can assist care partners as they understand the meaning and realize the impact of the medical information received. Recommendations to decrease the incidence or severity of post-intensive care syndrome include staff educated on assessing the needs of care partners and incorporating those needs into the plan of care, providing education about the intensive care environment and what to expect, providing frequent updates in language of patient or care partners, assessing preferred decision-making models/style, and involving care partners in the care of patients as appropriate and consistent with their comfort level – i.e., massage, passive range of motion, applying lotion, and lip balm.

Grief Support

There is evidence that caregivers experience loss through emotional strain, financial hardship, and physical health risks even if the patient is expected to survive the ICU stay. When care partners are expected to speak for the patient, they also struggle with internal emotional tension between their own emotional reaction to the experience and the desire to make the right decision for the patient. That tension may also originate from a difference of values and health-care goals from those of the patient. Ethical and legal models recognizing the surrogate decision-maker as only a spokesperson overlook the emotional needs of those care members and underestimate the influence that the fear of "giving up" on a loved one has on decision-making. Providing an interprofessional team with advanced skill in grief counseling can provide care partners with emotional support and a framework for future grief work. Sensitivity to how all will grieve the experience of the hospital stay and the patient's last days will incorporate individualized care, increase satisfaction with care, and establish a foundation of healing through the bereavement process.

Key Points

Cultivate a clinician–care partner relationship building practice by:

- Initiating contact upon admission to the unit
- Utilizing an interprofessional health-care team for additional support and continuity
- Organizing a Care Partner Conference within 72 h of admission to the unit and at regular intervals thereafter
- Planning to listen more and speaking less
- Acknowledging stressors using empathic statements
- Scheduling continuous and consistent communication
- Providing a route for easy access to team members familiar with the treatment plan

Suggested Reading

Abbott K, Sago J, Breen C, Abernethy A, Tulsky J. Families looking back: one year after discussion of withdrawal or withholding of life-sustaining support. Crit Care Med. 2001;29(1):197–201.

Azoulay E, Pochard F, Kentish-barnes N, et al. Risk of post-traumatic stress symptoms in family members of intensive care patients. Am J Respir Crit Care Med. 2005;171:987–94.

Curtis JR, White D. Practical guidance for evidence-based ICU family conferences. Chest. 2008;134:835–43.

Davidson JE, Jones C, Bienvenu OJ. Family response to critical illness: postintensive care syndrome-family. Crit Care Med. 2012;40:618–24.

Goldstein N, Back A, Morrison S. Titrating guidance: a model to guide physicians in assisting patients and family members who are facing complex decisions. Arch Intern Med. 2008;168(16):1733–9.

Haines KJ, Denehy L, Skinner EH, Warrillow S, Berney S. Psychosocial outcomes in informal caregivers of the critically ill: a systematic review. Crit Care Med. 2015;43:1112–20.

Hanson J. Shared decision-making: have we missed the obvious? Arch Intern Med. 2008;168(13):1368–70.

Maukisch L, Dugdale D, Dodson S, Epstein R. Relationship, communication, and efficiency in the medical encounter: creating a model from a literature review. Arch Intern Med. 2008;168(13):1387–95.

Quill T, Holloway R, Shah M, Caprio T, Storey P. Recommendations for conducting a family meeting when the patient is unable to participate. In: Quill T, Holloway R, Shah M, Caprio T, Storey P, editors. Primer of palliative care. 4th ed. Glenview: American Academy of Hospice and Palliative Medicine; 2004. p. 112–3.

Shalowitz D, Garrett-Mayer E, Wendler D. The accuracy of surrogate decision makers. Arch Intern Med. 2006;166:493–7.

Wendler D, Rid A. Systematic review: the effect on surrogates of making treatment decisions for others. Ann Intern Med. 2011;154:336–46.

White D, Braddock C, Bereknyei S, Curtis JR. Toward shared decision making at the end of life in intensive care units: opportunities for improvement. Arch Intern Med. 2007;167:461–7.

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https://doi.org/10.1007/978-3-030-17410-1