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Review Article

What Frequency of Ankle Pump Exercise is Optimal to Improve Lower Limb Hemodynamics? A Systematic Review and Network Meta-analysis

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SUMMARY

Purpose: Ankle pump exercises (APE) have been widely used in clinical practice. However, best practices for APE have not been established. Recognize the most effective frequency of APE for improving lower extremity hemodynamics and establish recommendations in clinical practice.
Methods: Therefore, a systematic review and network meta-analysis (NMA) was performed according to PRISMA-NMA. Six English databases (Pubmed, Medline, CINAHL, Embase, the Cochrane library and ProQuest) and four Chinese databases (CNKI, Wanfang, VIP and Sinomed) were searched. Randomized controlled trials (RCTs) and quasi-experimental studies investigating the effects of different frequencies of APE on lower limb hemodynamics published before July 2022 were included. The reference list was also searched. Seven studies (one RCTs and six quasi-experimental studies) were included in the systematic review and five studies (one RCTs and four quasi-experimental studies) were included in the NMA. The risk of bias was assessed using the Cochrane and Joanna Briggs Institute tools. The NMA was performed using the R software (version 4.2.1) and OpenBUGS (version 3.2.3).
Results: The results of the NMA showed that a frequency of every 3–4 s the most effective in improving lower extremity hemodynamics ($P = .85$), followed by every 1–2 s ($P = .81$), every 5–6 s ($P = .32$) and less than every 10 s ($P = .02$). Subgroup analysis failed to find a difference between healthy participants and those with unilateral total hip arthroplasty or fracture (MD = −0.23, 95% CI-5.92 to 4.61).
Conclusions: Consequencely, for adult patients, with or without lower extremity disease, a frequency of every 3–4 s can be recommended as the optimal frequency of APE in clinical care practice.
Registered number on PROSPERO: CRD42022349365.
https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=349365.

Introduction

Ankle pump exercise (APE), an exercise performed through plantar flexion and dorsiflexion of the ankle joint, promotes venous blood return to the lower extremities by contracting and relaxing the calf muscles [1,2] and is recommended as an effective method for preventing venous thromboembolism (VTE) [3–5]. In addition, APE improves calf muscle pump function and reduces venous stasis, which is beneficial in patients with chronic venous insufficiency (CVI) and venous leg ulcers (VLUs) [6,7]. However, the most effective frequency of APE has not been determined [8,9].

Traditional APE recommends holding plantarflexion and dorsiflexion for 10 s at a time, which corresponds to a frequency of 3 beats/min [8]. However, faster APE frequencies have recently been found to be more effective in accelerating blood flow velocity in the lower extremities, ranging from 6 to 100 beats/min [8–14]. Validating the most effective frequency for APE is difficult due to the

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wide range of frequencies and inconsistent results. There are no evidence-based studies to aid decision-making in clinical practice.

Traditional meta-analysis methods compare only two frequencies at a time, making it difficult to answer the question of which frequency is most effective [15]. Network meta-analysis (NMA), a technique that compares multiple treatments simultaneously in a single analysis by combining direct and indirect evidence [16], may be more appropriate for determining the best APE frequency from a variety of different frequencies.

Therefore, the objectives of this systematic review were to [1] recognize the most effective frequency of APE for improving lower extremity hemodynamics through an NMA and [2] establish recommendations for the frequency selection of APE in clinical care practice.

Methods

Registration

This systematic review and NMA is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-NMA) guidelines for extended reporting of NMAs [17]. The study protocol has been registered and updated on PROSPERO, an international systematic review prospective registry (ID: CRD42022349365).

Search strategy

Six English databases (Pubmed, Medline, CINAHL, Embase, the Cochrane library, and ProQuest) and four Chinese databases (CNKI, Wanfang, VIP, and SINOMED) were searched. The search strategy was established based on the PICOS tool: (P) population: adults (age $\geq$18 years) treated with APE; (I&C) interventions and comparators: different frequencies of APE; (O) outcomes: lower extremity hemodynamics; (S) studies: randomized controlled trials (RCTs) and quasi-experimental studies. For example, on Medline, search for “AB (ankle pump exercise or functional *training* or functional *exercise* or ankle motion or ankle plantarflexion or ankle valgus) and AB (frequency or number) and AB (lower extremity hemodynamics or blood flow rate or blood volume or venous blood return)". In addition to the database search, the reference lists of included studies were screened according to the inclusion criteria.

Inclusion criteria

RCTs and quasi-experimental studies conforming to the aforementioned PICOS, published by July 2022, written in English or Chinese, and peer-reviewed were included regardless of sample size. The frequency of APE was defined as any description that could indicate the number of APEs per minute or the interval between APEs. Low limb venous flow velocities, i.e., the velocity of blood in a specific vein, were used to measure lower limb hemodynamics and were assessed by a digital color Doppler ultrasound diagnostic system. For example, the time-averaged maximum flow velocity in the femoral vein is approximately 12.7 to 13.6 cm/s in the head-up position at rest [18,19].

Study selection

Two independent reviewers (X.W. and R.S.T.) screened the retrieved articles through Endnote X9 literature management software. Study selection consisted of three stages, evaluating articles in terms of title, abstract, and full text, respectively. Any disagreements were resolved through discussions between two reviewers or a third reviewer (B.H.L.). If necessary, a broader team meeting will be held to resolve disagreements.

Data extraction

A standardized data extraction form was used with two independent reviewers (X.W. & R.S.T.) to record data, including authors, year of publication, country, study design, study setting, sample size, population, intervention, measurements, funds, and differences in low limb venous flow velocity before and after APE.

Quality appraisal

Two independent reviewers (X.W. and R.S.T.) assessed the quality of eligible studies. For RCTs, the Cochrane Handbook version 5.2.0, which contains 13 items to assess the risk of bias (ROB), was used. The 13 items assessed performance bias, detection bias, attrition bias, and reporting bias, and assessed whether there were systematic differences in the care provided, outcome assessment, loss of participants between comparison groups, and the presence of selective reporting [20]. Trials were also categorized into three levels based on the presence of ROBs described in 13 items: high risk (five or more), moderate risk (three or four), and low risk (two or less). For quasi-experimental studies, the Joanna Briggs Institute (JBI) quality assessment tool, which consists of nine items, was used to assess ROB in multiple ways [21]. After discussion by the study team, studies that measured comparative outcomes in an inconsistent and unreliable manner were excluded.

Data analysis

Descriptive analyses included trials, characterized by different APE frequencies, and summarized the contribution to the overall evidence. Considering the similar and varying frequencies of APE, which can be supervised with a timer in order to facilitate in clinical practice, we classified APE into five frequencies (less than every 10 s, every 5–6 s, every 3–4 s, every 1–2 s, and greater than every 1 s) according to their intervals. Raw group data were combined into five frequencies, calculated from the mean, standard deviation (SD), and number of participants. To control for homogeneity, only studies that selected femoral vein velocity as an outcome were included in the NMA.

Meanwhile, the SEM was converted to SD by counting the number of participants. The Bayesian method was used as a statistical method for NMA [22], and it was performed by the “gemtc” package of R software (version 4.2.1) and OpenBUGS (version 3.2.3) [23]. Markov chain Monte Carlo (MCMC) simulation is a tool for Bayesian inference. In this study, we chose the consistency model and set the number of Markov chains to four with parameters set to n.adapt = 20,000, n.iter = 50,000, and thin = 1, which is the conventional setting for NMA [16]. Sensitivity analysis forest plots were examined for homogeneity analysis, while $I2 > 50\%$ was defined as having heterogeneity. Fixed-effects and random-effects models were selected based on I2 ($I2 < 50\%$: fixed-effects model, $I2 \geq 50\%$: random-effects model). The applicability of the NMA results was tested by nodal analysis as a consistency test with the NMA hypothesis to determine the selection of a consistent or inconsistent model.

The network plots show a direct comparison between the frequencies of APEs, while the edge thickness of the connected nodes implies the amount of data. MCMC simulations and convergence states are tested by trace and density plots, Gelman–Rubin statistical plots, and potential size reduction factors (PSRF).

Forest plots allow the graphical comparison of effect sizes by frequency of APE by NMA. The results are summarized as mean difference (MD) and 95% confidence interval (CI). Also, the surface under the cumulative ranking curve (SUCRA) was used to prioritize the different frequencies of APE. Subgroup analysis was used according to whether the participants were healthy or not. If 10 or more studies were included in the NMA, funnel plots were generated to assess publication bias.

Results

Literature selection

A total of 805 studies were initially identified. However, 451 studies were removed due to duplication, three studies were included from other sources, and 454 studies proceeded to title and abstract review. Following title and abstract review, nine studies proceeded to full text review. One study was excluded because it did not meet the inclusion criteria, and one study was excluded because we were unable to find the full text. Finally, seven studies were included [8–14]. The detailed process is shown in Figure 1.

Characteristic of included studies

The characteristics of the included studies are shown in Table 1. These studies were conducted in China (n = 4) and Japan (n = 3). Two studies recruited only men, while one study recruited only women, and the other studies recruited participants of all genders. The majority of included studies were conducted at universities or research institutions (71.4%, 5/7), and two studies were conducted in hospitals (28.6%). A total of 456 participants were included, ranging from 10 to 307, with a median sample size of 29 (IQR 10 to 63). The included participants included 337 healthy participants, 92 patients with unilateral total hip arthroplasty, and 30 patients with fractures. We combined 12 frequencies into the 5 previously described frequencies (Appendix II). A total of 411 participants were included less than every 10 s, 411 participants were included every 5–6 s, 90 participants were included every 3–4 s, 138 participants were included every 1–2 s, and 35 participants were included every 1 s or more. All studies reported outcomes for low limb venous blood flow velocity. One study reported the percentage of calf muscle hyperemia after APE, and six studies reported the velocity of lower extremity veins. Four studies reported blood flow velocity in one lower extremity vein, one study reported two lower extremity veins, while one study reported three lower extremity veins. Also, five studies reported on the velocity of blood flow in the common femoral vein, two studies reported on the velocity of blood flow in the popliteal vein, one study reported on the velocity of blood flow in the deep femoral vein, and one study reported on the velocity of blood flow in the external iliac vein, with three studies selecting the peak velocity of blood flow as the outcome and three studies selecting the average velocity of blood flow. The intervention time of APE ranged from 1 min to 5 min. A total of 12 different frequencies of APE were compared (Appendix I).

Risk of bias assessment

One RCT and six quasi-experimental studies were included. The ROB in the RCT was low in all domains except allocation bias, which was assessed as high. In the quasi-experimental study, the ROB was high for participant homogeneity and complete follow-up, while the other domains were assessed as low risk. Full details on the ROB assessment are reported in Appendix III.

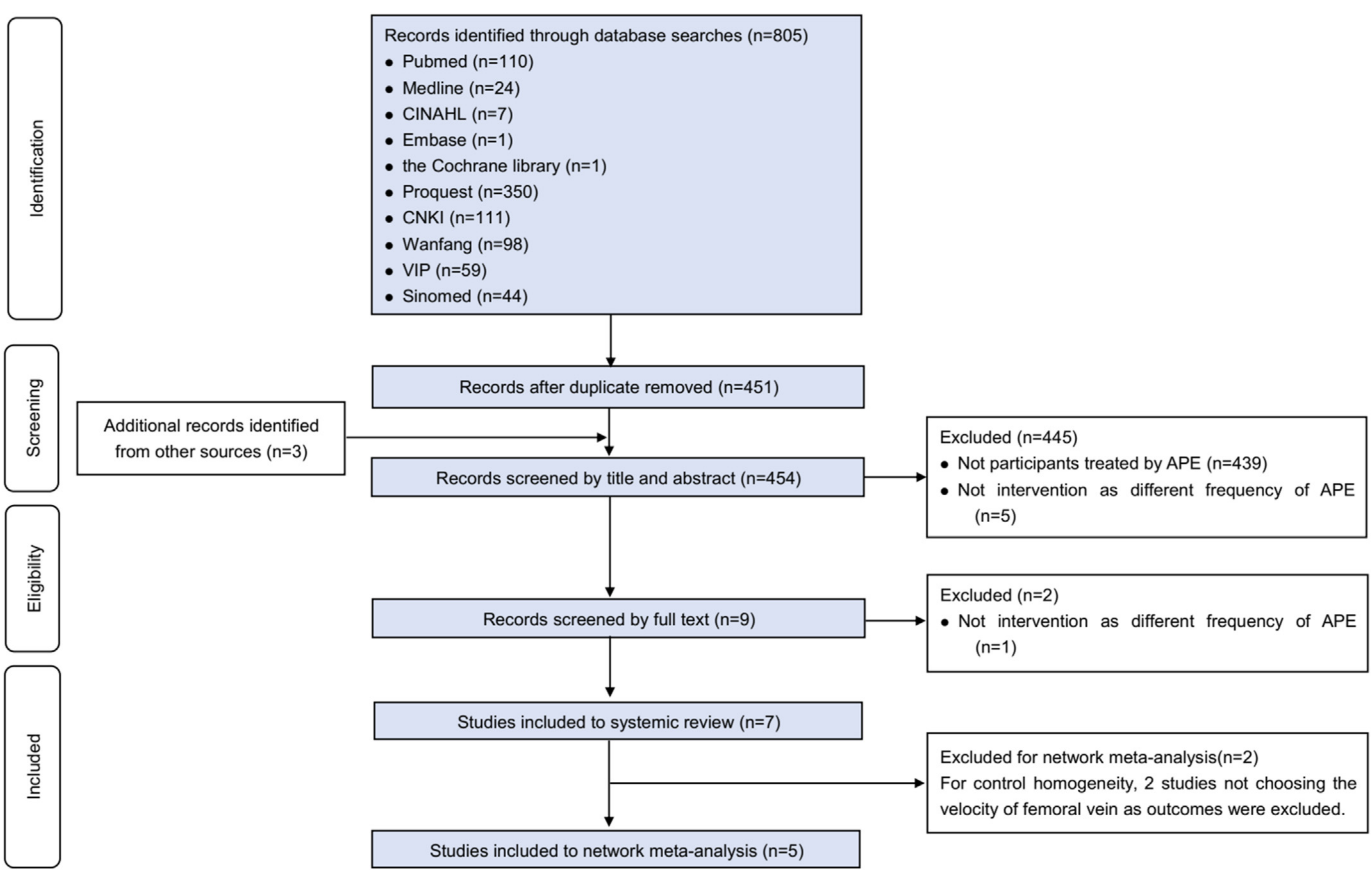

Figure 1. PRISMA-NMA Flow Chart.

Table 1 *Characteristics of Included Studies.*

Studies	Country	Study design	Research setting	N	Populations	Interventions	Original measurement mean (SD/SEM)	Post-combination frequencies Δ mean (SD)	Fund
Kagaya et al., 1991	Japan	Quasi-experimental study	Research Institute of Physical Fitness	6	Physically active women aged 21–22 years	Extend the ankle joint to 100°, then relaxed to return it to 90°, at frequencies of 20, 40, 60, 80, and 100 contractions/min	Post-exercise hyperemia of calf muscle 20 times/min:43.9 ± 5.3(SEM)% 40 times/min:44.3 ± 5.8 (SEM)% 60 times/min:53.6 ± 3.8 (SEM)% 80 times/min:47.4 ± 5.9 (SEM)% 100 times/min:60.9 ± 4.3 (SEM)%	Once every 3–4 s: 43.9 ± 12.98% Once every 1–2 s: 48.95 ± 12.38% More than once every 1 s: 54.15 ± 13.96%[s]	Not mentioned
Toya et al., 2016	Japan	Quasi-experimental study	University	10	Men without a history of cardiovascular diseases	Repeated dorsiflexion and plantarflexion with different frequencies: 15 times/min, 30 times/min, and 60 times/min.	Peak systolic velocity in the common femoral vein Baseline: 19.9 ± 1.9 cm/s 4 s rest exercise: 72.1 ± 10.4(SD)cm/s 2 s rest exercise: 61.0 ± 15.7(SD)cm/s no rest exercise: 73.7 ± 13.5(SD)cm/s	Once every 3–4 s: 52.2 ± 3.34 cm/s Once every 1–2 s: 47.45 ± 4.99 cm/s	Not mentioned
Nakayama et al.,2016	Japan	Quasi-experimental study	Rehabilitation department of a single private hospital.	29	Patients with unilateral total hip arthroplasty	Three different frequencies of active ankle movement: 40, 60, and 80 contractions per minute.	Mean velocity of blood flow in the profunda femoris Baseline: 11.9 ± 5.2(SD)cm/s 40 times/min: 20.2 ± 9.2(SD) cm/s 60 times/min: 29.4 ± 14.4(SD) cm/s 80 times/min: 26.0 ± 11.5(SD) cm/s	Once every 1–2 s: 12.90 ± 2.57 cm/s More than once every 1 s: 14.1 ± 2.34 cm/s[a]	None
Li et al., 2020	China	Quasi-experimental study	Third Hospital of Hebei Medical University	30	Patients with non-lower limb fracture/ patients with limb fracture	Ankle pump exercise with different frequencies: 6 times/min, 10 times/min, 30 times/min, and 60 times/min.	Time-averaged mean velocity (TAMV) of the common femoral venous blood flow patients with non-lower limb fracture: Baseline: 19.82 ± 3.86(SD)cm/s 6 times/min: 34.84 ± 8.30(SD) cm/s 10 times/min: 36.03 ± 9.60(SD) cm/s 30 times/min: 43.15 ± 9.12(SD) cm/s 60 times/min: 52.36 ± 11.69(SD)cm/s Patients with lower limb fracture: Baseline: 16.98 ± 3.01(SD)cm/s 6 times/min: 22.20 ± 4.96(SD) cm/s 10 times/min: 24.01 ± 5.78(SD) cm/s 30 times/min: 29.20 ± 7.05(SD) cm/s 60 times/min: 35.75 ± 9.28(SD) cm/s	Patients with non-lower limb fracture: Baseline: 19.82 ± 3.86 cm/s Less than once every 10 s: 13.96 ± 1.75 cm/s Once every 5–6 s: 17.24 ± 1.73 cm/s Once every 1–2 s: 28.18 ± 2.16 cm/s Patients with lower limb fracture: Baseline: 16.98 ± 3.01 cm/s Less than once every 10 s: 5.22 ± 1.06 cm/s Once every 5–6 s: 7.03 ± 1.19 cm/s Once every 1–2 s: 15.50 ± 1.70 cm/s	Yes
Zhao Huanli et al., 2020	China	Quasi-experimental study	Fourth Clinical Medical College of Yangzhou University	63	Patients after unilateral total hip arthroplasty	Maximum plantar flexion and dorsiflexion of the ankle with different frequencies: 6 times/min, 12 times/	Peak flow velocity of femoral vein of lower extremity Baseline: 29.17 ± 3.02(SD)cm/s 6 times/min: 36.20 ± 4.68(SD) cm/s	Less than once every 10 s: 7.03 ± 0.64 cm/s Once every 5–6 s: 10.05 ± 0.78 cm/s Once every 3–4 s:	Yes

						min, 15 times/min, 20 times/min, 30 times/ min, and 60 times/min.	12 times/min: 39.22 ± 5.44(SD) cm/s 15 times/min: 42.14 ± 6.14(SD) cm/s 20 times/min: 48.93 ± 6.31(SD) cm/s 30 times/min: 52.59 ± 6.79(SD) cm/s 60 times/min: 34.71 ± 5.73(SD) cm/s	16.37 ± 0.97 cm/s Once every 1–2 s: 14.48 ± 1.39 cm/s	
Zhou Shanshan et al., 2020	China	Quasi-experimental study	First Hospital of Nanjing Medical University	11	Healthy men	Ankle pump exercise with different frequencies: 5 times/ min, 10 times/min, and 15 times/min.	Peak flow velocity of femoral vein Baseline: 33.55 ± 5.67 (SD)cm/s 5 times/min: 45.45 ± 4.95(SD) cm/s 10 times/min: 52.55 ± 4.08(SD) cm/s 15 times/min: 56.09 ± 7.66(SD) cm/s Peak flow velocity of popliteal vein Baseline: 27.36 ± 5.46(SD)cm/s 5 times/min: 31.82 ± 4.90(SD) cm/s 10 times/min: 41.64 ± 5.67(SD) cm/s 15 times/min: 42.55 ± 8.30(SD) cm/s	Less than once every 10 s: 12.54 ± 2.07 cm/s Once every 5–6 s: 19.00 ± 2.11 cm/s Once every 3–4 s: 21.73 ± 3.25 cm/s	Yes
Li et al., 2022	China	RCT	Hospital	307	Healthy adults	Ankle pump exercise with different frequencies: 3 times/ min and 30 times/min.	Mean velocity of external iliac vein: Baseline: 21.36 ± 8.13(SD)cm/s 3 times/min: 25.49 ± 9.21(SD) cm/s 15 times/min: 25.98 ± 8.96(SD) cm/s Mean velocity of femoral vein: Baseline: 16.21 ± 6.56(SD)cm/s 3 times/min: 19.18 ± 6.96(SD) cm/s 15 times/min: 18.98 ± 6.63(SD) cm/s Mean velocity of popliteal vein: Baseline: 13.06 ± 5.02(SD)cm/s 3 times/min: 15.12 ± 5.76(SD) cm/s 15times/min: 15.12 ± 5.27(SD) cm/s	Less than once every 10 s: 2.97 ± 0.55 cm/s Once every 3–4 s: 2.77 ± 0.53 cm/s	Yes

Note. SD = standard deviation; SEM = standard error of mean.
[a] It was excluded for network meta-analysis.

Network meta-analysis for lower limb hemodynamics

Five studies with a combined total of 421 participants measured the velocity of the femoral vein (Table 1). In the absence of direct and indirect comparisons between more than once per second and other frequencies were excluded in the NMA. Figure 2 shows NMA plots examining the effect of four different frequencies of APE.

Frequencies of once every 3–4 s and once every 1–2 s were found to be more effective compared to frequencies of less than once every 10 s (MD = 10.00, 95% CI 5.40–15.00; MD = 9.90, 95% CI 5.70–14.00). The frequencies of once every 3–4 s and once every 1–2 s were also found to be more effective compared to once every 5–6 s (MD = 7.30, 95% CI 2.60–12.00; MD = 7.00, 95% CI 2.80–11.00) (Figure 3), with the same results. No other significant differences in lower extremity hemodynamics could be found among the different frequencies of APE.

Considering direct and indirect comparisons, a frequency of every 3–4 s had the best effect on improving lower extremity hemodynamics (p score = .85). Detailed results for APE frequency prioritization are presented in Table 2. In addition, subgroup analysis failed to find a difference between healthy participants and those with unilateral total hip arthroplasty or fracture (MD = −0.23, 95% CI −5.92 to 4.61), while the difference between studies conducted in China and Japan was also not significant (MD = 14.87, 95% CI −69.55 to 105.90).

The results of the homogeneity analysis showed that heterogeneity was clearly present (Appendix IV). The results of the nodal analysis confirm that there is no inconsistency in the model ($p > .050$) (Appendix V). The trace plots, density plots, and Gelman–Rubin statistical plots showed that MCMC simulations and convergence were in good condition, while PSRF converged to 1 (Appendices VI–VII). Also, publication bias was not assessed because fewer than 10 studies were included.

Discussion

To confirm the most effective frequency of APE and establish evidence-based recommendations for clinical practice, an NMA was conducted. A literature search identified 805 studies, and after removing duplicates, applying inclusion criteria, and completing a critical appraisal, seven studies were included for analysis. After direct and indirect comparisons of the NMA, evidence from different frequencies of APE was integrated, and the most effective frequency of the NMA was identified.

As an effective exercise to improve lower extremity hemodynamics [5], APE is popular in clinical care practice in patients lying in bed to prevent thrombosis [3,4]. However, although some studies have focused on the frequency selection of APE, there is no consensus on the frequency of APE. Therefore, there is a need to explore the most effective frequency of APE to guide clinical practice and improve the clinical outcomes of APE.

The results of the NMA showed that a frequency of every 3–4 s had the best effect on improving lower extremity hemodynamics, meaning that a frequency of every 3–4 s performed better than a frequency of every 1–2 s. This is quite different from previous studies, which found that faster APE performed better for improving lower extremity hemodynamics [11,13]. This may be because a single contraction of normal calf muscles can expel 60–90 ml of blood [24], whereas faster frequency APE can accomplish more contractions at the same time. Therefore, faster frequency APE can expel more blood at the same time. However, slower frequency of APE can increase the contraction force of calf muscles, which can promote more efficient venous blood return [11]. Thus, Toya et al found that a frequency of once every 4 s had a similar effect on lower limb hemodynamics as exercise without rest [9].

Our findings provide evidence-based recommendations for the frequency selection of APE in clinical practice, and patients will achieve the best clinical outcomes with APE at a frequency of every 3–4 s. Meanwhile, previous studies have found that APE every 3–4 s at 15–20 beats per minute has less post-exercise fatigue comparing to 60 beats per minute and 3 beats per minute [8,11], suggesting that APE every 3–4 s is clinically feasible and easily adhered to.

However, our study still contains some limitations. First, most of the included studies were quasi-experimental studies, and all participants in these studies experienced all sets of different frequencies [8–14]. Although the effect of APE on lower extremity hemodynamics is transient and participants experiencing multiple

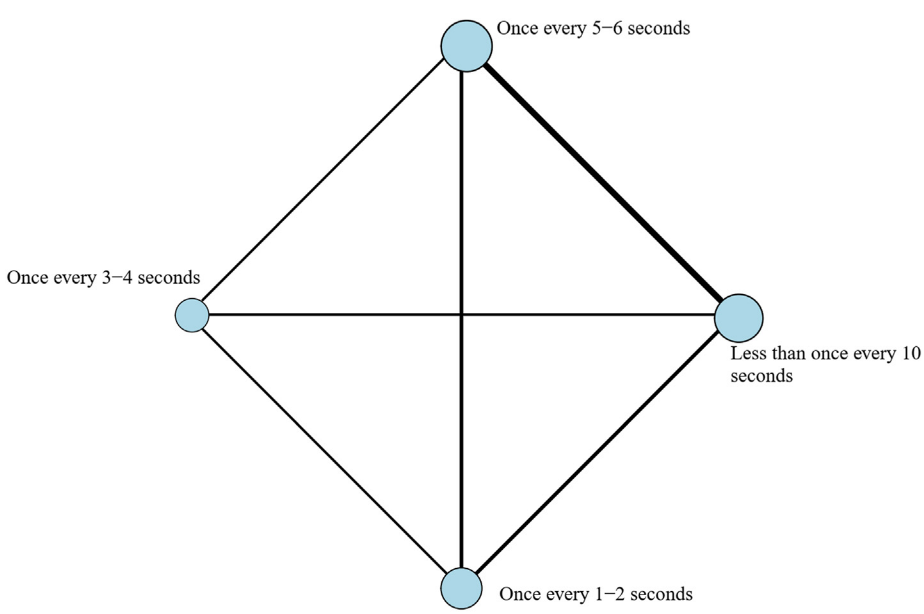

Figure 2. Network Meta-Analysis Maps of the Studies Examining the Effect of Five Different Frequencies of APE.
Note. The size of the nodes was related to the frequency of APEs that included participants, and the thickness of the lines was related to the number of studies for that comparison.

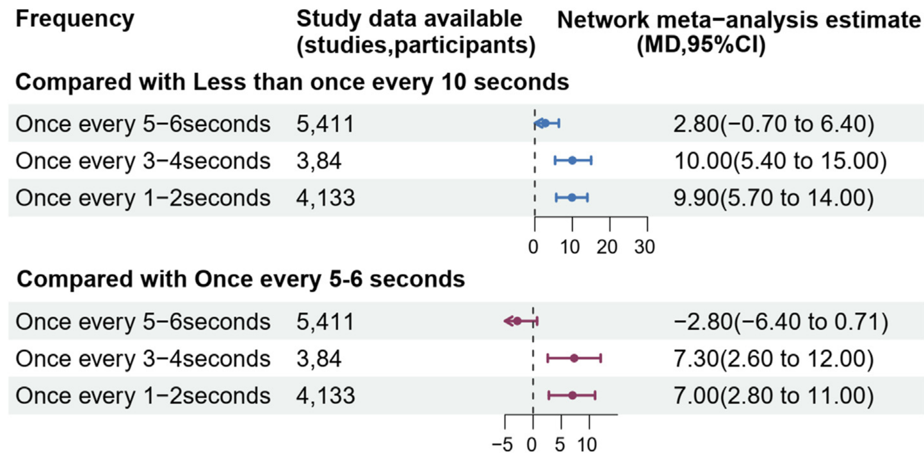

Figure 3. Summary Network Meta-Analysis Results for Each Ape Frequency Comparison.
Note. MD = mean difference; CI = confidence interval.

Table 2 *Ranking of Frequencies of APE in Order of Effectiveness.*

Frequency of APE	*p* score	Ranking
Less than once every 10 s	.02	4
Once every 5–6 s	.32	3
Once every 3–4 s	.85	1
Once every 1–2 s	.81	2

Note. APE = ankle pump exercise.

frequencies of APE at different times do not lead to inaccurate results, more RCTs are still needed. Moreover, all included studies were conducted in Asia, and there is a lack of data from other continents. We also searched Chinese local data, while the lack of local data of other countries. Third, the sample size of the included studies was limited. With the exception of one study with 307 participants, the number of participants in the other studies ranged from 6 to 63, which may increase the risk of false positive results in primary studies.

Conclusion

In this study, we provided evidenced-based recommendations for the clinical practice and standardization of APE through the NMA. APE every 3–4 s at 15–20 beats per minute is most effective in improving lower extremity hemodynamics with less post-exercise fatigue and should be recommended for widespread implementation in clinical practice.

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None.

Conflict of interest

The authors declare that they have no conflict of interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.03.001.

References

1. McNally MA, Cooke EA, Mollan RA. The effect of active movement of the foot on venous blood flow after total hip replacement. J Bone Jt Surg Am Vol. 1997;79(8):1198–201. Epub 1997/08/01. https://doi.org/10.2106/00004623-199708000-00012. PubMed PMID: 9278080.
2. Kwon OY, Jung DY, Kim Y, Cho SH, Yi CH. Effects of ankle exercise combined with deep breathing on blood flow velocity in the femoral vein. Aust J Physiother. 2003;49(4):253–8. Epub 2003/11/25. https://doi.org/10.1016/s0004-9514(14)60141-0. PubMed PMID: 14632624.
3. JCS. Guidelines for the diagnosis, treatment and prevention of pulmonary thromboembolism and deep vein thrombosis (JCS 2009). Circ J Off J Jpn Circ Soc. 2011;75(5):1258–81. Epub 2011/03/29. https://doi.org/10.1253/circj.cj-88-0010. PubMed PMID: 21441695.
4. Kehl-Pruett W. Deep vein thrombosis in hospitalized patients: a review of evidence-based guidelines for prevention. Dimensions of critical care nursing. DCCN. 2006;25(2):53–9. quiz 60-1. Epub 2006/03/23. https://doi.org/10.1097/00003465-200603000-00001. PubMed PMID: 16552270
5. Pi H, Ku H, Zhao T, Wang J, Fu Y. Influence of ankle active dorsiflexion movement guided by Inspiration on the venous return from the lower limbs: a prospective study. J Nurs Res. 2018;26(2):123–9. Epub 2017/09/01. https://doi.org/10.1097/jnr.0000000000000214. PubMed PMID: 28858972.
6. Orr L, Klement KA, McCrossin L, O'Sullivan Drombolis D, Houghton PE, Spaulding S, et al. A systematic review and meta-analysis of exercise intervention for the treatment of calf muscle pump Impairment in Individuals with chronic venous insufficiency. Ostomy/Wound Manag. 2017;63(8):30–43. Epub 2017/09/06. https://doi.org/10.25270/owm.2017.08.3043. PubMed PMID: 28873064.
7. O'Brien J, Finlayson K, Kerr G, Edwards H. Evaluating the effectiveness of a self-management exercise intervention on wound healing, functional ability and health-related quality of life outcomes in adults with venous leg ulcers: a randomised controlled trial. Int Wound J. 2017;14(1):130–7. Epub 2016/01/29. https://doi.org/10.1111/iwj.12571. PubMed PMID: 26817648; PubMed Central PMCID: PMCPMC7949716.
8. Li H, Zhang W, Lu Q, Wang J, Zhi Y, Zhang L, et al. Which frequency of ankle pump exercise should be chosen for the prophylaxis of deep vein thrombosis? Inquiry J Med Care Organ Provis Financ. 2022;59:469580221105989. https://doi.org/10.1177/00469580221105989. PubMed PMID: 35658650.
9. Toya K, Sasano K, Takasoh T, Nishimoto T, Fujimoto Y, Kusumoto Y, et al. Ankle positions and exercise intervals effect on the blood flow velocity in the common femoral vein during ankle pumping exercises. J Phys Ther Sci. 2016;28(2):685–8. https://doi.org/10.1589/jpts.28.685. PubMed PMID: 27065564.
10. Kagaya A. Reduced exercise hyperaemia in calf muscles working at high contraction frequencies. Eur J Appl Physiol Occup Physiol. 1992;64(4):298–303. https://doi.org/10.1007/BF00636215
11. Li T, Yang S, Hu F, Geng Q, Lu Q, Ding J. Effects of ankle pump exercise frequency on venous hemodynamics of the lower limb. Clin Hemorheol Microcirc. 2020;76(1):111–20. https://doi.org/10.3233/CH-200860. PubMed PMID: 2413995744; 32538827.
12. Nakayama T, Tsukada S, Hiyama T, Yamada T, Hirasawa N. Impact of active ankle movement frequency on velocity of lower limb venous flow following total hip arthroplasty. Adv Orthop. 2016;2016:7683272. Epub 2016/12/22. https://doi.org/10.1155/2016/7683272. PubMed PMID: 27999685; PubMed Central PMCID: PMCPMC5141543 or funding from any commercial party related directly or indirectly to the subject of this article.
13. Huanli Z, Aimei Z, Ya H, Lin C, Weihong F. Effects of different exercise duration of ankle joint active flexion and extension exercise on lower limb venous blood flow velocity after total hip arthroplasty. Nurs Integr Tradit Chin West Med. 2020;6(5):111–3. https://doi.org/10.11997/nitcwm.202005024

14. Shanshan Z, Qian M, Suyu M, Haiying J, Xiaodan B. Effect of ankle pump on venous blood flow and fibrinolysis of lower extremity. Mod Med J. 2020;48(12):1622–5. https://doi.org/10.3969/j.issn.1671-7562.2020.12.027. Chinese.
15. Hayden JA, Ellis J, Ogilvie R, Stewart SA, Bagg MK, Stanojevic S, et al. Some types of exercise are more effective than others in people with chronic low back pain: a network meta-analysis. J Physiother. 2021;67(4):252–62. Epub 2021/09/21. https://doi.org/10.1016/j.jphys.2021.09.004. PubMed PMID: 34538747.
16. Rouse B, Chaimani A, Li T. Network meta-analysis: an introduction for clinicians. Intern Emerg Med. 2017;12(1):103–11. Epub 2016/12/04. https://doi.org/10.1007/s11739-016-1583-7. PubMed PMID: 27913917; PubMed Central PMCID: PMCPMC5247317.
17. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann Intern Med. 2015;162(11):777–84. Epub 2015/06/02. https://doi.org/10.7326/m14-2385. PubMed PMID: 26030634.
18. Sakai K, Takahira N, Tsuda K, Akamine A. Effects of intermittent pneumatic compression on femoral vein peak venous velocity during active ankle exercise. J Orthop Surg. 2021;29(1):2309499021998105. https://doi.org/10.1177/2309499021998105. PubMed PMID: 33641535.
19. Toya K, Takahashi T, Fujimoto Y, Nishimoto T, Takasoh T, Sasano K, et al. Effect of elastic stockings and ankle positions on the blood velocity in the common femoral vein. J Phys Ther Sci. 2016;28(9):2608–10. Epub 2016/11/02. https://doi.org/10.1589/jpts.28.2608. PubMed PMID: 27799704; PubMed Central PMCID: PMCPMC5080186.
20. library C. Cochrane handbook for systematic reviews of interventions. 2011 https://training.cochrane.org/handbook [cited 2022 08/18].
21. Tufanaru CMZ, Aromataris E, Campbell J, Hopp L. In: Aromataris E, Munn Z, editors. Chapter 3. Systematic reviews of effectiveness. JBI Manual for Evidence Synthesis; 2020 https://jbi.global/critical-appraisal-tools [cited 2022 08/18].
22. Shim SR, Kim SJ, Lee J, Rücker G. Network meta-analysis: application and practice using R software. Epidemiol Health. 2019;41:e2019013. Epub 2019/04/20. https://doi.org/10.4178/epih.e2019013. PubMed PMID: 30999733; PubMed Central PMCID: PMCPMC6635665.
23. Van Valkenhoef G, Kuiper J. gemtc: network meta-analysis using Bayesian methods. R package version 1.0-1. https://doi.org/10.1002/jrsm.1167.
24. Ludbrook J. The musculovenous pumps of the human lower limb. Am Heart J. 1966;71(5):635–41. Epub 1966/05/01. https://doi.org/10.1016/0002-8703(66)90313-9. PubMed PMID: 5935855.

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Review Article

What Frequency of Ankle Pump Exercise is Optimal to Improve Lower Limb Hemodynamics? A Systematic Review and Network Meta-analysis

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SUMMARY

Purpose: Ankle pump exercises (APE) have been widely used in clinical practice. However, best practices for APE have not been established. Recognize the most effective frequency of APE for improving lower extremity hemodynamics and establish recommendations in clinical practice.
Methods: Therefore, a systematic review and network meta-analysis (NMA) was performed according to PRISMA-NMA. Six English databases (Pubmed, Medline, CINAHL, Embase, the Cochrane library and ProQuest) and four Chinese databases (CNKI, Wanfang, VIP and Sinomed) were searched. Randomized controlled trials (RCTs) and quasi-experimental studies investigating the effects of different frequencies of APE on lower limb hemodynamics published before July 2022 were included. The reference list was also searched. Seven studies (one RCTs and six quasi-experimental studies) were included in the systematic review and five studies (one RCTs and four quasi-experimental studies) were included in the NMA. The risk of bias was assessed using the Cochrane and Joanna Briggs Institute tools. The NMA was performed using the R software (version 4.2.1) and OpenBUGS (version 3.2.3).
Results: The results of the NMA showed that a frequency of every 3–4 s the most effective in improving lower extremity hemodynamics (P =.85), followed by every 1–2 s (P = .81), every 5–6 s (P=.32) and less than every 10 s (P =.02). Subgroup analysis failed to find a difference between healthy participants and those with unilateral total hip arthroplasty or fracture (MD = −0.23, 95% CI-5.92 to 4.61).
Conclusions: Consequencely, for adult patients, with or without lower extremity disease, a frequency of every 3–4 s can be recommended as the optimal frequency of APE in clinical care practice.
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https://www.crd.york.ac.uk/PROSPERO/display_record.php?RecordID=349365.

Introduction

Ankle pump exercise (APE), an exercise performed through plantar flexion and dorsiflexion of the ankle joint, promotes venous blood return to the lower extremities by contracting and relaxing the calf muscles [1,2] and is recommended as an effective method for preventing venous thromboembolism (VTE) [3–5]. In addition, APE improves calf muscle pump function and reduces venous stasis, which is beneficial in patients with chronic venous insufficiency (CVI) and venous leg ulcers (VLUs) [6,7]. However, the most effective frequency of APE has not been determined [8,9].

Traditional APE recommends holding plantarflexion and dorsiflexion for 10 s at a time, which corresponds to a frequency of 3 beats/min [8]. However, faster APE frequencies have recently been found to be more effective in accelerating blood flow velocity in the lower extremities, ranging from 6 to 100 beats/min [8–14]. Validating the most effective frequency for APE is difficult due to the

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wide range of frequencies and inconsistent results. There are no evidence-based studies to aid decision-making in clinical practice.

Traditional meta-analysis methods compare only two frequencies at a time, making it difficult to answer the question of which frequency is most effective [15]. Network meta-analysis (NMA), a technique that compares multiple treatments simultaneously in a single analysis by combining direct and indirect evidence [16], may be more appropriate for determining the best APE frequency from a variety of different frequencies.

Therefore, the objectives of this systematic review were to [1] recognize the most effective frequency of APE for improving lower extremity hemodynamics through an NMA and [2] establish recommendations for the frequency selection of APE in clinical care practice.

Methods

Registration

This systematic review and NMA is based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA-NMA) guidelines for extended reporting of NMAs [17]. The study protocol has been registered and updated on PROSPERO, an international systematic review prospective registry (ID: CRD42022349365).

Search strategy

Six English databases (Pubmed, Medline, CINAHL, Embase, the Cochrane library, and ProQuest) and four Chinese databases (CNKI, Wanfang, VIP, and SINOMED) were searched. The search strategy was established based on the PICOS tool: (P) population: adults (age ≥18 years) treated with APE; (I&C) interventions and comparators: different frequencies of APE; (O) outcomes: lower extremity hemodynamics; (S) studies: randomized controlled trials (RCTs) and quasi-experimental studies. For example, on Medline, search for “AB (ankle pump exercise or functional *training* or functional *exercise* or ankle motion or ankle plantarflexion or ankle valgus) and AB (frequency or number) and AB (lower extremity hemodynamics or blood flow rate or blood volume or venous blood return)". In addition to the database search, the reference lists of included studies were screened according to the inclusion criteria.

Inclusion criteria

RCTs and quasi-experimental studies conforming to the aforementioned PICOS, published by July 2022, written in English or Chinese, and peer-reviewed were included regardless of sample size. The frequency of APE was defined as any description that could indicate the number of APEs per minute or the interval between APEs. Low limb venous flow velocities, i.e., the velocity of blood in a specific vein, were used to measure lower limb hemodynamics and were assessed by a digital color Doppler ultrasound diagnostic system. For example, the time-averaged maximum flow velocity in the femoral vein is approximately 12.7 to 13.6 cm/s in the head-up position at rest [18,19].

Study selection

Two independent reviewers (X.W. and R.S.T.) screened the retrieved articles through Endnote X9 literature management software. Study selection consisted of three stages, evaluating articles in terms of title, abstract, and full text, respectively. Any disagreements were resolved through discussions between two reviewers or a third reviewer (B.H.L.). If necessary, a broader team meeting will be held to resolve disagreements.

Data extraction

A standardized data extraction form was used with two independent reviewers (X.W. & R.S.T.) to record data, including authors, year of publication, country, study design, study setting, sample size, population, intervention, measurements, funds, and differences in low limb venous flow velocity before and after APE.

Quality appraisal

Two independent reviewers (X.W. and R.S.T.) assessed the quality of eligible studies. For RCTs, the Cochrane Handbook version 5.2.0, which contains 13 items to assess the risk of bias (ROB), was used. The 13 items assessed performance bias, detection bias, attrition bias, and reporting bias, and assessed whether there were systematic differences in the care provided, outcome assessment, loss of participants between comparison groups, and the presence of selective reporting [20]. Trials were also categorized into three levels based on the presence of ROBs described in 13 items: high risk (five or more), moderate risk (three or four), and low risk (two or less). For quasi-experimental studies, the Joanna Briggs Institute (JBI) quality assessment tool, which consists of nine items, was used to assess ROB in multiple ways [21]. After discussion by the study team, studies that measured comparative outcomes in an inconsistent and unreliable manner were excluded.

Data analysis

Descriptive analyses included trials, characterized by different APE frequencies, and summarized the contribution to the overall evidence. Considering the similar and varying frequencies of APE, which can be supervised with a timer in order to facilitate in clinical practice, we classified APE into five frequencies (less than every 10 s, every 5–6 s, every 3–4 s, every 1–2 s, and greater than every 1 s) according to their intervals. Raw group data were combined into five frequencies, calculated from the mean, standard deviation (SD), and number of participants. To control for homogeneity, only studies that selected femoral vein velocity as an outcome were included in the NMA.

Meanwhile, the SEM was converted to SD by counting the number of participants. The Bayesian method was used as a statistical method for NMA [22], and it was performed by the “gemtc” package of R software (version 4.2.1) and OpenBUGS (version 3.2.3) [23]. Markov chain Monte Carlo (MCMC) simulation is a tool for Bayesian inference. In this study, we chose the consistency model and set the number of Markov chains to four with parameters set to n.adapt = 20,000, n.iter = 50,000, and thin = 1, which is the conventional setting for NMA [16]. Sensitivity analysis forest plots were examined for homogeneity analysis, while $I2 > 50\%$ was defined as having heterogeneity. Fixed-effects and random-effects models were selected based on I2 ($I2 < 50\%$: fixed-effects model, $I2 \geq 50\%$: random-effects model). The applicability of the NMA results was tested by nodal analysis as a consistency test with the NMA hypothesis to determine the selection of a consistent or inconsistent model.

The network plots show a direct comparison between the frequencies of APEs, while the edge thickness of the connected nodes implies the amount of data. MCMC simulations and convergence states are tested by trace and density plots, Gelman–Rubin statistical plots, and potential size reduction factors (PSRF).

Forest plots allow the graphical comparison of effect sizes by frequency of APE by NMA. The results are summarized as mean difference (MD) and 95% confidence interval (CI). Also, the surface under the cumulative ranking curve (SUCRA) was used to prioritize the different frequencies of APE. Subgroup analysis was used according to whether the participants were healthy or not. If 10 or more studies were included in the NMA, funnel plots were generated to assess publication bias.

Results

Literature selection

A total of 805 studies were initially identified. However, 451 studies were removed due to duplication, three studies were included from other sources, and 454 studies proceeded to title and abstract review. Following title and abstract review, nine studies proceeded to full text review. One study was excluded because it did not meet the inclusion criteria, and one study was excluded because we were unable to find the full text. Finally, seven studies were included [8–14]. The detailed process is shown in Figure 1.

Characteristic of included studies

The characteristics of the included studies are shown in Table 1. These studies were conducted in China (n = 4) and Japan (n = 3). Two studies recruited only men, while one study recruited only women, and the other studies recruited participants of all genders. The majority of included studies were conducted at universities or research institutions (71.4%, 5/7), and two studies were conducted in hospitals (28.6%). A total of 456 participants were included, ranging from 10 to 307, with a median sample size of 29 (IQR 10 to 63). The included participants included 337 healthy participants, 92 patients with unilateral total hip arthroplasty, and 30 patients with fractures. We combined 12 frequencies into the 5 previously described frequencies (Appendix II). A total of 411 participants were included less than every 10 s, 411 participants were included every 5–6 s, 90 participants were included every 3–4 s, 138 participants were included every 1–2 s, and 35 participants were included every 1 s or more. All studies reported outcomes for low limb venous blood flow velocity. One study reported the percentage of calf muscle hyperemia after APE, and six studies reported the velocity of lower extremity veins. Four studies reported blood flow velocity in one lower extremity vein, one study reported two lower extremity veins, while one study reported three lower extremity veins. Also, five studies reported on the velocity of blood flow in the common femoral vein, two studies reported on the velocity of blood flow in the popliteal vein, one study reported on the velocity of blood flow in the deep femoral vein, and one study reported on the velocity of blood flow in the external iliac vein, with three studies selecting the peak velocity of blood flow as the outcome and three studies selecting the average velocity of blood flow. The intervention time of APE ranged from 1 min to 5 min. A total of 12 different frequencies of APE were compared (Appendix I).

Risk of bias assessment

One RCT and six quasi-experimental studies were included. The ROB in the RCT was low in all domains except allocation bias, which was assessed as high. In the quasi-experimental study, the ROB was high for participant homogeneity and complete follow-up, while the other domains were assessed as low risk. Full details on the ROB assessment are reported in Appendix III.

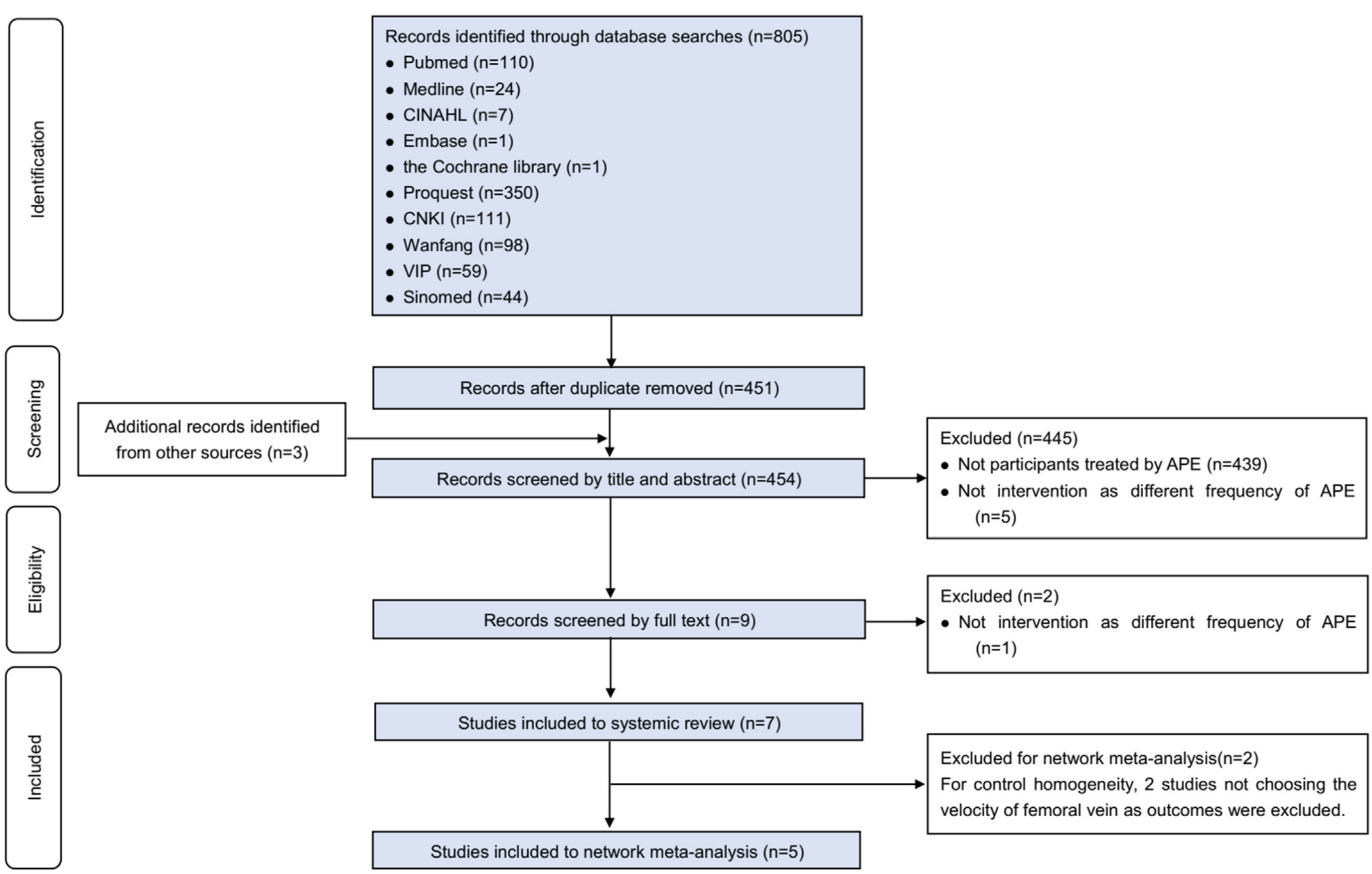

Figure 1. PRISMA-NMA Flow Chart.

Table 1 *Characteristics of Included Studies.*

Studies	Country	Study design	Research setting	N	Populations	Interventions	Original measurement mean (SD/SEM)	Post-combination frequencies Δ mean (SD)	Fund
Kagaya et al., 1991	Japan	Quasi-experimental study	Research Institute of Physical Fitness	6	Physically active women aged 21–22 years	Extend the ankle joint to 100°, then relaxed to return it to 90°, at frequencies of 20, 40, 60, 80, and 100 contractions/min	Post-exercise hyperemia of calf muscle 20 times/min:43.9 ± 5.3(SEM)% 40 times/min:44.3 ± 5.8 (SEM)% 60 times/min:53.6 ± 3.8 (SEM)% 80 times/min:47.4 ± 5.9 (SEM)% 100 times/min:60.9 ± 4.3 (SEM)%	Once every 3–4 s: 43.9 ± 12.98% Once every 1–2 s: 48.95 ± 12.38% More than once every 1 s: 54.15 ± 13.96%[s]	Not mentioned
Toya et al., 2016	Japan	Quasi-experimental study	University	10	Men without a history of cardiovascular diseases	Repeated dorsiflexion and plantarflexion with different frequencies: 15 times/min, 30 times/min, and 60 times/min.	Peak systolic velocity in the common femoral vein Baseline: 19.9 ± 1.9 cm/s 4 s rest exercise: 72.1 ± 10.4(SD)cm/s 2 s rest exercise: 61.0 ± 15.7(SD)cm/s no rest exercise: 73.7 ± 13.5(SD)cm/s	Once every 3–4 s: 52.2 ± 3.34 cm/s Once every 1–2 s: 47.45 ± 4.99 cm/s	Not mentioned
Nakayama et al.,2016	Japan	Quasi-experimental study	Rehabilitation department of a single private hospital.	29	Patients with unilateral total hip arthroplasty	Three different frequencies of active ankle movement: 40, 60, and 80 contractions per minute.	Mean velocity of blood flow in the profunda femoris Baseline: 11.9 ± 5.2(SD)cm/s 40 times/min: 20.2 ± 9.2(SD) cm/s 60 times/min: 29.4 ± 14.4(SD) cm/s 80 times/min: 26.0 ± 11.5(SD) cm/s	Once every 1–2 s: 12.90 ± 2.57 cm/s More than once every 1 s: 14.1 ± 2.34 cm/s[a]	None
Li et al., 2020	China	Quasi-experimental study	Third Hospital of Hebei Medical University	30	Patients with non-lower limb fracture/ patients with limb fracture	Ankle pump exercise with different frequencies: 6 times/min, 10 times/min, 30 times/min, and 60 times/min.	Time-averaged mean velocity (TAMV) of the common femoral venous blood flow patients with non-lower limb fracture: Baseline: 19.82 ± 3.86(SD)cm/s 6 times/min: 34.84 ± 8.30(SD) cm/s 10 times/min: 36.03 ± 9.60(SD) cm/s 30 times/min: 43.15 ± 9.12(SD) cm/s 60 times/min: 52.36 ± 11.69(SD)cm/s Patients with lower limb fracture: Baseline: 16.98 ± 3.01(SD)cm/s 6 times/min: 22.20 ± 4.96(SD) cm/s 10 times/min: 24.01 ± 5.78(SD) cm/s 30 times/min: 29.20 ± 7.05(SD) cm/s 60 times/min: 35.75 ± 9.28(SD) cm/s	Patients with non-lower limb fracture: Baseline: 19.82 ± 3.86 cm/s Less than once every 10 s: 13.96 ± 1.75 cm/s Once every 5–6 s: 17.24 ± 1.73 cm/s Once every 1–2 s: 28.18 ± 2.16 cm/s Patients with lower limb fracture: Baseline: 16.98 ± 3.01 cm/s Less than once every 10 s: 5.22 ± 1.06 cm/s Once every 5–6 s: 7.03 ± 1.19 cm/s Once every 1–2 s: 15.50 ± 1.70 cm/s	Yes
Zhao Huanli et al., 2020	China	Quasi-experimental study	Fourth Clinical Medical College of Yangzhou University	63	Patients after unilateral total hip arthroplasty	Maximum plantar flexion and dorsiflexion of the ankle with different frequencies: 6 times/min, 12 times/	Peak flow velocity of femoral vein of lower extremity Baseline: 29.17 ± 3.02(SD)cm/s 6 times/min: 36.20 ± 4.68(SD) cm/s	Less than once every 10 s: 7.03 ± 0.64 cm/s Once every 5–6 s: 10.05 ± 0.78 cm/s Once every 3–4 s:	Yes

						min, 15 times/min, 20 times/min, 30 times/min, and 60 times/min.	12 times/min: 39.22 ± 5.44(SD) cm/s 15 times/min: 42.14 ± 6.14(SD) cm/s 20 times/min: 48.93 ± 6.31(SD) cm/s 30 times/min: 52.59 ± 6.79(SD) cm/s 60 times/min: 34.71 ± 5.73(SD) cm/s	16.37 ± 0.97 cm/s Once every 1–2 s: 14.48 ± 1.39 cm/s	
Zhou Shanshan et al., 2020	China	Quasi-experimental study	First Hospital of Nanjing Medical University	11	Healthy men	Ankle pump exercise with different frequencies: 5 times/min, 10 times/min, and 15 times/min.	Peak flow velocity of femoral vein Baseline: 33.55 ± 5.67 (SD)cm/s 5 times/min: 45.45 ± 4.95(SD) cm/s 10 times/min: 52.55 ± 4.08(SD) cm/s 15 times/min: 56.09 ± 7.66(SD) cm/s Peak flow velocity of popliteal vein Baseline: 27.36 ± 5.46(SD)cm/s 5 times/min: 31.82 ± 4.90(SD) cm/s 10 times/min: 41.64 ± 5.67(SD) cm/s 15 times/min: 42.55 ± 8.30(SD) cm/s	Less than once every 10 s: 12.54 ± 2.07 cm/s Once every 5–6 s: 19.00 ± 2.11 cm/s Once every 3–4 s: 21.73 ± 3.25 cm/s	Yes
Li et al., 2022	China	RCT	Hospital	307	Healthy adults	Ankle pump exercise with different frequencies: 3 times/min and 30 times/min.	Mean velocity of external iliac vein: Baseline: 21.36 ± 8.13(SD)cm/s 3 times/min: 25.49 ± 9.21(SD) cm/s 15 times/min: 25.98 ± 8.96(SD) cm/s Mean velocity of femoral vein: Baseline: 16.21 ± 6.56(SD)cm/s 3 times/min: 19.18 ± 6.96(SD) cm/s 15 times/min: 18.98 ± 6.63(SD) cm/s Mean velocity of popliteal vein: Baseline: 13.06 ± 5.02(SD)cm/s 3 times/min: 15.12 ± 5.76(SD) cm/s 15times/min: 15.12 ± 5.27(SD) cm/s	Less than once every 10 s: 2.97 ± 0.55 cm/s Once every 3–4 s: 2.77 ± 0.53 cm/s	Yes

Note. SD = standard deviation; SEM = standard error of mean.
[a] It was excluded for network meta-analysis.

Network meta-analysis for lower limb hemodynamics

Five studies with a combined total of 421 participants measured the velocity of the femoral vein (Table 1). In the absence of direct and indirect comparisons between more than once per second and other frequencies were excluded in the NMA. Figure 2 shows NMA plots examining the effect of four different frequencies of APE.

Frequencies of once every 3–4 s and once every 1–2 s were found to be more effective compared to frequencies of less than once every 10 s (MD = 10.00, 95% CI 5.40–15.00; MD = 9.90, 95% CI 5.70–14.00). The frequencies of once every 3–4 s and once every 1–2 s were also found to be more effective compared to once every 5–6 s (MD = 7.30, 95% CI 2.60–12.00; MD = 7.00, 95% CI 2.80–11.00) (Figure 3), with the same results. No other significant differences in lower extremity hemodynamics could be found among the different frequencies of APE.

Considering direct and indirect comparisons, a frequency of every 3–4 s had the best effect on improving lower extremity hemodynamics (p score = .85). Detailed results for APE frequency prioritization are presented in Table 2. In addition, subgroup analysis failed to find a difference between healthy participants and those with unilateral total hip arthroplasty or fracture (MD = −0.23, 95% CI −5.92 to 4.61), while the difference between studies conducted in China and Japan was also not significant (MD = 14.87, 95% CI −69.55 to 105.90).

The results of the homogeneity analysis showed that heterogeneity was clearly present (Appendix IV). The results of the nodal analysis confirm that there is no inconsistency in the model ($p > .050$) (Appendix V). The trace plots, density plots, and Gelman–Rubin statistical plots showed that MCMC simulations and convergence were in good condition, while PSRF converged to 1 (Appendices VI–VII). Also, publication bias was not assessed because fewer than 10 studies were included.

Discussion

To confirm the most effective frequency of APE and establish evidence-based recommendations for clinical practice, an NMA was conducted. A literature search identified 805 studies, and after removing duplicates, applying inclusion criteria, and completing a critical appraisal, seven studies were included for analysis. After direct and indirect comparisons of the NMA, evidence from different frequencies of APE was integrated, and the most effective frequency of the NMA was identified.

As an effective exercise to improve lower extremity hemodynamics [5], APE is popular in clinical care practice in patients lying in bed to prevent thrombosis [3,4]. However, although some studies have focused on the frequency selection of APE, there is no consensus on the frequency of APE. Therefore, there is a need to explore the most effective frequency of APE to guide clinical practice and improve the clinical outcomes of APE.

The results of the NMA showed that a frequency of every 3–4 s had the best effect on improving lower extremity hemodynamics, meaning that a frequency of every 3–4 s performed better than a frequency of every 1–2 s. This is quite different from previous studies, which found that faster APE performed better for improving lower extremity hemodynamics [11,13]. This may be because a single contraction of normal calf muscles can expel 60–90 ml of blood [24], whereas faster frequency APE can accomplish more contractions at the same time. Therefore, faster frequency APE can expel more blood at the same time. However, slower frequency of APE can increase the contraction force of calf muscles, which can promote more efficient venous blood return [11]. Thus, Toya et al found that a frequency of once every 4 s had a similar effect on lower limb hemodynamics as exercise without rest [9].

Our findings provide evidence-based recommendations for the frequency selection of APE in clinical practice, and patients will achieve the best clinical outcomes with APE at a frequency of every 3–4 s. Meanwhile, previous studies have found that APE every 3–4 s at 15–20 beats per minute has less post-exercise fatigue comparing to 60 beats per minute and 3 beats per minute [8,11], suggesting that APE every 3–4 s is clinically feasible and easily adhered to.

However, our study still contains some limitations. First, most of the included studies were quasi-experimental studies, and all participants in these studies experienced all sets of different frequencies [8–14]. Although the effect of APE on lower extremity hemodynamics is transient and participants experiencing multiple

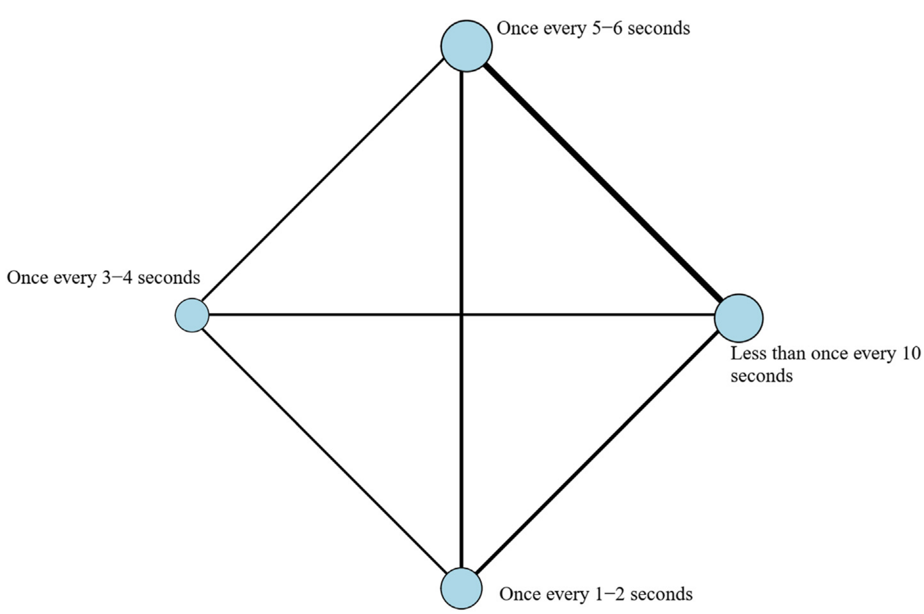

Figure 2. Network Meta-Analysis Maps of the Studies Examining the Effect of Five Different Frequencies of APE.
Note. The size of the nodes was related to the frequency of APEs that included participants, and the thickness of the lines was related to the number of studies for that comparison.

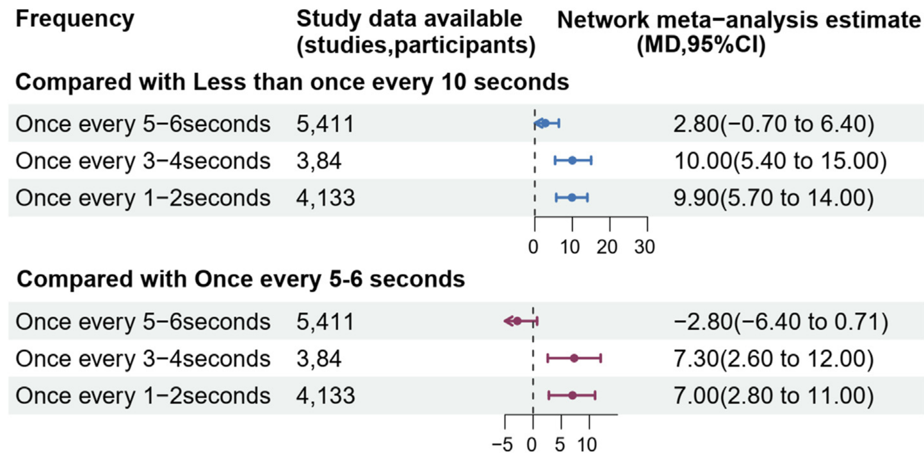

Figure 3. Summary Network Meta-Analysis Results for Each Ape Frequency Comparison.
Note. MD = mean difference; CI = confidence interval.

Table 2 *Ranking of Frequencies of APE in Order of Effectiveness.*

Frequency of APE	*p* score	Ranking
Less than once every 10 s	.02	4
Once every 5–6 s	.32	3
Once every 3–4 s	.85	1
Once every 1–2 s	.81	2

Note. APE = ankle pump exercise.

frequencies of APE at different times do not lead to inaccurate results, more RCTs are still needed. Moreover, all included studies were conducted in Asia, and there is a lack of data from other continents. We also searched Chinese local data, while the lack of local data of other countries. Third, the sample size of the included studies was limited. With the exception of one study with 307 participants, the number of participants in the other studies ranged from 6 to 63, which may increase the risk of false positive results in primary studies.

Conclusion

In this study, we provided evidenced-based recommendations for the clinical practice and standardization of APE through the NMA. APE every 3–4 s at 15–20 beats per minute is most effective in improving lower extremity hemodynamics with less post-exercise fatigue and should be recommended for widespread implementation in clinical practice.

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Conflict of interest

The authors declare that they have no conflict of interests.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.03.001.

References

1. McNally MA, Cooke EA, Mollan RA. The effect of active movement of the foot on venous blood flow after total hip replacement. J Bone Jt Surg Am Vol. 1997;79(8):1198–201. Epub 1997/08/01. https://doi.org/10.2106/00004623-199708000-00012. PubMed PMID: 9278080.
2. Kwon OY, Jung DY, Kim Y, Cho SH, Yi CH. Effects of ankle exercise combined with deep breathing on blood flow velocity in the femoral vein. Aust J Physiother. 2003;49(4):253–8. Epub 2003/11/25. https://doi.org/10.1016/s0004-9514(14)60141-0. PubMed PMID: 14632624.
3. JCS. Guidelines for the diagnosis, treatment and prevention of pulmonary thromboembolism and deep vein thrombosis (JCS 2009). Circ J Off J Jpn Circ Soc. 2011;75(5):1258–81. Epub 2011/03/29. https://doi.org/10.1253/circj.cj-88-0010. PubMed PMID: 21441695.
4. Kehl-Pruett W. Deep vein thrombosis in hospitalized patients: a review of evidence-based guidelines for prevention. Dimensions of critical care nursing. DCCN. 2006;25(2):53–9. quiz 60-1. Epub 2006/03/23. https://doi.org/10.1097/00003465-200603000-00001. PubMed PMID: 16552270
5. Pi H, Ku H, Zhao T, Wang J, Fu Y. Influence of ankle active dorsiflexion movement guided by Inspiration on the venous return from the lower limbs: a prospective study. J Nurs Res. 2018;26(2):123–9. Epub 2017/09/01. https://doi.org/10.1097/jnr.0000000000000214. PubMed PMID: 28858972.
6. Orr L, Klement KA, McCrossin L, O'Sullivan Drombolis D, Houghton PE, Spaulding S, et al. A systematic review and meta-analysis of exercise intervention for the treatment of calf muscle pump Impairment in Individuals with chronic venous insufficiency. Ostomy/Wound Manag. 2017;63(8):30–43. Epub 2017/09/06. https://doi.org/10.25270/owm.2017.08.3043. PubMed PMID: 28873064.
7. O'Brien J, Finlayson K, Kerr G, Edwards H. Evaluating the effectiveness of a self-management exercise intervention on wound healing, functional ability and health-related quality of life outcomes in adults with venous leg ulcers: a randomised controlled trial. Int Wound J. 2017;14(1):130–7. Epub 2016/01/29. https://doi.org/10.1111/iwj.12571. PubMed PMID: 26817648; PubMed Central PMCID: PMCPMC7949716.
8. Li H, Zhang W, Lu Q, Wang J, Zhi Y, Zhang L, et al. Which frequency of ankle pump exercise should be chosen for the prophylaxis of deep vein thrombosis? Inquiry J Med Care Organ Provis Financ. 2022;59:469580221105989. https://doi.org/10.1177/00469580221105989. PubMed PMID: 35658650.
9. Toya K, Sasano K, Takasoh T, Nishimoto T, Fujimoto Y, Kusumoto Y, et al. Ankle positions and exercise intervals effect on the blood flow velocity in the common femoral vein during ankle pumping exercises. J Phys Ther Sci. 2016;28(2):685–8. https://doi.org/10.1589/jpts.28.685. PubMed PMID: 27065564.
10. Kagaya A. Reduced exercise hyperaemia in calf muscles working at high contraction frequencies. Eur J Appl Physiol Occup Physiol. 1992;64(4):298–303. https://doi.org/10.1007/BF00636215
11. Li T, Yang S, Hu F, Geng Q, Lu Q, Ding J. Effects of ankle pump exercise frequency on venous hemodynamics of the lower limb. Clin Hemorheol Microcirc. 2020;76(1):111–20. https://doi.org/10.3233/CH-200860. PubMed PMID: 2413995744; 32538827.
12. Nakayama T, Tsukada S, Hiyama T, Yamada T, Hirasawa N. Impact of active ankle movement frequency on velocity of lower limb venous flow following total hip arthroplasty. Adv Orthop. 2016;2016:7683272. Epub 2016/12/22. https://doi.org/10.1155/2016/7683272. PubMed PMID: 27999685; PubMed Central PMCID: PMCPMC5141543 or funding from any commercial party related directly or indirectly to the subject of this article.
13. Huanli Z, Aimei Z, Ya H, Lin C, Weihong F. Effects of different exercise duration of ankle joint active flexion and extension exercise on lower limb venous blood flow velocity after total hip arthroplasty. Nurs Integr Tradit Chin West Med. 2020;6(5):111–3. https://doi.org/10.11997/nitcwm.202005024

14. Shanshan Z, Qian M, Suyu M, Haiying J, Xiaodan B. Effect of ankle pump on venous blood flow and fibrinolysis of lower extremity. Mod Med J. 2020;48(12): 1622–5. https://doi.org/10.3969/j.issn.1671-7562.2020.12.027. Chinese.
15. Hayden JA, Ellis J, Ogilvie R, Stewart SA, Bagg MK, Stanojevic S, et al. Some types of exercise are more effective than others in people with chronic low back pain: a network meta-analysis. J Physiother. 2021;67(4):252–62. Epub 2021/09/21. https://doi.org/10.1016/j.jphys.2021.09.004. PubMed PMID: 34538747.
16. Rouse B, Chaimani A, Li T. Network meta-analysis: an introduction for clinicians. Intern Emerg Med. 2017;12(1):103–11. Epub 2016/12/04. https://doi.org/10.1007/s11739-016-1583-7. PubMed PMID: 27913917; PubMed Central PMCID: PMCPMC5247317.
17. Hutton B, Salanti G, Caldwell DM, Chaimani A, Schmid CH, Cameron C, et al. The PRISMA extension statement for reporting of systematic reviews incorporating network meta-analyses of health care interventions: checklist and explanations. Ann Intern Med. 2015;162(11):777–84. Epub 2015/06/02. https://doi.org/10.7326/m14-2385. PubMed PMID: 26030634.
18. Sakai K, Takahira N, Tsuda K, Akamine A. Effects of intermittent pneumatic compression on femoral vein peak venous velocity during active ankle exercise. J Orthop Surg. 2021;29(1):2309499021998105. https://doi.org/10.1177/2309499021998105. PubMed PMID: 33641535.
19. Toya K, Takahashi T, Fujimoto Y, Nishimoto T, Takasoh T, Sasano K, et al. Effect of elastic stockings and ankle positions on the blood velocity in the common femoral vein. J Phys Ther Sci. 2016;28(9):2608–10. Epub 2016/11/02. https://doi.org/10.1589/jpts.28.2608. PubMed PMID: 27799704; PubMed Central PMCID: PMCPMC5080186.
20. library C. Cochrane handbook for systematic reviews of interventions. 2011 https://training.cochrane.org/handbook [cited 2022 08/18].
21. Tufanaru CMZ, Aromataris E, Campbell J, Hopp L. In: Aromataris E, Munn Z, editors. Chapter 3. Systematic reviews of effectiveness. JBI Manual for Evidence Synthesis; 2020 https://jbi.global/critical-appraisal-tools [cited 2022 08/18].
22. Shim SR, Kim SJ, Lee J, Rücker G. Network meta-analysis: application and practice using R software. Epidemiol Health. 2019;41:e2019013. Epub 2019/04/20. https://doi.org/10.4178/epih.e2019013. PubMed PMID: 30999733; PubMed Central PMCID: PMCPMC6635665.
23. Van Valkenhoef G, Kuiper J. gemtc: network meta-analysis using Bayesian methods. R package version 1.0-1. https://doi.org/10.1002/jrsm.1167.
24. Ludbrook J. The musculovenous pumps of the human lower limb. Am Heart J. 1966;71(5):635–41. Epub 1966/05/01. https://doi.org/10.1016/0002-8703(66)90313-9. PubMed PMID: 5935855.

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Research Article

Incidence and Risk Factors for Radiotherapy-Induced Oral Mucositis Among Patients With Nasopharyngeal Carcinoma: A Meta-Analysis

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SUMMARY

Purpose: To evaluate the incidence and identify the risk factors for radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma.
Methods: A meta-analysis was conducted. Eight electronic databases (Medline, Embase, Cochrane Library, CINAHL Plus with Full Text, Web of Science, China National Knowledge Infrastructure, Wanfang Database, and Chinese Scientific Journals Database) were systematically searched from inception to 4 March 2023 for relevant studies. Study selection and data extraction were conducted by two independent authors. The Newcastle–Ottawa scale was used for quality assessment among the included studies. Data synthesis and analyses were performed in R software package version 4.1.3 and Review Manager Software 5.4. The pooled incidence was calculated using proportions with 95% confidence intervals (CIs), and the risk factors were evaluated using the odds ratio (OR) with 95% CIs. Sensitivity analysis and predesigned subgroup analyses were also conducted.
Results: A total of 22 studies published from 2005 to 2023 were included. The results of the meta-analysis showed that the incidence of radiotherapy-induced oral mucositis was 99.0% among nasopharyngeal carcinoma patients, and the incidence of severe radiotherapy-induced oral mucositis was 52.0%. Poor oral hygiene, overweight before radiotherapy, oral pH < 7.0, the use of oral mucosal protective agents, smoking, drinking, combined chemotherapy, and the use of antibiotics at early treatment stage are risk factors for severe radiotherapy-induced oral mucositis. Sensitivity analysis and subgroup analyses also revealed that our results are stable and reliable.
Conclusions: Almost all patients with nasopharyngeal carcinoma have suffered from radiotherapy-induced oral mucositis, and more than half of patients have experienced severe oral mucositis. Facilitating oral health might be the key focus of reducing the incidence and severity of radiotherapy-induced oral mucositis among nasopharyngeal carcinoma patients.
Registration number: CRD42022322035.

Introduction

Nasopharyngeal carcinoma is the most common type of oto-rhinolaryngeal carcinoma, with 133354 new cases and 80008 deaths in 2020 [1]. Due to the deep-seated anatomic location and high sensitivity to ionizing radiation, radiotherapy is the mainstay treatment modality for patients with nasopharyngeal carcinoma. The radiotherapy techniques have progressed from conventional two-dimensional radiotherapy to 3D conformal radiotherapy and then to intensity-modulated radiotherapy over time. The locoregional control and survival have been enhanced by the parallel improved dosimetric properties [2]. Despite improvements in the radiotherapy techniques, the ongoing and intensive irradiation that is required might still cause the normal tissues around the tumor to suffer from a series of acute and chronic radiation toxicities, which lead patients to experience various treatment-related problems and poor quality of life [3]. Radiotherapy-induced oral mucositis is

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the most frequent and distressing radiation complication, with an incidence ranging from 85.0% to 100.0% among patients with head and neck cancer during therapy [4,5]. Great attention to this unpleasant complication is needed.

Radiotherapy-induced oral mucositis refers to erythematous and painful ulcerative lesions of the oral mucosa and is observed in patients who are treated with radiotherapy combined with or without chemotherapy [6]. The main symptoms of oral mucositis may range from mild discomfort and erythema to painful erythema, and edema and ulcerations [7]. The presence of severe radiotherapy-induced oral mucositis can have detrimental effects on patients' daily functioning and quality of life: unable to eat, drink, and talk due to painful ulceration, ultimately leading to weight loss, nutritional deficiencies, secondary infections, extended length of hospital stay, and increased associated economic costs [8]. What is worse, severe radiotherapy-induced oral mucositis might lead to dose reduction and treatment interruption, which could adversely affect the treatment effects and disease prognosis [9]. At present, the optimal prevention and treatment regimens for radiotherapy-induced oral mucositis are unclear [10]. Although a range of treatments have been used for oral mucositis, such as palifermin, growth factor, cryotherapy, and low-level laser treatment, no treatment is fully effective [11]. Active precaution for a complication beforehand is much easier and cheaper than treating it, and preventive strategies directed towards the risk factors for oral mucositis might effectively decrease the incidence of these complications [12]. Therefore, it is urgent and necessary to determine the risk factors and accordingly develop targeted preventive measures of radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma.

Currently, studies on radiotherapy-induced oral mucositis are mainly interventional studies that focus on symptom treatment and the effectiveness of these treatment measures [8,13]. There are only a small number of studies exploring the risk factors for radiotherapy-induced oral mucositis, and the limited studies are mostly focused on patients with head and neck cancer (such as oral cancer and oropharyngeal cancer) [14,15]. Although originating from similar cell or tissue lineages, nasopharyngeal carcinoma is distinctly different from other epithelial head and neck cancers [2]. In addition, the results of existing limited studies are inconsistent. For instance, Xu et al. [16] included 166 patients with nasopharyngeal carcinoma and found that smoking, poor oral hygiene, oral pH less than 7.0, and chemotherapy were risk factors for radiotherapy-induced oral mucositis. Dong et al. [17] explored the risk factors among 116 patients and found that smoking, oral pH less than 6.5, concurrent chemotherapy, and oral irradiation dose more than 32 Gy might contribute to the development of radiotherapy-induced oral mucositis. In addition, the incidence of severe radiotherapy-induced oral mucositis has varied in different studies, with a range from 30% to 100% [18,19]. To the best of our knowledge, no study has systematically explored the incidence and risk factors for radiotherapy-induced oral mucositis and its incidence among patients with nasopharyngeal carcinoma. Therefore, the objectives of our study are to (1) identify the incidence of radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma, (2) explore the possible risk factors for severe radiotherapy-induced oral mucositis in nasopharyngeal carcinoma patients, and (3) provide evidence-based references for developing targeted preventive measures of radiotherapy-induced oral mucositis.

Methods

This meta-analysis was registered with International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/PROSPERO), and it was performed and reported according to the updated Preferred Reporting Items for Systematic Review and Meta-analyses (PRISMA2020) guidelines [20].

Eligibility criteria

Two authors independently screened and selected all literature. Studies were included if they met the following inclusion criteria: (1) participants were patients diagnosed with nasopharyngeal carcinoma, aged over 18 years, and received radiotherapy; (2) the exact diagnostic criteria for radiotherapy-induced oral mucositis were available; (3) the incidence or risk factors for radiotherapy-induced oral mucositis were reported; (4) the research types were observational including cross-sectional studies, case-control studies, and cohort studies; and (5) the study language was English or Chinese. The exclusion criteria were as follows: (1) studies did not provide complete data; (2) the full-text of the study was unavailable; and (3) studies were conference abstracts, dissertations, study protocols, and duplicate reports.

Data sources and search strategies

Eight electronic databases, including Medline, Embase, Cochrane Library, CINAHL Plus with Full Text, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang Database, and Chinese Scientific Journals Database (VIP), were searched from inception to 4 March 2023 for all possible literature. The search strategies were established by using medical subject headings (MeSH) terms, text word searches, and Boolean calculation searches (see supplemental material Table 1). For instance, in Medline of Ovid, the search terms were as follows: Nasopharyngeal neoplasms [Mesh] or "nasopharyngeal neoplasms" or "nasopharynx cancer" or "nasopharyngeal cancer" or "nasopharynx neoplasms" or "nasopharyngeal carcinoma" or NPC OR (nasopharynx [Mesh] or nasopharynx or nasopharyngeal or nasopharyngitis * or rhinopharyngitis * or choanae) and (neoplasms [Mesh] or carcinoma* or cancer* or neoplasm* or tumor* or tumour* or malignancy* or onco*)), and "radiation-induced oral mucositis" or "radiotherapy oral mucositis" or RTOM or ((radiotherapy [Mesh] or radiotherapy* or irradiation* or "radiation therapy") and (Stomatitis [Mesh] or "oral mucositis" or stomatitis or stomatitides or oromucositis or oromucositides or (oral and (mucositis [Mesh] or mucositis or mucositides or mucosa inflammation). Additionally, the searches were limited to human adults, published in English or Chinese. The reference lists of the relevant studies were also screened for potentially relevant articles.

Study selection and data extraction

The reference management software EndNote X9 was used for data management. After removing duplicates, two authors independently screened the titles and abstracts of all citations in accordance with the inclusion and exclusion criteria. Then, the full-texts of citations were retrieved when considered potentially relevant by either investigator. Each article was evaluated by two independent authors for final study inclusion based on the eligibility criteria. The reference lists of the included studies were also screened for additional possible studies. Disagreements during the selection process were resolved by discussion or consultation with the third author.

Two independent authors extracted relevant data from the included studies using predesigned data collection forms. The following data were collected: the study author, date of publication, study site, study design, sample size, number of female and male patients, mean age, cancer stage, treatment regimen, diagnostic criteria, incidence of radiotherapy-induced oral mucositis, and assessed risk factors.

Quality assessment

Quality assessment was conducted by two independent authors. No cross-sectional studies were included in this study, and the quality of case–control studies and cohort studies was assessed using the Newcastle–Ottawa scale [21]. The scale evaluated the quality of the study from three domains: selection of subjects, comparability of study groups, and ascertainment of the exposure or outcome. The total score of the scale ranges from 0 to 9, with scores of 0–3, 4–6, and 7–9 indicating low, moderate, and high quality of each study, respectively.

Data synthesis and analysis

We used R software package version 4.1.3 and Review Manager Software 5.4 for the heterogeneity test and quantitative data synthesis. Heterogeneity among the included studies was evaluated

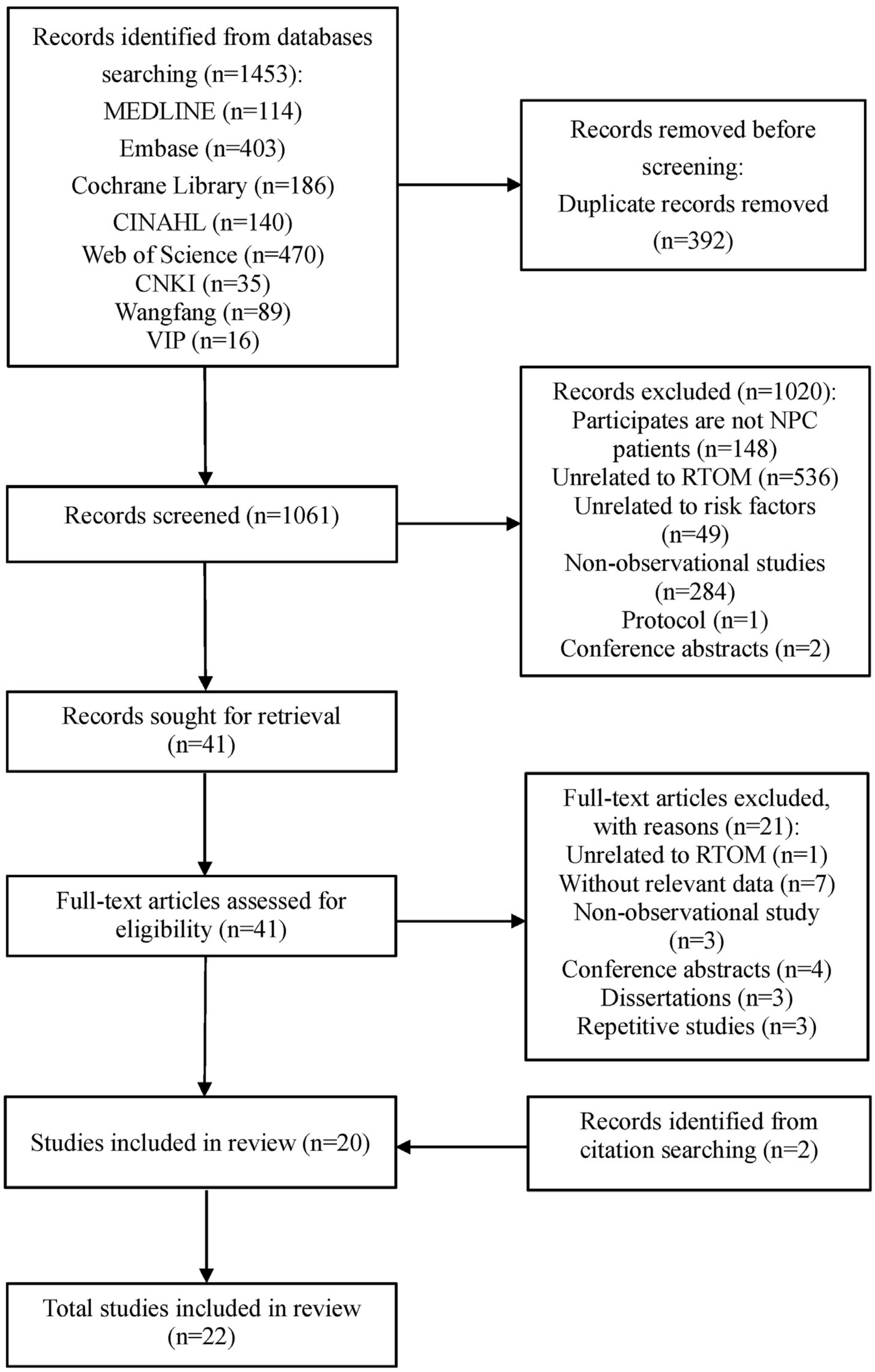


Figure 1. Flow Diagram of Study Selection. CNKI = China National Knowledge Infrastructure, VIP = Chinese Scientific Journals Database, NPC = nasopharyngeal carcinoma, RTOM = Radiotherapy-Induced Oral Mucositis.

using Cochrane's Q statistic, and the I^2 statistic and p value were used to assess the degree of heterogeneity. $I^2 \leq 50\%$ and a p value > .050 were regarded as indicating low heterogeneity and a fixed effect model was used to pool the results; otherwise, a random effect model was used to obtain more conservative pooled results. The incidence of radiotherapy-induced oral mucositis was presented as the proportion with 95% confidence intervals (CIs) and analysed using the Freeman-Turkey double-arcsine transformation random-effects model [22] in R software package version 4.1.3. The risk factors of severe radiotherapy-induced oral mucositis were determined by odds ratio (ORs) with 95% CIs in Review Manager Software 5.4. A two-sided p value less than .050 was used to indicate a statistically significant difference. In addition, predesigned subgroup analyses were performed according to the study characteristics and the different severities of oral mucositis. A sensitivity analysis was also conducted to test the stability and reliability of the pooled results of incidence and risk factors. Finally, a funnel plot and Egger's linear regression ($p < .100$ was considered as significant) method were used to evaluate the publication bias.

Results

Study selection

Our study selection process is presented in Fig. 1. A total of 1453 records were retrieved from eight electronic databases. After removing the duplicates ($n = 392$), another 1020 records were excluded according to the titles and abstracts because the participants were not patients with nasopharyngeal carcinoma ($n = 148$), the studies were not related to radiotherapy-induced oral mucositis ($n = 536$) nor to its risk factors ($n = 49$), and the studies were non–observational studies ($n = 284$), protocol ($n = 1$), and conference abstracts ($n = 2$). Next, the full-texts of 41 citations were retrieved and evaluated based on the eligibility criteria, and 21 studies were excluded for the reasons presented in Fig. 1. Finally, another two records were identified from citation searching were included, a total of 22 studies [16–19,23–40] were included in our systematic review and meta-analysis.

Characteristics of the included studies

Table 1 presents the characteristics of the included studies. The 22 included studies all were observational studies, 12 of which were prospective cohort studies, five was a retrospective cohort study, and another five studies were case–control studies. All these studies were published between 2005 and 2023, and they were from China ($n = 20$), Italy ($n = 1$), and Japan ($n = 1$). The sample size of the included studies ranged from 22 to 1674, and the total sample size was 4507. The mean ages of all the participants ranged from 46.3 to 64.3 years old. Most studies ($n = 17$) included all stages of patients with nasopharyngeal carcinoma, one study included patients at stage, one study included patients at stage T3-4NxM0 or TxN2-3M0 following the Union for International Cancer Control (2010), and three studies included only locally advanced patients (stage). All participants were treated with radiotherapy alone or combined with chemotherapy. The diagnostic criteria of radiotherapy-induced oral mucositis varied in these included studies, grade 2 or above was defined as severe radiotherapy-induced oral mucositis. Specifically, 10 studies [17,23,24,27,28,33,35,38–40] used the Radiation Therapy Oncology Group criteria of acute effects for mucous membranes to assess the grade of oral mucositis. Five studies [16,18,30,32,36] used the World Health Organization oral mucositis grading scale to evaluated the severity of oral mucositis. Five studies [19,25,26,31,34] used the Common Terminology Criteria for Adverse Events to assess the oral mucositis grade. Two studies [29,37] did not report the details of the assessment tool for oral mucositis.

Quality of the included studies

All the included studies were evaluated using the Newcastle–Ottawa scale, and the results are presented in Table 1. Nineteen studies [16–19,24–28,30–32,34–40] were rated as having high quality and low risk of bias, and another three studies [23,29,33] were rated as having moderate quality and moderate risk of bias. In addition, the funnel plots and Egger's linear regression indicated that there was no significant publication bias ($p = .224$) in these included studies (see supplemental material Fig. 1).

Meta-analysis

Incidence of radiotherapy-induced oral mucositis

A total of 20 studies with 4135 participants were included in the quantitative meta-analysis, and the incidence of radiotherapy-induced oral mucositis ranged from 50% to 100%. In detail, 16 studies reported that all the participants experienced radiotherapy-induced oral mucositis with an incidence of 100%. In addition, four studies [24,33,35,37] reported that the incidences of oral mucositis were 98%, 90%, 84%, and 50%, respectively. As a high level of heterogeneity ($I^2 = 97\%$, $p < .01$) existed among these studies, a random-effect model was used to obtain more conservative results, and the pooled results (Fig. 2) showed that the incidence of radiotherapy-induced oral mucositis was 99% (95% CI: 96% to 100%).

A sensitivity analysis was performed using a one-study-out method to test the stability and reliability of the pooled results. The pooled estimated incidence of radiotherapy-induced oral mucositis did not change significantly, ranging from 99% (95% CI: 96–100%) to 100% (95% CI: 99–100%) (see supplemental material Fig. 2).

Subgroup analysis

The results of the subgroup analysis showed that the incidences of mild and severe radiotherapy-induced oral mucositis were 46% (95% CI: 36–55%, $I^2\% = 97\%$) and 52% (95% CI: 43–61%, $I^2\% = 98\%$), respectively (Fig. 3). In addition, the subgroup analyses conducted based on the participant characteristics (gender, cancer stage, and treatment regimen) and study characteristics (study design, study language, sample size, and diagnostic criteria) showed that there were no significant differences no matter the participant and study characteristics (see supplemental material Table 2).

Risk factors for severe radiotherapy-induced oral mucositis

Of the 22 included studies, 17 studies [16,17,19,23,24,27,29,31–40] reported at least one risk factor that was available for data synthesis, and another five studies [18,25,26,28,30] did not report relevant data for meta-analysis. The potential risk factors from the included studies were categorized into demographic factors (gender and age), health-related factors (such as BMI, weight loss, oral pH, diabetes, cancer stage, and oral hygiene), and lifestyle-related factors (such as smoking and drinking). Among these factors, nine factors (oral hygiene, oral pH, the use of oral mucosal protective agents, smoking, drinking, overweight before radiotherapy, combined chemotherapy, and the use of antibiotics at early treatment stage, and diabetes) from 14 studies had data that could be used for quantitative meta-analysis. The pooled results showed that poor oral hygiene (OR = 4.78, 95% CI: 2.56–8.91), oral pH < 7.0 (OR = 3.56, 95% CI: 2.58–4.91), smoking (OR = 3.60, 95% CI: 2.59–5.01), drinking (OR = 3.24, 95% CI: 1.92–5.46), overweight

Table 1 *Characteristics of Included Studies.*

Study ID	Country	Study design	Sample size	Women/Men	Mean age	Cancer stage	Treatment regimen	Diagnostic criteria	Incidence of RTOM	Assessed risk factors	NOS score/risk of bias
Chen et al., 2021a	China	Case-control study	240	71/169	51.3	All stages	Chemo-radiotherapy	RTOG criteria	131/240	Concurrent chemotherapy, mean oral cavity dose, Vitamin B2, Vitamin C	6/moderate
Cheng et al., 2014	China	Prospective cohort study	85	28/57	50	Stage II-IV	Chemo-radiotherapy	RTOG criteria	83/85	Smoking, diabetes, BMI	8/low
Dong et al., 2021	China	Prospective cohort study	115	34/81	54.4	All stages	Chemo-radiotherapy	RTOG criteria	115/115	Smoking history, oral pH $\leq$ 6.5, concurrent chemotherapy, oral mucosa dose$\geq$32 Gy, did not use mouthwash	8/low
Kawashita et al., 2023	Japan	Retrospective cohort study	22	NA	64.5	All stages	Radiotherapy or chemo-radiotherapy	CTCAE V5.0	22/22	/	7/low
Li & Zheng, 2011	China	Prospective cohort study	150	66/84	50	All stages	Radiotherapy	WHO OM Grading scale	150/150	/	8/low
Li et al., 2013	China	Prospective cohort study	114	36/78	49.6	All stages	Radiotherapy or chemo-radiotherapy	CTCAE V3.0	114/114	/	9/low
Li et al., 2017	China	Prospective cohort study	92	25/67	NA	Stage T3-4NxM0 or TxN2-3M0	Chemo-radiotherapy	RTOG criteria	92/92	Body weight loss, V30 $\geq$ 70%	9/low
Li et al., 2020a	China	Prospective cohort study	270	207/63	50	All stages	Chemo-radiotherapy	RTOG criteria	270/270	/	9/low
Li et al., 2020b	China	Case-control study	120	44/76	NA	All stages	Radiotherapy	NA	120/120	BMI>24, smoking, drinking, oral care, oral pH < 7.0, antibiotics, oral mucosal protective agents, chemotherapy	6/moderate
Liu et al., 2023	China	Retrospective cohort study	190	135/55	46.3	All stages	Chemo-radiotherapy	WHO OM grading scale	190/190	/	8/low
Luo et al., 2005	China	Prospective cohort study	102	34/68	47.9	All stages	Radiotherapy or chemo-radiotherapy	CTCAE V2.0	102/102	Chemotherapy, oral hygiene, antibiotics, smoking	9/low
Orlandi et al., 2018	Italy	Retrospective cohort study	132	40/92	49	Stage II-IVB	Chemo-radiotherapy	CTCAE V4.0	40/132	BMI $\geq$ 30 kg/m^2, combined parotid glands EUD	7/low
Pang & Yi, 2020	China	Prospective cohort study	120	59/61	53.8	All stages	Radiotherapy	WHO OM grading scale	120/120	Smoking, oral care, mouth PH < 7.0, antibiotics, chemotherapy, oral mucosal protective agents	9/low
Peng et al., 2016	China	Case-control study	1674	434/1240	48	All stages	Radiotherapy	RTOG criteria	1500/1674	Diabetes, prediabetes, smoking, cancer stage	6/moderate
Song et al., 2023	China	Retrospective cohort study	228	59/169	NA	All stages	Radiotherapy or chemo-radiotherapy	CTCAE V5.0	228/228	Modified nutrition index	8/low
Sun et al., 2020	China	Prospective cohort study	96	36/60	59.2	Stage II-IV	Chemo-radiotherapy	RTOG criteria	81/96	Smoking, diabetes, white blood cell	8/low
Study ID	Country	Study design	Sample size	Female/male	Mean age	Cancer stage	Treatment regimen	Diagnostic criteria	Incidence of RTOM	Assessed risk factors	NOS score/risk of bias
Wang et al., 2017	China	Prospective cohort study	92	39/53	52.4	All stages	Radiotherapy	WHO OM grading scale	92/92	Smoking, oral care, oral pH < 7.0, antibiotics, oral mucosal protective agents, chemotherapy	9/low
Wang et al., 2022	China	Case-control study	172	77/95	53.1	All stages	Radiotherapy or chemo-radiotherapy	NA	86/172	Smoking, oral hygiene, drinking, oral pH < 7.0, overweight, antibiotics, chemotherapy, oral mucosal protective agents	7/low

Wu et al., 2022	China	Prospective cohort study	88	28/60	54.4	Stage I-III	Radiotherapy or chemo-radiotherapy	RTOG criteria	88/88	Smoking, diabetes, oral pH < 7.0	7/low
Xu et al., 2019	China	Case-control study	166	74/92	NA	All stages	Radiotherapy	WHO OM grading scale	166/166	Smoking, oral hygiene, chemotherapy, oral pH, oral mucosal protective agents, antibiotics	7/low
Yuan et al., 2022	China	Retrospective cohort study	183	34/149	NA	All stages	Radiotherapy or chemo-radiotherapy	RTOG criteria	183/183	Chemotherapy, white blood cell, hemoglobin	8/low
Zhu et al., 2014	China	Prospective cohort study	56	16/40	47	All stages	Radiotherapy	RTOG criteria	56/56	White blood cell, diabetes	7/low

Abbreviations: BMI = Body Mass Index, CTCAE = Common Terminology Criteria for Adverse Events, EUD = Equivalent Uniform Dose, NA = Not Accessible, , NOS = Newcastle-Ottawa scale, RTOG = Radiation Therapy Oncology Group, RTOM = Radiotherapy-Induced Oral Mucositis WHO = World Health Organization, OM = Oral Mucositis, ,.

before radiotherapy (OR = 4.72, 95% CI: 2.45–9.09), and combined chemotherapy (OR = 7.89, 95% CI: 3.66–16.99) were significant risk factors, while the use of oral mucosal protective agents (OR = .26, 95% CI: .14–.48) and the use of antibiotics at early treatment stage (OR = .30, 95% CI: .13–.68) were protective factors of radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma. In addition, results showed that patient with diabetes (OR = 1.33, 95% CI: .45–3.91) was a risk factor but with no statistical significance (Fig. 4).

Discussion

To our knowledge, this is the first meta-analysis to estimate the incidence and to explore risk factors for radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma. Most of the included studies in our review were from China, which resulted from the extremely uneven geographical global distribution, with more than 70.0% new cases per year are in East and Southeast Asia [2]. High rates of nasopharyngeal carcinoma have long been observed in the population of Southern China, with an age-standardized rate (world) of 3.0/100000 [2,41], and accounting for almost a half of nasopharyngeal carcinoma patients worldwide [42]. Although nasopharyngeal carcinoma is relatively uncommon compared with other cancers, it remains a significant public health problem in East and Southeast Asia [43]. Based on the comprehensive search strategy from eight electronic databases and systematic review of relevant studies, our study results provided evidence-based references for developing targeted preventive measures of radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma.

Incidence of radiotherapy-induced oral mucositis

The pooled results of the meta-analysis revealed that almost all patients with nasopharyngeal carcinoma have experienced oral mucositis during the radiotherapy process, with a pooled incidence of 99.0%, and more than half (52.0%) of patients suffered from severe oral mucositis, which is as high as that among patients with head and neck cancers [6,44]. On the one hand, the persistent and concentrated high-dose irradiation can inevitably induce acute and chronic toxicity reactions including radiotherapy-induced oral mucositis [2] in spite of the modern advances in radiotherapy technology. On the other hand, currently, the consistent and targeted assessment tools for oral mucositis are insufficient [45], nurses are unable to evaluate radiotherapy-induced oral mucositis comprehensively during clinical practice, which might cause inadequate attention and underestimation of the severity of oral mucositis among patients with nasopharyngeal carcinoma. In addition, consistent with other countries in the world, patients with nasopharyngeal carcinoma in China usually are treated with outpatient radiotherapy, which means they were inaccessible to systemic and structured professional care and support compared to the inpatient setting [46], such as basic oral care, oral health education, and coping skills for oral mucositis. Thus, patients with nasopharyngeal carcinoma often suffer from high incidence of radiotherapy-induced oral mucositis, and it is urgent and necessary to pay more attention to nasopharyngeal carcinoma patients and take effective measures for the early identification and prevention of oral mucositis during their treatment process.

To test the reliability and stability of pooled results and explore the potential sources of heterogeneity, we also conducted subgroup analyses on the basis of participant characteristics (gender, cancer stage, and treatment regime) and study characteristics (study design, study language, sample size, and diagnostic

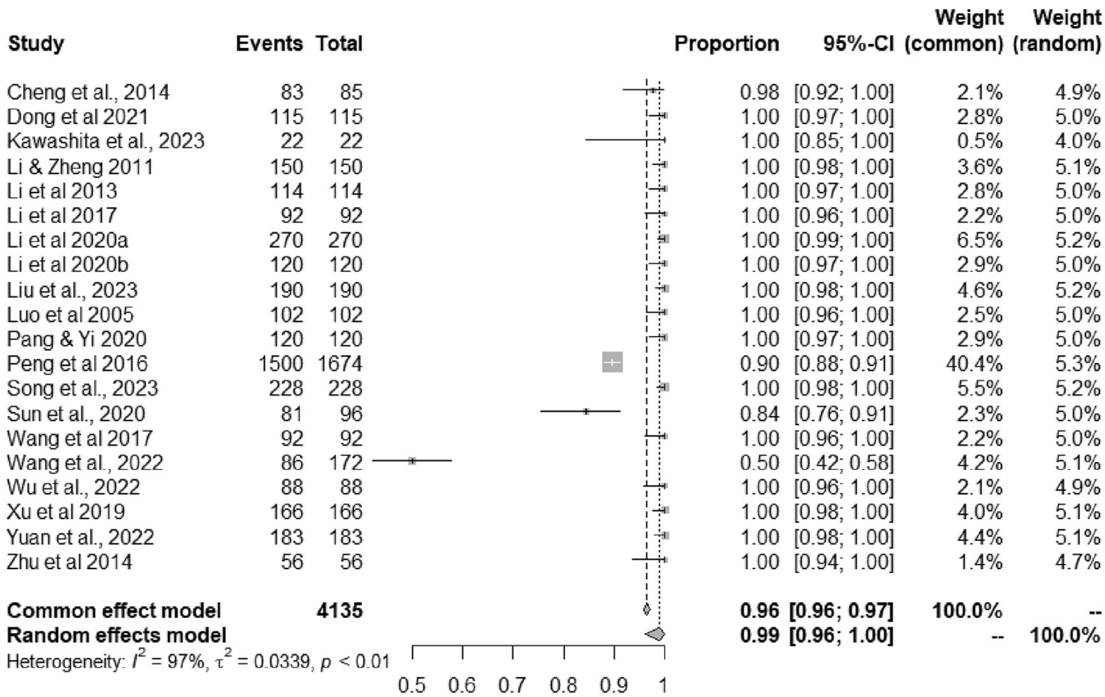


Figure 2. Forest Plot of Incidence of Radiotherapy-Induced Oral Mucositis. CI = Confidence Interval.

criteria). The results showed that the incidence of radiotherapy-induced oral mucositis was similar within subgroups, which suggested that the results were stable and reliable, but there might be other possible sources of heterogeneity among these included studies. For example, the sample sources and age groups varied among the different studies, which might contribute to the high heterogeneity of our study.

Risk factors for severe radiotherapy-induced oral mucositis

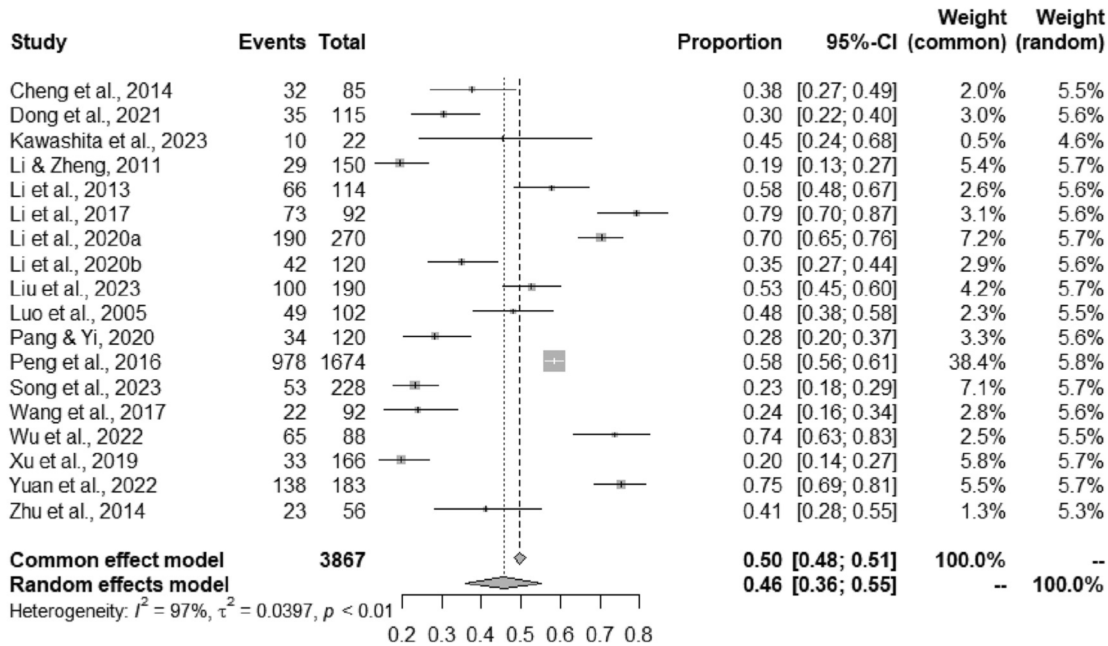
This study identified eight significant risk factors for severe radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma, including poor oral hygiene, oral pH less than 7.0, the use of oral mucosal protective agents, overweight before radiotherapy, smoking, drinking, combined chemotherapy, and the use of antibiotics.

Poor oral hygiene, oral pH less than 7.0, and the use of oral mucosal protective agents are three oral health-related risk factors for severe radiotherapy-induced oral mucositis, among which poor oral hygiene is the most significant risk factor. Previous studies also showed that the status of oral health and hygiene is a risk factor for radiotherapy-induced oral mucositis [47]. However, it was reported that 64.4% of patients who received radiotherapy had poor oral hygiene, and the proportion of poor oral hygiene was much higher among patients with oral mucositis (69.1%) than among patients without oral mucositis (42.9%) [48]. Oral health, starting with good oral hygiene, is essential for patient wellness, and providing oral health education and prevention interventions to promote good oral hygiene can prevent infection by oral bacteria and consequently could reduce the risk and severity of oral mucositis [49,50,58]. In addition, previous studies have already identified that the use of oral mucosal protective agents and interventions promoting the oral pH to shift from an acidic to alkaline could enhance oral protection against mucositis and decrease the susceptibility to oral mucositis among patients [51,52]. Thus, preventive strategies are needed to target facilitating oral health during and even prior to radiation treatment to decrease the risk and severity of oral mucositis among patients with nasopharyngeal carcinoma [50].

Unsurprisingly, smoking and drinking were two other risk factors for severe radiotherapy-induced oral mucositis. A previous study [53] conducted among patients with head and neck carcinoma also revealed that smoking was a risk factor for radiotherapy-induced oral mucositis. Although drinking was not identified as a risk factor in previous studies, alcohol use is one of the leading risk factors for a range of diseases and injury conditions, and there is even a causal relationship between them [54]. As common lifestyle-related risk factors, further targeted strategies and interventions are needed to reduce the utilization of tobacco and alcohol among patients.

This meta-analysis showed that overweight before radiotherapy was a risk factor for radiotherapy-induced oral mucositis, which was inconsistent with Saito et al. [55] who reported significant association between low BMI and oral mucositis. However, as oral mucositis might lead to anorexia, dysphagia, and low BMI during radiotherapy, it is difficult to confirm whether low BMI caused oral mucositis, or the oral mucositis resulted in low BMI. For our result, a previous study [56] has identified the significant correlation between overweight and poor oral conditions, and the possible mechanism is that adipose tissue could cause increased levels of IL-6, IL-8, and TNF- α, resulting in raised leukocytes, which might activate systemic inflammation. Therefore, overweight status before radiotherapy also might be the focus for preventing severe oral mucositis.

Our study showed that concomitant chemotherapy and the use of antibiotics at early treatment stage were treatment-related risk factors for radiotherapy-induced oral mucositis. Although identified as a potential protective factor of oral mucositis, the use of antibiotics at early treatment stage for prevention oral mucositis was not recommended by any guidelines to be used in the prevention of oral mucositis, and caution is needed for antibiotic utilization among patients [57]. Moreover, due to the toxicity of chemotherapeutics, patients who receive radiotherapy combined



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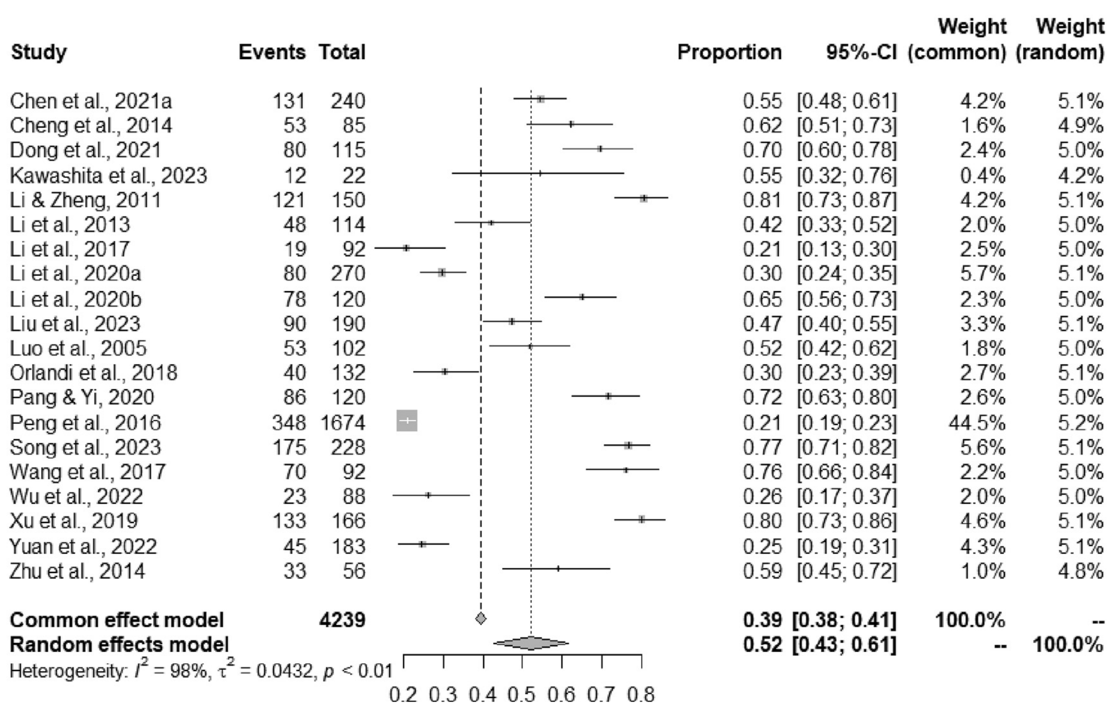

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Figure 3. (A) Forest Plot of Incidence of Mild Radiotherapy-Induced Oral Mucositis. (B) Forest Plot of Incidence of Severe Radiotherapy-Induced Oral Mucositis. CI = Confidence Interval.

with chemotherapy can be definitely more prone to experiencing severe oral mucositis [58], and more attention is needed to patients who receive chemoradiotherapy when providing preventive measures of oral mucositis.

Limitations

Some limitations should be considered when interpreting the results: (1) due to the inconsistent characteristics among the

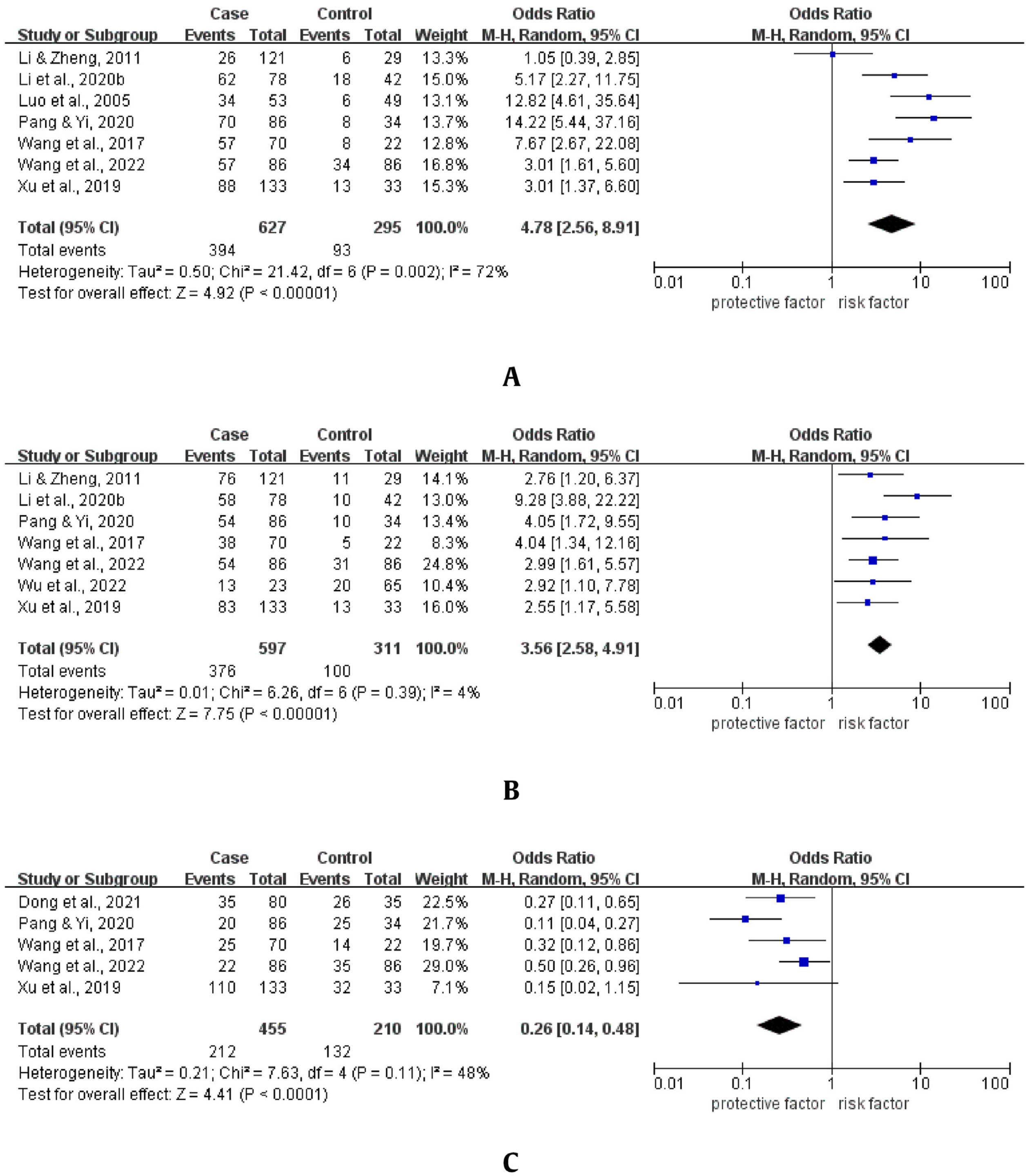
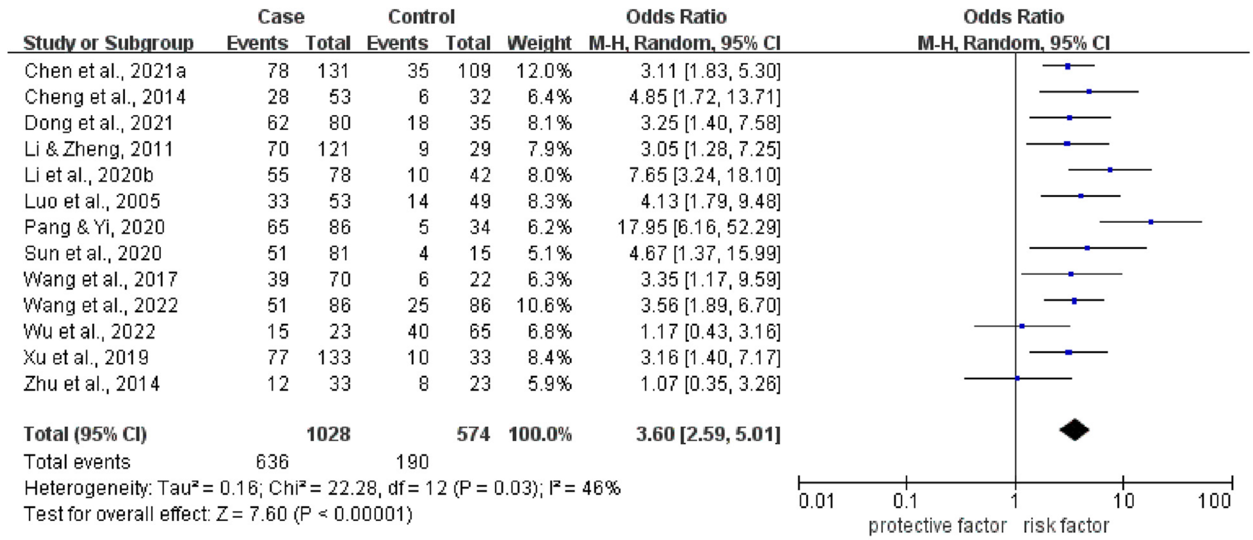


Figure 4. (A) Forest Plot of Odds Ratio of Poor Oral Hygiene. (B) Forest Plot of Odds Ratio of Oral pH < 7.0. (C) Forest Plot of Odds Ratio of the Use of Oral Mucosal Protective Agents. (D) Forest Plot of Odds Ratio of Smoking. (E) Forest Plot of Odds Ratio of Drinking. (F) Forest Plot of Odds Ratio of Overweight Before Radiotherapy. (G) Forest Plot of Odds Ratio of Combined Chemotherapy. (H) Forest Plot of Odds Ratio of the Use of Antibiotics. (I) Forest Plot of Odds Ratio of the Use of Diabetes. CI = Confidence Interval, BMI = Body Mass Index.

included studies, high heterogeneity existed in our study; (2) some potential risk factors were not available for meta-analysis because they were reported in less than three studies, or reported with incomplete data; and (3) due to the geographical features of nasopharyngeal carcinoma, most of the studies included in our study were published in China. Wider researches with larger sample sizes are needed to further identify the incidence and risk factors for radiotherapy-induced oral mucositis.

Implications for further research and nursing practice

The results of this study showed that almost all nasopharyngeal carcinoma patients inevitably experienced radiotherapy-induced



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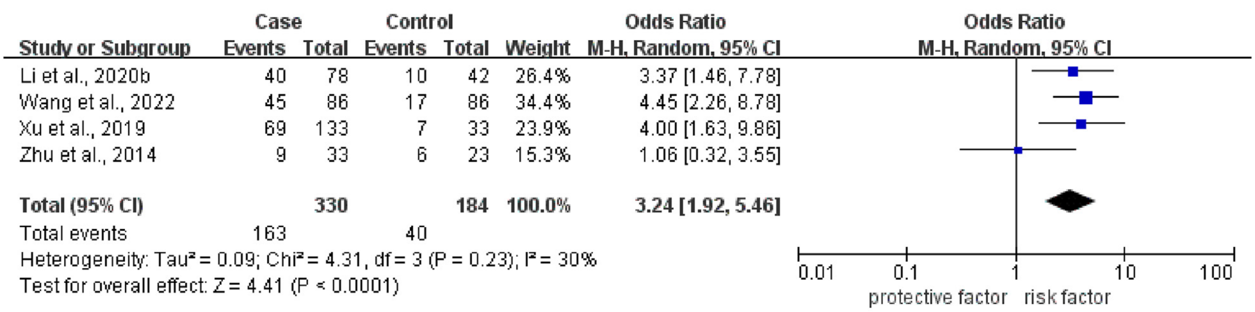

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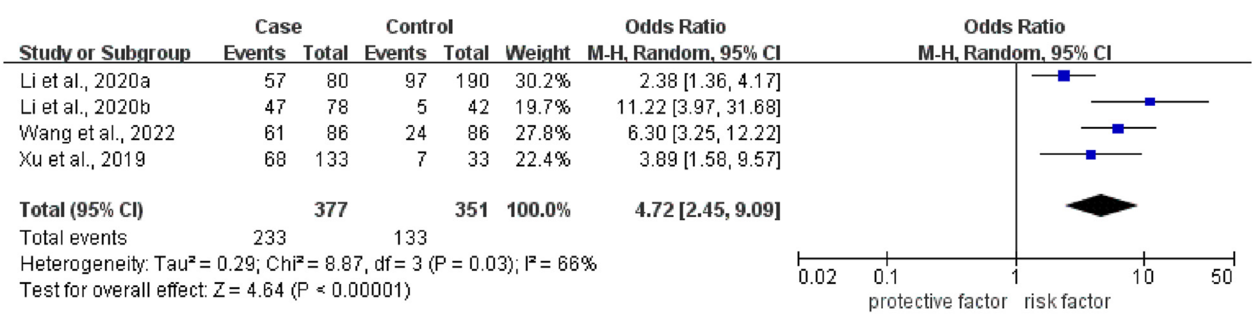
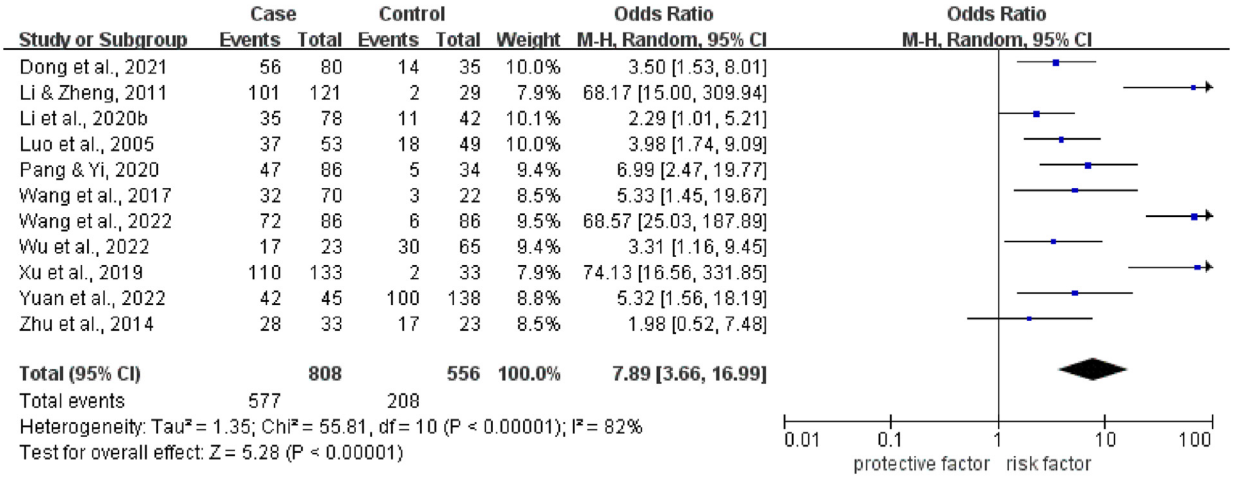


F

Figure 4. (*continued*).

oral mucositis, and more than half of patients even suffered from severe oral mucositis during radiotherapy. Radiotherapy-induced oral mucositis poses negative effects on patients' physical, emotional, and social dimensions and quality of life [58], which should be highly valued as an interdisciplinary problem during clinical practice. Therefore, interventions for effective management of oral mucositis should cover interdisciplinary professionals, including oncology, stomatology, psychology, and nutritional science. For instance, in addition to the symptom management of oral mucositis, it is also essential for regular clinical screening the risk of nutritional and psychological problems [59]. In addition, most risk factors for oral mucositis in our study were modifiable, including oral hygiene, oral pH, the use of oral mucosal protective agents, smoking, drinking, and overweight. Further studies and clinical practitioners should focus on the controllable risk factors and should accordingly develop targeted preventive measures for radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma.



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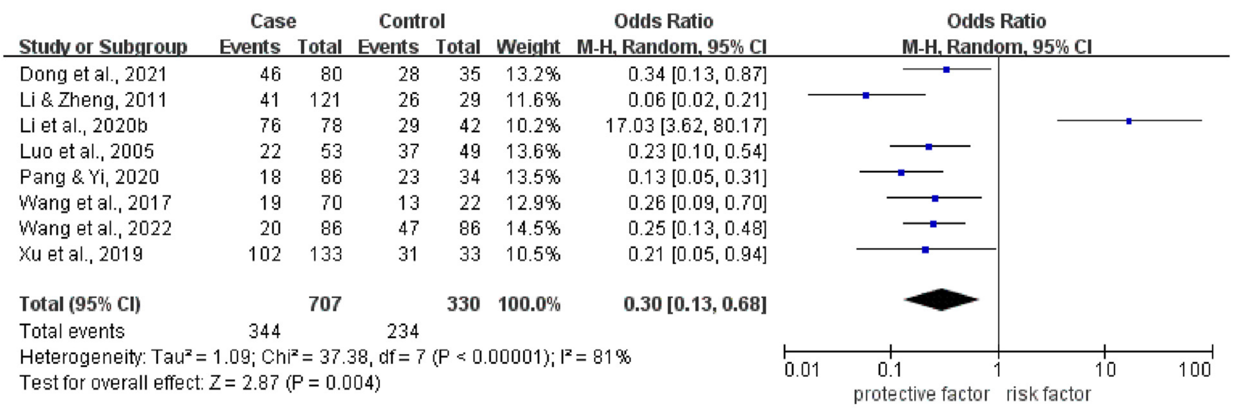

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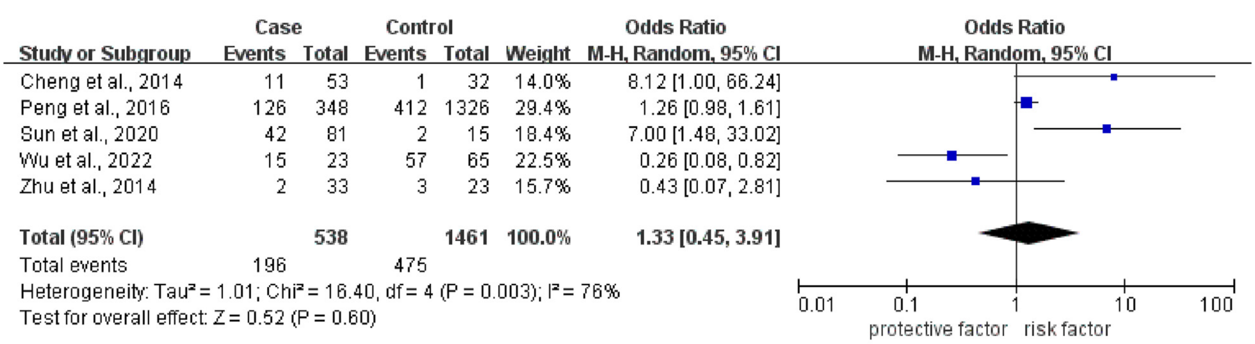

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Figure 4. (*continued*).

Conclusions

This study found that almost all patients with nasopharyngeal carcinoma have experienced radiotherapy-induced oral mucositis, and more than half of patients have suffered from severe oral mucositis during radiation therapy. Poor oral hygiene, oral pH less than 7.0, use of protective agents, smoking, drinking, overweight before radiotherapy, combined chemotherapy, and the use of antibiotics at early treatment stage are risk factors for severe radiotherapy-induced oral mucositis. Wider and larger well-designed studies are needed to explore the risk factors for radiotherapy-induced oral mucositis, and promoting oral health, especially good oral hygiene, might be the key focus of decreasing the risk and severity of radiotherapy-induced oral mucositis among patients with nasopharyngeal carcinoma.

Contributions

Study Design and writing: JJL, XLH and CMZ.
Data Collection: JJL, YZ, CG and QW.
Data Analysis and Interpretation: JJL, CMZ, YXD and XLH.
Manuscript Writing: JJL and XLH.

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Ethical statement

Informed consent and ethical approval were unnecessary, as the data used in this study came from already published studies.

Data availability statement

The authors confirm that the data supporting the findings of this study are available within the article and its supplementary materials.

Conflict of interest

No conflict of interest exists in the submission of this manuscript.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.04.002.

References

1. International Agency for Research on Cancer. https://gco.iarc.fr/today/data/factsheets/cancers/4-Nasopharynx-fact-sheet.pdf (26 March 2022 accessed).
2. Chen YP, Chan ATC, Le QT, Blanchard P, Sun Y, Ma J. Nasopharyngeal carcinoma. Lancet. 2019;394(10192):64–80. https://doi.org/10.1016/S0140-6736(19)30956-0
3. Li J, Liu Y, Jiang J, Peng X, Hu X. Effect of telehealth interventions on quality of life in cancer survivors: a systematic review and meta-analysis of randomized controlled trials. Int J Nurs Stud. 2021;122:103970. https://doi.org/10.1016/j.ijnurstu.2021.103970
4. Yang G, Feng D, Li F, Luo B, Zhu J, Yang Q, et al. A randomized, controlled phase II trial of maxillofacial and oral massage in attenuating severe radiotherapy-induced oral mucositis and lipid metabolite changes in nasopharyngeal carcinoma. Radiother Oncol. 2021;163:76–82. https://doi.org/10.1016/j.radonc.2021.07.024
5. Zheng B, Zhu X, Liu M, Yang Z, Yang L, Lang J, et al. Randomized, double-blind, placebo-controlled trial of shuanghua baihe tablets to prevent oral mucositis in patients with nasopharyngeal cancer undergoing chemoradiation therapy. Int J Radiat Oncol Biol Phys. 2018;100(2):418–26. https://doi.org/10.1016/j.ijrobp.2017.10.013
6. Daugėlaitė G, Užkuraitytė K, Jagelavičienė E, Filipauskas A. Prevention and treatment of chemotherapy and radiotherapy induced oral mucositis. Medicina (Kaunas). 2019;55(2):25. https://doi.org/10.3390/medicina55020025
7. Plevova P. Prevention and treatment of chemotherapy- and radiotherapy-induced oral mucositis: a review. Oral Oncol. 1999;35(5):453–70. https://doi.org/10.1016/s1368-8375(99)00033-0
8. Davy C, Heathcote S. A systematic review of interventions to mitigate radiotherapy-induced oral mucositis in head and neck cancer patients. Support Care Cancer. 2021;29(4):2187–202. https://doi.org/10.1007/s00520-020-05548-0
9. Peng H, Chen BB, Chen L, Chen YP, Liu X, Tang LL, et al. A network meta-analysis in comparing prophylactic treatments of radiotherapy-induced oral mucositis for patients with head and neck cancers receiving radiotherapy. Oral Oncol. 2017;75:89–94. https://doi.org/10.1016/j.oraloncology.2017.11.001
10. Tian X, Xu L, Liu X, Wang CC, Xie W, Jiménez-Herrera MF, et al. Impact of honey on radiotherapy-induced oral mucositis in patients with head and neck cancer: a systematic review and meta-analysis. Ann Palliat Med. 2020;9(4):1431–41. https://doi.org/10.21037/apm-20-44
11. Lima ICGDS, de Fátima Souto Maior L, Gueiros LAM, Leão JC, Higino JS, Carvalho AAT. Clinical applicability of natural products for prevention and treatment of oral mucositis: a systematic review and meta-analysis. Clin Oral Invest. 2021;25(6):4115–24. https://doi.org/10.1007/s00784-020-03743-1
12. Karagözoğlu S, Filiz Ulusoy M. Chemotherapy: the effect of oral cryotherapy on the development of mucositis. J Clin Nurs. 2005;14(6):754–65. https://doi.org/10.1111/j.1365-2702.2005.01128.x
13. Yang C, Gong G, Jin E, Han X, Zhuo Y, Yang S, et al. Topical application of honey in the management of chemo/radiotherapy-induced oral mucositis: a systematic review and network meta-analysis. Int J Nurs Stud. 2019;89:80–7. https://doi.org/10.1016/j.ijnurstu.2018.08.007
14. Nishii M, Soutome S, Kawakita A, Yutori H, Iwata E, Akashi M, et al. Factors associated with severe oral mucositis and candidiasis in patients undergoing radiotherapy for oral and oropharyngeal carcinomas: a retrospective multicenter study of 326 patients. Support Care Cancer. 2020;28(3):1069–75. https://doi.org/10.1007/s00520-019-04885-z
15. Soutome S, Yanamoto S, Nishii M, Kojima Y, Hasegawa T, Funahara M, et al. Risk factors for severe radiation-induced oral mucositis in patients with oral cancer. J Dent Sci. 2021;16(4):1241–6. https://doi.org/10.1016/j.jds.2021.01.009
16. Xu F, Teng HR, Wang YX, He Y. Analysis of relevant factors of radiotherapy-induced oral mucositis after radiotherapy in patients with nasopharyngeal carcinoma. Pract Prev Med. 2019;26(12):1476–9. https://doi.org/10.3969/j.issn.1006-3110.2019.12.019
17. Dong KC, Zhang M, Xia L, Liang Y, Zhang MJ, Fei XX. Analysis of risk factors for severe oral mucositis in intensity-modulated radiotherapy for nasopharyngeal carcinoma. World Journal of Integrated Traditional and Western Medicine (China). 2021;16(10):1924–8. https://doi.org/10.13935/j.cnki.sjzx.211032
18. Li XD, Zheng XY. Analysis of main associated factors of radiation therapy-induced oral mucositis during intensity-modulated radiotherapy among patients with nasopharyngeal carcinoma. J Nan Jing Med Univ. 2011;11(4):134–7.
19. Orlandi E, Iacovelli NA, Rancati T, Cicchetti A, Bossi P, Pignoli E, et al. Multivariable model for predicting acute oral mucositis during combined IMRT and chemotherapy for locally advanced nasopharyngeal cancer patients. Oral Oncol. 2018;86:266–72. https://doi.org/10.1016/j.oraloncology.2018.10.006
20. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. https://doi.org/10.1136/bmj.n71
21. Wells GA, Shea B, O'Connell D, Peterson J, Welch V, Losos M, et al. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomised studies in meta-analyses. 2022. accessed) http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp
22. Lin L, Xu C. Arcsine-based transformations for meta-analysis of proportions: pros, cons, and alternatives. Health Sci Rep. 2020;3(3):e178. https://doi.org/10.1002/hsr2.178
23. Chen G, Jiang H, Jiang D, Wu Q, Li Z, Hua X, et al. Pretreatment serum vitamin level predicts severity of radiation-induced oral mucositis in patients with nasopharyngeal carcinoma. Head Neck. 2021a;43(4):1153–60. https://doi.org/10.1002/hed.26576
24. Cheng H, Wu H, Lu X, Xu J. Clinical observation of acute skin and oral mucous membrane reactions in patients with nasopharyngeal carcinoma treated with concurrent radiochemotherapy and correlated factors. Chin J Radiol Med Prot. 2014;34(5):351–4. https://doi.org/10.3760/cma.j.issn.0254-5098.2014.05.008
25. Kawashita Y, Soutome S, Umeda M, Saito T. Predictive risk factors associated with severe radiation-induced mucositis in nasopharyngeal or oropharyngeal cancer patients: a retrospective study. Biomedicines. 2022;10(10):2661. https://doi.org/10.3390/biomedicines10102661
26. Li H, You Y, Lin C, Zheng M, Hong C, Chen J, et al. XRCC1 codon 399Gln polymorphism is associated with radiotherapy-induced acute dermatitis and mucositis in nasopharyngeal carcinoma patients. Radiat Oncol. 2013;8:31. https://doi.org/10.1186/1748-717X-8-31
27. Li K, Yang L, Xin P, Chen Y, Hu QY, Chen XZ, et al. Impact of dose volume parameters and clinical factors on acute radiation oral mucositis for locally advanced nasopharyngeal carcinoma patients treated with concurrent

intensity-modulated radiation therapy and chemoradiotherapy. Oral Oncol. 2017;72:32–7. https://doi.org/10.1016/j.oraloncology.2017.06.026
28. Li PJ, Li KX, Jin T, Lin HM, Fang JB, Yang SY, et al. Predictive model and precaution for oral mucositis during chemo-radiotherapy in nasopharyngeal carcinoma patients. Front Oncol. 2020a;10:596822. https://doi.org/10.3389/fonc.2020.596822
29. Li SE, Wei WH, Lv ZQ. Associated factors of radiotherapy-induced oral mucositis after radiotherapy in patients with nasopharyngeal carcinoma. China Practical Medical (China). 2020b;15(20):110–2. https://doi.org/10.14163/j.cnki.11-5547/r.2020.20.045
30. Liu Z, Huang L, Wang H, Shi Z, Huang Y, Liang L, et al. Predicting nomogram for severe oral mucositis in patients with nasopharyngeal carcinoma during intensity-modulated radiation therapy: a retrospective cohort study. Curr Oncol. 2022;30(1):219–32. https://doi.org/10.3390/curroncol30010017
31. Luo DH, Hong MH, Guo L, Cao KJ, Deng MQ, Mo HY. Analysis of oral mucositis risk factors during radiotherapy for nasopharyngeal carcinoma patients and establishment of a discriminant model. Chin J Cancer. 2005;24(7):850–4. https://doi.org/10.3969/j.issn.1000-467X.2005.07.017
32. Pang SH, Yi YL. Relevant factors of radiation-induced oral mucositis in patients with nasopharyngeal carcinoma undergoing intensity-modulated radiotherapy. Drug Evaluation (China). 2020;17(2):59–60, 62 https://doi.org/10.3969/j.issn.1672-2809.2020.02.030.
33. Peng W, Chen J, Jiang CH, Su GJ, Xiao YP, Chen Y. Correlation of blood glucose level with radiation oral mucositis after radiation therapy in nasopharyngeal carcinoma: a study of 1 674 patients. Journal of Diagnostics Concepts & Practice (China). 2016;15(3):317–21. https://doi.org/10.16150/j.1671-2870.2016.03.026
34. Song X, Su L, Lin Q, Liu S, Zhang W, Hong J. Effect of nutritional status before radiotherapy on radiation-induced acute toxicities in patients with nasopharyngeal carcinoma. Head Neck. 2023;45(3):620–8. https://doi.org/10.1002/hed.27275
35. Sun J, Cheng M, Huang X. Associated risk factors of acute mucosa reaction in patients with nasopharyngeal carcinoma after radiotherapy and chemotherapy and application of OREM self-protection theory. J Clin Pathol Res. 2020;40(3):711–7. https://doi.org/10.3978/j.issn.2095-6959.2020.03.027
36. Wang L, Cao YM, Shi JY. Risk factors of radiation induced oral mucositis after intensity-modulated radiotherapy for nasopharyngeal carcinoma. Chinese Journal of Otorhinolaryngology In Integrative Medicine (China). 2017;25(6):456–9. https://doi.org/10.16542/j.cnki.issn.1007-4856.2017.06.016
37. Wang Y, Cheng N, Shi B, Wu D. Influactors of radiation oral mucositis after radiotherapy in nasopharyngeal patients. Prac J Cancer. 2022;37(6):907–9. https://doi.org/10.3969/j.issn.1001-5930.2022.06.011, 916.
38. Wu J, Wang A, Zou J. Correlation analysis between prognostic nutritional index before radiotherapy and severity of acute oral mucositis in patients with nasopharyngeal carcinoma. J Multidis Cancer Manag (Electronic version). 2022;8(4):76–80. https://doi.org/10.12151/JMCM.2022.04-13
39. Yuan H, Wei Y, Liang G. Analysis of risk factors for severe radiotherapy-induced oral mucositis in patients with nasopharyngeal carcinoma. Mode Med J Chin. 2022;24(7):35–8. https://doi.org/10.3969/j.issn.1672-9463.2022.07.007
40. Zhu XX, Chen LH, Chao YL. An analysis on risk factors of radiation-induced oral mucositis in patients with nasopharyngeal carcinoma. The Journal of Practical Medicine (China). 2014;30(16):2583–5. https://doi.org/10.3969/j.issn.1006-5725.2014.16.018
41. Chang ET, Ye W, Zeng YX, Adami HO. The evolving epidemiology of nasopharyngeal carcinoma. Cancer Epidemiol Biomarkers Prev. 2021;30(6):1035–47. https://doi.org/10.1158/1055-9965.EPI-20-1702
42. Min Y, Wei X, Xia X, Wei Z, Li R, Jin J, et al. Hepatitis B virus infection: an insight into the clinical connection and molecular interaction between hepatitis B virus and host extrahepatic cancer risk. Front Immunol. 2023;14:1141956. https://doi.org/10.3389/fimmu.2023.1141956
43. Chen YP, Ismaila N, Chua MLK, Colevas AD, Haddad R, Huang SH, et al. Chemotherapy in combination with radiotherapy for definitive-intent treatment of stage II-IVA nasopharyngeal carcinoma: CSCO and ASCO guideline. J Clin Oncol. 2021b;39(7):840–59. https://doi.org/10.1200/JCO.20.03237
44. Hong CHL, Gueiros LA, Fulton JS, Cheng KKF, Kandwal A, Galiti D, et al. Systematic review of basic oral care for the management of oral mucositis in cancer patients and clinical practice guidelines. Support Care Cancer. 2019;27(10):3949–67. https://doi.org/10.1007/s00520-019-04848-4
45. Pulito C, Cristaudo A, Porta C, Zapperi S, Blandino G, Morrone A, et al. Oral mucositis: the hidden side of cancer therapy. J Exp Clin Cancer Res. 2020;39(1):210. https://doi.org/10.1186/s13046-020-01715-7
46. Hiatt J, Young A, Brown T, Banks M, Segon B, Bauer J. A qualitative comparison of the nutrition care experiences of carers supporting patients with head and neck cancer throughout surgery and radiation treatment and survivorship. Support Care Cancer. 2022;30(11):9359–68. https://doi.org/10.1007/s00520-022-07348-0
47. Musha A, Hirai C, Kitada Y, Tsunoda A, Shimada H, Kubo N, et al. Relationship between oral mucositis and the oral bacterial count in patients with head and neck cancer undergoing carbon ion radiotherapy: a prospective study. Radiother Oncol. 2022;167:65–71. https://doi.org/10.1016/j.radonc.2021.12.010
48. Gao Y. Analysis of related factors and oral health-related quality of life in patients with radiation-induced oral mucositis. Shanxi (China): Shanxi Medical University; 2020.
49. Bezerra PMM, Sampaio MEA, Dos Santos FG, Ribeiro ILA, Santiago BM, de Sousa SA, et al. The effectiveness of an oral health education and prevention program on the incidence and severity of oral mucositis in pediatric cancer patients: a non-randomized controlled study. Support Care Cancer. 2021;29(12):7877–85. https://doi.org/10.1007/s00520-021-06387-3
50. Cullen L, Baumler S, Farrington M, Dawson C, Folkmann P, Brenner LCE. Oral care for head and neck cancer symptom management. Am J Nurs. 2018;118(1):24–34. https://doi.org/10.1097/01.NAJ.0000529694.30568.41
51. Baysal E, Sari D, Vural F, Çağırgan S, Saydam G, Töbü M, et al. The effect of cryotherapy on the prevention of oral mucositis and on the oral pH value in multiple myeloma patients undergoing autologous stem cell transplantation. Semin Oncol Nurs. 2021;37(3):151146. https://doi.org/10.1016/j.soncn.2021.151146
52. Wei J, Wu J, Wang H, Wang B, Zhao T, Meng L, et al. A bioadhesive barrier-forming oral liquid gel improved oral mucositis and nutritional status in patients with head and neck cancers undergoing radiotherapy: a retrospective single center study. Front Oncol. 2021;11:617392. https://doi.org/10.3389/fonc.2021.617392
53. Tao Z, Gao J, Qian L, Huang Y, Zhou Y, Yang L, et al. Factors associated with acute oral mucosal reaction induced by radiotherapy in head and neck squamous cell carcinoma: a retrospective single-center experience. Medicine (Baltimore). 2017;96(50):e8446. https://doi.org/10.1097/MD.0000000000008446
54. World Health Organization. https://www.who.int/news-room/fact-sheets/detail/alcohol
55. Saito N, Imai Y, Muto T, Sairenchi T. Low body mass index as a risk factor of moderate to severe oral mucositis in oral cancer patients with radiotherapy. Support Care Cancer. 2012;20(12):3373–7. https://doi.org/10.1007/s00520-012-1620-7
56. Thanakun S, Pornprasertsuk-Damrongsri S, Izumi Y. Increased oral inflammation, leukocytes, and leptin, and lower adiponectin in overweight or obesity. Oral Dis. 2017;23(7):956–65. https://doi.org/10.1111/odi.12679
57. Lalla RV, Bowen J, Barasch A, Elting L, Epstein J, Keefe DM, et al. MASCC/ISOO clinical practice guidelines for the management of mucositis secondary to cancer therapy. Cancer. 2014;120(10):1453–61. https://doi.org/10.1002/cncr.28592
58. Kusiak A, Jereczek-Fossa BA, Cichońska D, Alterio D. Oncological-therapy related oral mucositis as an interdisciplinary problem-literature review. Int J Environ Res Publ Health. 2020;17(7):2464. https://doi.org/10.3390/ijerph17072464
59. Hu X, Huang W. Protecting the psychological well-being of healthcare workers affected by the COVID-19 outbreak: perspectives from China. Nurs Health Sci. 2020;22(3):837–8. https://doi.org/10.1111/nhs.12727

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Research Article

Fatigue and Quality of Life Among Patients with Diabetes and Non-diabetes Receiving Primary Percutaneous Coronary Interventions

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SUMMARY

Purpose: Few studies have examined the effect of diabetes mellitus (DM) on patients with coronary artery disease. The relationships between quality of life (QoL), risk factors, and DM of patients receiving percutaneous coronary interventions (PCIs) are poorly understood. We investigated the influence of DM on fatigue and QoL over time among patients receiving PCIs.
Methods: An observational cohort study with a longitudinal, repeated-measures design was used to investigate fatigue and QoL among 161 Taiwanese patients with coronary artery disease with/without DM who received primary PCIs between February and December 2018. Participants provided demographic information and their Dutch Exertion Fatigue Scale and the 12-Item Short-Form Health Survey scores before the PCI and two weeks, three months, and six months post-discharge.
Results: Seventy-seven PCI patients were in the DM group (47.8%; mean age = 67.7 [SD = 10.4] years). The mean scores of fatigue, physical component scale (PCS), and mental component scale (MCS) were 7.88 (SD = 6.74), 40.74 (SD = 10.05), and 49.44 (SD = 10.57), respectively. DM did not affect the magnitude of change in fatigue or QoL over time. Patients with DM perceived similar fatigue as those without DM before PCI and two weeks, three and six months post-discharge. Patients with DM perceived lower psychological QoL than those without DM two weeks post-discharge. Compared to pre-surgery scores, patients without DM perceived lower fatigue at two weeks, three months, and six months post-discharge, and higher physical QoL at three- and six-months post-discharge.
Conclusions: Compared with DM patients, patients without DM had higher pre-intervention QoL and better psychological QoL two weeks post-discharge, and DM did not influence fatigue or QoL of patients receiving PCIs over six months. DM may affect patients in the long term; therefore, nurses should educate patients to regularly take medication, maintain proper habits, notice comorbidities, and follow rehabilitation regimes after PCIs to improve prognosis.

Introduction

Diabetes mellitus (DM) is a serious chronic disease [1], affecting approximately 537 million adults worldwide [2]. DM, hyperglycemia, insulin resistance, and hyperinsulinemia often trigger vascular smooth muscle cell proliferation, inflammation, dyslipidemia, and endothelial dysfunction, resulting in a higher risk of cardiovascular disease [1]—a major independent risk factor for coronary artery disease (CAD) [3]. Reports show that around 68% of patients with DM aged older than 65 years die from heart disease [4].

CAD often causes myocardial ischemia, fatigue [5], and declining quality of life (QoL) [6]. Insulin resistance hinders protein to synthesize muscles, and high blood sugar promotes muscles to break down, which affects patients' activities of daily living. Thus, patients with DM experience increased feelings of fatigue [1]. Fatigue is defined as a subjective sense of tiredness and lack of energy that negatively influences physical and mental capacity [7]. Research shows that most patients with CAD perceive fatigue after heart attacks, which has a substantial adverse effect on QoL [8].

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Abbreviations: CAD, coronary artery disease; DM, diabetes mellitus; PCI, percutaneous coronary intervention; QoL, quality of life.

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Therefore, early revascularization, which has been shown to have a certain effect on QoL, is vital for patients with CAD. Percutaneous coronary intervention (PCI) has become the most effective revascularization therapy for CAD [9]. Fatigue is the most intense symptom experienced by patients with CAD six months after PCI [5]. Moreover, one year after PCI, both fatigue and depression affected the perception of illness in patients with CAD and subsequently influenced their QoL [6].

There are few studies about the effect of CAD on patients with DM, and the relationship between QoL, risk factors, and DM remains unclear. Pischke et al. found that patients with CAD and DM reported lower QoL than those without DM, especially women [10]. Their study also showed that men with DM had CAD and hypertension more often than men without DM [10]. However, this study is relatively old and recruited relatively few patients with DM; as such, the results might not accurately describe changes in QoL of patients with CAD and DM after PCI treatment. In 2013, national guidelines indicated that DM increases the risk of progression of CAD and causes cardiovascular complications [11]. Male patients with both DM and CAD had a mortality rate that was thrice than that of patients with CAD but without DM [11]; however, the aforementioned study is only a CAD guideline, not a research study.

The relationship between QoL of patients with CAD, which is affected by several comorbidities [12], and fatigue, which influences QoL among patients with DM [13], is poorly understood. An underlying cause of CAD is DM, which often triggers vascular smooth muscle cell proliferation, inflammation, and endothelial dysfunction, resulting in deterioration of CAD progression. Therefore, this study examined the relationship between fatigue and QoL among patients with diabetes and non-diabetes receiving primary PCI.

Methods

Study design and participants

This was an observational cohort study using a longitudinal, repeated-measures design to investigate fatigue and QoL among 165 patients with CAD with/without DM who received primary PCIs between February and December 2018. Patients were recruited from coronary care units of one large hospital in Taiwan. The researcher checked the list of hospitalizations for primary PCI daily and explained the study aim to the PCI patients in order to obtain their informed consent letters. Then, the researcher reviewed PCI patients' medical records to confirm if patients have a diagnosis of DM under DM drugs. Participants were thereby allocated to two groups: DM ($n = 78$) and non-DM ($n = 87$). The inclusion criteria were as follows: (1) aged $\geq$20 years, (2) with/without DM and diagnosed by a cardiologist as requiring PCI, and (3) attended regular outpatient follow-ups. Exclusion criteria were (1) hemodynamic instability or (2) the presence of pregnancy, cancer, or severe heart failure.

G*Power version 3.1.9.2 was used to calculate the required sample size, given a two groups $\times$ four time points repeated-measures analysis of variance with a medium effect size (f) of 0.25 [14], α of .05, and power of 0.8. The minimum sample size in each group was calculated as 41 (82 for both groups). The total number of participants recruited was 165. Four patients did not complete the study because of heart surgery or death; therefore, 161 patients were included (DM group, $n = 77$; non-DM group, $n = 84$).

Instruments

Demographics questionnaire

This survey was conducted while patients were in hospital but before PCI. The questionnaire assessed 15 items: age, sex, body mass index (BMI), education, marital status, living situation, monthly income, smoking and drinking habits, diagnosis, puncture site, number and degree of coronary artery occlusions, PCI stenting, and comorbidities. All 15 items were found to be related to CAD in the previous literature [15–17].

Dutch exertion fatigue scale (DEFS)

Tiesinga et al. developed the nine-item DEFS for self-evaluating fatigue while executing daily activities [18]. Each item is rated using a five-point Likert scale ranging from 0 (*never*) to 4 (*always*). Total score ranges from 0 to 36; higher scores indicate a higher level of fatigue. This questionnaire was translated verbatim into Chinese by the researchers (who speak both English and Chinese) and then back-translated to English for comparison according to the procedure proposed by Guillemin et al. [19]. To achieve optimal translation, two native English speakers and two Chinese nursing experts participated in the translation process. The content validity index (CVI) of this questionnaire was 93.8%, determined by using the ratings of item relevance and agreement among the five experts, including two cardiologists, two senior cardiovascular nurses, and one nursing professor. The number of items that were rated as a 3 or 4 were divided by the total number of items. Moreover, the authors separately read the response format reported by the content experts and evaluated the wording of each item. For face validity, we applied cognitive assessment to evaluate how the PCI patients understood and responded to items. Face validity was established by 10 PCI patients and one senior cardiovascular nurse. By using the verbal probe method, the cardiovascular nurse collected information about the respondents' understanding of each item and their questions. Ten PCI patients fully understood the items, and no changes were needed. The Cronbach's α coefficient was .71 in the main study.

The 12-item short-form health survey (SF-12)

This questionnaire comprises 12 questions that evaluate physical and mental health-related QoL. Ware et al. developed the 12-Item Short-Form Health Survey which comprises two subscales: the physical component scale (PCS) and the mental component scale (MCS) [20]. Each item response was converted into physical and mental standardized values and then summed to PCS and MCS scores. Both subscale scores ranged from 0–100. The higher the score, the greater the QoL. The SF-12 scale has been effectively used in many countries worldwide, with a wide range of applications, and is suitable for all age groups. The researchers obtained the Chinese version of SF-12 from the website of the Government Research Bulletin (GRB), Taiwan [21]. We searched the Chinese SF-12 scale through the retrieval system (http://www.grb.gov.tw/search;keyword=Sf-12;type=GRB05), which is completely free and open to use [21]. Moreover, Lam et al. found that the Chinese version of SF-12 can be effectively applied to Asians, and its internal consistency and test-retest reliabilities are good (range 0.67–0.82) [22]. It's Cronbach's alpha in our present study was 0.92, showing good reliability.

Procedure and data collection

Measurement reliability and validation was verified through a pilot study of 10 PCI patients whose data were not used in the main study. For reliability, in the pilot study, the coefficients of internal consistency of Chinese DEFS and SF-12 were good (0.89 and 0.8), indicating good interrelatedness of the items. For validity, we used content validity and face validity. The CVI was 93.8%, as determined by a panel of five experts, showing good content validity. Face validity was established by 10 PCI patients. They fully understood the items of each questionnaire, and advised no changes were

Table 1 *Participants' Demographics Characteristics.*

Variable	DM (n = 77)		Non-DM (n = 84)		Total (N = 161)		t/χ^2	p
	n	%	n	%	n	%		
Gender								
Men	53	68.8	62	73.8	115	71.4	.488	.485[a]
Women	24	31.2	22	26.2	46	28.6		
Education level							1.09	.161[a]
< Junior high school	32	41.6	26	31.0	58	36.0		
≥ Junior high school	45	58.4	58	69.0	103	64.0		
Marital status							4.83	.028[*,a]
Married	60	77.9	76	90.5	136	84.5		
Single, divorced, widowed	17	22.1	8	9.5	25	15.5		
Living situation							4.52	.211[a]
Living alone	4	5.2	4	4.8	8	5.0		
Living with family	69	89.6	80	95.2	149	92.5		
Living with friends	1	1.3	0	00.0	1	0.6		
Living with caretaker	3	3.9	0	00.0	3	1.9		
Monthly income (US dollars)							5.19	.075[a]
<1,275	61	79.2	53	63.9	114	71.3		
1,276–2,234	12	15.6	19	22.9	31	19.4		
>2,235	4	5.2	11	13.3	15	9.4		
Smoking							.20	.652[a]
No	67	87.0	71	84.5	138	85.7		
Yes	10	13.0	13	15.5	23	14.3		
Drinking alcohol							1.66	.198[a]
No	68	88.3	68	81.0	136	84.5		
Yes	9	11.7	16	19.0	25	15.5		
Age, mean (SD)	67.7 (10.4)		64.5 (10.8)		66.0 (10.7)		−1.87	.063[b]
Body Mass Index, mean (SD)	27.1 (3.9)		26.3 (4.0)		26.7 (3.9)		−1.27	.208[b]
Diagnosis							3.84	.147[a]
Unstable angina	45	58.4	61	72.6	106	65.8		
Myocardial infarction	4	5.2	4	4.8	8	5.0		
Coronary artery disease	28	36.4	19	22.6	47	29.2		
Puncture site							6.00	.050[*,a]
Transfemoral	20	26.0	13	15.5	33	20.5		
Transradial	57	74.0	67	79.8	124	77.0		
Both	0	00.0	4	4.8	4	2.5		
Number of coronary artery occlusions							4.51	.034[*,a]
< 3	51	66.2	68	81.0	119	73.9		
≥ 3	26	33.8	16	19.0	42	26.1		
Degree of coronary artery occlusion							.25	.616[a]
< 70.0%	2	2.6	3	3.6	5	3.1		
70–89.0%	51	66.2	52	61.9	103	64.0		
> 90.0%	24	31.2	29	34.5	53	32.9		
PCI stenting							.29	.593[a]
Yes	52	70.3	53	66.3	105	68.2		
No	25	29.7	31	33.7	56	31.8		
Comorbidities								
Hyperlipidemia	17	22.1	13	15.5	30	18.6	1.15	.283[a]
Hypertension	57	74.0	48	57.1	105	65.2	5.05	.025[*,a]
Stroke	12	15.6	2	2.4	14	8.7	8.82	.003[*,a]
Kidney disease	3	3.9	0	0.0	3	1.9	3.34	.068[a]

Note. DM: diabetes mellitus; PCI: percutaneous coronary intervention; SD: standard deviation.
[*] $p < .05$, two-tailed.
[a] Chi-square.
[b] Independent t-test.

needed. The main data were collected from February to December 2018. A total of 161 participants with PCIs completed the self-rated questionnaires, consisting of demographic characteristics, the DEFS, and the SF-12 at Time 1 (T1; during hospitalization, one day before receiving PCI), Time 2 (T2; two weeks after discharge), Time 3, (T3; three months after discharge), and Time 4 (T4; six months after discharge). Measurements at T2 to T4 were obtained when participants visited the outpatient department or through phone calls by the researchers.

Ethical considerations

Prior to conducting this study, approval from the institutional review board of Taichung Veterans General Hospital was obtained (no. SE17198 A). All participants provided written, informed consent prior to beginning the first questionnaire.

Data analysis

SPSS 24.0 (IBM, Armonk, NY) was utilized to analyze the data. The Chi-square and Independent t-test analyzed the demographic variables and found that five types of demographic data (marital status, puncture site, the number of coronary artery occlusions, a diagnosis of hypertension or stroke) were to be heterogeneous and regarded as control variables that acted as covariates in the generalized estimating equation (GEE) analysis into three measurements. Independent t-tests were used to measure differences in fatigue and QoL between groups (DM versus non-DM) at each

Table 2 *Difference in Fatigue and Quality of Life at Each Time Point.*

Variable		DM (n = 77)	Non-DM (n = 84)	T	p
		Mean (SD)	Mean (SD)		
Fatigue					
T1	Baseline	8.40 (7.41)	7.40 (6.06)	−0.93	.349
T2	Two weeks	6.58 (6.52)	5.56 (4.35)	−1.18	.239
T3	Three months	4.84 (4.10)	4.81 (4.22)	−0.053	.958
T4	Six months	4.71 (4.54)	4.14 (3.71)	−.88	.381
SF-12					
PCS					
T1	Baseline	38.94 (10.48)	42.39 (9.40)	2.21	.029*
T2	Two weeks	41.01 (9.83)	43.02 (8.98)	1.36	.176
T3	Three months	43.34 (9.53)	45.21 (8.93)	1.29	.201
T4	Six months	44.83 (9.23)	46.72 (8.42)	1.36	.176
MCS					
T1	Baseline	47.68 (11.15)	51.06 (9.79)	2.05	.042*
T2	Two weeks	48.66 (9.47)	51.45 (7.78)	2.04	.043*
T3	Three months	49.30 (9.01)	51.41 (7.86)	1.59	.115
T4	Six months	49.49 (8.60)	50.73 (8.33)	0.94	.351

Note. DM: diabetes mellitus; MCS: mental component scale; PCS: physical component scale; SD: standard deviation; SF-12: The 12-Item Short-Form Health Survey; T1: hospitalization (baseline); T2: two weeks after discharge; T3: three months after discharge; T4: six months after discharge. *$p < .05$, two-tailed.

time point. The GEE was used to analyze the changes in fatigue and QoL over the four time points. The GEE mode included the main effects of group (DM = 1 vs. non-DM = 0), time point (T1, T2, T3, T4), and interaction effect (group × time point), and the previously mentioned five demographic variables as covariates. The main effects and interactions were utilized to measure the extent of changes in fatigue and QoL of patients with PCI over time. A p-value of less than 0.05 was used as the criterion for statistical significance.

Results

Demographic characteristics

Table 1 shows that the 77 PCI patients in the DM group (47.8%) had a mean age of 67.7(*SD* = 10.4) years and a mean BMI of 27.1(*SD* = 3.9). A total of 161 participants with PCIs were included; most participants were men (71.4%), married (84.5%), had a monthly income of less than US$ 1,275 (71.3%), lived with family (92.5%), did not smoke (85.7%) or drink alcohol (84.5%), had a diagnosis of unstable angina (65.8%), had 70–89.0% coronary artery occlusion (64.0%), had hypertension (65.2%), and had PCI through a radial artery (77%). The mean scores of fatigue, PCS, and MCS of all participants were 7.88 (*SD* = 6.74), 40.74 (*SD* = 10.05), and 49.44 (*SD* = 10.57), respectively.

There were significant differences in the demographic data of marital status, puncture site, the number of coronary artery occlusions, hypertension, and stroke between DM and non-DM groups, indicating heterogeneous.

Differences in fatigue and QoL at each time point

Independent *t*-tests were utilized to measure the differences in fatigue and QoL between patients with/without DM at the four time points (Table 2). Although the fatigue scores of the DM group were slightly higher than non-DM group, no significant differences were found in fatigue between both groups at T1 ($p = .349$), T2 ($p = .239$), T3 ($p = .958$), or T4 ($p = .381$). QoL (PCS and MCS) scores were lower for the DM group than for the non-DM group; there were significant differences between DM and non-DM groups in PCS at T1 ($p = .029$) and in MCS at T1 ($p = .042$) and T2 ($p = .043$).

Magnitude of change in fatigue and QoL at each time point

Table 3 presents the change in fatigue between four time points through GEE analysis. Considering the non-DM group's T1 fatigue score (7.405) as the reference, the DM group's fatigue score at T1 was 0.998 units higher than that of the non-DM group ($p = .349$), indicating no significant pre-surgery difference between the groups. At T2, T3, and T4, the fatigue scores of the non-DM group were significantly lower (all *ps* < .001) than those at T1, showing that the growth effect decreased over time. Considering the DM group's T1 fatigue score (8.403) as the reference, at T2, T3, and T4, the fatigue scores of the DM group were significantly lower (all *ps* < .001) than those at T1, showing that the growth effect decreased over time. After adjusting for the pre-test differential effect and growth effects, the magnitude of changes in the DM group's fatigue scores were .027, −.963, and −.426 compared to those of the non-DM group from T1 to T2 ($p = .253$), T1 to T3 ($p = .252$), and T1 to T4 ($p = .625$), respectively. This indicates that the extent of change in fatigue was not

Table 3 *Magnitude of Change in Fatigue at Each Time Point By Group.*

Variable	β	SE	95% CI	Wald test	p
Marital status	−2.20	1.16	−4.47, .068	3.615	.057
Puncture site	−1.613	.98	−3.53, .34	2.72	.099
Number of coronary artery occlusions	.226	.87	−1.47, 1.93	.068	.794
Comorbidities-Hypertension	.583	.75	−0.89, 2.06	.599	.439
Comorbidities-Stroke	−1.066	1.26	−3.53, 1.40	.720	.396
DEFS of Non-DM patients at T1 (reference)	7.405	0.66	6.12, 8.69	127.004	<.001***
DEFS at T1 (DM patients compared to non-DM patients)	0.998	1.07	−1.09, 3.09	0.877	.349
DEFS of Non-DM patients (T2 compared to T1)	−1.845	0.39	−2.61, −1.09	22.687	<.001***
DEFS of Non-DM patients (T3 compared to T1)	−2.595	0.53	−3.63, −1.56	24.048	<.001***
DEFS of Non-DM patients (T4 compared to T1)	−3.262	0.54	−4.33, −2.20	35.986	<.001***
DEFS of DM patients at T1 (reference)	8.403	0.84	6.76, 10.05	100.071	<.001***
DEFS of DM patients (T2 compared to T1)	−1.818	0.52	−2.83, −0.80	12.223	<.001***
DEFS of DM patients (T3 compared to T1)	−3.558	0.65	−4.84, −2.28	29.963	<.001***
DEFS of DM patients (T4 compared to T1)	−3.688	0.68	−5.03, −2.35	29.415	<.001***
Magnitude of change in DEFS in both groups from T1 to T2	0.027	0.65	−1.24, 1.30	0.002	.253
Magnitude of change in DEFS in both groups from T1 to T3	−0.963	0.84	−2.61, 0.68	1.314	.252
Magnitude of change in DEFS in both groups from T1 to T4	−0.426	0.87	−2.14, 1.28	0.239	.625

Note. β: beta coefficients; CI: confidence interval; DEFS: Dutch Exertion Fatigue Scale; DM: diabetes mellitus; SE: standard error; T1: hospitalization (baseline); T2: two weeks after discharge; T3: three months after discharge; T4: six months after discharge. *p < .05, **p < .01, ***$p < .001$, two-tailed.

Table 4 *Magnitude of Change in Physical Component Scale (PCS) Scores at Each Time Point By Group.*

Variable	β	SE	95% CI	Wald test	*p*
Marital status	2.69	2.23	−1.69, 7.06	1.452	.228
Puncture site	1.539	1.71	−1.82, 4.90	.808	.369
Number of coronary artery occlusions	.314	1.61	−2.83, 3.46	.038	.845
Comorbidities-Hypertension	−3.28	1.41	−6.05, −.52	5.404	.020*
Comorbidities-Stroke	.941	2.42	−3.80, 5.69	.151	.697
PCS of non-DM patients at T1 (reference)	42.393	1.02	40.39, 44.39	1727.585	<.001***
PCS at T1 (DM patients compared to non-DM patients)	−3.455	1.56	−6.52, −0.39	4.877	.027*
PCS of Non-DM patients (T2 compared to T1)	0.629	0.65	−0.65, 1.91	0.928	.335
PCS of Non-DM patients (T3 compared to T1)	2.819	0.80	1.26, 4.38	12.529	<.001***
PCS of Non-DM patients (T4 compared to T1)	4.326	0.78	2.80, 5.86	30.719	<.001***
PCS of DM patients at T1 (reference)	38.938	1.19	36.61, 41.26	1070.664	<.001***
PCS of DM patients (T2 compared to T1)	2.072	0.75	0.61, 3.54	7.632	0.006**
PCS of DM patients (T3 compared to T1)	4.404	0.80	2.85, 5.96	30.305	<.001***
PCS of DM patients (T4 compared to T1)	5.890	0.83	4.27, 7.51	50.359	<.001***
Magnitude of change in PCS in both groups from T1 to T2	1.443	0.99	−0.50, 3.39	2.113	.146
Magnitude of change in PCS in both groups from T1 to T3	1.585	1.13	−0.62, 3.79	1.986	.159
Magnitude of change in PCS in both groups from T1 to T4	1.564	1.14	−0.67, 3.80	1.889	.169

Note. β: beta coefficients; CI: confidence interval; MCS: physical component scale (MCS); DM: diabetes mellitus; SE: standard error; T1: hospitalization (baseline); T2: two weeks after discharge; T3: three months after discharge; T4: six months after discharge. *p < .05, **p < .01, ***p < .001, two-tailed.

significantly higher in the DM group than in the non-DM group from hospitalization (baseline) to two weeks, three months, and six months after discharge.

Table 4 shows the change in PCS at each time point. Considering the T1 PCS score (42.393) of the non-DM group as the reference, T1 PCS scores of the DM group were 3.455 points lower than those of the non-DM group ($p = .027$), indicating there was a significant pre-surgery difference between the groups. At T3 and T4, the PCS scores of the non-DM group were significantly higher (all *ps* < .001) than those at T1, showing a growth effect over time. Considering the T1 PCS score (38.938) of the DM group as the reference, at T2, T3, and T4, the PCS scores of the DM group were significantly higher (all *ps* < .01) than those at T1, showing a growth effect over time. After adjusting for the pre-test effect and growth effects of the control group, the DM group's PCS were 1.443, 1.585, and 1.564 units lower than those of the non-DM group from T1 to T2 ($p = .146$), T1 to T3 ($p = .159$), and T1 to T4 ($p = .169$), respectively. This indicated that there was no significant difference in the extent of change in PCS scores between the two groups from hospitalization (baseline) to two weeks, three months, and six months after discharge.

Table 5 shows the change in MCS at each time point. Considering the T1 MCS scores (51.057) of the non-DM group as the reference, T1 MCS scores of the DM group were 3.377 points lower than those of the non-DM group ($p = .041$), indicating there was a significant difference between the groups at T1. The non-DM group exhibited a slight increase in MCS at T2 (0.389, $p = .556$) and T3 (0.356, $p = .688$), and a decrease at T4 (0.322, $p = .714$) than those at T1, showing no growth effect over time. Considering the T1 MCS scores (47.680) of the DM group as the reference, the DM group exhibited a slight increase in MCS at T2 (0.985, $p = .107$) and T3 (1.625, $p = .056$), and at T4 (1.808, $p = .054$). After adjusting for the pre-test value and growth effects in the non-DM group, the extent of changes in the MCS scores of the DM group were 0.596, 1.269, and 2.130 points higher than those of the non-DM group from T1 to T2 ($p = .098$), T1 to T3 ($p = .301$), and T1 to T4 ($p = .099$) (all *ps* > .05), respectively. This indicated that there was no significant difference in the extent of change in MCS in both groups from hospitalization (baseline) to two weeks, three months, and six months after discharge.

Discussion

Participants' characteristics regarding sex and presence of hypertension were consistent with the previously reported data, which indicated that patients with CAD often have hypertension and men have a higher CAD prevalence rate than women [5,15].

Table 5 *Magnitude of Change in Mental Component Scale (MCS) Scores at Each Time Point By Group.*

Variable	β	SE	95% CI	Wald test	*p*
Marital status	2.38	2.07	−1.67, 6.43	1.325	.250
Puncture site	.698	1.61	−2.46, 3.86	.187	.665
Number of coronary artery occlusions	−.615	1.59	−3.73, 2.50	.150	.699
Comorbidities-Hypertension	−1.475	1.38	−4.18, 1.23	1.141	.285
Comorbidities-Stroke	1.747	2.22	−2.60, 6.09	.621	.431
MCS of non-DM patients at T1 (reference)	51.057	1.06	48.98, 53.14	2312.988	<.001***
MCS at T1 (DM patients compared to non-DM patients)	−3.377	1.65	−6.61, −0.14	4.190	.041*
MCS of Non-DM patients (T2 compared to T1)	0.389	0.66	−0.90,1.68	0.346	.556
MCS of Non-DM patients (T3 compared to T1)	0.356	0.87	−1.382,2.093	0.161	.688
MCS of Non-DM patients (T4 compared to T1)	−0.322	0.88	−2.05,1.40	0.134	.714
MCS of DM patients at T1 (reference)	47.680	1.26	45.21, 50.16	1431.962	<.001***
MCS of DM patients (T2 compared to T1)	0.985	0.61	−0.21, 2.18	2.607	.107
MCS of DM patients (T3 compared to T1)	1.625	0.85	−0.04, 3.29	3.655	.056
MCS of DM patients (T4 compared to T1)	1.808	0.94	−0.03, 3.65	3.699	.054
Magnitude of change in MCS in both groups from T1 to T2	0.596	0.90	−1.17,2.36	0.439	.098
Magnitude of change in MCS in both groups from T1 to T3	1.269	1.23	−1.14, 3.68	1.068	.301
Magnitude of change in MCS in both groups from T1 to T4	2.130	1.28	−0.39, 4.65	2.742	.099

Note. β: beta coefficients; CI: confidence interval; MCS: mental component scale (MCS); DM: diabetes mellitus; SE: standard error; T1: hospitalization (baseline); T2: two weeks after discharge; T3: three months after discharge; T4: six months after discharge. *p < .05, **p < .01, ***p < .001, two-tailed.

However, our results contradict those that showed that female PCI patients receiving a drug-eluting stent had a higher incidence of DM than male PCI patients ($p = .485$) [5]. The prevalence of radial artery puncture in this present study differs from Faridi et al.'s study, which found that in the US, >80.0% of patients with CAD received PCI in the femoral artery [16]. Su et al. indicated that when patients with CAD have acute myocardial ischemia onset or narrow coronary arteries, the transfemoral approach is often chosen for PCI [9]. Although the participants in Faridi et al.'s study and the present study involved non-emergency PCIs, the major puncture sites were different [16]. Thus, this requires further study.

Our results regarding smoking and dringing alcohol habits among patients with CAD were consistent with a prior study that found that 53.0% of patients with CAD ($n = 200$) were non-smokers [17]. However, our results contradict those of Ram and Trivedi's study, which indicated that smokers in Turkey had a higher prevalence of CAD (around 3.72 times higher) than those who had quit smoking [23]. A possible reason for these differences is that most studies simply investigated current smoking or non-smoking and rarely focused on patients' history of smoking, daily use of cigarettes, and time since quitting smoking, which may also affect the prevalence of CAD. Moreover, Su and He found that Type D personality is associated with CAD prevalence and may raise the mortality rate [24]. The risk factors for triggering CAD may also include personality traits or comorbidities such as DM.

Difference and magnitude of change in fatigue at each time point

Fatigue scores at T1 indicated that before PCI, patients with CAD experienced mild-to-moderate fatigue irrespective of DM comorbidity. This is consistent with a study that found that fatigue was the most common symptom experienced by patients with CAD [25]. The present study also found no significant differences in fatigue between DM and non-DM groups at T2, T3, and T4; although, both groups' fatigue scores decreased compared to pre-PCI (T1). Our results contradict a study that found that fatigue was the most intense symptom in the first month after PCI [5]. Duijndam et al. indicated that within a year after PCI, fatigue continued to affect the perception of illness and QoL [6]. Patients' perceived concentration problems were associated with decreased QoL, possibly owing to fatigue, negative mood, and older age [6]. However, these two studies were subject to some limitations: the participants in Kim et al.'s study were all outpatients with acute coronary syndrome [5], and the time points assessed in Duijndam et al.'s study were after PCI (baseline), and at one-month and one-year follow-ups [6]. They did not consider the influence of DM in patients with CAD who received PCI, although DM damages the vascular system and nerves [1] and is detrimental to patients with CAD [11]. When the vascular endothelial cells are damaged, patients with CAD are prone to fatigue [5]. Therefore, longitudinal studies are needed to examine the degree of fatigue and seriousness of DM among patients with CAD before and after receiving PCI.

Notably, our GEE analyses indicated that fatigue scores in the DM and non-DM groups at T2, T3, and T4 were significantly lower than those at pre-PCI (T1), showing that fatigue significantly decreased over time. This result is consistent with a study that found that patients with myocardial infarction immediately felt well and perceived a decrease in fatigue after PCI [8]. This may be because PCI is the most effective revascularization therapy for CAD as it can quickly destroy arterial plaque and subsequently relieve fatigue [9], no matter CAD patients with or without DM. Ayton et al. found that patients with CAD ($n = 32$) perceived physical symptoms (e.g., fatigue) and psychological symptoms (e.g., anxiety, depression, and uncertainty) and were relieved after PCI, but continued to worry about mortality and incapability of performing daily physical activities [26]. Therefore, we suggest that clinical nurses should enhance patients' awareness and management of physical and psychological symptoms after PCI and possible comorbidities, as education regarding lifestyle changes, taking medication regularly, and following rehabilitation regimes after PCI improves prognosis.

Our study revealed that the magnitude of change in fatigue was not significant in the DM group compared to the non-DM group from T2 to T1, T3 to T1, and T4 to T1. This result contradicts Ayton et al.'s study, which found that six months after PCI, patients perceived a significant improvement in fatigue, shortness of breath, and angina [26]. A possible reason for this discrepancy could be that they conducted a qualitative study with a small sample size and considered neither DM nor fatigue change at different time points after PCI, which may have influenced their outcomes. Moreover, fatigue may be caused by a variety of factors: lifestyle-related, nutritional, medical, psychological, glycemic/diabetes-related, endocrine, and iatrogenic [27]. Thus, we suggest that further studies consider these related factors and the influence of time to better understand the efficacy of PCI for patients with CAD and DM.

Difference and magnitude of change in QoL at each time point

Patients' QoL decreased because of CAD, especially for patients with CAD and DM. This is consistent with Srivastava et al.'s study, which found that the CAD group's physical and social QoL were significantly lower than a healthy control group [28].

The DM group's MCS scores were lower than those of the non-DM group at T2; however, there was no difference in PCS scores between groups at T2. Our results contradict Moriel et al.'s study, which found that PCI patients ($n = 78$) who had DM comorbidity experienced low physical and psychological QoL, especially women [29]. Moreover, Kim et al. found that the average QoL scores of patients with CAD with and without DM were not significantly different (67.81 ± 14.96 vs. 67.87 ± 16.70, $p > .05$) [5]. However, their study only explored postoperative QoL a month after PCI without comparing pre-PCI QoL and used a different measurement tool (Seattle Angina Questionnaire) to evaluate QoL. Thus, based on these contradictory results, we suggest that further studies consider DM and participants' sex, using consistent ways of assessing different aspects of QoL, to verify the influence of DM on the health-related QoL of patients with CAD.

Notably, our GEE analysis showed that PCS scores in the non-DM group at T3 and T4, and in the DM group at T2, T3, and T4 were significantly higher than those at T1; that is, both groups' PCS scores significantly increased over time. This result is consistent with Uchmanowicz et al.'s study, which evaluated the impact of DM on QoL of 120 patients with CAD [30]. Non-diabetic patients had better QoL than patients with DM at both baseline and six months after PCI. Negative predictors of PCS scores were diabetes, multivessel disease, high triglyceride level, and hypertension; regarding MCS, negative predictors were DM, history ofmyocardial infarction, and high triglyceride level. Edward et al. found that PCS scores six months after PCI (51.4 ± 10.5) were higher than those after 12 months (39.7 ± 10.8) among 40 Australian patients with CAD [31].

However, no significant changes in MCS scores were found among three time points in both groups. Britneff et al. found that DM is a common comorbid medical condition in patients of CAD and when the condition occurs together, such patients are vulnerable for depression, anxiety, and psychosocial problems [32]. However, this study did not investigate the difference in depression in patients with and without DM; thus, further study is still needed concerning depression after patients with DM receive PCI.

Our study also revealed that the magnitude of change in QoL of PCI patients with/without DM did not significantly differ at T2, T3, and T4. This result is consistent with Pischke et al.'s study, which showed that there was no significant difference in QoL at a one-year follow-up among patients with CAD with/without DM who received PCI [10]. Tareen and Tareen proposed that DM is a debilitating chronic illness with a complex pathophysiology that often damages kidney and cardiovascular function, resulting in emotional distress and significantly affecting patients' QoL [33]. DM has been associated with lower QoL among patients with CAD [29]. However, Kim et al. found that QoL scores in patients with CAD with and without DM did not significantly differ (67.81 ± 14.96 vs. 67.87 ± 16.70, $p > .05$) [5]. This may be because after PCI treatment, patients' coronary arteries recanalize, and chest tightness and chest pain gradually improve. If patients with DM regularly take heart and DM medication along with implementing a proper cardiac rehabilitation exercise program, they may not perceive any noteworthy QoL improvement. Nevertheless, DM has been found to decrease cardiovascular function and induce heart disease, especially in Asia [34]. Current treatment and control of DM have improved. Thus, we suggest that future transnational studies related to PCI prognosis, DM comorbidity, and QoL in patients who receive PCI be conducted to increase the awareness of nurses' roles in CAD care, DM care, strengthen communication among interdisciplinary teams, and provide necessary support to help patient recovery after PCIs.

Limitations

This study took place in Taiwan; thus, our results may not be generalizable to global populations. Further, the time since DM diagnosis and condition of DM control were not explored in this study, and both may influence levels of fatigue and QoL. Moreover, living with one's extended family is common in traditional Chinese culture, especially older adults being looked after by their children (i.e., *filial piety*). However, whether living with family members and social support affect the fatigue or QoL of patients with DM receiving PCIs needs further study. In addition, other factors could be confounded with fatigue and QoL scores such as marital status; puncture site; number of coronary artery occlusions; and comorbidities such as hypertension, unstable angina, and stroke. Thus, further studies with a transnational, transcultural, and longitudinal design and longer follow-ups are recommended.

Conclusions

Patients with DM had lower pre-intervention QoL and lower psychological QoL two weeks after discharge than those with non-DM. By three and six months after discharge, DM did not affect the magnitude of changes in fatigue and QoL in patients who received PCIs over three or six months. Patients without DM perceived lower fatigue at two weeks, three months, and six months after discharge, and higher physical QoL at three and six months after discharge. DM may affect patients with CAD over the long term. Thus, nurses should educate patients to regularly take medication, notice blood sugar, change life habits, notice comorbidities, and follow rehabilitation regimes after PCIs for better prognosis.

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Conflict of interest statement

There are no relevant financial or non-financial competing interests to report.

Ethical approval

This study was performed after receiving approval (no. SE17198 A) from the research ethics committee of Taichung Veterans General Hospital. The researchers informed patients undergoing percutaneous coronary interventions about the aims, procedures, anonymity, and human rights associated with this study. All participants provided informed, written consent.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.02.001.

References

1. World Health Organization. Diabetes [Internet]. Geneva: WHO; 2018 [cited 2021 Dec 25]. Available from: https://www.who.int/news-room/fact-sheets/detail/diabetes
2. International Diabetes Federation. IDF diabetes atlas [Internet]. Amsterdam: IDF; 2022 [cited 2022 Feb 16]. Available from: https://diabetesatlas.org/
3. Khanam PA, Begum T, Chowdhury A, Habib SH. Coronary artery disease with type 2 diabetes and other risk factors: a tertiary care hospital in Bangladesh. Bangladesh Crit Care J. 2019;7(1):20–5. https://doi.org/10.3329/bccj.v7i1.40759
4. American Diabetes Association. 10. Cardiovascular disease and risk management: standards of medical care in diabetes-2019. Diabetes Care. 2019;42(Suppl 1):S103–23. https://doi.org/10.2337/dc19-S010
5. Kim HS, Kim HK, Kang KO, Kim YS. Determinants of health-related quality of life among outpatients with acute coronary artery disease after percutaneous coronary intervention. Jpn J Nurs Sci. 2019;16(1):3–16. https://doi.org/10.1111/jjns.12209
6. Duijndam S, Denollet J, Nyklíček I, Kupper N. Perceived cognition after percutaneous coronary intervention: association with quality of life, mood and fatigue in the THORESCI study. Int J Behav Med. 2017;24(4):552–62. https://doi.org/10.1007/s12529-016-9624-1
7. Li J, Yuan Y, Wang M, Zhang J, Zhang L, Jiang S, et al. Alterations in regional homogeneity of resting-state brain activity in fatigue of Parkinson's disease. *J Neural Transm*. 2017;124(10):1187–95. https://doi.org/10.1007/s00702-017-1748-1
8. Iles-Smith H, Deaton C, Campbell M, Mercer C, McGowan L. The experiences of myocardial infarction patients readmitted within six months of primary percutaneous coronary intervention. J Clin Nurs. 2017;26(21–22):3511–8. https://doi.org/10.1111/jocn.13715
9. Su SF, Chang MY, Wu MS, Liao YC. Safety and efficacy of using vascular closure devices for hemostasis on sheath removal after a transfemoral artery percutaneous coronary intervention. Jpn J Nurs Sci. 2019;16(2):172–83. https://doi.org/10.1111/jjns.12221
10. Pischke CR, Weidner G, Elliott-Eller M, Scherwitz L, Merritt-Worden TA, Marlin R, et al. Comparison of coronary risk factors and quality of life in coronary artery disease patients with versus without diabetes mellitus. Am J Cardiol. 2006;97(9):1267–73. https://doi.org/10.1016/j.amjcard.2005.11.051
11. Task Force Members, Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, et al. 2013 ESC guidelines on the management of stable coronary artery disease: the task force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013;34(38):2949–3003. https://doi.org/10.1093/eurheartj/eht296
12. Darvishpour A, Javadi-Pashaki N, Salari A, Sadeghi T, Taleshan-Nejad M. Factors associated with quality of life in patients undergoing coronary angioplasty. Int J Health Sci. 2017;11(4):35–41. PMID: 29085266, PMCID: PMC5654185.
13. Singh R, Teel C, Sabus C, McGinnis P, Kluding P. Fatigue in type 2 diabetes: impact on quality of life and predictors. PLoS One. 2016;11(11):e0165652. https://doi.org/10.1371/journal.pone.0165652
14. Cohen J. Statistical power analysis for the behavioral sciences. 2nd ed. NY: Routledge; 1988.
15. Su SF, Chang MY, He CP. Social support, unstable angina, and stroke as predictors of depression in patients with coronary heart disease. J Cardiovasc Nurs. 2018;33(2):179–86. https://doi.org/10.1097/JCN.0000000000000419
16. Faridi KF, Rymer JA, Rao SV, Dai D, Wojdyla D, Yeh RW, et al. Ad hoc percutaneous coronary intervention in patients with stable coronary artery disease: a report from the National Cardiovascular Data Registry CathPCI Registry. Am Heart J. 2019;216:53–61. https://doi.org/10.1016/j.ahj.2019.07.004

17. Chiou AF, Hsu SP, Hung HF. Predictors of health-promoting behaviors in Taiwanese patients with coronary artery disease. Appl Nurs Res. 2016;30:1–6. https://doi.org/10.1016/j.apnr.2015.08.008
18. Tiesinga LJ, Dassen TWN, Halfens RJG. DUFS and DEFS: development, reliability and validity of the Dutch fatigue scale and the Dutch exertion fatigue scale. Int J Nurs Stud. 1998;35(1–2):115–23. https://doi.org/10.1016/s0020-7489(98)00005-4
19. Guillemin F, Bombardier C, Beaton D. Cross-cultural adaptation of health-related quality of life measures: literature review and proposed guidelines. J Clin Epidemiol. 1993;46(12):1417–32. https://doi.org/10.1016/0895-4356(93)90142-N
20. Ware Jr JE, Kosinski M, Keller SD. A 12-Item Short-Form Health Survey: construction of scales and preliminary tests of reliability and validity. Med Care. 1996;34(3):220–33. https://doi.org/10.1097/00005650-199603000-00003
21. Government Research Bulletin (GRB). [Internet]. Taiwan, Chinese SF12 scale. 2018 [cited 2018 Feb 1]. Available from: http://www.grb.gov.tw/search;keyword=Sf-12;type=GRB05
22. Lam ET, Lam CL, Fong DY, Huang WW. Is the SF-12 version 2 Health Survey a valid and equivalent substitute for the SF-36 version 2 Health Survey for the Chinese? J Eval Clin Pract. 2013;19(1):200–8. https://doi.org/10.1111/j.1365-2753.2011.01800.x
23. Ram RV, Trivedi AV. Behavioral risk factors of coronary artery disease: a paired matched case control study. J Cardiovasc Dis Res. 2012;3(3):212–7. https://doi.org/10.4103/0975-3583.98896
24. Su SF, He CP. Type D personality, social support, and depression among ethnic Chinese coronary artery disease patients undergoing a percutaneous coronary intervention: an exploratory study. Psychol Rep. 2019;122(3):988–1006. https://doi.org/10.1177/0033294118780428
25. Kim HL, Jang JS, Kim MA, Seo JB, Chung WY, Kim SH, et al. Gender differences of in-hospital outcomes in patients undergoing percutaneous coronary intervention in the drug-eluting stent era. Med (Baltim). 2019;98(20):e15557. https://doi.org/10.1097/MD.0000000000015557
26. Ayton DR, Barker AL, Peeters GMEE, Berkovic DE, Lefkovits J, Brennan A, et al. Exploring patient-reported outcomes following percutaneous coronary intervention: a qualitative study. Health Expect. 2018;21(2):457–65. https://doi.org/10.1111/hex.12636
27. Kalra S, Sahay R. Diabetes fatigue syndrome. Diabetes Ther. 2018;9(4):1421–9. https://doi.org/10.1007/s13300-018-0453-x
28. Srivastava S, Shekhar S, Bhatia MS, Dwivedi S. Quality of life in patients with coronary artery disease and panic disorder: a comparative study. Oman Med J. 2017;32(1):20–6. https://doi.org/10.5001/omj.2017.04
29. Moriel G, Roscani MG, Matsubara LS, Cerqueira AT, Matsubara BB. Qualidade de vida em pacientes com doença ateroclerótica coronariana grave e estável [Quality of life in patients with severe and stable coronary atherosclerotic disease]. Arq Bras Cardiol. 2010;95(6):691–7. https://doi.org/10.1590/S0066-782X2010005000151. Portuguese.
30. Uchmanowicz I, Loboz-Grudzien K, Jankowska-Polanska B, Sokalski L. Influence of diabetes on health-related quality of life results in patients with acute coronary syndrome treated with coronary angioplasty. Acta Diabetol. 2013;50(2):217–25. https://doi.org/10.1007/s00592-011-0280-2
31. Edward KL, Stephenson J, Giandinoto JA, Wilson A, Whitbourn R, Gutman J, et al. An Australian longitudinal pilot study examining health determinants of cardiac outcomes 12 months post percutaneous coronary intervention. BMC Cardiovasc Disord. 2016;16:31. https://doi.org/10.1186/s12872-016-0203-9
32. Britneff E, Winkley K. The role of psychological interventions for people with diabetes and mental health issues. J Diabetes Nurs. 2013;17(8):305–10. Corpus ID: 12061739.
33. Tareen RS, Tareen K. Psychosocial aspects of diabetes management: dilemma of diabetes distress. Transl Pediatr. 2017;6(4):383–96. https://doi.org/10.21037/tp.2017.10.04
34. Yang JJ, Yu D, Wen W, Saito E, Rahman S, Shu XO, et al. Association of diabetes with all-cause and cause-specific mortality in Asia: a pooled analysis of more than 1 million participants. JAMA Netw Open. 2019;2(4):e192696. https://doi.org/10.1001/jamanetworkopen.2019.2696

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Research Article

Advanced Practice Nurses' Organization Commitment: Impact of Job Environment, Job Satisfaction, and Person-Organization Fit☆

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SUMMARY

Purpose: The demand for advanced practice nurses (APNs) has increased globally due to a shortage of physicians and an increased demand for high-quality healthcare. Research is needed on the enhancement of advanced practice nurses' organization commitment. Organization commitment (OC) directly impacts the retention of APNs. This study aims to identify the key factors affecting the OC of advanced practice nurses.
Method: A cross-sectional survey was conducted at the largest hospital in South Korea. A total of 189 APNs answered survey questions. A partial least squares-structural equation modeling method was employed to analyze the survey responses.
Results: A pay scale of APNs is positively associated with person-organization fit (POF). However, the effect of job location and computer self-efficacy on POF is not significant. Job satisfaction plays a salient direct role in supervision and POF. Job satisfaction is also a significant moderator in the relationship between supervision and POF. POF is significantly associated with both OC and supervision. Supervision has a positive effect on organization commitment.
Conclusions: Pay scale, job satisfaction, supervision, and POF are significant factors affecting organization commitment. Establishing an intra-organization entity, such as APN steering committee, to ensure mutual consensus and transparent communication between administrators and APNs would enhance POF, the rating of supervision, and organization commitment.

Introduction

Advanced practice nurses (APNs) are registered nurses working as “nurse practitioners, clinical nurse specialists, nurse anesthetists, and nurse midwives” [1]. They are “registered nurses who have acquired the expert knowledge base, complex decision-making skills, and clinical competencies needed for expanded practice, the characteristics of which are shaped by the context and/or country in which she/he is credentialed to practice” [2]. The demand for APNs has increased globally [3]. There are two major reasons. One is a shortage of physicians. The other is the need to deliver quality healthcare at lower medical costs. In many countries, APNs perform primary physician duties and/or work alongside physicians as full team members. As a strong force contributing to increased access to quality healthcare at lower costs [4], APNs have been described as hidden but essential healthcare workers [2,5].

APNs, however, encounter barriers in many countries. Barriers include lack of autonomy, professional under-recognition, lack of understanding of their unique role, and lack of support from administrations and from other clinicians [6]. These barriers can

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prevent APNs from fulfilling their responsibilities and fully integrating themselves within the healthcare system. There is much work to be done to utilize APNs to the fullest extent possible, but there has been little research on the improvement of the work conditions for APNs and the efficient management and retention of APNs. The relatively recent emergence of APNs in healthcare systems and the relatively small number of APNs in the general nurse population contribute to the scant research on them. Given the crisis in healthcare, however, the demand for APNs has increased and will continue to increase. The retention of APNs and the enhancement of their commitment to their profession and organization have thus become crucial global topics in healthcare management.

The current study focuses on the organization commitment (OC) of APNs. OC is defined as “an individual's loyalty or bond to his or her employing organization” [7]. It is an established finding that a high level of OC plays an important role in determining employee retention, low overall turnover in a profession, and the sustainability of the organization itself [8].

Researchers have identified a number of factors impacting OC. They include motivation, job satisfaction, job environment, interrelationships within the workplace, person-organization fit (POF), and turnover intentions [7]. So far, most nursing research has focused on two or three factors impacting OC among nurses [9].

Among various factors affecting organization commitment, our study employs job environment (pay scale, supervision, and job location), job satisfaction, computer self-efficacy (CSE), and POF as variables. Job location and pay scale are, respectively, measures that reflect the adjustment to the working environment and monetary magnitude of a person's job performance [10]. Supervision is defined as “the provision of guidance or direction, evaluation and follow-up by the supervisor” [11]. CSE refers to “judgment of one's capability to use a computer” [12, p. 192]. POF is defined as “the compatibility between people and organizations that occurs when: (a) at least one entity provides what the other needs, or (b) they share similar fundamental characteristics, or (c) both” [13, pp. 4–5]. Job satisfaction is defined as a positive feeling that one holds toward one's job, resulting from the appraisement and various experiences one has at a workplace [14].

Given these definitions, we posit direct and moderating effects among variables. For example, pay scale and job location are posited as positively associated with POF as direct effects. Job satisfaction is posited as moderating the relationship between POF and supervision. The Theoretical Background and Research Model section discusses detailed associations among these perceptional constructs.

The goal of our study is to examine direct and moderating effects on APNs' OC using partial least squares - structural equation modeling (PLS-SEM). This is done to (1) explore precursory job environmental factors affecting APNs' perception of POF, (2) identify moderating factors affecting POF and supervision, and (3) understand the direct effects of POF and supervision on APNs' OC. The Partial Least Squares (PLS) is a unique assessment method that can identify the direct effects of variables and moderating effects on a dependent variable (e.g., commitment).

The current study was conducted on APNs in the largest hospital in South Korea (‘Korea’ hereafter). This hospital has employed the largest number of APNs ($n = 378$) and has the longest-running (20 years) APN program in Korea. The Korean healthcare system exceeds global standards for excellent medical care, and APNs play a pivotal role in it. However, the Korean healthcare system is experiencing the same problems that healthcare systems over the world are: physician shortages in residency programs and an urgent need to deliver optimal care at low costs. In Korea, as in many other countries, APNs perform some of the functions that physicians do or work as full team members with physicians. They are experiencing the same barriers experienced the world over by APNs. The findings of this study are likely to have relevant implications for APNs in general.

Literature review and theoretical background

Some research on various factors affecting OC has been previously conducted. A brief review of the research on the six factors under consideration in our study– pay scale, job location, supervision, job satisfaction, CSE, and POF follows.

Job environment − pay scale, job location, and supervision

Our study considers three aspects of the job environment and personal fit: pay scale, supervision [15], and job location [10]. A prior study suggested that these factors play an important role in determining the personal expectations of a job position and in building a strong connection between employees and organizations [15]. According to Porter & Steers (1973), immediate work environment, job satisfaction, and pay scale are three essential elements influencing employee turnover rate and absenteeism. In our study, supervision is taken to be a part of the immediate work environment, while pay scale counts as an organization-wide factor.

Pay scale measures an employee's emotional satisfaction at a pay level and reflects the organization's judgment of employee work performance. Pay scale is considered a salient factor, along with promotion, affecting an employee's compensation for her job performance and the potential possibility of withdrawal from her duties [16].

Job location is an important part of the job environment. Job location matching an employee's interests and values boosts his/her job satisfaction [17].

Supervision is an important immediate work environment factor within an organization [15]. Studies on supervision have focused on well-fitted dyadic relationships between a supervisor and a subordinate. For instance, similar personalities, similar values, and goal congruity among supervisors and subordinates are considered important factors in achieving a strong supervisor-employee relationship [10]. A supervisor's support for employees is crucial in securing positive employee responses and behaviors in challenging and troublesome situations [18]. Our study focuses on the relation of APNs' pay scale and job location to her OC, and on supervisors' support for APNs' performance, recognition of successful job performance, and assistance to APNs in resolving conflicts in the medical setting.

Job satisfaction

In general, satisfaction is defined as “the summary psychological state resulting when emotion surrounding disconfirmed expectation is coupled with the consumer's prior feelings about the consumption experience” [19]. Specifically, job satisfaction is referred to as a positive feeling that one holds toward one's job, resulting from the appraisement and various experiences one has at a workplace [14,20]. Our study focuses specifically on the satisfaction that an APN experiences in 1) providing medical interventions to clients/patients, 2) being recognized by the supervisor because of successful performance of duties, and 3) interacting with patients/clients. A study of APNs' job satisfaction reveals that it is an integral part of healthcare performance, retention, and the delivery of quality work [21]. It is also an important factor affecting turnover intention [15].

Prior studies also emphasized that job satisfaction can be salient in playing a direct role but also in becoming a moderator among various employee perceptions. Accordingly, we consider all of the above theoretical characteristics of job satisfaction as a direct indicator and a moderator between constructs within our research framework in the APNs' OC context.

Based on the theoretical characteristics of job satisfaction as a direct indicator and a moderator between constructs, we employed job satisfaction to examine its both direct and moderating effects on other variables to APNs' path to OC within our research frameworks.

Computer self-efficacy

CSE is rooted in the original concept of self-efficacy, which can be defined as the judgment of one's own capability to organize and execute courses of action required to attain designated types of performances [17]. Thus, an individual's degree of self-efficacy affects the selection of behavioral activities and their eventual performance, given their current state of motivation [22]. CSE can be defined as "a judgment of one's capability to use a computer" [12] to organize and execute computer-related courses of action. Since self-efficacy affects our behaviors and performances, it is likely that CSE does the same.

In today's work environment, CSE can be essential to the performance of an APNs' daily duties. CSE is not simply measuring an APN's computing proficiency in hardware and software management for the assigned daily duties. Rather, an APN's CSE reflects his or her judgment of capability to organize and execute computer-related medical duties assigned to him/her. Recent studies note a positive relation among CSE, work performance, and job satisfaction in a variety of work contexts [22]. In all likelihood, an APN with a higher level of CSE is capable of successfully mastering a more comprehensive array of duties in a computing environment than an APN with lower CSE. Almost by definition, a higher level of CSE indicates a greater ability to work in a clinical environment with diverse software or hardware. Belief in one's mastery of computer-related daily duties would produce higher job satisfaction for an APN. In our study, we did not measure "internet self-efficacy" which can be essential to the performance of APNs' daily duties and to job satisfaction.

Person-organization fit (POF)

POF indicates the congruence of values between an individual and an organization. In detail, unlike person-job fit, which concerns aspects of people's job-related qualifications (e.g., skill, knowledge, and capability), POF concerns an individual's and an organization's congruence of beliefs, values, and norms [23]. For instance, a good POF implies a close alignment of an individual's values with an organization's aims. If people perceive themselves as fitting well within an organization, they tend to regard themselves as a part of the organization and are more likely to join a "psychological group" within an organization [24]. This type of POF is the one under consideration in our research. Other types of POF include *needs – supplies fit* and *demands – abilities fit* [25,26]. *Needs – supplies fit* occurs when an organization fulfills an individual's needs and desires in response to or in return for an individual's service [24]. A *demands – abilities fit* between an organization and an individual occurs when an individual is capable of satisfying the organization's demands, resulting in high job performance [13].

Another significant aspect of POF is the distinction between actual and perceived POF. While actual POF refers to "the actual similarity of an employee and an organization on fundamental characteristics," perceived POF refers to "the extent to which individuals believe they fit the organization" [27]. In our research, we focus on perceived POF, since our research is based on the perception of APNs.

Little work has been done on APNs' POF and its significance. Organizations have simply assumed that APNs have or will adopt their beliefs, values, and norms; mutual congruence has not been a question that organizations have had in mind [28]. But a study of RNs employed in a Midwestern hospital system shows that perceived POF produces positive work outcomes and impact [29].

Hypotheses development and research model

Based on a comprehensive literature review and the theoretical background stated above, we constructed a theoretical conceptual framework that organizational commitment is explained by Person-Job Environment, POF, CSE, and Job Satisfaction (see Figure S1 in the Supplementary Tables and Figures).

We developed the following six hypotheses on the direct and indirect associations of the variables affecting APNs' OC and a research model to test those hypotheses (see Figure 1).

The role of job environment (job location, pay scale), computer self-efficacy, and POF

Individuals who fit well in their job environment showed a high degree of job satisfaction, job motivation, mental health, socialization, and OC [12]. However, financial, structural, and social barriers in the job environment adversely affect individuals' work performance [30]. An organization that provides a better job environment will positively affect employees' POF. The literature indicates that job location and pay scale, as aspects of the job environment, influence APNs' POF. In particular, fewer environmental barriers in pay scale and job location tend to result in the perception of higher compatibility with an organization.

The concept of CSE records a computer user's self-judgment about his or her capability to use a computer to successfully complete a specific task, as well as his or her perception of what can be done in the future [31]. In today's work environment, CSE is essential to the performance of an APN's daily duties. In all likelihood, an APN with a higher level of CSE is capable of successfully mastering a more comprehensive array of skills in a computing environment than an APN with lower CSE. A study found that an individual's anxiety about computer capability is a barrier to successful performance and liable to result in a lower perception of POF [32]. We claim that APNs who have successfully adapted to a work environment and attained high CSE tend to share their organization's values and beliefs and positively perceive their fit to the organization (H3). Thus, we posit:

H1-3. An APN's job location (**H1**), pay scale (**H2**), and CSE (**H3**) are positively associated with his or her POF.

The role of job satisfaction, POF, and supervision

An APN's job satisfaction is an integral factor affecting retention and the delivery of quality work [21]. It is also a crucial factor affecting an employee's turnover intention [15].

Higher job satisfaction is derived from active and positive interactions with other organization members. Prior studies show that APNs' job satisfaction is positively associated with supervision. Thus, we argue that job satisfaction increases when APNs are acknowledged by their supervisors or other nurses [6,21,33]. A supervisor is an active member of an organization who represents the organization's values and who interacts directly with APNs. Job satisfaction is derived from interactions with other organization members. Accordingly, APNs with higher job satisfaction tend to perceive supervision more positively if a little conflict occurs, and harmonious job performance is

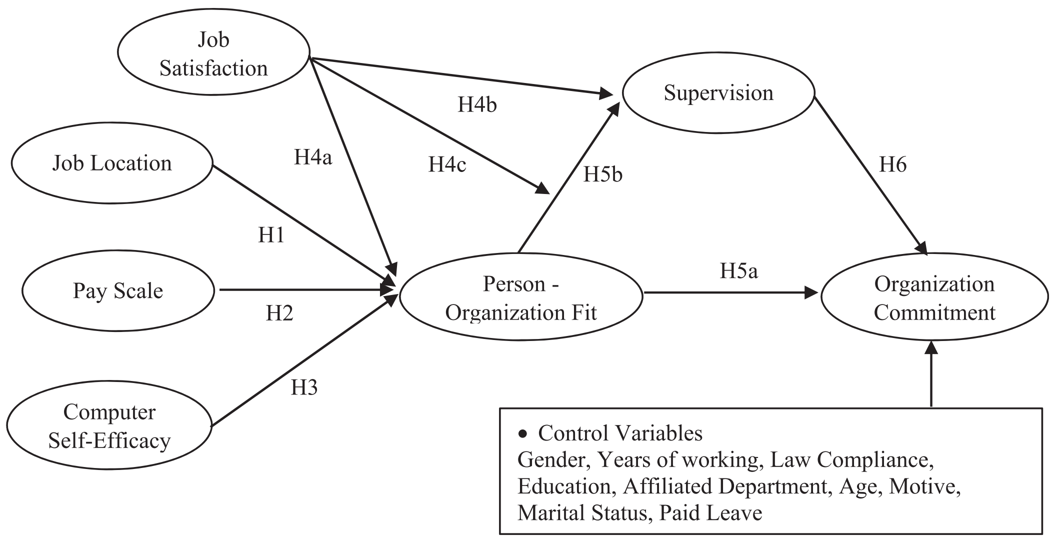

Figure 1. Research Model and Hypotheses.

achieved through smooth interaction with a supervisor. Job satisfaction is also significantly associated with POF [34]. The degree of APNs' job satisfaction is likely to affect the perceived value of the employer organization, the hospital.

Based on the review of the literature, we posit that job satisfaction positively affects both POF and supervision. Since APNs with high perception POF are likely to rate supervision more positively if they are satisfied with their jobs, we claim that APNs' job satisfaction moderates the relationship between POF and supervision. That is, we posit

H4. An APN's job satisfaction is positively associated with his or her POF (**H4a**) and supervision (**H4b**).

H4c. An APN's job satisfaction positively moderates the relationship between POF and supervision.

The role of person-organization fit (POF)

POF concerns an individual's and an organization's congruence of beliefs, values, and norms [23]. High POF indicates a close alignment of an individual's beliefs, values, and norms with those of an organization. Multiple studies show that POF has a significant effect on job satisfaction, commitment, and intention to leave a position [35].

An individual's desire to remain in an organization is stronger if his/her perceived POF is positive. That, in turn, affects employee turnover [36]. Highly positive POF is correlated with strong OC and a low turnover rate [37]. In addition, positive POF provides an employee with a sense of meaningfulness and psychological attachment to an organization. That leads to a higher employee engagement level and consequently a lower turnover rate [38].

Organizations have simply assumed that APNs have or will adopt the beliefs, values, and norms of their organizations; mutual adjustment has not been a question for organizations [28]. A study of RNs employed in a Midwestern hospital system, however, shows that highly positive POF, conceptualized in terms of supplementary adjustment and congruence, produces positive work outcomes [29]. Supplementary congruence occurs when an organization and an individual share similar fundamental characteristics [25]. Given these findings, we claim 1) that an individual's willingness to remain in an organization tends to be stronger if he/she perceives high congruence of his/her beliefs, values, and norms with those of the employing health care organization.

Research has also found that employees' POF plays a vital role in supervisor ratings and career success [27]. With organizational assimilation, based on shared values and organizational goals, mentees' relationships with mentors evolve positively [23]. A supervisor's role in supporting APNs is particularly significant as far as the POF perspective is concerned. APNs' supervision ratings are positive when they believe that their values and beliefs coincide with those of supervisors. Supervisors represent and promulgate a healthcare organization's culture when they support and assist APNs. The higher the perceived POF, the more positive the supervision rating [33]. Thus, we claim 2) that POF influences APNs' rating of supervision. On the basis of 1) and 2), we posit:

H5. An APN's POF is positively associated with his/her OC (**H5a**) and supervision performed within the healthcare organization (**H5b**).

The role of supervision

Supervision is referred to as a supervisor's managing style toward his or her subordinate, interaction with a working unit and peers, providing feedback based on his or her working experience, and the receipt of recognition as an important immediate job environment factor within an organization [15].

Supervisors can significantly influence workers' wellbeing, personal growth, and development. Workers who receive guidance and support from their supervisors exhibit higher OC levels [39]. Supervisors support for employees is crucial in securing positive employee responses and behaviors in challenging and troublesome situations [18]. An employee's relationship with his/her supervisor plays an important role in his/her OC [40]. In addition, a positive relationship between supervisors and employees is strongly associated with lower employee turnover rates, a more positive job attitude, and a higher satisfaction level [10]. When APNs perceive that their supervisors “are on their side” as far as their professional work and growth are concerned, their emotional bonds with them deepen and a strong OC results [33]. Given these findings, we claim that a higher APN rating of supervision leads to a stronger commitment to a healthcare organization.

H6. Supervision is positively associated with OC.

Table 1 *Characteristics of Participants.*

Characteristics	N (%)
Gender	
Men	2 (1.1)
Women	184 (98.4)
No response	1 (0.5)
Age	
21–30	12 (6.4)
31–40	113 (60.4)
41–50	59 (31.6)
51–60	2 (1.1)
No response	1 (0.5)
Marital status	
Married	141 (75.4)
Single	45 (24.1)
Divorced	1 (0.5)
Education	
AND	3 (1.6)
BSN	54 (28.9)
Master	124 (66.3)
Ph.D.	6 (3.2)
Affiliated department	
Nursing	183 (97.9)
Medical	1 (0.5)
Others	2 (1.1)
No response	1 (0.5)
Paid leave	
Yes	34 (18.2)
No	152 (81.3)
No response	1 (0.5)
Years of working	
3–5 years	2 (1.1)
6–10 years	32 (17.1)
11–15 years	48 (25.7)
16–20 years	68 (36.4)
21–25 years	29 (15.5)
26 years or more	7 (3.7)
No response	1 (0.5)
Law compliance	
Yes	159 (85.0)
No	28 (15.0)
Motive	
Being assigned/transferred	17 (9.1)
Being interested in	18 (9.6)
Working in a more professional position	119 (63.6)
To avoid a work shift (e.g., 8-hours or night shift)	10 (5.3)
To pursue a self-development	22 (11.8)
Others	1 (0.5)

Note. ADN = Associate Degree in Nursing; BSN = Bachelor of Science in Nursing.

The research model from the literature review and the hypotheses we posit is shown in Figure 1.

Research method

Study design

Our study identifies inter-relationships among the key factors affecting APNs' OC: job environment, job satisfaction, POF, and supervision. To this end, a cross-sectional research design employing a survey was used. Hypotheses were tested using the PLS method. The PLS method is one of the two analysis methods of the structural equation model (SEM). One method is covariance-based, the other is variance-based. The PLS method offers benefits that include: identifying the possible existence of nonlinear relationships among measured constructs, being well-suited for a small sample size, and recognizing mediating or moderating effects among constructs [41,42]. In addition, the PLS is well known for its capability to explore significant associations among latent variables. That is a welcomed benefit: our research model recognizes the possibility of just such significant associations among latent variables.

Ethical considerations

The current study (Proposal #2018-1400) was approved by the IRB in the Asan Medical Center in which the research was conducted.

Selection of measurement items

To measure the core dependent variable of organization commitment, five measurement items were adopted from a prior study [43]. Selected survey items correspond to organization commitment, defined as “the strength of an individual's identification with and involvement in a particular organization” [16]. Next, three items to measure POF were adopted [24]. The items represent employees' perception of organization fitting, with organization fit conceptualized in terms of congruence of personal values with an organization's culture [24]. APNs' job satisfaction (three items), supervision (three items), and pay scale (two items) were adopted from Sutton and Griffin [15] The items measure APNs' emotional responses to their daily duties, current working environment, and position compensation. Five items to measure CSE were adopted from Compeau and Higgins [12]. All five are rooted in the theory of self-efficacy proposed by Bandura [17]. The theory is constructed to explain “people's judgments of their capabilities to organize and execute courses of action to attain designated types of performance”. Finally, two items measure APNs' perceptions of job location as an environmental factor affecting POF. Nine additional items concern demographics for control variables (gender, years of working, law compliance, education, affiliated department, age, motive, marital status, and paid leave).

All survey items were assessed using a 7-point Likert scale ranging from “1 (strongly disagree)” to “7 (strongly agree)”, except for the construct of CSE. The CSE items were measured using a bipolar continuum of 10 scales. Survey questions were translated into Korean by the authors. Four bilingual nursing professionals with a master's or higher degree validated the translation. One author later reverse-translated the survey questions into English and confirmed the validity of the Korean translations.

With PLS-SEM/variance-based SEM models as guides, three or four items were selected for each construct on the basis of cross-loadings. It indicated the best reflective latent variable and qualified the uni-dimensionality and the maximum of latent variable identification of each construct [44].

Participants

The survey was conducted at the largest hospital in South Korea. The hospital is located in Southeast Seoul. It has 2705 beds and serves, on average, 11,885 outpatients and 2540 inpatients per day. The survey was limited to APNs. APNs are divided into two groups: clinical nurse specialists (CNSs) and physician assistants. The hospital employs approximately 120 CNSs. Nurses are certified as CNSs through a CNS exam. CNSs have been engaged in nursing research, have acquired professional knowledge in clinical nursing, and have served patients in practice areas designated by the APN executive council. The hospital also employs 258 physician assistants. Among them, 86 are members of the Department of Medical Specialty, while 172 are members of the Department of Nursing.

Table 2 *Summary Statistics of Constructs, Convergent Validity and HTMT.*

Constructs	Items	M ± SD	Composite Reliability	Cronbach's α	Heterotrait-Monotrait Ratio (HTMT)						
					OC	SUP	JS	PAY	POF	JL	CSE
Organization Commitment (OC)	OC1	5.85 ± 0.94	.90	.86	1.00						
	OC2	6.06 ± 0.90									
	OC3	5.86 ± 1.03									
	OC4	5.75 ± 1.23									
	OC5	6.43 ± 0.84									
Supervision (SUP)	SUP1	5.28 ± 1.21	.86	.76	.48	1.00					
	SUP2	4.93 ± 1.37									
	SUP3	4.83 ± 1.34									
Job satisfaction (JS)	JS1	5.83 ± 0.86	.89	.81	.71	.55	1.00				
	JS2	5.88 ± 0.80									
	JS3	5.71 ± 0.91									
Pay Scale (PAY)	PAY1	4.83 ± 1.24	.94	.87	.37	.41	.45	1.00			
	PAY2	4.75 ± 1.27									
Person-Organization Fit (POF)	POF1	5.44 ± 0.92	.96	.93	.69	.50	.72	.48	1.00		
	POF2	5.39 ± .95									
	POF3	5.33 ± 0.98									
Job Location (JL)	JL1	5.50 ± 1.29	.84	.62	.48	.32	.53	.46	.50	1.00	
	JL2	4.96 ± 1.39									
Computer Self Efficacy (CSE)	CSE1	8.42 ± 1.421	.93	.90	.36	.30	.46	.19	.36	.42	1.00
	CSE2	8.57 ± 1.30									
	CSE3	9.16 ± 1.09									
	CSE4	9.06 ± 1.09									
	CSE5	8.77 ± 1.27									

Note. CSE = Computer Self-Efficacy; JL = Job Location; JS = Job Satisfaction; PAY = Pay Scale; POF = Person-Organization Fit; SUP = Supervision; OC = Organizational Commitment.

Paper survey materials were sent to 200 APNs in the hospital. One hundred and eighty-nine participants (95.5%) answered and returned the survey. In determining the minimum sample size, a prior study suggested calculating the statistical power and effect sizes *a priori* [45]. Assessing *a priori* by power analysis in PLS-SEM benefits minimizing Type II errors (false negative − not declining a false hypothesis). Therefore, we set the standard values of effect size f^2 (a value of .1), error probability α (a value of .05), and power (1-α) (a value of .8) using G*Power 3.1 [46] to gain prior knowledge of the required sample size. Doing so enables the avoidance of Type II errors [47]. The number of predictors is set for two reasons. First, the maximum number of paths directed to a single construct in a valid research model is four; and second, on the research model, POF is influenced by job satisfaction, job location, pay scale, and CSE [42]. The minimum required sample size for securing valid results was determined to be 125. Detailed demographic information about the participants is shown in Table 1.

Ninety-eight percent ($n = 184$) of ANPs surveyed were female. The age range was 21 to 60 and was divided into four groups. Ninety-two percent of the participants ($n = 172$) fell into two age groups. The range of the two age groups was 31 to 50. Seventy-five percent of participants were married at the time of the survey. More than 60.0% of the participants had earned a master's degree, and more than 90.0% at least a bachelor's degree. Almost all participants (98.0%) were working in the nursing department. 152 participants (81.3%) answered that they did not have paid leave.

Data collection process

After the IRB approval, a briefing on the research was conducted at a meeting of APNs at the hospital. Names of volunteering APNs were collected by the Department of Nursing and sent to the research team. The research team then sent emails to volunteering APNs to confirm their willingness to participate in the study. APNs who confirmed their willingness to participate received a package in which the paper survey, a consent form, and a self-addressed and stamped envelope were included. Participating APNs completed the survey, signed the consent form, and mailed them to the research team. After remaining sealed for two weeks, the surveys were opened for analysis.

Data analysis

WarpPLS 7.0 software was used to test the hypotheses and analyze the research model [48]. Two model assessments of the data were conducted. A measurement assessment confirmed the validity and reliability of the data, measured by convergent validity and discriminant validity. A structural model assessment identified path coefficients, effect sizes, and *p*-values. Details can be found below.

Results

Measurement model assessment

We assessed a measurement model using internal consistency, convergent validity, and discriminant validity per PLS-SEM reporting standard [42]. Internal consistency is examined by composite reliability and Cronbach's α. Convergent validity is examined by indicator reliability. Our analysis shows that the composite reliabilities ranged from .96 to .84 and Cronbach's α ranged from .62 to .93 (see Table 2). All indicator reliabilities are higher than the minimum of 0.6 (see Table 2). Thus, measures of internal consistency and convergent validity met or surpassed the recommended minimum thresholds [42,44].

Discriminant validity is identified by the heterotrait-monotrait ratio of correlations and examined by the cross-loadings of each construct. All heterotrait-monotrait ratio values in our measurement model are smaller than the conservative threshold of 0.85 [42]. Thus, all constructs are conceptually distinct (see Table 2). The rotated cross-loadings of each construct are much less than the indicator's outer loadings (see Table S1 in the Supplementary Tables and Figures). Thus, all results support discriminant validity.

Structural model assessment and hypothesis testing

In testing the hypotheses, our results show that APNs' pay scale is positively associated with POF ($\beta = 0.21$, $p < .001$), indicating that H2 is supported (see Figure 2).

Table 3 *Total and Specific Indirect Effects.*

Constructs		Indirect Paths	Specific indirect effects (*p*-value)	Total Indirect Effect (*p*-value)
OC	PAY	PAY → POF → SUP → OC	0 (.428)	.09 (.033)
		PAY → POF → OC	.09 (.045)	
	JS	JS → POF → OC	.20 (<.001)	.26 (<.001)
		JS → POF → SUP → OC	.02 (.338)	
		JS → SUP → OC	.04 (<.001)	
	CSE	CSE → POF → OC	−.03 (.264)	−.03 (.246)
		CSE → POF → SUP → OC	0 (.473)	
	JL	JL → POF → OC	.05 (.186)	.05 (.166)
		JL → POF → SUP → OC	0 (.462)	
	POF	POF → SUP → OC	.04 (.239)	.04 (.239)
SUP	PAY	PAY → POF → SUP	.06 (.138)	.06 (.138)
	JS	JS → POF → SUP	.13 (.006)	.13 (.006)
	CSE	CSE → POF → SUP	−.02 (.342)	−.02 (.342)
	JL	JL → POF → SUP	.03 (.282)	.03 (.282)

Note. CSE = Computer Self-Efficacy; JL = Job Location; JS = Job Satisfaction; PAY = Pay Scale; POF = Person-Organization Fit; SUP = Supervision; OC = Organizational Commitment.

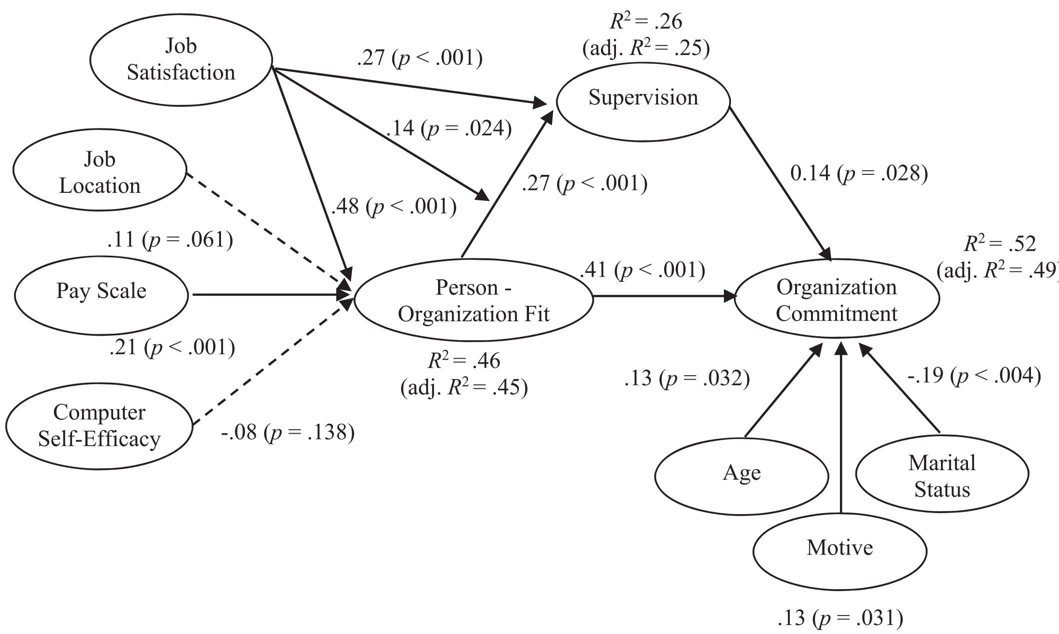

Figure 2. Testing Hypotheses. Note: Control variables – only statistically significant variables are included in the figure.

However, job location and CSE are not associated significantly with POF (respectively: $\beta = 0.11, p = .061; \beta = -0.8, p = .138$). H1 and H3 are thus not supported. As for H4, job satisfaction has a significant effect on both POF and supervision (respectively: $\beta = 0.48, p < .001; \beta = 0.27, p < .001$). H4a and H4b are thus supported. The results also show that job satisfaction positively and significantly moderates the relationship between a supervisor and person-organization fit ($\beta = 0.14, p = .024$). H4c is thus supported. In particular, supervision is influenced by APNs' low and high job satisfaction levels as the degree of POF increases (that is, as toward the right side of the POF axis. See Figure S2 in the Supplementary Tables and Figures). Given a low job satisfaction level, the effect of supervision gets suddenly weaker when the POF becomes positive on the POF axis. However, given a high job satisfaction level, the supervision effect is greater when the POF increases. Note that the WarpPLS application assumes nonlinear relationships among people's perceptions and behaviors. This is because such nonlinear relationships are common and well-established in social studies [41].

Regarding H5, POF is positively and significantly associated with both an APN's commitment to healthcare organization and supervision (respectively: $\beta = 0.41, p < .001; \beta = 0.27, p < .001$). H5 is thus supported. Supervision has a positive effect on OC ($\beta = 0.14, p = .028$). H6 is thus also supported. Among control variables, only age, motive, and marital status are statistically significant (respectively: $\beta = 0.13, p = .032; \beta = 0.13, p = .031; \beta = -0.19, p < .004$).

Total indirect effects and specific indirect effects in this model are listed in Table 3. In examining indirect effects, the path of job satisfaction → POF → OC indicates both the highest total and specific indirect effects.

Discussion

The study investigated the key factors affecting APNs' OC in their healthcare organization. The results provide a number of insights.

The aspects of the work environment (i.e., job location – H1 and pay scale – H2) show mixed relations, resulting in mixed outcomes. Pay scale for APNs is a significant factor for POF, but job location is not. In the case of job location, 93.0% of the survey participants reported that they had worked in the hospital for more than 8 years. We infer that their place of residence is within a readily commutable distance; thus, job location does not significantly affect POF. Participants considered pay scale an important factor impacting POF. This finding aligns with the findings from prior studies [49]. Well-paid APNs tend to perceive high congruence with their organizations.

CSE was examined in relation to APNs' years of working experience, in conjunction with the length of electronic health records (EHR) and EHRs use in the hospital. Our finding is that CSE is not a significant factor affecting APNs' perceived POF. Some APNs, however, expressed a desire for hospital assistance with new EHRs systems. This indicates a need for future research concerning APNs' perception of CSE in updated computing environments and the impact of such perception on POF.

The study also shows that job satisfaction is a salient factor underlying precursory factors (e.g., supervision and POF) affecting OC. Job satisfaction thus plays a dual role: 1) it is a direct antecedent factor influencing both supervision and POF and 2) it is a simultaneous moderator between POF and supervision. In particular, in the examination of the moderating effects between POF and supervison, the level of job satisfaction plays a crucial role in explaining the relationship between POF and supervision; given a high job satisfaction level, POF and supervision are positively associated with each other; given a low job satisfaction level, POF and supervision are negatively associated with each other at a certain point.

Another salient aspect of job satisfaction is found in the path of JS → POF → OC in Table 3. This path shows the strongest indirect effect (.20) among other specific indirect effects. The total indirect effect between JS and OC is the greatest (.26) among all total indirect effects. Our findings indicate that APNs' job satisfaction cannot sufficiently explain his or her OC if the APNs' perception of POF is not considered in the relationship between JS and OC.

The findings point to an effective potential resource for the retention of APNs and for the improvement of overall quality healthcare: the enhancement of APNs' job satisfaction. APNs' job satisfaction can be enhanced effectively when patients and supervisors recognize the contribution and value of APNs' performances. Well-crafted institutional programs can promote such recognition and thus enhance APNs' job satisfaction.

Concerning POF, the findings indicate the important role of POF on supervision and OC. Both our research and earlier studies support POF's association with OC. Survey participants are strongly committed to their organizations when their perceived organization values fit well with their own personal values. Another significant finding is an association of POF with supervision rating. This finding deserves the attention of healthcare organizations because personal value congruence with an organization's value is strongly associated with the interaction between an individual and his or her supervisor at their duty stations.

The congruence of APNs' aims and values with those of their organization is not easy to achieve. Values tend to diverge in an institutional setting, but one-sided assimilation of APNs' values to those of a health organization is neither desirable nor possible. Neither is the converse assimilation. Necessary is a mutual effort by both parties through transparent communication and negotiation of values, led by the healthcare organization [50]. Such congruence requires that the organization strive to establish ethical and socially acceptable mission/value statements and policies on promotion, reward, and the resolution of conflicts and to secure the acceptance of such statements and policies from organization stakeholders, including APNs. Efforts need to be made to know and reflect on APNs' values and goals and to include APNs in the decision-making process. The decision-making process must be inclusive, transparent, and equitable for APNs and all stakeholders. APNs' POF would be best promoted with committed organizational support for the mutual congruence between APNs and their organizations. Committees or programs constructed to serve that purpose are indirect routes to improved POF.

The construct of supervision influences OC directly. Our finding is in keeping with other studies: a more supportive and helpful supervisor enhances APNs' commitment to a healthcare organization [21,33]. Our findings suggest that supervisors of APNs should develop positive relationships with them and be supportive in guiding, evaluating, and assisting them. Positive supervision results from a committed organizational effort to initiate and support clear and transparent communication and the professionalism of supervisors. Committed organizational support for effective supervision of supervisors for APNs is much needed.

Implications

Our discussion has indicated the need for committed organizational support to enhance job satisfaction, POF, and supervision for the OC of APNs. At the hospital where the research was conducted, there is an APN steering committee which manages APN job duties. The committee consists of top-ranking officers and APN supervisor representatives in the hospital. Among its powers and duties are setting pay rates, promoting APNs, evaluation and recognition of job performance of APNs, and communication with supervisors regarding organization policies and activities. This steering committee has been recognized as an effective instrument in managing the APN system. APNs are managed by supervisors who communicate with administrators and convey organizational values and norms to APNs. The APN steering committee has been instrumental in enhancing the positive ratings of supervision, POF, and OC. Our results thus have important practical implications for reducing the APN turnover rate. They suggest that establishing an APN steering committee or establishing a procedure that ensures direct and transparent communication among the healthcare organization, supervisors, and APNs may help achieve high POF and high ratings of supervision, as well as secure higher OC levels.

Limitations

Our research has limitations as follows; first, studies of the OC of APNs are relatively rare. Our findings are based only on data collected at a single hospital in Korea. Even though it is the largest hospital in Korea, the findings need to be further validated. To increase confidence in the results, more research in different social and cultural settings is needed. Additional research will help clinical policymakers devise effective strategies to improve APNs' OC.

Second, given that our data are cross-sectional, causal relationships cannot be inferred from our findings. For example, (1) job satisfaction can play a role as both an antecedent condition and as a target variable, and (2) POF may be, given only our data, an outcome variable influenced by supervision. Cross-sectional data alone are not sufficient to confirm the causal relationships that our results may suggest. Confirmation requires not just the collection and analysis of similar data over periods of time but a more rigorous test to draw inferences about causal relationships among constructs.

Last, our study offers useful insights into APNs' OC level at a specific place and point in time, but OC is always at least partly a function of place and time. We thus suggest that culturally disparate and in-depth longitudinal studies of APNs' OC be conducted. This is of some importance. Shortages of APNs already exist, and duties, positions, status, staffing, institutional arrangements, and other variables are ever changing. Identifying factors which significantly impact OC can provide a deeper managerial insight and thereby help to improve APN loyalty and enhance APN retention.

Conclusions

Our conclusions are: 1) Job satisfaction significantly impacts APNs' POF and supervision. 2) POF significantly impacts APNs' OC. 3) Supervision has a high impact on APNs' OC. These findings suggest that healthcare organizations strive to retain APNs primarily by enhancing their job satisfaction, their POF, and supervision. If our study suggests one practical implication for nursing management, it is to establish an entity such as the APN steering committee or an official procedure to establish and enhance mutual consensus and transparent communication between administrators and APNs.

Authors' contributions

Project administration: MHJ. Funding acquisition: YHK. Research Conceptualization: SIS, MHJ, YHK. Overall Introduction: YHK, MHJ. Hypotheses and research model development: SIS, MHJ, HKK. Data curation: YHK, MHJ. Formal analysis: SIS. Methodology: SIS, MHJ. Writing – original draft: SIS, HKK, MHJ. Writing – review & editing: MHJ, HKK, YHK, WM.

Conflict of interest

No potential conflict of interest relevant to this article was reported.

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Appendix 1. Measurement Items

Organization Commitment

OC1. I talk up my healthcare organization to my friends as a great place to work.
OC2. I am proud to tell others that I am part of my healthcare organization.
OC3. I am extremely glad that I chose this healthcare organization to work for over others I was considering at the time I joined.
OC4. For me, this is the best of all possible healthcare organizations to work.
OC5. Deciding to work for my healthcare organization was a definite mistake on my part (RC).

Supervision

SUP1. My Clinic Manager is helpful in resolving issues of conflict.
SUP2. My Clinic Manager is supportive when I need to increase or decrease my scope of practice for the needs of my patients.
SUP3. Good performance is acknowledged.

Job Satisfaction

JS1. Patients and my Clinic Manager value my intervention.
JS2. Work is rewarding.
JS3. My intervention makes a difference to patients and my Clinic Manager.

Pay Scale

PAY1. I am content with my level of compensation.
PAY2. My compensation is an adequate reflection of my performance.

Job Location

JL1. My clinic location fits my interests.
JL2. My community matches my interests for outside of work activities.

Person-Organization Fit

POF1. The things that I value in life are very similar to the things that my healthcare organization values.
POF2. My personal values match my healthcare organization's values and culture.
POF3. My healthcare organization's values and culture provide a good fit with the things that I value in life.

Computer Self-Efficacy

I could complete the job using the software package…..

CSE1 …. If I could call someone for help if I got stuck:
CSE2 …. If someone else had helped me get started:
CSE3 …. If I had a lot of time to complete the job for which the software was provided:
CSE4 …. If I had just the built-in help facility for assistance:
CSE5 …. If someone showed me how to do it first:

Demographic Information

(Gender) What is your gender?

1. Male
2. Female

(Age) What is your age? ( )
(Affiliated Department) Please select your current working department

1. Nursing office
2. Medical office
3. Others

(Marital Status) Please select your marital status

1. Married
2. Single
3. Divorced

(Motive) Please select your motivation to become an NP or ANP

1. Being assigned/transferred
2. Being interested in
3. Working in a more professional position
4. To avoid a work shift (e.g., 8-hours or night shift)
5. To pursue self-development
6. Others

(Years of working) Please indicate years of working in the current hospital ( )
(Paid leave) I can use all my available vacation or leave days whenever I wish.

1. Yes
2. No

(Law compliance) I am worried about working in the current position of NP or ANP because of a lack of relevant protective laws and compliance.

1. Yes
2. No

(Education) Please indicate your terminal degree.

1. AND
2. NSN
3. Master
4. Ph.D.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.anr.2023.03.002.

References

1. American Nurses Association (ANA). Advanced practice registered nurses (APRN) [Internet]: American Nurses Association, American Nurses Credentialing Center, American Nurses Foundation [cited 2022 December 31]. Available from: https://www.nursingworld.org/practice-policy/aprn/.
2. International Council of Nurses. Guidelines on advanced practice nursing. Geneva, Switzerland: ICN; 2020 [cited 2023 January 8]. Available from: https://www.icn.ch/sites/default/files/inline-files/ICN_APN%20Report_EN_WEB.pdf
3. Schober M. Global emergence of nurse practitioner/advanced practice nursing roles. J Am Assoc Nurse Pract. 2018;30(4):182–4. https://doi.org/10.1097/JXX.0000000000000029
4. George C. The future of health care depends on reducing cost and raising quality [Internet]. Texas Medical Center; 2018, April 13 [cited 2022 February 22]. Available from: https://www.tmc.edu/news/2018/04/the-future-of-health-care-depends-on-reducing-cost-and-raising-quality/#single-article-body
5. Choi SJ, Kim YH, Lim KC, Kang Y. Advanced practice nurse in South Korea and current issues. J Nurse Pract. 2022. https://doi.org/10.1016/j.nurpra.2022.10.015
6. Faris JA, Douglas MK, Maples DC, Berg LR, Thrailkill A. Job satisfaction of advanced practice nurses in the Veterans Health Administration. J Am Acad Nurse Pract. 2010;22(1):35–44. https://doi.org/10.1111/j.1745-7599.2009.00468.x
7. Bozeman DP, Perrewé PL. The effect of item content overlap on organizational commitment questionnaire–turnover cognitions relationships. J Appl Psychol. 2001;86(1):161–73. https://doi.org/10.1037/0021-9010.86.1.161
8. Benson J, Brown M. Knowledge workers: what keeps them committed; what turns them away. Work Employ Soc. 2007;21(1):121–41. https://doi.org/10.1177/0950017007073623
9. Bratt MM, Felzer HM. Predictors of new graduate nurses' organizational commitment during a nurse residency program. J Nurses Staff Dev. 2012;28(3):108–19. https://doi.org/10.1097/NND.0b013e31825515c4
10. Tak J. Relationships between various person–environment fit types and employee withdrawal behavior: a longitudinal study. J Vocat Behav. 2011;78(2):315–20. https://doi.org/10.1016/j.jvb.2010.11.006
11. Finkelman AW. Professional nursing concepts: competencies for quality leadership. Burlington, MA: Jones & Bartlett Learning; 2023.
12. Compeau DR, Higgins CA. Computer self-efficacy - development of a measure and initial test. MIS Q. 1995;19(2):189–211. https://doi.org/10.2307/249688
13. Kristof AL. Person-organization fit: an integrative review of its conceptualizations, measurement, and implications. Pers Psychol. 1996;49(1):1–49. https://doi.org/10.1111/j.1744-6570.1996.tb01790.x
14. Blegen MA, Mueller CW. Nurses' job satisfaction: a longitudinal analysis. Res Nurs Health. 1987;10(4):227–37. https://doi.org/10.1002/nur.4770100405
15. Sutton G, Griffin MA. Integrating expectations, experiences, and psychological contract violations: a longitudinal study of new professionals. J Occup Organ Psychol. 2004;77(4):493–514. https://doi.org/10.1348/0963179042596487
16. Porter LW, Steers RM, Mowday RT, Boulian PV. Organizational commitment, job satisfaction, and turnover among psychiatric technicians. J Appl Psychol. 1974;59(5):603–9. https://doi.org/10.1037/h0037335
17. Bandura A. Social foundations of thought and action. 1st ed. Englewood Cliffs: Prentice Hall; 1986.
18. Chen CC, Chiu SF. An integrative model linking supervisor support and organizational citizenship behavior. J Bus Psychol. 2008;23(1-2):1–10. https://doi.org/10.1007/s10869-008-9084-y
19. Oliver RL. Measurement and evaluation of satisfaction processes in retail settings. J Retailing. 1981;57(3):25–48.
20. Locke EA, Dunnette MD. Chapter, The nature and causes of job satisfaction. In: The handbook of industrial and organizational psychology. Chicago: Skokie: Rand McNally; 1976. p. 1297–349.
21. Steinke MK, Rogers M, Lehwaldt D, Lamarche K. An examination of advanced practice nurses' job satisfaction internationally. Int Nurs Rev. 2018;65(2):162–72. https://doi.org/10.1111/inr.12389
22. Abun D, Javier JPG, Gamponia JIB, Magallanes T, Julian FP. The effect of employees' computer and internet self-efficacy on job satisfaction. IJRBS [Internet]. 2022;11(3):130–4. https://doi.org/10.20525/ijrbs.v11i3.1727
23. Wan CS, Yang Jt, Cheng Sy, Su C. A longitudinal study on internship effectiveness in vocational higher education. Educ Rev (Birm). 2012;65(1):36–55. https://doi.org/10.1080/00131911.2011.634969
24. Cable DM, DeRue DS. The convergent and discriminant validity of subjective fit perceptions. J Appl Psychol. 2002;87(5):875–84. https://doi.org/10.1037/0021-9010.87.5.875
25. Kim S. Does person-organization fit matter in the public -sector? Testing the mediating effect of person-organization fit in the relationship between public service motivation and work attitudes. Public Adm Rev. 2012;72(6):830–40. https://doi.org/10.1111/j.1540-6210.2012.02572.x
26. Caplan RD. Person-environment fit theory and organizations: commensurate dimensions, time perspectives, and mechanisms. J Vocat Behav. 1987;31(3):248–67. https://doi.org/10.1016/0001-8791(87)90042-X
27. McCulloch MC, Turban DB. Using person-organization fit to select employees for high-turnover jobs. Int J Sel Assess. 2007;15(1):63–71. https://doi.org/10.1111/j.1468-2389.2007.00368.x
28. Kwon JO, Kang JM. The effect of person-environment fit (person-job fit, person-organization fit, person-supervisor fit) and job embeddedness on turnover intention in clinical nurses. J Korean Converg Soc. 2019;10(3):307–17. https://doi.org/10.15207/JKCS.2019.10.3.307
29. Risman KL, Erickson RJ, Diefendorff JM. The impact of person-organization fit on nnurse job satisfaction and patient care quality. Appl Nurs Res. 2016;31:121–5. https://doi.org/10.1016/j.apnr.2016.01.007
30. Duffy RD, Autin KL, Bott EM. Work volition and job satisfaction: examining the role of work meaning and person-environment fit. Career Dev Q. 2015;63(2):126–40. https://doi.org/10.1002/cdq.12009
31. Sam HK, Othman AEA, Nordin ZS. Computer self-efficacy, computer anxiety, and attitudes toward the internet: a study among undergraduates in Unimas. J Educ Technol Soc. 2005;8(4):205–19 https://www.jstor.org/stable/jeductechsoci.8.4.205
32. Thatcher JB, Perrewe PL. An empirical examination of individual traits as antecedents to computer anxiety and computer self-efficacy. MIS Q. 2002;26(4):381–96. https://doi.org/10.2307/4132314
33. Seong JS, Yeom EY. Experience of the performance of the Korean physician assistants duties. J Qual Res. 2015;16(2):122–34. https://doi.org/10.22284/qr.2015.16.2.122
34. Chen X, Liu M, Liu C, Ruan F, Yuan Y, Xiong C. Job satisfaction and hospital performance rated by physicians in China: a moderated mediation analysis on the role of income and person-organization fit. Int J Environ Res Public Health. 2020;17(16):5846. https://doi.org/10.3390/ijerph17165846
35. Verquer ML, Beehr TA, Wagner SH. A meta-analysis of relations between person-organization fit and work attitudes. J Vocat Behav. 2003;63(3):473–89. https://doi.org/10.1016/S0001-8791(02)00036-2
36. Kristof-Brown AL, Zimmerman RD, Johnson EC. Consequences of individuals' fit at work: a meta-analysis of person-job, person-organization, person-group, and person-supervisor fit. Pers Psychol. 2005;58(2):281–342. https://doi.org/10.1111/j.1744-6570.2005.00672.x
37. Saks AM, Ashforth BE. A longitudinal investigation of the relationships between job information sources, applicant perceptions of fit, and work outcomes. Pers Psychol. 1997;50(2):395–426. https://doi.org/10.1111/j.1744-6570.1997.tb00913.x
38. Memon MA, Salleh R, Baharom MNR, Harun H. Person-organization fit and turnover intention: the mediating role of employee engagement. Global Bus Manag Res. 2014;6(3):205–9.
39. Frederico Ferreira MM. Organizational commitment and supervisor support, perception of procedural fairness, tenure in the hospital: the mediating effect of work-life balance - study in nurses. Clin Nurs Stud. 2014;3(2):17–23. https://doi.org/10.5430/cns.v3n2p17
40. Casper WJ, Harris C, Taylor-Bianco A, Wayne JH. Work–family conflict, perceived supervisor support and organizational commitment among Brazilian professionals. J Vocat Behav. 2011;79(3):640–52. https://doi.org/10.1016/j.jvb.2011.04.011
41. Kock N. Using WarpPLS in e-collaboration studies: an overview of five main analysis steps. Int J e-Collab. 2010;6(4):1–11. https://doi.org/10.4018/jec.2010100101
42. Hair JF, Hult GTM, Ringle C, Sarstedt M. A primer on partial least squares structural equation modeling (PLS-SEM). 2nd ed. Los Angeles: Sage Publications; 2016.
43. Mowday RT, Steers RM, Porter LW. The measurement of organizational commitment. J Vocat Behav. 1979;14(2):224–47. https://doi.org/10.1016/0001-8791(79)90072-1
44. Hair JF. Multivariate data analysis. 6th ed. Upper Saddle River, N.J: Pearson Prentice Hall; 2006.
45. Cohen J. Quantitative methods in psychology: a power primer. Psychol Bull. 1992;112(1):155–9. https://doi.org/10.1037//0033-2909.112.1.155

46. Faul F, Erdfelder E, Buchner A, Lang AG. Statistical power analyses using G*Power 3.1: tests for correlation and regression analyses. Behav Res Methods. 2009;41(4):1149–60. https://doi.org/10.3758/BRM.41.4.1149
47. Russo D, Stol KJ. PLS-SEM for software engineering research. ACM Comput Surv. 2022;54(4):1–38. https://doi.org/10.1145/3447580
48. Kock N. WarpPLS User Manual: Version 7.0 [Internet]. Laredo: ScriptWarp Systems; 2021 [cited 2022 August 18]. Available from: https://www.scriptwarp.com/warppls/UserManual_v_7_0.pdf
49. Salami SO. Demographic and psychological factors predicting organizational commitment among industrial workers. Anthropologist. 2017;10(1):31–8. https://doi.org/10.1080/09720073.2008.11891026
50. Marquis BL, Huston CJ. Leadership roles and management functions in nursing: theory and application. 10th ed. PA: Wolters Kluwer Health/LWW; 2022.

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Research Article

Validity and Reliability of the Korean Version of the Paternal Postnatal Attachment Scale

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SUMMARY

Purpose: The study aimed to translate the Paternal Postnatal Attachment Scale (PPAS) into Korean and to evaluate the validity and reliability of the Korean version of the PPAS (K-PPAS).
Methods: The PPAS was translated, back-translated, and reviewed by 12 experts and 5 fathers following the World Health Organization's guideline. A convenience sample of 396 fathers with infants in their first 12 months participated in this study. For construct validity, an underlying factor structure and model fit was assessed with an exploratory and confirmatory factor analysis. Convergent and discriminant validity and reliability of the K-PPAS were evaluated.
Results: The construct validity of the K-PPAS with 11 items was identified by two-factor structures: healthy attachment relationship, and patience and tolerance. The final model fit was shown acceptable with the normed chi-square = 1.94, comparative fit index = .94, Tucker–Lewis index = .92, root mean square error of approximation = .07, and standardized root mean square residual = .06. This model had acceptable convergent and discriminant validity for each construct with the values of the composite reliability and heterotrait–monotrait ratio at a satisfactory level. Discriminant validity with known groups showed that fathers with no postnatal depression had significantly higher scores on the K-PPAS than those with postnatal depression. Cronbach's α and McDonald's omega coefficient of the K-PPAS was .84 and .83.
Conclusions: The K-PPAS would be beneficial to measure postnatal attachment among fathers with infants aged 12 months or younger in Korea. However, further studies are suggested to evaluate the applicability of the scale considering the various family structures, such as single or foster parents and multicultural families that exist within the Korean population.

Introduction

A father-infant attachment emerges as an important mechanism in raising a child and influences the biological, psychological, and social aspects of a child's development [1]. From biological aspects, a secure attachment in infants has been associated with stimulating an infant's brain growth and development and allowing strong emotional immunity to form, making them more tolerant to stress [1]. Also, a positive paternal attachment in the early infant phase of childrearing greatly influences the child's later cognitive development [2], and these children also grew up to exhibit fewer behavioral problems, including emotional symptoms, conduct problems, hyperactivity, peer relationship problems, and prosocial behavior [3]. In contrast, the children of fathers with disengaged interactions even at 3 months of age were to manifest early behavioral problems such as aggression, rebellion, and hyperactivity [4].

Many scholars in pediatric and child psychology suggest that maternal and paternal roles in caregiving are separate systems from the evolutionary perspective [5]. When comparing both parents, mothers as the primary caregiver spend more time with their children even in the case of both parents having to work full time [6]. Previous studies had mainly addressed maternal attachment to a child's developmental outcomes as mothers were considered to be a more influential figure to children. However, the growing interest in fathers' involvement in childrearing has become an increasing trend with nuclear families and dual-income households being more prevalent in Korea [7]. Women's participation in the

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workforce might have led to changes in the perceptions of fathers and mothers sharing parenting and housework [8]. With this transition, recent studies have explored the role of Korean fathers as caregivers and their impact on children's development [9,10].

Although recent studies have highlighted the importance of paternal involvement in early attachment with their infants [11,12], evidence concerning paternal attachment towards an infant was less examined in comparison to maternal attachment due to a limited number of valid assessment tools available in Korea [13]. Several maternal attachment measures varying from self-report questionnaires to observational approaches have been translated into Korean, such as the Maternal Postnatal Attachment Scale [14], Maternal Attachment Inventory [53], and Attachment Q-sort [15].

However, only one scale, the Paternal Attachment Scale (PAS) [16], has been available to assess paternal attachment in infancy in Korea. The PAS [16] is developed from the father's perspective to describe the involvement with his neonate, who refers to a child aged under 28 days [17]. It is a self-report measure of 35 items with seven subscales, which assess traits such as absorption, preoccupation, and interest exhibited in fathers who have formed bonds with their newborns. Often the term “infant” has been used interchangeably with the term “neonate” regarding paternal attachment in Korea. While the PAS measures paternal attachment in neonates, it has been referred to and used in previous studies to describe paternal attachment in infants [18,19], which is an unsuitable usage of the tool for fathers of infants as old as 24 months [17]. Moreover, the use of the PAS in cross-cultural studies may also be limited with its measuring concepts developed and addressed in Korean. Hence, to accurately assess the correct age group of the infants, tools that assess mother-infant attachment were used by modifying words such as “mother” to “father” [20]. Nonetheless, this is still inadequate because mothers and fathers develop attachments differently [21]. Therefore, a tool that specifically assesses father-infant attachment more accurately with infants correctly termed is in need.

On the other hand, the Paternal Postnatal Attachment Scale (PPAS) [22] consists of 19 items with 3 subscales that measure the affective and cognitive part of paternal attachment by considering the subjective experience of a father in forming an attachment with his infant up to 12 months. The formation of a father's attachment with an infant up to 1-year-old has been considered a crucial developmental milestone for infants [11], as the growth and development of major functional networks occur within the first year of life [23]. Likewise, according to Bowlby [24], the sensitive period for the development of infant attachment is from 6 to 24 months. In contrast to the PAS, the PPAS properly captures the crucial period in which infants develop an attachment with their fathers, and a further assessment has proven it to be an acceptable measure for paternal attachment with infants that are 24 months old [25]. Thus, regardless of the terms of age used in the original study, the PPAS has been shown to assess the important developmental period of attachment across infancy. Moreover, because it has been used in many studies worldwide and was translated and adapted for use across diverse cultures with good validity and reliability to the original scale [26–28], it can also be used in cross-cultural studies. In light of the aforementioned gap in the postnatal field, a cross-culturally validated tool like the PPAS that evaluates attachment between fathers and infants of ages up to 12 months is required in Korea.

Hence, the aim of this study is to translate and adapt the PPAS into Korean and examine the validity and reliability of the Korean version of the PPAS (K-PPAS). The results of this study will provide a foundation for future research measuring and understanding Korean fathers' attachment to their infants.

Methods

Study design

In this validation study, a cross-sectional study was applied to evaluate the validity and reliability of the Korean version of the PPAS. The PPAS was translated into Korean following the four phases of the guideline of the World Health Organization: forward and back translation, cultural adaptation with an expert panel, content validity, and pretesting and cognitive interviewing [29]. The psychometric properties of the translated version of the PPAS were examined among Korean fathers. Permission to use and translate the PPAS was acquired by the copyright holder prior to this study.

Translation process

Forward and back translation

Firstly, two independent pediatric nurses, who are fluent in both Korean and English, translated the PPAS into two initial versions. These two initial versions were synthesized into one version by reviewing and resolving any inadequately translated expressions or concepts with an initial team of experts, comprising a professor, a researcher from the department of psychiatric mental health nursing, and three pediatric nurses with clinical experience of more than 6 years. The synthesized version was back translated into an English version by a bilingual professor in pediatric nursing, who has studied and worked in the United States.

Cultural adaptation with expert panel

A panel of 6 experts consisted of the initial team of 5 experts in the previous phase of forward and back translation and the bilingual professor in pediatric nursing. They ensured cultural and conceptual equivalence and reconcile any discrepancies between the back translated and the original. The panel agreed on maintaining item 1 (“When I take care of my child, I get bored or annoyed”) as the words “annoyance” and “irritation” used in the original tool were difficult to distinguish in general terms used in Korean. They also discussed to keep the change of item 13's response from “Neither” to “I don't care about the amount of time that I spend with my child” as the original option was unable to adequately convey the meaning needed for a person to answer a question. However, the panel suggested that consistency in response options for the scale should be needed for less confusion, and all back translated items were adapted into a 5-point Likert scale. After a consensus was reached within the panel of experts, the preliminary version of the tool was produced from this process.

Content validity

The final confirmation of the scale was assessed independently by a panel of 7 different experts with three professors and two researchers from the department of pediatric nursing and two senior pediatric nurses with more than 10 years of clinical experience. Experts were asked to evaluate each item on a 4-point Likert scale (1 = not relevant, 2 = item needs some revision, 3 = relevant but needs minor revision, and 4 = very relevant). The values of the item-level content validity index for each item and the scale-level content validity index based on the average method above .78 and .90, respectively, were considered adequate for content validity [30].

Pretesting and cognitive interviewing

The pretesting of the preliminary version of the K-PPAS was carried out using a purposive sampling method to recruit 5 fathers who have infants in their first 12 months. These participants were first-time fathers, with mean age of 34.60 (SD = 5.86) years. All of them were married with undergraduate degrees and worked full-time earning middle-class income. Interviews were performed to probe about the clarity of words or expressions used in questions. No problems were raised regarding clarity and comprehension of all items, and hence, a final version of the K-PPAS was created.

Setting and Samples

The survey for this study was conducted through online child-rearing communities in Korea. Convenience sampling was adopted to recruit fathers. The inclusion criteria were as follows: fathers aged 18 to 65 with infants in their first 12 months and have no problem communicating and answering questionnaires written in Korean, and have given a statement of consent prior to the study. A total of 396 fathers participated in this study, excluding four fathers who provided incomplete and inconsistent responses to survey questionnaires. To assess the construct validity of the scale, the necessary sample size for factor analysis was suggested as a minimum of 10 participants per item for exploratory factor analysis (EFA) and 200~300 participants for confirmatory factor analysis (CFA) [31]. Based on this, the data sample size was appropriate to conduct the factor analysis.

Ethical Considerations

The current study was conducted after receiving ethical approval from the Institutional Review Board at Ewha Womans University (Approval no. ewha-202203-0045-01). Participants were all informed about this study, and consent was gathered before commencing data collection.

Instruments

The PPAS [28] is a self-report measure that assesses the emotional responses of fathers to their infants during the first year of life in relation to the father-to-infant attachment. It comprises 19 items grouped in three subscales: patience and tolerance (PT) (8 items), pleasure in interaction (7 items), and affection and pride (4 items). Each item is scored with two to five response options. The score in the questionnaire ranges from 19 to 95, with a higher score indicating greater father-infant attachment. The PPAS has demonstrated adequate construct validity and reliability, and Cronbach's α coefficient ranged from .78 to 81 in the original study.

The K-Edinburgh Postnatal Depression Scale (EPDS) [32] translated from the original EPDS [33] is administered to assess postnatal depression. This 10-item scale is scored on a 4-point rating with a higher score indicating a greater level of postnatal depression. Cronbach's α coefficient of the K-EPDS and the EPDS was .84 and .87, respectively. As paternal depression is conceptually differentiated from father-infant attachment [34], the K-EPDS was used to examine discriminant validity.

Data Collection

This study recruited participants from online childrearing communities throughout April 2022. Prior to conducting data collection, consent from the administrators of online childrearing communities was obtained with a clear explanation regarding the study's purpose. The details of this study and a URL to the online survey were posted on each permitted online community. Participants were informed that their responses would remain anonymous and confidential, and assured of their right to refuse or withdraw their consent at any stage of this study without any consequences. A statement of consent was obtained from all participants before the survey began by allowing only those who have pressed “I consent” to continue onto the questionnaires. A gift voucher was given upon the completion of the questionnaires.

Data Analysis

The data were analyzed using IBM SPSS 28.0 and SPSS AMOS 28.0 programs (IBM Corp., Armonk, NY, USA). For the item analysis, means, standard deviations, skewness (<3), and kurtosis (<10) of an item's normal distribution [35] and item-total correlations ($\geq$.30) were assessed [36].

Construct validity was evaluated with EFA and CFA. The data collected were divided randomly to perform the EFA (n = 190) and CFA (n = 206). To determine the underlying factor structure, principal axis factoring with varimax rotation was used in the EFA [37]. The Kaiser–Meyer–Olkin (KMO >.60) and Bartlett's test of sphericity ($p < .05$) were used to confirm data suitability [38]. The optimum number of factors was extracted in accordance with an eigenvalue of 1 or above the elbow represented in a scree plot [37]. Items with loading onto their primary factors of .40 or above, alternative factors of .30 or below, and having a loading difference of .20 between their primary and alternative factors were considered acceptable [38]. For model fit verification, the CFA was performed with normed chi-square ($\chi 2$/df), comparative fit index (CFI), Tucker–Lewis index (TLI), root mean square error of approximation (RMSEA), and standardized root mean square residual (SRMR). The model fit was evaluated using the following criteria: $\chi 2/\text{df} \leq 3$, CFI and TLI $\geq$.90, RMSEA $\leq$.08, and SRMR $\leq$.06 [39,40].

Convergent validity and discriminant validity for each construct in the model were evaluated using the values of the composite reliability (CR) and heterotrait–monotrait ratio with the CFA data set [41,42]. Discriminant validity with known groups was assessed with the scores determined from the K-EPDS [32], comparing the scores of the postnatal depressed (K-EPDS $\geq$10) and the normal (K-EPDS <10) group. Cronbach's α and McDonald's omega coefficients ($\geq$.70) were assessed to determine acceptable internal consistency [41].

Results

Sample Characteristics

The sample consisted of 396 fathers with data distributed randomly to have necessary sample sizes for both the EFA and CFA. The mean age of the total sample was 34.07 (SD = 3.86). The majority of fathers were married (98.7%) and living together with someone (97.7%). Most were first-time fathers (83.3%), and slightly more than half of the children were male (50.5%). Other characteristics of the fathers and their children are shown in Table 1.

Item Analysis

The results of the item analysis are shown in Table 2. The skewness and kurtosis of each item of the initial 19-item K-PPAS ranged from −.87 to .30 and −.49 to 1.83, respectively, meeting the criteria for normality. No items were additionally deleted with the initial item-total correlation coefficients ranging from .30 to .71.

Content Validity

The item-level content validity index value for each item was above .78, with all items scoring 1.00 except .85 for item 8; however, still demonstrated excellent content validity for 11 items [30]. The scale-level content validity index based on the average method value scored .99, with the above recommended value of .90 [30], also satisfying the criterion for good content validity, and thus all items were retained.

Construct Validity

Both EFA and CFA were performed to determine underlying factor structures that might exist as cultural adaptation and confirm any possibilities for reclassifying the items from the

Table 1 *General Characteristics of the Participants (N = 396).*

	Characteristics	Categories	Total (n = 396)	EFA (n = 190)	CFA (n = 206)
			Mean ± SD or n (%)	Mean ± SD or n (%)	Mean ± SD or n (%)
Father	Age (years)		34.07 ± 3.86	34.44 ± 3.98	33.72 ± 3.71
	Marital status	Unmarried	5 (1.3)	2 (1.1)	3 (1.5)
		Married	391 (98.7)	188 (98.9)	203 (98.5)
	Educational level	High school or less	24 (6.0)	11 (5.8)	13 (6.3)
		College/university	325 (82.1)	173 (91.0)	152 (73.8)
		Graduate or above	47 (11.9)	6 (3.2)	41 (19.9)
	Job status	Yes	382 (96.5)	181 (95.3)	201 (97.6)
		No	14 (3.5)	9 (4.7)	5 (2.4)
	Family structure	Alone	9 (2.3)	3 (1.6)	6 (2.9)
		Nuclear family	353 (89.1)	181 (95.3)	172 (83.5)
		Parents/parents-in-law	33 (8.3)	6 (3.1)	27 (13.1)
		Others	1 (0.3)		1 (0.5)
	Planned pregnancy	Yes	319 (80.6)	148 (77.9)	171 (83.0)
		No	77 (19.4)	42 (22.1)	35 (17.0)
	Number of children	First	330 (83.3)	160 (84.2)	170 (82.5)
		Second	60 (15.2)	28 (14.7)	32 (15.5)
		Third or more	6 (1.5)	2 (1.1)	4 (2.0)
	Childrearing (hours)	Weekdays	3.65 ± 2.36	3.67 ± 2.65	3.63 ± 2.06
	Childrearing (hours)	Weekends	8.68 ± 4.30	7.99 ± 4.08	9.32 ± 4.42
	Childrearing support	None	125 (31.6)	74 (38.9)	51 (24.8)
		Parents/parents-in-law	243 (61.4)	99 (52.7)	144 (69.8)
		Others	28 (7.0)	17 (8.4)	11 (5.4)
Child	Age (months)		8.47 ± 2.77	8.61 ± 2.51	8.33 ± 2.99
	Gender	Men	200 (50.5)	95 (50.0)	105 (51.0)
		Women	192 (48.5)	93 (48.9)	99 (48.0)
		Twins or more	4 (1.0)	2 (1.1)	2 (1.0)
	Gestational age (weeks)		37.19 ± 3.55	37.08 ± 3.53	37.29 ± 3.58
	Birth weight (grams)		3069.35 ± 368.09	3127.32 ± 396.74	3146.47 ± 375.41

Note. CFA = confirmatory factor analysis; EFA = explanatory factor analysis; SD = standard deviation.

original PPAS. The KMO was .89, and Bartlett's test of sphericity was $\chi2 = 1559.02$ ($p < .001$), indicating adequate sampling and suitability for factor analysis. The principal axis factoring and varimax rotation revealed two factors with eigenvalues above 1 and consistent with the scree plot. The criteria for primary and alternative factor loadings and their differences [38] were considered in addition to content coherence with the original scale [22]. As a result, items 10, 12, 13, 14, 15, 16, 18, and 19 were deleted.

EFA was performed again with a final 11 items, resulting in a KMO of .84 and Bartlett's test of sphericity of $\chi2 = 790.95$ ($p < .001$), demonstrating suitability for factor analysis. With eigenvalues above 1 and based on the elbow in the scree plot, the final factor structure consisted of two factors. The two-factor structure accounted for

Table 2 *Item Analysis and Factor Analysis of the K-PPAS (N = 396).*

Factors	Item no.	Mean ± SD	ITC	EFA (n = 190)				CFA (n = 206)		CR
				Initial factor structure		Final factor structure		FL	*p*	
				1	2	1	2			
Healthy attachment relationship	Item 3	3.98 ± 0.75	.59	.50	.31	.49	.28	.64	<.001	.81
	Item 4	3.53 ± 0.83	.39	.58	.00	.65	−.03	.48	<.001	
	Item 5	3.68 ± 0.72	.48	.62	.08	.72	.06	.61	<.001	
	Item 7	3.87 ± 0.85	.59	.60	.28	.59	.28	.64	<.001	
	Item 8	3.96 ± 0.71	.55	.61	.20	.69	.18	.58	<.001	
	Item 9	3.56 ± 0.89	.46	.49	.15	.49	.17	.67	<.001	
	Item 10	3.45 ± 0.87	.30	.31	−.07					
	Item 11	3.99 ± 0.64	.65	.65	.34	.54	.29	.66	<.001	
	Item 12	3.96 ± 0.76	.57	.49	.37					
	Item 13	3.96 ± 0.74	.65	.59	.37					
	Item 14	4.07 ± 0.71	.71	.55	.50					
	Item 15	4.13 ± 0.73	.69	.55	.48					
	Item 16	3.95 ± 0.80	.65	.55	.45					
	Item 19	3.58 ± 0.76	.39	.36	.22					
Patience and tolerance	Item 1	3.68 ± 0.87	.58	.10	.81	.11	.84	.80	<.001	.65
	Item 2	3.85 ± 0.9	.60	.13	.81	.18	.79	.68	<.001	
	Item 6	3.70 ± 0.98	.56	.18	.70	.19	.72	.43	<.001	
	Item 17	3.65 ± 1.00	.50	.11	.68	.16	.64	.30	<.001	
	Item 18	3.05 ± 0.97	.31	.12	.35					
	Eigenvalue (%)			34.09	7.78	35.40	12.84			
	Cumulative (%)			34.09	41.88	35.40	48.24			

Note. CFA = confirmatory factor analysis; CR = composite reliability; EFA = explanatory factor analysis; FL = standardized factor loading; ITC = item-total correlation; K-PPAS = Korean version of Paternal Postnatal Attachment Scale; SD = standard deviation.

48.2% of the total variance, having a similar result to the PPAS [22] that accounted for 45% of the total variance, and meeting the total variance criteria of 40-60% [39,43]. The percentages of the variance explained by each factor are presented in Table 2. Factor 1 was labeled "healthy attachment relationship (HAR)" (items 3, 4, 5, 7, 8, 9, and 11) and factor 2 was labeled "PT"' (item 1, 2, 6, and 17). Factor loadings of all the 11 items ranged from .49 to .84, with each factor consisting of more than three items (Table 2).

Based on the result of the EFA, the assumption of multivariate normality was tested by calculating Mardia's coefficient of multivariate kurtosis before conducting maximum likelihood estimation for CFA. The value of Mardia's coefficient multivariate kurtosis and the critical ratio was 110.91 and 47.07, which was greater than the threshold criteria of the multivariate kurtosis <5 and critical ratio <1.96 [44]. Thus, multivariate normality was not met, and the Bollen-Stine bootstrap [45] method using recommended 250 bootstrap samples was applied [46]. The initial fit indices of the two-factor structure were Bollen-Stine bootstrap p = .056, $\chi2$/df = 2.85, CFI = .87, TLI = .83, RMSEA = .10, and SRMR = .07. The initial model showed a poor fit to the data with CFI, TLI, RMSEA, and SRMR not meeting the criteria for good fit indices [39,40]. The modification index (MI) values were inspected, and the covariance modification between error terms could significantly improve the initial model fit. The MI values of 3.84 or above suggested a need for model improvement [39]; however, a threshold of 10 was used for greater efficiency [44]. After considering the items' content and MI values, the initial model was revised by setting the covariance of the error term to item 6 and 17 (MI = 30.41), and the fit indices of the new model were Bollen-Stine bootstrap p = .291, $\chi2$/df = 2.12, CFI = .92, TLI = .89, RMSEA = .07, and SRMR = .06. This model fit was improved than the initial model, but TLI of .89 still suggested a poor fit. The covariance of the error term was additionally set to items 4 and 5 (MI = 10.20), and the fit indices of the revised model were Bollen-Stine bootstrap p = .422, $\chi2$/df = 1.94, CFI = .94, TLI = .92, RMSEA = .07, and SRMR = .06 (Table 3). The difference in the CFI value between model 1 and model 2 indicates a substantial improvement in the model fit. Additionally, the final model showed a better model fit than model 2 [35]. The fit indices of this revised model were improved substantially compared with the initial model by having all the criteria met for fit indices: $\chi2$/df ≤ 3; CFI and TLI ≥.90, RMSEA ≤.08, and SRMR ≤.06 [39,40]. The final model was confirmed (Figure 1). As shown in Table 2, the standardized factor loadings of all the 11 items in the final model ranged from .30 to .80, with all factor loading coefficients reaching significance (p < .001). In terms of the rule of thumb, a standardized factor loading >.50 is ideal in CFA. However, the results were considered acceptable and in agreement given that each loading coefficient was statistically significant (p < .001) and had a minimum value of .30 [39]. In addition, the revised model revealed to have adequate convergent validity for each construct in the model with the CR values of the two factors as .81 and .65 (Table 2), meeting the criterion of CR > .60 [41]. Discriminant validity was also supported by the heterotrait−monotrait ratio of .66, meeting the criterion of < .85 [42].

Table 3 *Goodness of Model Fit Indices of the K-PPAS (N = 206).*

Modified model	Bollen-Stine bootstrap (p)	Absolute fit index			Incremental fit index		
		$\chi2$/df	RMSEA	SRMR	CFI	Difference value of CFI	TLI
1	.056	2.85	.10	.07	.87		.83
2	.291	2.12	.07	.06	.92	.05	.89
Final	.422	1.94	.07	.06	.94	.02	.92

Note. $\chi2$/df = chi-square minimum/degree of freedom; CFI = comparative fit index; RMSEA = root mean square error of approximation; SRMR = standard root mean residual; TLI = Tucker-Lewis index.

Discriminant Validity (known groups)

The results of the discriminant validity using known groups are shown in Table 4. The group of fathers with no postnatal depression (K-EPDS <10) scored significantly higher on the K-PPAS (t = −9.97, p < .001) than those who did (K-EPDS ≥10). Similar significances were found in the subscales of the K-PPAS, with HAR (t = −12.01, p < .001) and PT (t = −5.77, p < .001) scoring higher in a group with the absence of postnatal depression.

Reliability

Cronbach's α coefficient for 11 items of the K-PPAS was .84, with .81 and .85 for the subscales of HAR and PT, respectively. The McDonald's omega coefficient for the scale was .83 and for the subscales of HAR and PT was .81 and .85. An acceptable internal consistency of the K-PPAS was demonstrated with the result of all coefficient values above .70.

Discussion

In this study, the PPAS was culturally adapted into Korean and had its psychometric properties evaluated among 396 Korean fathers with infants up to 12 months old. The results revealed that the 11-item K-PPAS had acceptable validity and reliability to assess the construct of father-infant attachment in Korea. The use of this tool may contribute to gaining knowledge and supporting further studies on father-infant attachment to bring about positive outcomes in an infant's later development.

The two-factor structure of 11-item K-PPAS was identified by conducting factor analysis: healthy attachment relationship, and patience and tolerance. This result was not consistent with the three-factor structure of the original PPAS ("patience and tolerance", "pleasure in interaction", and "affection and pride") [22], as well as the 15-item Spanish [26] and 18-item Turkish [28]. On the other hand, compared to the three-factor, the findings in this study were similar to the two-factor structure in the 16-item Portuguese version ("quality of attachment" and "patience and tolerance") [27]. One of the reasons for these differences in the factor structure may be due to not performing CFA in the original study to support its structure and items [26]. The absence of CFA may leave how well the proposed factor structure fits with observed data unexplored [32]. However, cultural differences may have also influenced the inequivalent number of factors and item placements. Therefore, it is advised to use the K-PPAS after careful consideration.

One strength of this study is that both EFA and CFA were performed to validate the factor structure among 396 fathers with infants, who were randomly divided into two data, one for EFA and the other for CFA. The results showed a total of 11 items after removing 8 items (10, 12, 13, 14, 15, 16, 18, and 19) from the original 19-item PPAS. Consistent with this study by conducting both factor analyses, the Spanish version had 4 items (6, 8, 9, and 15) and the Turkish version had 1 item (16) omitted. Although item deletion happened in all studies above, it was incomparable with the findings of this study as the cultural context was not dealt with as one of its reasons. In contrast, the cultural context was dealt with as having contributed to all 8 item deletions in this study as low parental responsibilities were observed in Korean fathers, who believe that being involved in childrearing is important but still perceive themselves to be in assisting roles in childrearing [47]. The Confucian culture, which has deeply rooted in the Korean society, influenced a physical and psychological gap to form between the Korean

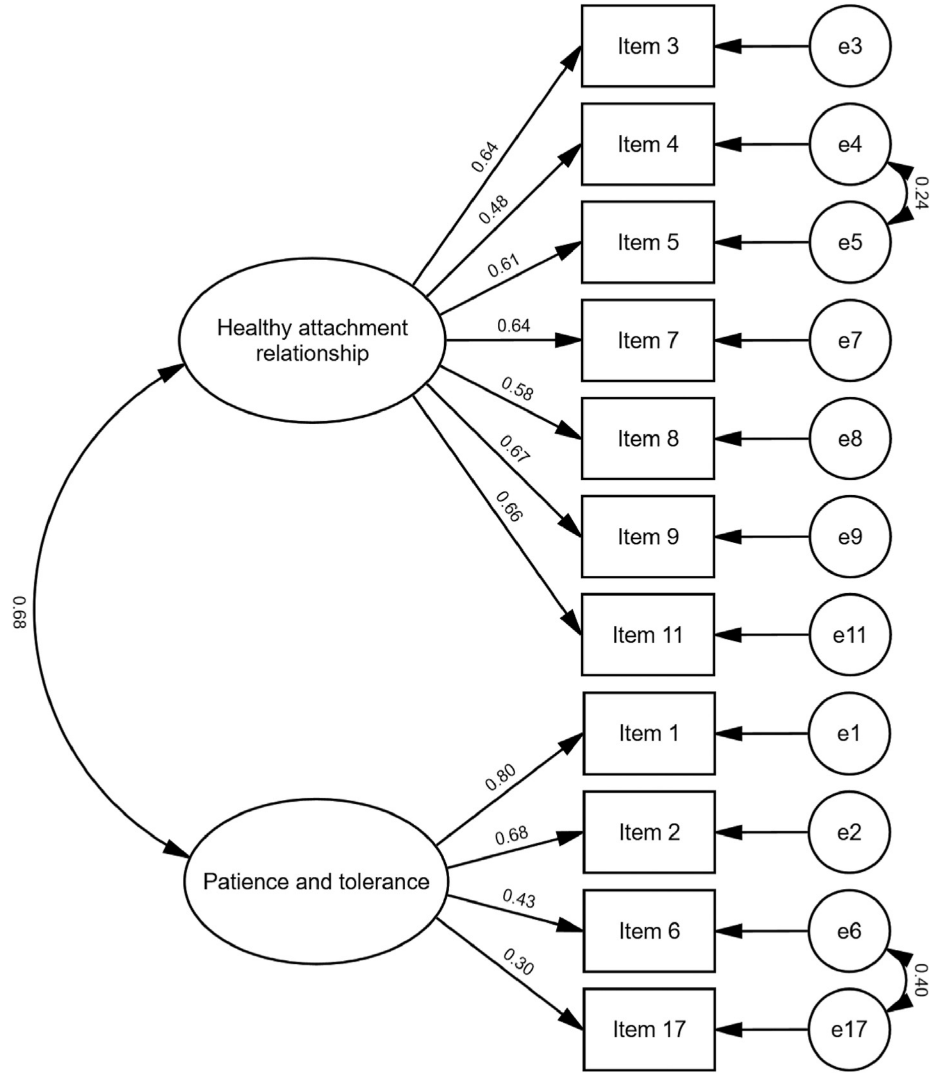

Figure 1. Confirmatory Factor Analysis of the Korean Version of the Paternal Postnatal Attachment Scale.

men and women [48]. This has typically made Korean fathers to be the financial providers of their families and lacked opportunities to be involved with their children [49]. Likewise, with a majority of Korean fathers in this study holding a job, conflict in the work-life balance may have also influenced responses to be inconsistent with these items. Therefore, characteristics such as being apart from one's infant (item 10, 12, and 14), balancing time spent on one's infant and for oneself (item 13 and 18), feeling affectionate (item 15), accepting the infant as one's own (item 16), and being patient (item 19) may have differed from the study's participants.

The K-PPAS has two subscales of “HAR (7 items)” and “PT (4 items)”, which differed from the original PPAS consisting of three subscales: “PT (8 items)”, “pleasure in interaction (7 items)”, and “affection and pride (4 items)”. The “HAR” subscale is a combination of items from the “pleasure in interaction” and “affection and pride” subscales of the original PPAS and contains similar items of the “quality of attachment” and “quality of bonding” from the Portuguese and Spanish versions, respectively. While these translated versions focus on the aspect of “quality”, the K-PPAS emphasizes the “healthy” part of attachment, the quality, and nature of

Table 4 *Known Group Validity of the K-PPAS with K-EPDS (N = 396).*

Factors	Known group Validity Mean (SD)		t(*p*)	Cohen's *d*
	Normal group (K-EPDS <10)	Depressed group (K-EPDS ≥10)		
Healthy attachment relationship	16.57 (2.09)	13.00 (3.18)	−12.01 (<.001)	1.40
Patience and tolerance	28.13 (3.88)	25.65 (4.50)	−5.77 (<.001)	0.60
K-PPAS	76.64 (8.46)	67.3 (9.69)	−9.97 (<.001)	1.04

Note. K-EPDS = Korean version of Edinburgh Postnatal Depression Scale; K-PPAS = Korean version of Paternal Postnatal Attachment Scale; SD = standard deviation.

the actual relationship between the parent and infant that is formed from repetitive nurturing behaviors involving interaction and affectionate touches [50]. These characteristics of a healthy attachment relationship between the father and infant include being attentive to the infant's needs with warmth and care and having conversational interactions and positive attitudes [51]. Likewise, item 8 (“I try to involve myself as much as possible in childrearing”), included only in the K-PPAS, captures the aspect of a healthy attachment relationship representing a father's active involvement with his infant. This demonstrated the difference between the two translated versions' subscales and the “HAR” of the K-PPAS, as not only this subscale assesses the father's capability of childrearing but also their will to maintain healthier attachment relationships with their infants.

The second subscale of the K-PPAS represents the degree of PT that fathers have when interacting with their infants [22]. The 4 items (1, 2, 6, and 17) of this subscale were in correspondence to the “patience and tolerance” subscale of the original PPAS, the Turkish, and Portuguese versions. This may suggest that “PT' represents a common quality among fathers despite cultural differences. Fathers' high level of PT to infants help them become more engaged as a father and cope with difficult situations in parenting [52], which in turn may promote father-infant attachment. The cultural context of low parental responsibilities in Korean fathers [47] and having low paid paternity leave [53] may have contributed to low factor loading on item 17, as some fathers may not be involved enough with their children to feel like they have given up on things. However, item 17 was retained for the importance it would have in the near future as the current trend of Korean fathers' involvement in childrearing [7] and more paid leave entitlements being available for fathers [53] may affect perceptions and parenting practices among Korean fathers.

Moreover, the discriminant validity using known groups demonstrated that discrimination existed between nondepressed and postnatal depressed fathers in relation to attachment formed with their infants. The finding was similar to the systematic review examining the use and performance of father-child relationship tools [34], in which nondepressed fathers formed a higher level of attachment with their infants than depressed fathers. Fathers with postnatal depression are shown to have more withdrawn parental behaviors and are less involved in interacting with their infants [54]. Hence, this may suggest that further studies are in need to interpret this occurrence of depressed fathers during the postnatal period in association with the attachment towards their infants.

The present study had some limitations. First, the K-PPAS was culturally adapted by applying a 5-point Likert scale to all items of the original PPAS, which is from a 2- to 5-point Likert scale. This resulted in difficulty in comparing this study's findings with other studies due to items' response options all being modified. Second, test-retest reliability to investigate the internal consistency of the K-PPAS was unable to be performed because online surveys have difficulty in gathering the same participants. Thirdly, an online survey has made it difficult to examine any physical, psychological, and social problems in fathers and infants that could interrupt the formation of father-infant attachment prior to the study. Future research should consider this in the exclusion criteria. Lastly, other influences including cultural differences may be suggested as the reason behind the inconsistency of the number of factors between the K-PPAS, the original, and the other translated versions. Hence, future studies should be performed to further examine the psychometric properties and application of the K-PPAS in a broader Korean population considering the various family structures and cultural diversity that exist within the Korean population.

Conclusion

The 11-item K-PPAS adapted from the original PPAS for the assessment of the father-infant attachment in the postnatal period consists of two aspects: “healthy attachment relationship” and “patience and tolerance”. However, inconsistencies in the structure compared to the original scale could have occurred with cultural differences, and thus, it is recommended to carefully consider all the necessary aspects when using the K-PPAS in the Korean population.

Conflicts of interest

There are no conflicts of interest and ethical adherence of this manuscript, and the authorship belongs to Yookyung CHOI and Suk-Sun KIM.

Ethical approval

The study was approved by the Institutional Review Board of Ewha Womans University (ewha-202203-0045-01). All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee.

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References

1. Moullin S, Waldfogel J, Washbrook E. Baby bonds: parenting, attachment and a secure base for children [Internet]. London: The Sutton Trust; 2014 [cited 2014 Mac 21]. Available from: www.suttontrust.com/researcharchive/baby-bonds/
2. Sethna V, Perry E, Domoney J, Iles J, Psychogiou L, Rowbotham NEL, et al. Father-child interactions at 3 months and 24 months: contributions to children's cognitive development at 24 months. Infant Ment Health J. 2017;38(3):378–90. https://doi.org/10.1002/imhj.21642
3. Opondo C, Redshaw M, Savage-McGlynn E, Quigley MA. Father involvement in early child-rearing and behavioural outcomes in their pre-adolescent children: evidence from the ALSPAC UK birth cohort. BMJ Open. 2016;6(11):e012034. https://doi.org/10.1136/bmjopen-2016-012034
4. Ramchandani PG, Domoney J, Sethna V, Psychogiou L, Vlachos H, Murray L. Do early father-infant interactions predict the onset of externalising behaviours in young children? Findings from a longitudinal cohort study. JCPP (J Child Psychol Psychiatry). 2013;54(1):56–64. https://doi.org/10.1111/j.1469-7610.2012.02583.x
5. Moller EL, Majdandzic M, de Vente W, Bogels SM. The evolutionary basis of sex differences in parenting and its relationship with child anxiety in western societies. J Exp Psychopathol. 2013;4(2):88–117. https://doi.org/10.5127/jep.026912
6. Yee YH. A comparative study on time of child caring between father and mother. J Children Rights. 2012;16(3):471–95.
7. Statistics Korea. 2020 Population and housing census (register-based census) [Internet]. Daejeon: Statistics Korea; 2021 [cited 2021 Jul 29]. Available from: http://kostat.go.kr/portal/eng/pressReleases/8/7/index.board?bmode=read&aSeq=391585&pageNo=&rowNum=10&amSeq=&sTarget=&sTxt=
8. Statistics Korea. Women's lives through statistics in 2020 [Internet]. Daejeon: Statistics Korea; 2020 [cited 2020 Sep 2]. Available from: https://kostat.go.kr/portal/eng/pressReleases/13/1/index.board?bmode=read&bSeq=&aSeq=385880&pageNo=1&rowNum=10&navCount=10&currPg=&searchInfo=&sTarget=title&sTxt=
9. Kim M, Kang SK, Yee B, Shim SY, Chung M. Paternal involvement and early infant neurodevelopment: the mediation role of maternal parenting stress. BMC Pediatr. 2016;16(1):212. https://doi.org/10.1186/s12887-016-0747-y
10. Shim SY, Lim SA. Paternal self-efficacy, fathering, and children's behavioral problems in Korea. J Child Fam Stud. 2019;28(3):851–9. https://doi.org/10.1007/s10826-018-01310-7
11. Bakermans-Kranenburg MJ, Lotz A, Alyousefi-van Dijk K, van Ijzendoorn M. Birth of a father: fathering in the first 1,000 days. Child Dev Perspect. 2019;13(4):247–53. https://doi.org/10.1111/cdep.12347
12. Taing R, Galescu O, Noble L, Hand IL. Factors influencing paternal attachment among preterm infants in an urban neonatal intensive care unit. Cureus. 2020;12(6):e8476. https://doi.org/10.7759/cureus.8476

13. Trombetta T, Giordano M, Santoniccolo F, Vismara L, Della Vedova AM, Rollè L. Pre-natal attachment and parent-to-infant attachment: a systematic review. Front Psychol. 2021;12:620942. https://doi.org/10.3389/fpsyg.2021.620942
14. Condon JT, Corkindale CJ. The assessment of parent-to-infant attachment: development of a self-report questionnaire instrument. J Reprod Infant Psychol. 1998;16(1):57—76. https://doi.org/10.1080/02646839808404558
15. Waters E, Deane KE. Defining and assessing individual differences in attachment relationships: Q-methodology and the organization of behavior in infancy and early childhood. Monogr Soc Res Child Dev. 1985;50(1-2):41—65. https://doi.org/10.2307/3333826
16. Kim JY. The degree of paternal attachment to neonate. J Korean Acad Nurs. 1995;25(2):330—40. https://doi.org/10.4040/jnas.1995.25.2.330
17. US Food and Drug Administration. Pediatric medical devices. US food and drug administration [Internet]. Maryland: US Food and Drug Administration; 2022 [cited 2022 Apr 26]. Available from: https://www.fda.gov/medical-devices/products-and-medical-procedures/pediatric-medical-devices
18. Choi MR, Kim HK. Effects of a paternal participation program during cesarean section on paternal infant attachment. Korean J Women Health Nurs. 2013;19(2):75—87. https://doi.org/10.4069/kjwhn.2013.19.2.75
19. Kim MA, Kim SJ, Cho H. Effects of tactile stimulation by fathers on physiological responses and paternal attachment in infants in the NICU: a pilot study. J Child Health Care. 2017;21(1):36—45. https://doi.org/10.1177/1367493516666729
20. Hwang HJ. A study on father's attachment to infant and related variables. Korean J Child Care Educ. 2012;73:81—99.
21. Lee E. A phenomenological study on becoming a father: experience in parenting young children. Korean J Child Care Educ. 2020;16(2):179—94. https://doi.org/10.14698/jkcce.2020.16.02.179
22. Condon JT, Corkindale CJ, Boyce P. Assessment of postnatal paternal-infant attachment: development of a questionnaire instrument. J Reprod Infant Psychol. 2008;26(3):195—210. https://doi.org/10.1080/02646830701691335
23. Gao W, Alcauter S, Elton A, Hernandez-Castillo CR, Smith JK, Ramirez J, et al. Functional network development during the first year: relative sequence and socioeconomic correlations. Cereb cortex. 2015;25(9):2919—28. https://doi.org/10.1093/cercor/bhu088
24. Bowlby J. Attachment and loss. Volume 1: attachment. 2nd ed. New York: Basic Books; 1982.
25. de Cock ESA, Henrichs J, Klimstra TA, Janneke BM, Maas A, Vreeswijk CMJM, et al. Longitudinal associations between parental bonding, parenting stress, and executive functioning in toddlerhood. J Child Fam Stud. 2017;26(6):1723—33. https://doi.org/10.1007/s10826-017-0679-7
26. Riera-Martin A, Oliver-Roig A, Martinez-Pampliega A, Cormenzana-Redondo S, Clement-Carbonell V, Richart-Martínez M. A single Spanish version of maternal and paternal postnatal attachment scales: validation and conceptual analysis. PeerJ. 2018;6:e5980 https://peerj.com/articles/5980/
27. Pires M, Nunes O, Brites R, Hipolito J, Vasconcelos M, Spitz E. Paternal post-attachment scale (PPAS): validation studies to the Portuguese population. Eur Health Psychol [internet]. 2014 Aug [cited 2021 Sep 21];16:888. Available from: https://www.ehps.net/ehp/index.php/contents/article/view/679
28. Guleç D, Kavlak O. The study of reliability and validity of paternal-infant attachment scale in Turkish society. Int J Hum Sci. 2013;10(2):170—81 https://www.j-humansciences.com/ojs/index.php/IJHS/article/view/2590
29. World Health Organization. Process of translation and adaptation of instruments [Internet]. Geneva, Switzerland: World Health Organization; 2015 [cited 2021 Oct 12]. Available from: http://www.who.int/substance_abuse/research_tools/translation/en/
30. Polit DF, Beck CT, Owen SV. Is the CVI an acceptable indicator of content validity? Appraisal and recommendations. Res Nurs Health. 2007;30(4):459—67. https://doi.org/10.1002/nur.20199
31. Boateng GO, Neilands TB, Frongillo EA, Melgar-Quinonez HR, Young SL. Best practices for developing and validating scales for health, social, and behavioral research: a primer. Front Public Health. 2018;6:149. https://doi.org/10.3389/fpubh.2018.00149
32. Kim YK, Hur JW, Kim KH, Oh KS, Shin YC. Clinical application of Korean version of Edinburgh postnatal depression scale. J Korean Neuropsychiatr Assoc. 2008;47(1):36—44.
33. Cox J, Holden J, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. Br J Psychiatry. 1987;150:782e6. https://doi.org/10.1192/bjp.150.6.782
34. Siew J, Iles J, Domoney J, Bristow F, Darwin ZJ, Sethna V. The applicability and performance of tools used to assess the father-offspring relationship in relation to parental psychopathology and offspring outcomes. Front Psychiatr. 2021;11:596857. https://doi.org/10.3389/fpsyt.2020.596857
35. Kline RB. Principles and practice of structural equation modeling. 4th ed. New York: The Guilford Press; 2016. p. 76—7, 400.
36. Field A. Discovering Statistics using IBM SPSS statistics. 5th ed. London: Sage Publications Ltd; 2018. p. 1050.
37. Shrestha N. Factor analysis as a tool for survey analysis. Am J Appl Math Stat. 2021;9(1):4—11 http://pubs.sciepub.com/ajams/9/1/2
38. Howard MC. A review of exploratory factor analysis decisions and overview of current practices: what we are doing and how can we improve? Int J Hum Comput Interact. 2016;32(1):51—62. https://doi.org/10.1080/10447318.2015.1087664
39. Hair JF, Black WC, Babin BJ, Anderson RE. Multivariate data analysis. 8th ed. Hampshire, Winchester: Cengage Learning EMEA; 2018.
40. Keith TZ. Multiple regression and beyond: an introduction to multiple regression and structural equation modeling. London: Routledge; 2019. p. 327.
41. Fornell C, Larcker DF. Evaluating structural equation models with unobservable variables and measurement error. J Market Res. 1981;18(1):39—50. https://doi.org/10.1177/002224378101800104
42. Henseler J, Ringle CM, Sarstedt M. A new criterion for assessing discriminant validity in variance-based structural equation modeling. J Acad Market Sci. 2015;43(1):115—35. https://doi.org/10.1007/s11747-014-0403-8
43. Tavsancil E. Measurement of attitudes and data analysis with SPSS. Ankara: Nobel; 2002.
44. Byrne BM. Structural equation modeling with AMOS: basic concepts, applications, and programming. 2nd ed. New York: Taylor and Francis Group; 2016.
45. Bollen KA, Stine RA. Bootstrapping goodness-of-fit measures in structural equation models. Socio Methods Res. 1992;21:205—29.
46. Nevitt J, Hancock GR. Performance of bootstrapping approaches to model test statistics and parameter standard error estimation in structural equation modeling. Struct Equ Model. 2001;8(3):353—77.
47. An S, Lee M. Determinants of parental involvement and responsibility among fathers with young children. Korean J Child Care Educ policy. 2020;14(1):3—25.
48. Yang JA. Fathering and children's sex role orientation in Korea. Adolescence. 2000;35(140):731—45.
49. Kim KK, Chung J. The role of Korean fathers: a study of Korean fathering practices in the United States. Int J Child Care Educ Policy. 2011;5:47—55. https://doi.org/10.1007/2288-6729-5-2-47
50. Perry BD. Bonding and attachment in maltreated children: consequences of emotional neglect in childhood. ChildTrauma Acad [Internet]. 1999;1(3):1—10 [cited 2022 Sep 30] https://www.childtrauma.org/child-dev-early-childhood
51. Shafie R. Healthy attachment and parent-child relationships [dissertation]. [Arizona]: Grand Canyon University; 2017. p. 269.
52. Dewitte L, Granqvist P, Dezutter J. Meaning through attachment: an integrative framework. Psychol Rep. 2019;122(6):2242—65. https://doi.org/10.1177/0033294118799739
53. Organization for Economic Co-operation and Development (OECD). Parental leave systems [Internet]. Paris: OECD; 2022 [cited 2023 Mar 3]. Available from: https://www.oecd.org/els/soc/PF2_1_Parental_leave_systems.pdf
54. Sethna V, Murray L, Netsi E, Psychogiou L, Ramchandani PG. Paternal depression in the postnatal period and early father-infant interactions. Parent Sci Pract. 2015;15(1):1—8. https://doi.org/10.1080/15295192.2015.992732

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Research Article

Performance of Early Warning Scoring Systems Regarding Adverse Events of Unanticipated Clinical Deterioration in Complementary and Alternative Medicine Hospitals

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ABSTRACT

Purpose: This study aims to examine the performance of early warning scoring systems regarding adverse events of unanticipated clinical deterioration in complementary and alternative medicine hospitals.
Methods: A medical record review of 500 patients from 5-year patient data in two traditional Korean medicine hospitals was conducted. Unanticipated clinical deterioration events included unexpected in-hospital mortality, cardiac arrest, and unplanned transfers to acute-care conventional medicine hospitals. Scores of the Modified Early Warning Score (MEWS), National Early Warning Score (NEWS), and National Early Warning Score 2 (NEWS2) were calculated. Their performance was evaluated by calculating areas under the receiver-operating characteristic curve for the event occurrence. Multiple logistic regression analyses were performed to determine the factors associated with event occurrence.
Results: The incidence of unanticipated clinical deterioration events was 1.1% (225/21101). The area under the curve of MEWS, NEWS, and NEWS2 was .68, .72, and .72 at 24 hours before the events, respectively. NEWS and NEWS2, with almost the same performance, were superior to MEWS ($p = .009$). After adjusting for other variables, patients at low-medium risk (OR = 3.28; 95% CI = 1.02–10.55) and those at medium and high risk (OR = 25.03; 95% CI = 2.78–225.46) on NEWS2 scores were more likely to experience unanticipated clinical deterioration than those at low risk. Other factors associated with the event occurrence included frailty risk scores, clinical worry scores, primary medical diagnosis, prescribed medicine administration, acupuncture treatment, and clinical department.
Conclusions: The three early warning scores demonstrated moderate-to-fair performance for clinical deterioration events. NEWS2 can be used for early identification of patients at high risk of deterioration in complementary and alternative medicine hospitals. Additionally, patient, care, and system factors need to be considered to improve patient safety.

Introduction

Improving patient safety is a public health issue [1]. Unexpected in-hospital mortality, cardiac arrest, and unplanned transfer to higher-acuity units, such as intensive care units in hospitalized patients, are serious adverse events [2]. Since physiological instability is usually preceding clinical deterioration, therefore early warning scoring systems (EWSs), which are mainly based on routinely collected vital sign observations, have been developed to identify clinically deteriorating patients and avoid preventable adverse events [3,4]. Their use has been expanded to the

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emergency department and prehospital settings and further to deteriorating COVID-19 patients [5,6].

Prior research has shown that EWSs' performance varied depending on patient population and clinical settings [4,6,7]. For instance, studies have found that widely used EWSs of the Modified Early Warning Score (MEWS), National Early Warning Score (NEWS), and NEWS version 2 (NEWS2) demonstrated good ability to predict clinical deterioration in acute-care conventional medicine hospitals [8–10]. However, other studies reported poor performance of MEWS, NEWS, and NEWS2 in care settings including long-term acute-care hospitals [11–13]. In addition, there were variations in the performance by EWS type. A study reported that NEWS showed better discrimination than NEWS2 [14]. Another study found that NEWS2 had a better performance than MEWS and NEWS [15]. These findings may indicate the necessity of additional studies on the performance of EWSs when we consider implementing an EWS in practice.

Along with aging and increased chronic diseases, utilization of complementary and alternative medicine (CAM), also known as traditional medicine, has also increased [16,17]. There are 528 Traditional Korean Medicine (TKM) hospitals, which comprise 23.0% of acute-care hospitals in the Korean healthcare system [18]. Studies revealed that approximately 11.0% of inpatients in CAM hospitals have experienced adverse events, including unanticipated clinical deterioration [19]. Although the comprehensive plans for patient safety based on the Patient Safety Act in Korea recommend the establishment of a rapid response team in hospitals [20], there is no study on a rapid response system in CAM hospitals. Furthermore, there is a lack of data regarding the serious adverse events attributable to unanticipated clinical deterioration in CAM hospitals. In this context, a tool for predicting sudden clinical deterioration is critical for improving patient safety. Although existing EWSs have been validated, the performance of EWSs is unknown in CAM hospitals.

Researchers have suggested that patient, care, and system factors may affect clinical deterioration and patient outcomes [21,22]. However, there are inconsistent findings. While some studies showed that severity of illness, comorbidity, and type of care were significant factors associated with the occurrence of unanticipated clinical deterioration and patient outcomes [15,22], another study found that these were not significant predictors of clinical deterioration [11]. These findings may indicate the necessity of additional study. A better understanding of the factors associated with the occurrence of unanticipated clinical deterioration will help identify high-risk patients and reduce preventable serious adverse events.

This study aimed to explore the performance of EWSs as predictors of unanticipated clinical deterioration in CAM hospitals. Specifically, we examined the performance of MEWS, NEWS, and NEWS2 in CAM hospitals. Furthermore, we investigated the factors associated with unanticipated clinical deterioration. The findings of this study will contribute to facilitating early detection and timely response to patients at risk of sudden clinical deterioration, thereby improving patient safety in CAM hospitals.

Methods

Research design

We employed a retrospective review research design. A medical record review of (1) all patients with events of unexpected clinical deterioration during the 5-year period in two TKM hospitals and (2) a random sample of patients without events during the same period was conducted.

Sample and setting

The sample comprised 500 patients from two university-affiliated TKM hospitals from January 1, 2015, to December 31, 2019. The study hospitals had electronic medical record systems with full accredited status by the Korea Institute of Healthcare Accreditation. The annual number of inpatients was 2,177 in Hospital A and 1,006 in Hospital B in 2020. Nurse staffing level was grade 3 (3.0–3.5 patients per nurse) and grade 2 (2.5–3.0 patients per nurse). TKM subspecialty includes internal medicine, gynecology, pediatrics, eyes-ear-nose-throat-dermatology, neuropsychology, rehabilitation, Sasang constitutional medicine, and acupuncture.

We included patients aged ≥19 years with a length of stay ≥1 day. Unanticipated clinical deterioration events included unexpected in-hospital mortality, cardiopulmonary resuscitation, and unplanned transfer to a higher-acuity bed outside CAM hospitals due to deteriorating conditions. Exclusion criteria were (1) cases with a do-not-resuscitate order and (2) planned transfers to other hospitals due to other reasons except for clinical deterioration. We included only transfers to university-affiliated conventional medicine hospitals or tertiary hospitals due to deteriorating conditions. If the reason for the transfer was not clearly recorded, the inclusion of the case was decided at the discretion of our research team. Patients without events were randomly sampled from patients residing in the same care unit during the same period using the Research Randomizer [23].

A priori sample size of approximately 500 was determined based on the recommendations of 10 to 20 cases per predictor in multiple logistic regression [24]. The final sample consisted of 500 patients (225 with events and 275 without events) (Figure 1).

Measures

MEWS parameters are systolic blood pressure, heart rate, respiration rate, body temperature, and level of consciousness [8]. NEWS parameters are respiration rate, oxygen saturation (SpO_2), oxygen supplement, systolic blood pressure, pulse, body temperature, and level of consciousness [9]. In addition to NEWS parameters, NEWS2 includes the SpO_2 scale 2 for patients with hypercapnic respiratory failure and new confusion as part of the assessment of consciousness [9,10]. Based on the predefined criteria in their scoring systems, a score (range = 0–3) was assigned for each parameter and then a risk stratification was determined for the summed scores. MEWS scores (range = 0–14) were categorized into low (0–2), medium (3–4), and high (≥5) risk groups [8,25]. NEWS and NEWS2 scores (range = 0–20 for both systems) were categorized into low (0–4), low-medium (extreme score of 3 in a single parameter), medium (5–6), and high (≥7) risk groups [10,15].

Data collection

Medical records were reviewed by two nurses and three TKM physicians in the hospitals. The first author (JH), who had expertize in the application of early warning scoring systems and medical record review methodologies, trained the reviewers individually in two half-day sessions in each hospital, using the subsets of the medical records assigned to each reviewer. It was challenging to train them simultaneously due to work schedules and the COVID-19 pandemic. Inter-rater reliability between the first author and each reviewer was assessed using kappa values. The values ranged from 0.84 to 0.97, indicating the "almost perfect agreement" of 0.81–0.99 [26].

We calculated the MEWS, NEWS, and NEWS2 scores 24 hours before the events. For the usual group, the scores were calculated using vital sign observations at 24 hours postadmission to obtain the highest score based on previous studies [8,15]. For cases with no

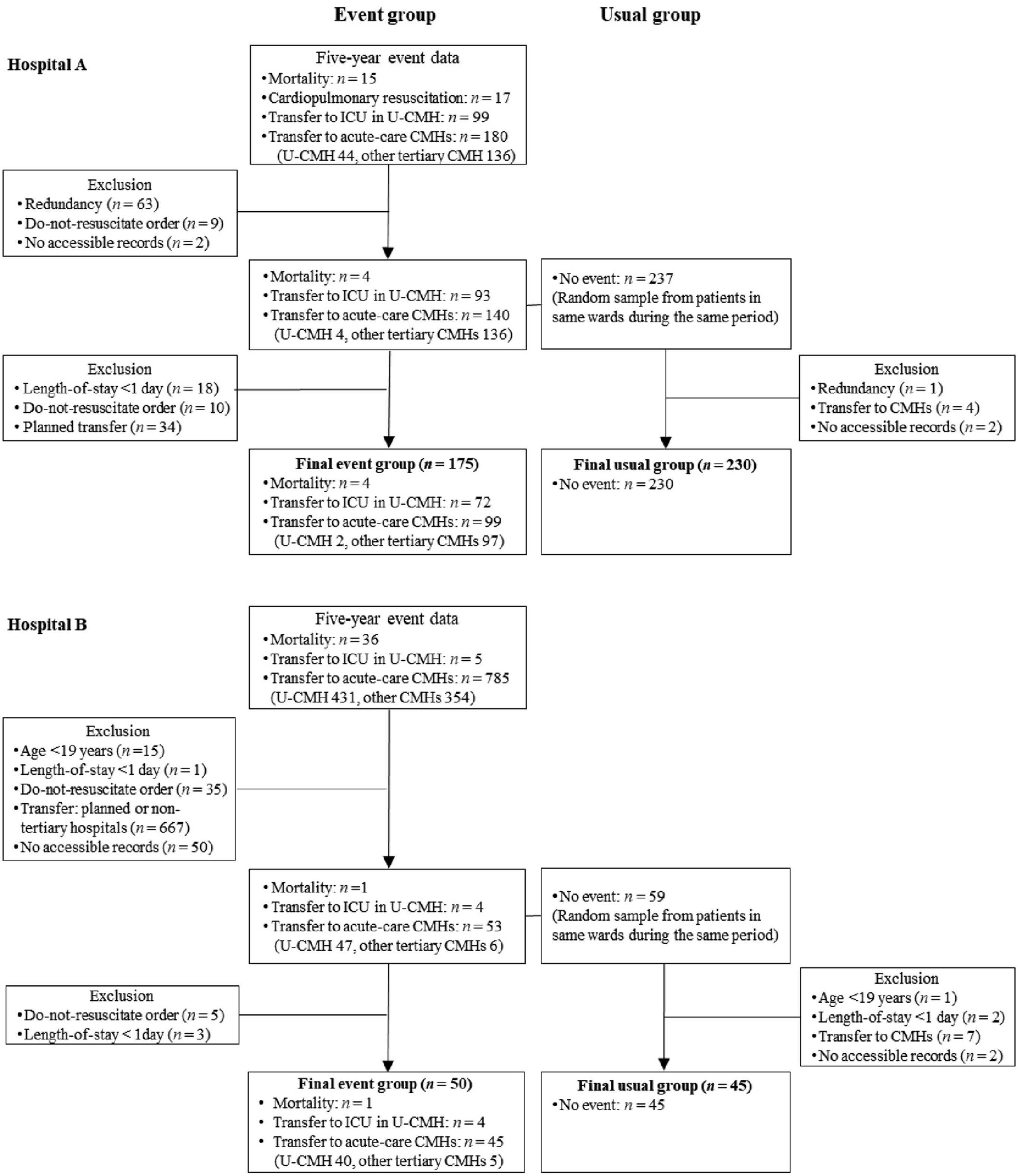

Figure 1. Flow Chart of the Sample Selection in the Hospital A and Hospital B. Note. ICU = intensive care unit; U-CMH = university-affiliated conventional medicine hospital; CMH = conventional medicine hospital.

recording of certain vital sign values, we used the values at the closest time point. If SpO_2 values were null, score 0 for this parameter was assigned [15].

We collected data on patient, care, and system factors based on previous studies regarding clinical deterioration [21,22]. Patient- and disease-related variables included age, gender, educational level, body mass index (BMI), frailty risk, clinical worry score (CWS), primary medical diagnosis, comorbidities, and admission route. Frailty risk was measured using the Morse fall scale (MFS) and Braden scale scores at admission [27–29]. If there were no recordings of these scores at admission, the values at the closest time point was used. Nine cases with no recording on the frailty risk were considered as low risk after reviewing the records. CWS was measured using the Dutch-Early-Nurse-Worry-Indicator-Score scale comprising of nine indicators of respiration change, circulation change, temperature, mentation change, agitation, pain, unexpected trajectory, patient comments, and subjective observations [30]. The applicability of this scale has been validated in Korean hospitals [15]. After the presence of each indicator was coded as 1 and the other as 0, a sum score (range = 0–9) was calculated. The Charlson comorbidity index (CCI) was calculated [31,32].

Care- and treatment-related variables included the use of prescribed medicine, herbal medication, acupuncture, moxibustion, cupping, physical therapies (e.g., infrared therapy, transcutaneous electrical nerve stimulation, interferential current therapy, and chuna), and length of hospital stay. The uses of prescribed medicine and herbal medication were reviewed for the following day post-admission to reflect the acuity, which was also consistent with the time point for EWSs' calculation [8,15]. Since there was no intensive care unit, surgical operation room, and rapid response team in the CAM hospitals, variables on care intensity and types were not included. System- and organization-related variables included hospital type, nurse staffing level, and clinical department. Since the nurse staffing level was determined at the hospital level, we included only the hospital type. We also collected event-related data such as the time of event occurrence (07:01–15:00, 15:01–18:00, 18:01–22:00, and 22:01–07:00), the day of the week (weekday and weekend), and length to event occurrence postadmission.

A random sample of 52 medical records were rereviewed by the first author. The overall agreement rate was 75.0% (39/52) at the patient level and 96.5% (637/660) at the indicator level of CWS.

Ethical considerations

The study protocol was approved by the Institutional Review Boards of two study hospitals (no. 2019-12-001 and 2019-12-005).

Data analysis

Data were analyzed using the SAS program (version 9.4; Cary, NC, USA). Patients' general characteristics were summarized using descriptive statistics. Interrater reliability was calculated using Kappa values [26]. Independent t tests and chi-square tests were conducted to identify differences between the event group and the usual group according to patients' general characteristics. We calculated the areas under the receiver operating characteristic curves (AUCs) to evaluate the performance of MEWS, NEWS, and NEWS2.

Multiple logistic regression analyses were performed to determine factors associated with the occurrence of unanticipated clinical deterioration. Model calibration was assessed using the Hosmer-Lemeshow goodness-of-fit test. Odds ratios (ORs) and 95% confidence intervals (CIs) were also calculated. For a sensitivity analysis, we performed additional analysis after excluding cases with missing data on frailty risk scores (n = 9). Statistical significance was set at a two-tailed $p < .05$.

Results

Patients' general characteristics and event characteristics

The patients' general characteristics are shown in Table 1. Of the 500 patients, 56.4% were women, with a mean age of 63.72 ± 16.01 years (range = 19.00–98.00). The mean length of hospitalization was 25.27 days (95% CI = 21.57–28.97). Most patients (89.4%) were discharged with improved status. There were significant differences between the event group and the usual group by patients' gender, age, education, BMI, fall risk, pressure ulcer risk, CWS, primary medical diagnosis, CCI, admission route, prescribed medicine use, uses of CAM treatment, length of stay, and clinical department (Table 1).

The incidence of unanticipated clinical deterioration events was 1.1% (i.e., 225 out of 21101 patients over the 5-year period). The time spent to event occurrence since admission was a median of 14.00 days (interquartile range = 5.79–38.00). Most events occurred on weekdays (n = 195, 86.7%) and during daytime between 07:01 and 18:00 (n = 182, 80.9%).

Performance of EWSs

MEWS, NEWS, and NEWS2 well discriminated patients with events from those without (Table 2). The AUC was .68 (95% CI = .64–.72), .72 (95% CI = .67–.76), and .72 (95% CI = .67–.76), respectively (Figure 2). In pairwise comparisons, there were significant differences between NEWS2 and MEWS (p = .009), but there was no difference between NEWS and NEWS2.

Factors associated with unanticipated deterioration event occurrence

Based on the findings of the univariate analyses, multiple logistic regression analyses were performed. The "medium (5–6)" and "high (≥7)" risk stratification on NEWS2 scores were merged into one category (≥5) due to low frequency of the categories. The results showed that NEWS2, fall risk, pressure ulcer risk, CWS, primary medical diagnosis, use of prescribed medicine, acupuncture treatment, and clinical department were significant factors associated with event occurrence (Max-rescaled R^2 = 59.0%, $p < .001$; c-statistic = 0.90; Hosmer-Lemeshow goodness-of-fit test, p = .057).

Specifically, patients at low-medium risk (OR = 3.28; 95% CI = 1.02–10.55) and those at medium and high risk (OR = 25.03; 95% CI = 2.78–225.46) on NEWS2 scores were more likely to experience unanticipated deterioration events than patients at low risk. In addition, patients at medium risk on the MFS were more likely to experience the events than those at low risk on the MFS (OR = 2.98; 95% CI = 1.48–6.02). Those at a high risk of pressure ulcer on the Braden scale were more likely to experience the events than others (OR = 4.33; 95% CI = 2.12–8.84). Patients with higher CWSs were more likely to experience the events (OR = 1.91; 95% CI = 1.29–2.84). Patients with "circulatory system diseases" (OR = 3.44; 95% CI = 1.64–7.23), "neoplasm" (OR = 12.98; 95% CI = 3.92–43.00), and "injuries and other consequences of external causes" (OR = 5.21; 95% CI = 1.43–18.94) were more likely to experience the events than those with "others" diseases (Table 3).

Patients treated with prescribed medicine in CAM hospitals were more likely to experience the events than those without (OR = 4.34; 95% CI = 1.42–13.28). In addition, those receiving acupuncture treatment (OR = 0.09; 95% CI = 0.01–0.97) and those who were admitted to CAM rehabilitation department (OR = 0.26; 95% CI = 0.12–0.60) were less likely to experience unanticipated deterioration events (Table 3).

Discussion

Improving patient safety in CAM practices is a global concern [16]. Early identification of patients at high risk of unanticipated clinical deterioration and appropriate responses are important to avoid unnecessary harm to patients. This is the first study to explore the performance of MEWS, NEWS, and NEWS2 for unanticipated clinical deterioration in CAM hospitals. Moreover, this is

Table 1 *Patients' General Characteristics and Differences Between Event Group and Usual Group.*

Variable	Category	*n*	%	Event group		Usual group		χ^2/t	*p*
				n	%	*n*	%		
Gender	Men	218	43.6	112	22.4	106	21.2	6.35	.012
	Women	282	56.4	113	22.6	169	33.8		
Age (years)	19–50	97	19.4	24	4.8	73	14.6	39.06	<.001
	51–65	153	30.6	59	11.8	94	18.8		
	66–75	116	23.2	56	11.2	60	12.0		
	76–99	134	26.8	86	17.2	48	9.6		
Education level	Middle school or lower	167	33.4	88	17.6	79	15.8	12.76	.005
	High school	106	21.2	42	8.4	64	12.8		
	College or higher	164	32.8	60	12.0	104	20.8		
	Others[a]	63	12.6	35	7.0	28	5.6		
Body mass index,[b] *Mean* ± *SD*		23.41 ± 3.66		22.95 ± 3.73		23.82 ± 3.54		2.49	.013
Fall risk	Low	230	46.0	59	11.8	171	34.2	67.85	<.001
	Medium	176	35.2	101	20.2	75	15.0		
	High	94	18.8	65	13.0	29	5.8		
Pressure ulcer risk	High	166	33.2	133	26.6	33	6.6	123.84	<.001
	Low	334	66.8	92	18.4	242	48.4		
Clinical worry score, *Mean* ± *SD*		0.68 ± 0.84		0.89 ± 1.01		0.50 ± 0.62		−5.01	<.001
Primary medical diagnosis	Circulatory system disease	163	32.6	105	21.0	58	11.6	82.65	<.001
	Nervous system disease	88	17.6	25	5.0	63	12.6		
	Neoplasm	44	8.8	34	6.8	10	2.0		
	Musculoskeletal system disease	44	8.8	9	1.8	35	7.0		
	Injuries, consequences of external causes	38	7.6	20	4.0	18	3.6		
	Others	123	24.6	32	6.4	91	18.2		
Number of comorbidity, *Mean* ± *SD*		3.47 ± 2.38		3.50 ± 2.39		3.45 ± 2.38		−0.24	.811
Charlson comorbidity index, *Mean* ± *SD*		1.29 ± 3.14		2.01 ± 4.29		0.70 ± 1.45		−4.4	<.001
Admission route	Outpatient department	446	89.2	192	38.4	254	50.8	6.35	.012
	Others	54	10.8	33	6.6	21	4.2		
Use of prescribed medicine		380	76.0	195	86.7	185	67.3	25.52	<.001
Use of herbal medication		479	95.8	213	94.7	266	96.7	1.31	.253
CAM treatment	Acupuncture	490	98.0	216	96.0	274	99.6	8.35	.007[c]
	Moxibustion	373	74.6	145	64.4	228	82.9	22.27	<.001
	Cupping	219	43.8	71	31.6	148	53.8	24.92	<.001
	Physical therapy	267	53.4	81	36.0	186	67.6	49.77	<.001
Length of stay (day)	1 to 7	137	27.4	76	15.2	61	12.2	34.94	<.001
	8 to 14	136	27.2	38	7.6	98	19.6		
	15 to 21	62	12.4	19	3.8	43	8.6		
	22 or longer	165	33.0	92	18.4	73	14.6		
Hospital type	A	405	81.0	175	35.0	230	46.0	2.76	.097
	B	95	19.0	50	10.0	45	9.0		
Clinical department	Internal medicine	261	52.2	145	29.0	116	23.2	33.21	<.001
	Rehabilitation	118	23.6	29	5.8	89	17.8		
	Acupuncture	71	14.2	27	5.4	44	8.8		
	Others	50	10.0	24	4.8	26	5.2		

Note. SD = standard deviation; CAM = complementary and alternative medicine.
[a] It includes no response.
[b] *n* = 435.
[c] Fisher's exact test.

the first report on the incidence of unanticipated clinical deterioration events in CAM hospitals.

In this study, the EWSs showed moderate to fair ability in predicting unanticipated clinical deterioration in CAM hospitals. The study found that patient, care, and system factors, along with EWSs, were significantly associated with the occurrence of unanticipated clinical deterioration. These findings indicate that using EWSs can help in the early identification of patients at risk of deterioration in CAM hospitals. Furthermore, patient, care, and system factors (i.e., frailty risk scores, CWS, primary medical diagnosis, treatment modality, and clinical department) should be considered along with EWS scores to better identify patients at high risk of clinical deterioration and to avoid preventable adverse events in CAM hospitals.

Although three EWSs showed reasonable discrimination ability, their AUCs were lower than .8, indicating a threshold of good performance [33]. The values were lower than those in previous studies [14,15], but they were higher than those for composite outcomes of acute-care hospital transfer and mortality in long-term acute-care hospitals [13]. These differences may be attributable to the characteristics of patient groups and care settings [7]. In this study, most events were transfer cases, and nearly half scored 0 on the NEWS2. In addition, routine vital sign measurements are sometimes performed twice a day in CAM hospitals. Thus, vital sign values for EWSs' calculation can be distant from the time point of 24 hours before the event. These might result in low prognostic accuracy of the EWSs. Specifically, NEWS and NEWS2, showing better performance than MEWS, demonstrated similar performance. This was different from the findings of previous studies [14,15]. A possible reason can be due to the limited number of patients with hypercapnic respiratory failure. Since NEWS2 has the benefit of a separate oxygen saturation scoring system for COPD patients, the use of NEWS2 is suggested.

Additionally, we examined the improvement in EWSs' models by including other variables. Based on existing research [34], adding an age variable to the models improved their performance, indicating fair discrimination (AUC = .76, .77, and .77 for MEWS, NEWS, and NEWS2, respectively). However, the values were still

Table 2 *Performance of the MEWS, NEWS, and NEWS2.*

Variable	*n*	%	Event group		Usual group		χ^2/t	*p*	AUC
			n	%	*n*	%			
MEWS, *mean (95% CI)*			1.79	(1.65–1.94)	1.13	(1.07–1.19)	−8.34	<.001	0.68
Low risk	446	89.2	175	35.0	271	54.2	55.50	<.001	
Medium risk	50	10.0	46	9.2	4	0.8			
High risk	4	0.8	4	0.8	0	0.0			
NEWS, *mean (95% CI)*			2.50	(2.16–2.85)	0.64	(0.53–0.74)	−10.20	<.001	0.72
Low risk	413	82.6	148	29.6	265	53.0	83.85	<.001	
Low-medium risk	42	8.4	33	6.6	9	1.8			
Medium risk	26	5.2	25	5.0	1	0.2			
High risk	19	3.8	19	3.8	0	0.0			
NEWS2, *mean (95% CI)*			2.48	(2.14–2.82)	0.64	(0.53–0.74)	−10.16	<.001	0.72
Low risk	414	82.8	149	29.8	265	53.0	82.19	<.001	
Low-medium risk	42	8.4	33	6.6	9	1.8			
Medium risk	26	5.2	25	5.0	1	0.2			
High risk	18	3.6	18	3.6	0	0.0			

Note. AUC = area under the receiver operating characteristic curve; CI = confidence interval.

lower than .8. Therefore, future studies are necessary to further improve the prognostic accuracy of EWSs in CAM hospitals.

Significant factors to predict unanticipated clinical deterioration included NEWS2 scores, frailty risk scores, CWS, primary medical diagnosis, treatment modality, and clinical department. After controlling for other characteristics, patients with NEWS2 scores of ≥5 were approximately 25 times more likely to experience unanticipated clinical deterioration events than those in the low-risk group on NEWS2 scores of 0–4. Additionally, those with extreme scores of any single parameter were slightly over three times more likely to experience the events. This finding supports the relevance of NEWS2 as a monitoring tool for clinical deterioration.

Among patient factors, MFS scores were positively associated with clinical deterioration event occurrence. In particular, patients at medium-level fall risk experienced unanticipated clinical deterioration more frequently than those at low-level fall risk. In addition, patients at high risk of pressure ulcers were more likely to experience unanticipated clinical deterioration. This was similar to

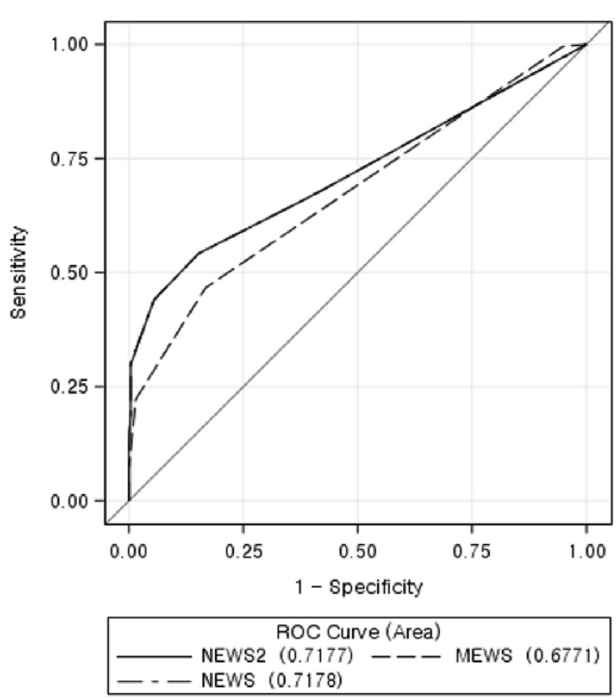

Figure 2. Receiver Operating Characteristic Curves of MEWS, NEWS, and NEWS2.

the finding that the Braden score was a predictor of adverse events in geriatric surgical patients [27]. However, these findings were different from the finding that the MFS and Braden scale scores were not significant independent factors for predicting mortality in patients with heart failure [28]. Since recordings on fall and pressure ulcer risk assessments were not mandatory in the hospitals during the study period, we used frailty risk scores at admission. In addition, we used MFS and Braden scale scores as readily available data on frailty risk [29]. We recommend that future studies on the predictive abilities of frailty risk scores 24 hours before adverse events be conducted using other measures developed for frailty risk assessments [35,36]. Furthermore, CWS was positively associated with event occurrence. This is consistent with the findings of previous studies [15,30]. These findings indicate the importance of nurses' assessment on subjective and objective signs and symptoms of patients. Therefore, the use of a systematic tool to measure clinical concerns needs to be considered for early detection of unanticipated deterioration events. Patients with circulatory system diseases, neoplasms, and injuries experienced unanticipated clinical deterioration more frequently than others. This is similar to the findings of previous studies [15]. These findings might reflect disease characteristics. Therefore, patients with such diseases need to be monitored closely.

In relation to care and treatment, patients who needed prescribed medicine were more likely to experience unanticipated deterioration events. Studies have recommended the use of integrated therapies in CAM hospitals, rather than CAM therapies alone, especially for inpatients whose conditions are severe and highly complex, such as intractable cancer patients [37,38] and stroke rehabilitation patients [39]. In this regard, the use of prescribed medicine during hospitalization in CAM hospitals may reflect patient conditions with high morbidity, which can easily contribute to sudden deterioration. Therefore, patients who require prescribed medication to be administered in addition to CAM therapies need to be closely observed for deterioration risk. In addition, patients who received acupuncture treatment were less likely to experience unanticipated deterioration events. This finding may relate to the fact that acupuncture treatment is not recommended for patients with septic conditions, acute hemorrhagic stroke, unstable seizures, or confusion. Generally, acupuncture therapy has been applied as a general treatment mode for common conditions and diseases such as acute and chronic noncancer pain, nausea, and vomiting, rather than complex and severe diseases [40,41]. However, additional study on the relationship between clinical deterioration risk and acupuncture treatment is suggested.

Table 3 *Logistic Regression Results for Unanticipated Clinical Deterioration Event Occurrence.*

Variable	Odds ratio	95% Confidence interval
NEWS2		
Medium and high risk	25.03	(2.78–225.46)*
Low-medium risk	3.28	(1.02–10.55)*
Low risk	reference	
Gender		
Men	1.28	(0.72–2.27)
Women	reference	
Age (years)	1.00	(0.98–1.03)
Education level		
College or higher	0.82	(0.37–1.84)
High school	0.55	(0.26–1.20)
Others	0.67	(0.27–1.64)
Middle school or lower	reference	
Body mass index	0.96	(0.89–1.04)
Fall risk		
High	2.07	(0.86–4.49)
Medium	2.98	(1.48–6.02)*
Low	reference	
Pressure ulcer risk		
High	4.33	(2.12–8.84)*
Low	reference	
Clinical worry score	1.91	(1.29–2.84)*
Primary medical diagnosis		
Circulatory system disease	3.44	(1.64–7.23)*
Nervous system disease	1.80	(0.69–4.74)
Neoplasm	12.98	(3.92–43.00)*
Musculoskeletal system disease	1.37	(0.43–4.41)
Injuries, other consequences of external causes	5.21	(1.43–18.94)*
Others	reference	
Charlson comorbidity index	1.07	(0.95–1.20)
Admission route		
Outpatient department	0.98	(0.37–2.58)
Others	reference	
Use of prescribed medicine	4.34	(1.42–13.28)*
Complementary and alternative medicine treatment		
Acupuncture	0.09	(0.01–0.97)*
No acupuncture	reference	
Moxibustion	0.74	(0.39–1.41)
No moxibustion	reference	
Cupping	1.03	(0.57–1.86)
No cupping	reference	
Physical therapy	0.79	(0.44–1.43)
No physical therapy	reference	
Length of stay (days)	1.00	(0.99–1.01)
Clinical department		
Rehabilitation	0.26	(0.12–0.60)*
Acupuncture	0.73	(0.32–1.65)
Others	0.71	(0.24–2.07)
Internal medicine	reference	

Note. This analysis was performed using 435 patient data due to the missing values of body mass index.
*$p < .05$.

Patients who were hospitalized in the rehabilitation department were less likely to experience unanticipated clinical deterioration. It may reflect that patients who were admitted to CAM hospitals for rehabilitation have relatively stable conditions. Therefore, clinical departments will be considered in managing high-risk patients.

Overall, the findings of this study indicate that NEWS2 can be used to predict the risk of clinical deterioration in CAM practices. NEWS2 will be utilized as a common language for communicating the clinical deterioration risk between healthcare teams comprising of various healthcare professionals, which will facilitate timely interdisciplinary interventions. Therefore, hospital executives and nurse managers should support the use of EWSs in CAM practice. Setting a protocol including the escalation of care in CAM hospitals will be a fundamental step. Furthermore, a rapid response system between CAM hospitals and conventional medicine hospitals needs to be implemented.

The findings of this study also indicate that EWSs' predictive abilities need to be further improved. Based on the findings of this study, patient, care, and system factors can be used to detect patients at high risk of clinical deterioration. Using multiple predictors will contribute to reducing false alarms and increasing EWSs' predictive ability.

However, this study has several limitations. First, this study was conducted only in two CAM hospitals. Thus, the generalizability of the findings is limited. However, we analyzed 5-year data, which also met the recommendation of including at least 100 event cases [42]. Second, most event cases were transfers to other conventional medicine hospitals. Thus, we could not analyze patient outcomes after transfer. Third, we collected data based on recordings using a retrospective study design. Since documentation could not be prioritized in busy clinical environments, EWSs' performance can be different in real-world practice. In addition, we did not include variables such as the degrees of vital signs' derangement over time and their temporal characteristics, laboratory test results, and care team factors that may affect the performance of EWSs and patient outcomes. Lastly, we assigned risk stratification values to the cases with missing data of frailty risk through medical record reviews ($n = 9$). It can cause bias. However, additional analyses, after excluding such cases, demonstrated that the results were consistent. Thus, we suggest future studies with more cases of mortality and cardiac arrest, including various CAM hospitals. Furthermore, a prospective study on the impact of using EWSs on patient outcomes is recommended.

Conclusion

This study provides evidence on the performance of EWSs in CAM hospitals for predicting high-risk patients who especially require rapid transfer to acute-care conventional medicine hospitals due to unanticipated clinical deterioration. Using NEWS2 will help identify high-risk patients in CAM hospitals. At the same time, patient, care, and system factors should be considered to avoid preventable adverse events and improve patient safety. This study finding will contribute to expanding the applicability of EWSs to CAM hospitals.

Conflict of interest

The authors declared no conflict of interest.

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Ethical approval

This research was approved by the Institutional Review Boards of the study hospitals (no. 2019-12-001 and 2019-12-005).

Data availability

The data presented in this study are available from the corresponding author upon reasonable request and with permission of the institutional review boards of the study hospitals.

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References

1. World Health Organization. Global patient safety action plan 2021–2030: towards eliminating avoidable harm in health care. Geneva: WHO; 2021.
2. Alam N, Hobbelink EL, van Tienhoven AJ, van de Ven PM, Jansma EP, Nanayakkara PW. The impact of the use of the Early Warning Score (EWS) on patient outcomes: a systematic review. Resuscitation. 2014;85(5):587–94. https://doi.org/10.1016/j.resuscitation.2014.01.013
3. Lee JR, Kim EM, Kim SA, Oh EG. A systematic review of early warning systems' effects on nurses' clinical performance and adverse events among deteriorating ward patients. J Patient Saf. 2020;16(3):e104–13. https://doi.org/10.1097/PTS.0000000000000492
4. Fu LH, Schwartz J, Moy A, Knaplund C, Kang MJ, Schnock KO, et al. Development and validation of early warning score system: a systematic literature review. J Biomed Inf. 2020;105:103410. https://doi.org/10.1016/j.jbi.2020.103410
5. Kostakis I, Smith GB, Prytherch D, Meredith P, Price C, Chauhan A, et al. The performance of the National Early Warning Score and National Early Warning Score 2 in hospitalised patients infected by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Resuscitation. 2021;159:150–7. https://doi.org/10.1016/j.resuscitation.2020.10.039
6. Guan G, Lee CMY, Begg S, Crombie A, Mnatzaganian G. The use of early warning system scores in prehospital and emergency department settings to predict clinical deterioration: a systematic review and meta-analysis. PLoS One. 2022;17(3):e0265559. https://doi.org/10.1371/journal.pone.0265559
7. Alhmoud B, Bonnici T, Patel R, Melley D, Williams B, Banerjee A. Performance of universal early warning scores in different patient subgroups and clinical settings: a systematic review. BMJ Open. 2021;11(4):e045849. https://doi.org/10.1136/bmjopen-2020-045849
8. Subbe CP, Kruger M, Rutherford P, Gemmel L. Validation of a modified early warning score in medical admissions. QJM. 2001;94(10):521–6. https://doi.org/10.1093/qjmed/94.10.521
9. Royal College of Physicians. National Early Warning Score (NEWS): standardising the assessment of acute-illness severity in the NHS. London: RCP; 2012.
10. Royal College of Physicians. National Early Warning Score (NEWS) 2: standardising the assessment of acute-illness severity in the NHS. London: RCP; 2017.
11. Wang J, Hahn SS, Kline M, Cohen RI. Early in-hospital clinical deterioration is not predicted by severity of illness, functional status, or comorbidity. Int J Gen Med. 2017;10:329–34. https://doi.org/10.2147/IJGM.S145933
12. Bedoya AD, Clement ME, Phelan M, Steorts RC, O'Brien C, Goldstein BA. Minimal impact of implemented early warning score and best practice alert for patient deterioration. Crit Care Med. 2019;47(1):49–55. https://doi.org/10.1097/CCM.0000000000003439
13. Churpek MM, Carey KA, Dela Merced N, Prister J, Brofman J, Edelson DP. Validation of early warning scores at two long-term acute care hospitals. Crit Care Med. 2019;47(12):e962–5. https://doi.org/10.1097/CCM.0000000000004026
14. Pimentel MAF, Redfern OC, Gerry S, Collins GS, Malycha J, Prytherch D, et al. A comparison of the ability of the National Early Warning Score and the National Early Warning Score 2 to identify patients at risk of in-hospital mortality: a multi-centre database study. Resuscitation. 2019;134:147–56. https://doi.org/10.1016/j.resuscitation.2018.09.026
15. Hwang JI, Chin HJ. Relationships between the National Early Warning Score 2, clinical worry and patient outcome at discharge: retrospective observational study. J Clin Nurs. 2020;29(19-20):3774–89. https://doi.org/10.1111/jocn.15408
16. World Health Organization. WHO traditional medicine strategy: 2014–2023. Geneva: WHO; 2013.
17. Ministry of Health and WelfareNational Development Institute of Korean Medicine. Herbal medicine use survey: fundamental report, 2020. Seoul: NIKOM; 2021.
18. Statistics Korea. The Korean Statistical Information Service: National Health Insurance statistics [Internet]. [cited 2022 November 1] Available from: https://kosis.kr/statHtml/statHtml.do?orgId=354&tblId=DT_MIRE01&vw_cd=MT_ZTITLE&list_id=354_MT_DTITLE&scrId=&seqNo=&lang_mode=ko&obj_var_id=&itm_id=&conn_path=MT_ZTITLE&path=%252FstatisticsList%252FstatisticsListIndex.do.
19. Hwang JI, Kim J, Park JW. Adverse events in Korean traditional medicine hospitals: a retrospective medical record review. J Patient Saf. 2018;14(3):157–63. https://doi.org/10.1097/PTS.0000000000000190
20. Ministry of Health and Welfare of Korea. The first comprehensive plans for patient safety (2018–2022) [cited 2023 Feb 22]. Available from: https://www.mohw.go.kr/react/jb/sjb030301vw.jsp?PAR_MENU_ID=03&MENU_ID=0319&CONT_SEQ=344873; 2018
21. Jones D, Mitchell I, Hillman K, Story D. Defining clinical deterioration. Resuscitation. 2013;84(8):1029–34. https://doi.org/10.1016/j.resuscitation.2013.01.013
22. Stelfox HT, Bagshaw SM, Gao S. Characteristics and outcomes for hospitalized patients with recurrent clinical deterioration and repeat medical emergency team activation. Crit Care Med. 2014;42(7):1601–9. https://doi.org/10.1097/CCM.0000000000000315
23. Churpek MM, Yuen TC, Huber MT, Park SY, Hall JB, Edelson DP. Predicting cardiac arrest on the wards: a nested case-control study. Chest. 2012;141(5):1170–6. https://doi.org/10.1378/chest.11-1301
24. Polit DF. Statistics and data analysis for nursing research. 2nd ed. New Jersey: Pearson Education; 2010.
25. Kim WY, Shin YJ, Lee JM, Huh JW, Koh Y, Lim CM, et al. Modified Early Warning Score changes prior to cardiac arrest in general wards. PLoS One. 2015;10(6):e0130523. https://doi.org/10.1371/journal.pone.0130523
26. Viera AJ, Garrett JM. Understanding interobserver agreement: the kappa statistic. Fam Med. 2005;37(5):360–3.
27. Cohen RR, Lagoo-Deenadayalan SA, Heflin MT, Sloane R, Eisen I, Thacker JM, et al. Exploring predictors of complication in older surgical patients: a deficit accumulation index and the Braden scale. J Am Geriatr Soc. 2012;60(9):1609–15. https://doi.org/10.1111/j.1532-5415.2012.04109.x
28. Carazo M, Sadarangani T, Natarajan S, Katz SD, Blaum C, Dickson VV. Prognostic utility of the Braden scale and the Morse fall scale in hospitalized patients with heart failure. West J Nurs Res. 2017;39(4):507–23. https://doi.org/10.1177/0193945916664077
29. Tapper EB, Finkelstein D, Mittleman MA, Piatkowski G, Lai M. Standard assessments of frailty are validated predictors of mortality in hospitalized patients with cirrhosis. Hepatology. 2015;62(2):584–90. https://doi.org/10.1002/hep.27830
30. Douw G, Huisman-de Waal G, van Zanten AR, van der Hoeven JG, Schoonhoven L. Nurses' 'worry' as predictor of deteriorating surgical ward patients: a prospective cohort study of the Dutch-Early-Nurse-Worry-Indicator-Score. Int J Nurs Stud. 2016;59:134–40. https://doi.org/10.1016/j.ijnurstu.2016.04.006
31. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. J Chronic Dis. 1987;40(5):373–83. https://doi.org/10.1016/0021-9681(87)90171-8
32. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi JC, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005;43(11):1130–9. https://doi.org/10.1097/01.mlr.0000182534.19832.83
33. Smith GB, Prytherch DR, Meredith P, Schmidt PE, Featherstone PI. The ability of the National Early Warning Score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. Resuscitation. 2013;84(4):465–70. https://doi.org/10.1016/j.resuscitation.2012.12.016
34. Shamout F, Zhu T, Clifton L, Briggs J, Prytherch D, Meredith P, et al. Early warning score adjusted for age to predict the composite outcome of mortality, cardiac arrest or unplanned intensive care unit admission using observational vital-sign data: a multicentre development and validation. BMJ Open. 2019;9(11):e033301. https://doi.org/10.1136/bmjopen-2019-033301
35. Sutton JL, Gould RL, Daley S, Coulson MC, Ward EV, Butler AM, et al. Psychometric properties of multicomponent tools designed to assess frailty in older adults: a systematic review. BMC Geriatr. 2016;16:55. https://doi.org/10.1186/s12877-016-0225-2
36. Gilbert T, Neuburger J, Kraindler J, Keeble E, Smith P, Ariti C, et al. Development and validation of a Hospital Frailty Risk Score focusing on older people in acute care settings using electronic hospital records: an observational study. Lancet. 2018;391(10132):1775–82. https://doi.org/10.1016/S0140-6736(18)30668-8
37. Greenlee H, DuPont-Reyes MJ, Balneaves LG, Carlson LE, Cohen MR, Deng G, et al. Clinical practice guidelines on the evidence-based use of integrative therapies during and after breast cancer treatment. CA Cancer J Clin. 2017;67(3):194–232. https://doi.org/10.3322/caac.21397
38. Mao JJ, Pillai GG, Andrade CJ, Ligibel JA, Basu P, Cohen L, et al. Integrative oncology: addressing the global challenges of cancer prevention and treatment. CA Cancer J Clin. 2022;72(2):144–64. https://doi.org/10.3322/caac.21706
39. Zhong LL, Zheng Y, Lau AY, Wong N, Yao L, Wu X, et al. Would integrated Western and traditional Chinese medicine have more benefits for stroke rehabilitation? A systematic review and meta-analysis. Stroke Vasc Neurol. 2022;7(1):77–85. https://doi.org/10.1136/svn-2020-000781
40. Chon TY, Lee MC. Acupuncture. Mayo Clin Proc. 2013;88(10):1141–6. https://doi.org/10.1016/j.mayocp.2013.06.009
41. Van Hal M, Dydyk AM, Green MS. Acupuncture. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing; 2022 [cited 2023 Feb 22]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK532287/
42. Gerry S, Bonnici T, Birks J, Kirtley S, Virdee PS, Watkinson PJ, et al. Early warning scores for detecting deterioration in adult hospital patients: systematic review and critical appraisal of methodology. BMJ. 2020;369:m1501. https://doi.org/10.1136/bmj.m1501