PMAC
PRINCE MAHIDOL AWARD CONFERENCE 2025

E-ISSN 2228-8082
Volume 77, Number 10, October 2025

SMJ

Siriraj Medical Journal

The world-leading biomedical science of Thailand

MONTHLY

Anesthesiology

ORIGINAL ARTICLE REVIEW ARTICLE

Indexed by Scopus® DOAJ EBSCO

https://he02.tci-thaijo.org/index.php/sirirajmedj/index
E-mail: sijournal92@gmail.com

SMJ
Siriraj Medical Journal
The world-leading biomedical science of Thailand
Volume 77 Number 10
October 2025

ORIGINAL ARTICLE

REVIEW ARTICLE

SIRIRAJ MEDICAL JOURNAL

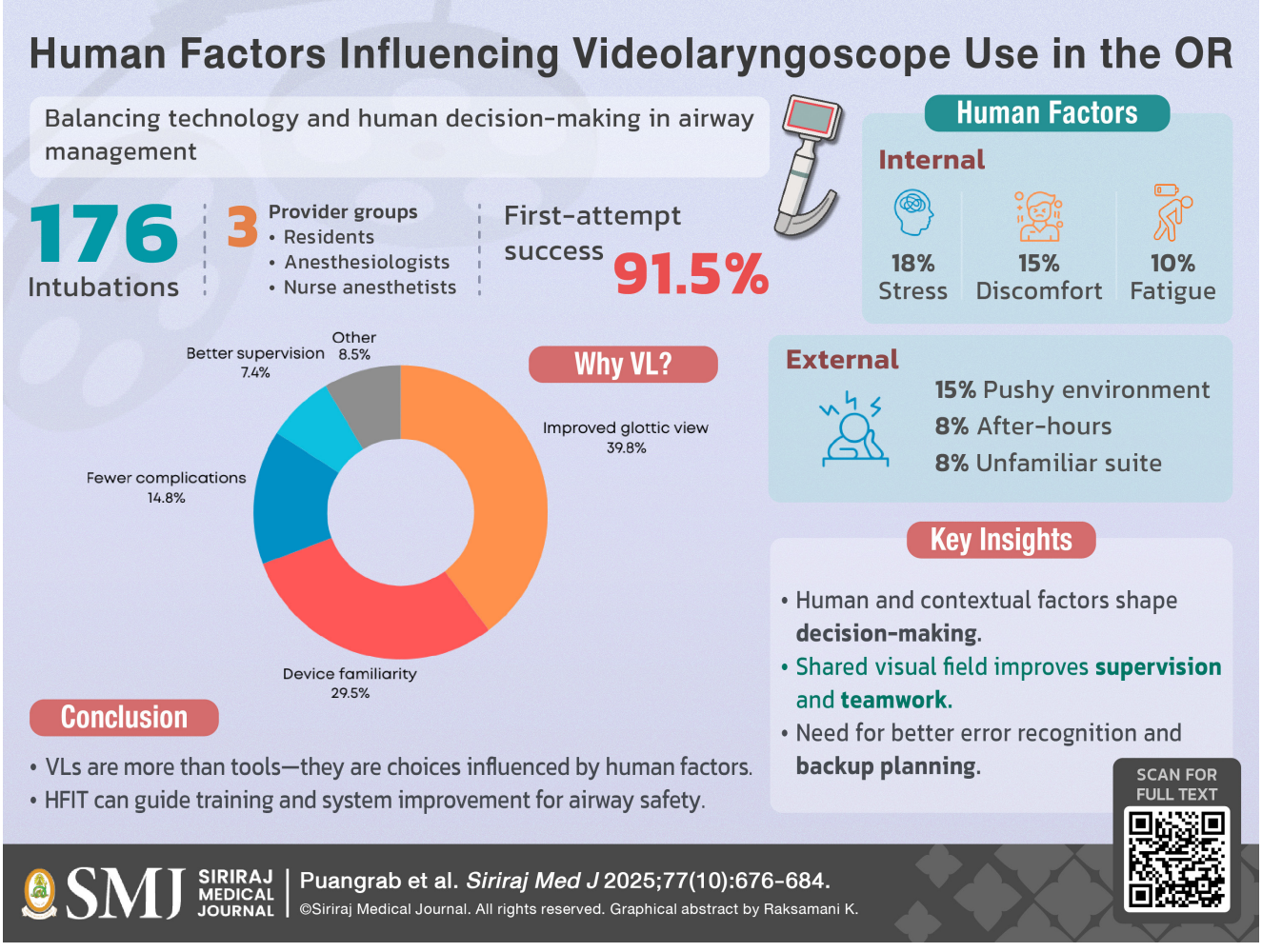
https://he02.tci-thaijo.org/index.php/sirirajmedj/index

Office: His Majesty the King's 80th Birthday Anniversary 5th December 2007 Building (SIMR), 2nd Fl., Room No.207
Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand
E-mail: sijournal92@gmail.com

Human Factors Influencing the Decision to Use Videolaryngoscopes for Intubation in the Operating Room

Siwatus Puangrab, M.D.[1,2], Atip Youngyoodee, M.D.[1,3], Tachawan Jirativanont, M.D.[1], Kasana Raksamani, M.D.[1,*]

[1]Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [2]Department of Anesthesiology, School of Medicine, Walailak University, Nakhon Si Thammarat, Thailand, [3]Department of Anesthesiology, Nakhonpathom Hospital, Nakhon Pathom, Thailand.



*Corresponding author: Kasana Raksamani
E-mail: kasana.rak@mahidol.edu
Received 13 May 2025 Revised 30 June 2025 Accepted 30 June 2025
ORCID ID:http://orcid.org/0000-0003-4524-4781
https://doi.org/10.33192/smj.v77i10.275409

ABSTRACT

Objective: This study aimed to explore (1) the human factors influencing the decision to use videolaryngoscopes (VLs) instead of conventional Macintosh blades for intubation in operating room settings, and (2) the reasons anesthesia providers report for selecting VLs in clinical practice.

Materials and Methods: A prospective observational study was conducted from September 2020 to June 2021 among anesthesia personnel at Siriraj Hospital. Eligible participants included anesthesiologists, anesthesia residents, and nurse anesthetists who used a VL for intubating adult patients under general anesthesia. Participants completed a structured questionnaire based on the Human Factors Investigation Tool (HFIT) model, which captured internal and external human factors, device selection rationale, and self-assessed performance. Data were analyzed using descriptive and inferential statistics.

Results: A total of 176 VL intubation events were analyzed. Internal human factors such as stress (18.2%), discomfort (15.3%), and fatigue (10.2%), along with external factors like a pushy environment (15.3%) and after-hours work (7.9%), influenced VL use. The most cited reasons for choosing VLs included improved glottic visualization (39.8%), device familiarity (29.5%), fewer complications (14.8%), and better supervision (7.4%). These findings align with key domains of the HFIT model, including situational awareness, decision-making, and environmental conditions.

Conclusion: This study demonstrates that the decision to use VLs is shaped not only by technical considerations but also by a range of human and contextual factors. The HFIT model provided a valuable framework for understanding how providers navigate complex clinical environments. These insights support targeted interventions in training and workplace design to enhance decision-making and airway safety.

Keywords: Videolaryngoscopes; human factors; airway management (Siriraj Med J 2025; 77: 676-684)

INTRODUCTION

Videolaryngoscopes (VL) have demonstrated superiority over traditional direct laryngoscopy in both anticipated and unanticipated difficult airways by increasing first-attempt success rates and reducing airway trauma.[1-5] Their ability to provide an enhanced glottic view without requiring alignment of the oral, pharyngeal, and laryngeal axes makes them especially useful for patients with restricted neck movement or limited mouth opening.[6] Additionally, VLs reduce the physical force needed during intubation, which minimizes upper airway injuries and improves safety, particularly in patients with fragile airway conditions.[3-5]

Beyond their utility in difficult airway scenarios, VLs are increasingly used in patients with normal airway anatomy due to their benefits in reducing soft tissue trauma, improving visualization, and facilitating teaching and supervision.[1,6] Studies have shown that VLs can reduce intubation time and post-procedural complications such as sore throat or hoarseness.[7]

Their widespread use in routine cases may also enhance familiarity with the device, better preparing providers for high-stakes or emergency situations.[6,7]

Using VL can enhance human factors, including non-technical aspects of airway management, especially during difficult laryngoscopy and intubation.[8-10] Teamwork, communication, and overall team performance can be improved by providing a shared visual of the airway.[9-12] Human factors play a critical role in airway management and have been implicated in 40% of adverse outcomes related to difficult airway complications, as highlighted in the NAP4 report.[13] To prevent such complications, anesthesia providers must be proficient not only in clinical skills but also in understanding and managing human factors at both individual and systemic levels.[14] A recent multicenter study reported that airway and respiratory complications occurred in 9.6% of obese patients undergoing general anesthesia, with pregnancy, obesity class, and high Mallampati score being significant risk factors.[15] Non-technical skills are increasingly recognized as a complementary and independent area of competence in anesthesiology.[16,17] To address these concerns, *Flin et al.* developed the Simplified Human Factors Investigation Tool (HFIT) model to investigate difficult airway events.[18] This study aims to identify the human factors, using the HFIT framework, that influence the decision to use VLs as intubation devices instead of conventional Macintosh blades in operating room settings.

MATERIALS AND METHODS

This observational study was conducted in the Department of Anesthesiology at Siriraj Hospital, Faculty of Medicine Mahidol University, from September 2020 to June 2021. The primary aim was to identify the human

factors influencing the decision to use VLs for intubation instead of conventional Macintosh blades in the operating rooms. This study received approval from The Siriraj Institutional Review Board (COA no Si 679/2020).

Eligible participants included attending anesthesiologists, anesthesia residents, and certified registered nurse anesthetists from the Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, who performed tracheal intubation using VLs for adult patients (>18 years) undergoing general anesthesia. To ensure homogeneity of clinical context and reduce confounding variables, data from pediatric, trauma, obstetric, and COVID-19-related patients were excluded. These patient groups often require distinct airway management protocols, equipment, or infection control measures that differ significantly from routine adult elective and emergency surgical cases. This exclusion helped maintain consistency in evaluating human factors specific to standard operating room settings. Eligible participants volunteered to take part in the study and were asked to complete a structured questionnaire immediately following the intubation event.

To systematically assess human factors, we developed the "Human Factors Analysis Form" based on the Human Factors Investigation Tool (HFIT) model proposed by Flin et al.[18] The HFIT framework is designed to investigate the role of non-technical skills and contextual factors in clinical decision-making. The form was translated and validated in Thai and structured to collect detailed information across four key domains: user demographics, patient characteristics, airway device details, and a self-assessment of the intubation event (Supplemental File 1). The self-assessment section was the core component reflecting the HFIT model, designed to evaluate five domains of human performance—situational awareness, decision-making, task management, teamwork, and environmental conditions. Each domain was assessed through targeted questions that captured internal factors such as stress, fatigue, and discomfort, as well as external factors like operating room conditions, time pressure, and unfamiliar settings. Among the environmental factors assessed were noise, lighting, temperature, unfamiliar operating environments, and what was defined in this study as a *"pushy environment"*. This term referred to clinical settings where participants felt under increased pressure to perform rapidly or precisely due to perceived urgency, hierarchical dynamics, or expectations conveyed by surgical teams, supervisors, or the overall pace of the operating room. This operational definition helped capture the subjective experience of performance pressure that may influence decision-making in real-time clinical scenarios.

To quantify the likelihood of a difficult airway, a scoring system was used based on seven established predictors: limited mouth opening (<3 cm), limited neck movement, reduced thyromental distance (<6 cm), presence of a receding mandible, prominent upper incisors, Mallampati classification III or IV, and history of difficult intubation. Each positive predictor was assigned 1 point, resulting in a total difficulty score ranging from 0 to 7, with higher scores indicating increased risk of intubation difficulty. Moreover, a difficult airway was operationally defined as a failed intubation using conventional direct laryngoscopy, followed by a request to use a VL as a rescue device.

The questionnaire underwent expert validation by two independent anesthesiologists with expertise in airway management and human factors. Both experts assessed the content for relevance, clarity, and representativeness. The calculated Content Validity Index (CVI) was 0.96, indicating a high level of agreement and excellent content validity.

The HFIT-based questionnaire was administered immediately after each intubation event to capture the provider's reflections on the decision-making process, human factors, and contextual influences while the experience was still fresh and accurately recalled. Participants were asked to reflect on the specific conditions under which they chose to use a VL, providing insights into both conscious and contextual influences on their clinical choices. The questionnaire also included space for free-text responses to allow further elaboration beyond the structured items.

The primary outcome was the successful intubation using a VL. In cases of unanticipated difficult airway—defined as failed intubation using conventional direct laryngoscopy followed by a request for VL—success was defined as successful endotracheal intubation on the first attempt with VL.

The sample size was calculated to estimate the proportion of anesthesia providers whose decision to use VLs is influenced by human factors, assuming a prevalence of 70% based on prior observational studies.[13] Using a 95% confidence level and a precision of ±7%, the required sample size was 165.

All questionnaire items were optional, and participants were allowed to skip questions without penalty. Missing responses were treated as missing completely at random and were excluded from item-level percentage calculations without imputation. No statistical adjustments were made for missing data, in keeping with the exploratory nature of the study. For data analysis, descriptive statistics such as means and standard deviations (SDs) were used

to describe continuous data, while frequencies and percentages were used to analyze categorical data. For inferential statistics, the Chi-square test was employed to compare two independent proportions for categorical endpoints. A p-value of < 0.05 was considered statistically significant. All statistical analyses were conducted using SPSS software version 29.0 (SPSS Inc., Chicago, USA).

RESULTS

A total of 176 intubation events using videolaryngoscopes in anesthesia settings were recorded from September 2020 to June 2021. Among the respondents who opted to use VLs, 111 (63.1%) were anesthesia residents, 33 (18.8%) were attending anesthesiologists, and 32 (18.2%) were certified registered nurse anesthetists. The respondents included 50 males (28.4%) and 126 females (71.6%), with a mean age of 32.4 ± 9.6 years (Table 1).

Successful intubation on the first attempt was achieved in 161 cases (91.5%), while 15 cases (8.5%) were unsuccessful. Among the 176 patients, 97 (55.1%) were male and 79 (44.9%) were female, with a mean age of 57.6 ± 19.5 years. Emergency cases accounted for 21 (11.9%) of the total. The distribution by service units included 18 (10.2%) in cardiovascular and thoracic surgery, 54 (30.7%) in otorhinolaryngologic surgery, 27 (15.3%) in general surgery, 19 (10.8%) in neurosurgery, 28 (15.9%) in orthopedic surgery, and 30 (17.1%) in other units.

Across 176 events, the chosen VLs were Macintosh blade VLs in 116 cases (65.9%) and angulated blade VLs in 60 cases (34.1%). Participants reported various internal human factors affecting their decision to request VLs: stress in 32 cases (18.2%), discomfort in 27 cases (15.3%), fatigue in 18 cases (10.2%), and hunger in 8 cases (4.5%), while 120 participants (68.2%) reported no internal factors. External factors influencing the decision included a pushy environment in 27 cases (15.3%), after-hours situations in 14 cases (7.9%), unfamiliar suites in 14 cases (7.9%), too many people involved in 14 cases (7.9%), extreme temperature conditions (too hot or too cold) in 10 cases (5.7%), noisy conditions in 8 cases (4.5%), and improper lighting in 8 cases (4.5%) (Table 2). Meanwhile, 120 participants reported no external factors. A human factors analysis of both successful and unsuccessful first-attempt intubations revealed no significant differences between the groups, as demonstrated in Table 3. The primary reasons participants cited for selecting VLs were improved glottic visualization (70 cases, 39.8%), familiarity with the devices (52 cases, 29.5%), confidence that VL would result in fewer complications (26 cases, 14.8%), reduced intubation time (13 cases, 7.4%), and better supervision (13 cases, 7.4%).

The decision to request alternative airway devices was made in the operating theaters before induction in 88 cases (50.0%), during preanesthetic visits in 74 cases

TABLE 1. Demographic data of respondents.

Variable	Successful intubation on the first attempt (n=161)	Unsuccessful intubation on the first attempt (n=15)	p value
Sex (Male), n (%)	41 (25.5)	6 (40.0)	0.36
Age (year), mean (SD)	32.0 (8.5)	31.9 (8.4)	0.97
Type of respondent, n (%)			0.33
Attending anesthesiologist	34 (21.1)	2 (13.3)	
Anesthesia resident	98 (60.9)	8 (53.3)	
Certified register nurse anesthetist	29 (18.0)	5 (33.3)	
Experience of respondent, n (%)			0.53
0-5 years	129 (80.1)	13 (86.7)	
5-10 years	4 (2.5)	1 (6.7)	
10-15 years	15 (9.3)	1 (6.7)	
More than 15 years	13 (8.1)	0 (0.0)	

TABLE 2. Human Factors Reported to Influence the Decision to Use Videolaryngoscopes (n=176).

Category	Factor	Number of Cases	Percentage (%)
Internal Factors	Stress	32	18.2
	Discomfort	27	15.3
	Fatigue	18	10.2
	Hunger	8	4.5
External Factors	Pushy environment	27	15.3
	After-hours situations	14	7.9
	Unfamiliar suite	14	7.9
	Too many people involved	14	7.9
	Extreme temperature	10	5.7
	Noisy conditions	8	4.5
	Improper lighting	8	4.5
Technical Considerations	Improved glottic view	70	39.8
	Familiarity with device	52	29.5
	Fewer complications expected	26	14.8
	Better supervision	13	7.4

TABLE 3. Participant responses to non-technical skill statements adapted from the Human Factors Investigation Tool (HFIT) framework, targeting domains such as decision-making, teamwork, and situational awareness. These human factors were analyzed in relation to successful and unsuccessful first-attempt intubations.

Category	Question	Success in the first attempt (n=161)	Unsuccess in first attempt (n=15)	p
Task management	Do you know how to assess difficult airways?	161 (100%)	15 (100%)	
	Did you notice the personnel action error?	15 (9.3%)	3 (20.0%)	0.186
	Are you aware of the difficult airway management guideline?	158 (98.1%)	15 (100%)	1.00
	Did you follow the difficult airway management guideline?	151 (93.8%)	14 (93.3%)	1.00
Teamworking	Did your team have a clear role?	160 (99.4%)	15 (100%)	1.00
	Did the assigned role appropriate to the team member?	161 (100%)	15 (100%)	
	Did your teamwork collaborate?	160 (99.4%)	14 (93.3%)	0.16
	Did the information exchange appropriately?	150 (93.2%)	14 (93.3%)	0.43
	Did your team encourage each other?	148 (91.9%)	14 (93.3%)	1.00
Situation awareness	Did you notice the difficult airway beforehand?	155 (96.3%)	13 (86.7%)	0.14
	Did you plan for alternative airway instruments in advance?	149 (92.5%)	13 (86.7%)	0.34
Decision making	Did you aware of the pros and cons of the instrument chosen?	139 (86.3%)	10 (66.7%)	0.58
	Did you have another backup plan?	109 (67.7%)	10 (66.7%)	1.00

(42.0%), and after failed intubation with a Macintosh blade #3 in 12 unanticipated difficult airway cases (6.8%). The success rate of VLs in unanticipated difficult airway cases, defined as successful intubation on the first attempt using VL, was 10 out of 12 (83.3%). The mean intubation difficulty score was 2.03 (±1.6), and there was no significant difference between the success and unsuccessful groups.

DISCUSSION

This study demonstrated a high first-attempt intubation success rate (91.5%) using videolaryngoscopes (VL) in anesthesia settings. The primary reasons for selecting VL included improved glottic visualization, device familiarity, reduced complications, and enhanced supervision. Both internal (e.g., stress, discomfort) and external (e.g., pushy environment, after-hours situations) factors influenced the decision to use VL.

The high first-attempt success rate highlights the effectiveness of VL in clinical practice. Our findings align with previous studies reporting high success rates with VL in both difficult and non-difficult airway situations.[1,7] When comparing success rates of VL and conventional Macintosh laryngoscopes, the literature consistently shows higher first-attempt success rates with VL due to its superior glottic visualization and improved angle of view, which enhances the likelihood of successful intubation on the first attempt, reducing the incidence of failed intubations and associated complications.[1,3,13]

The study highlights several reasons for selecting VL for intubation, including improved glottic visualization, device familiarity, reduced complications, and better supervision during intubation. VL devices are equipped with video cameras that provide a high-resolution view of the glottis and surrounding structures.[1,19] This enhanced visualization is particularly beneficial in patients with difficult airways, where direct laryngoscopy often fails to provide a clear view.[19,20] Studies have shown that VL significantly improves the Cormack-Lehane grade and offers superior visualization compared to Macintosh laryngoscopes, especially in patients with difficult airways.[2,21] The improved visualization also enhances team coordination by allowing all members to share the visual field and maintain situational awareness during the procedure.[22] This shared view enables the team to assist with additional airway maneuvers, such as applying external laryngeal pressure or providing secretion suction when needed. Familiarity with the VL device is another crucial human factor influencing its selection as the first-choice intubation tool.[14,23] This is particularly important in emergency situations where quick and efficient airway management is critical.[4,5] Knowing how to operate and locate the device is vital for effective airway management.[4,5,9] Another significant reason for choosing VL is the improved supervision and support it offers during intubation, making it valuable in both routine and emergency settings. The shared glottic view allows supervisors to guide the intubation process, provide immediate feedback, and intervene when necessary to prevent complications.[24-26] Ensuring that practitioners are familiar with VL through regular use can further improve outcomes.

This study examined the influence of human factors, such as stress, pushy environment, discomfort, fatigue/after-hours situations, and hunger, on the decision to use VL for intubation. Anesthesia induction and intubation are high-stakes procedures that demand rapid decision-making and precise clinical skills. Human factors can significantly impact the performance of anesthesia providers during these critical moments.[11,12,18] Studies have shown that stress/ pushy environments can reduce working memory capacity and hinder problem-solving abilities, potentially affecting the choice of intubation device.[5,13] Stress-induced physiological changes, such as increased heart rate and elevated cortisol levels, can also impair coordination and fine motor skills.[9] Discomfort, often due to poor ergonomic conditions, can negatively affect concentration and efficiency.[9] Inadequate workstation setups, improper posture, and prolonged standing may lead to musculoskeletal pain and distraction. Additionally, environmental factors, such as extreme temperatures, noise, and psychological discomfort (i.e., anxiety) in unfamiliar environments can increase cognitive load and reduce situational awareness, complicating decision-making during anesthesia.[27] Fatigue also negatively affects cognitive and physical performance, impairing attention, memory, and executive function. It slows reaction times and increases error rates, with performance degradation comparable to alcohol intoxication.[27] This is particularly concerning in the high-stakes anesthesia settings. Understanding and addressing human factors such as stress, discomfort and fatigue through targeted interventions can improve clinical performance and patient safety.[12] Strategies like simulation training, ergonomic improvements, fatigue management, and promoting proper nutrition can mitigate the adverse effects of human factors and enhance the overall effectiveness of anesthesia providers in high-pressure situations.

This study employed the HFIT model to create a questionnaire assessing various aspects of intubation practices. The results showed a high proportion of affirmative responses across multiple items in Table 3—for example, 91.5% reported knowing their roles during

intubation and 89.2% indicated clear communication with team members—indicating general competence and situational awareness among respondents. However, the self-analysis method used to assess human factors presents certain limitations.[27] Healthcare providers tend to report their non-technical skills higher than when observed in simulation settings.[28] Moreover, the relatively low proportions of respondents who reported having a backup plan (67.7%) or observed errors during intubation (64.2%) are concerning. These findings, as shown in Table 3, may indicate under-preparedness or a tendency to underrecognize or underreport errors during airway management. This finding could imply the need for better education and culture around error reporting and analysis.[9,18] Similarly, the relatively low score on the backup intubation planning reveals a significant gap in airway management preparedness. Having a comprehensive backup plan is essential, especially in difficult airway scenarios, to ensure prompt, effective, and successful management when unexpected situations arise.[4,5] These findings emphasize the importance of continued focus on developing and implementing robust backup plans in airway management protocols and training programs.

Limitations

While this study offers useful insight into the human factors that prompt clinicians to select VLs and highlights the value of backup plans during difficult intubations, several limitations warrant consideration. First, the analysis is inherently subject to selection bias: only intubations in which providers had already chosen a VL were captured, and participation was voluntary. Because no comparison cohort of conventional direct-laryngoscopy cases was included, causal inference regarding device choice cannot be made.[29] Second, the observational, single-center design further limits causal interpretation and external validity. Clinical practices, resource availability, and patient characteristics at Siriraj Hospital may differ from those in other institutions or healthcare systems, constraining generalizability. Third, all human-factor data were obtained from immediate post-procedure self-reports. Although this timing minimizes recall decay, it remains vulnerable to recall and social-desirability bias; providers may under- or over-estimate non-technical behaviors such as situational awareness or error recognition.[30] Additionally, the study was not powered for inferential subgroup comparisons, and multivariate analysis was not feasible due to the limited number of unsuccessful intubation cases. Finally, unmeasured confounders—including provider experience, institutional culture, and contemporaneous pandemic-related practice changes—may have influenced both human-factor ratings and intubation outcomes. These limitations underscore that the present findings are exploratory and hypothesis-generating, with the primary aim of informing the design of future studies rather than guiding immediate changes in clinical practice. Future multi-center studies with objective behavioral assessment and a control group of direct-laryngoscopy cases are needed to confirm and extend these observations.

Strengths and implications

Despite these limitations, this study offers several noteworthy strengths. It is among the few to systematically apply the HFIT to explore decision-making in airway management in real-world operating room settings. By capturing responses immediately after intubation, the study provides timely insights into how internal (e.g., stress, fatigue) and external (e.g., time pressure, communication dynamics) human factors influence the choice to use VLs. The inclusion of multiple provider types—attending anesthesiologists, residents, and nurse anesthetists—adds to the contextual relevance of the findings.

Importantly, the study highlights actionable gaps in current practices, particularly in error recognition and backup planning, which are critical to patient safety. Based on our findings, integrating the HFIT model into airway management practice has several potential applications. It can support routine post-intubation debriefings by enabling systematic reflection on technical and non-technical contributors to performance. HFIT domains can also be used to design simulation scenarios that help trainees recognize and manage system-based challenges, such as communication breakdowns or equipment availability. Finally, embedding HFIT principles into formal airway training programs may enhance decision-making, preparedness, and team coordination, ultimately improving safety and efficiency in airway management.

CONCLUSION

This study identified key human factors influencing the decision to use VLs instead of Macintosh blades in the operating room. Internal factors such as stress and fatigue, along with external pressures like time constraints and high-demand environments, played a significant role in decision-making. Participants cited improved glottic visualization, device familiarity, and enhanced supervision as primary reasons for choosing VLs. By applying the HFIT model, this study systematically captured the interplay of cognitive, organizational, and environmental influences on airway management. The

findings underscore the importance of incorporating HFIT-based frameworks into training, debriefing, and system-level strategies to support safe and efficient intubation practices.

Data Availability Statement

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ACKNOWLEDGEMENTS

The authors thank Ms. Nerisa Thornsri, Dr. Saowalak Hunnangkul for statistical support and our research team members including Assoc. Prof. Nantthasorn Zinboonyahgoon, Assist. Prof. Suratsawadee Wangnamthip and Ms. Natsupa Wiriyakulsit for administrative support.

DECLARATIONS

Grants and Funding Information

This research project was supported by Siriraj Research Fund, Grant number (IO) R016431003, Faculty of Medicine Siriraj Hospital, Mahidol University.

Conflict of Interest

None declared.

Registration Number of Clinical Trial

The study did not involve any intervention or prospective assignment of participants; therefore, clinical trial registration was not applicable.

Author Contributions

Conceptualization and Methodology: SP, AY, TJ, KR; Literature review, Investigation, Formal analysis and Writing original draft: SP, AY; Writing review & editing, Data interpretation and Supervision: KR, T.J. All the authors read and agreed with the final version of the manuscript.

Use of Artificial Intelligence

Not applicable.

REFERENCES

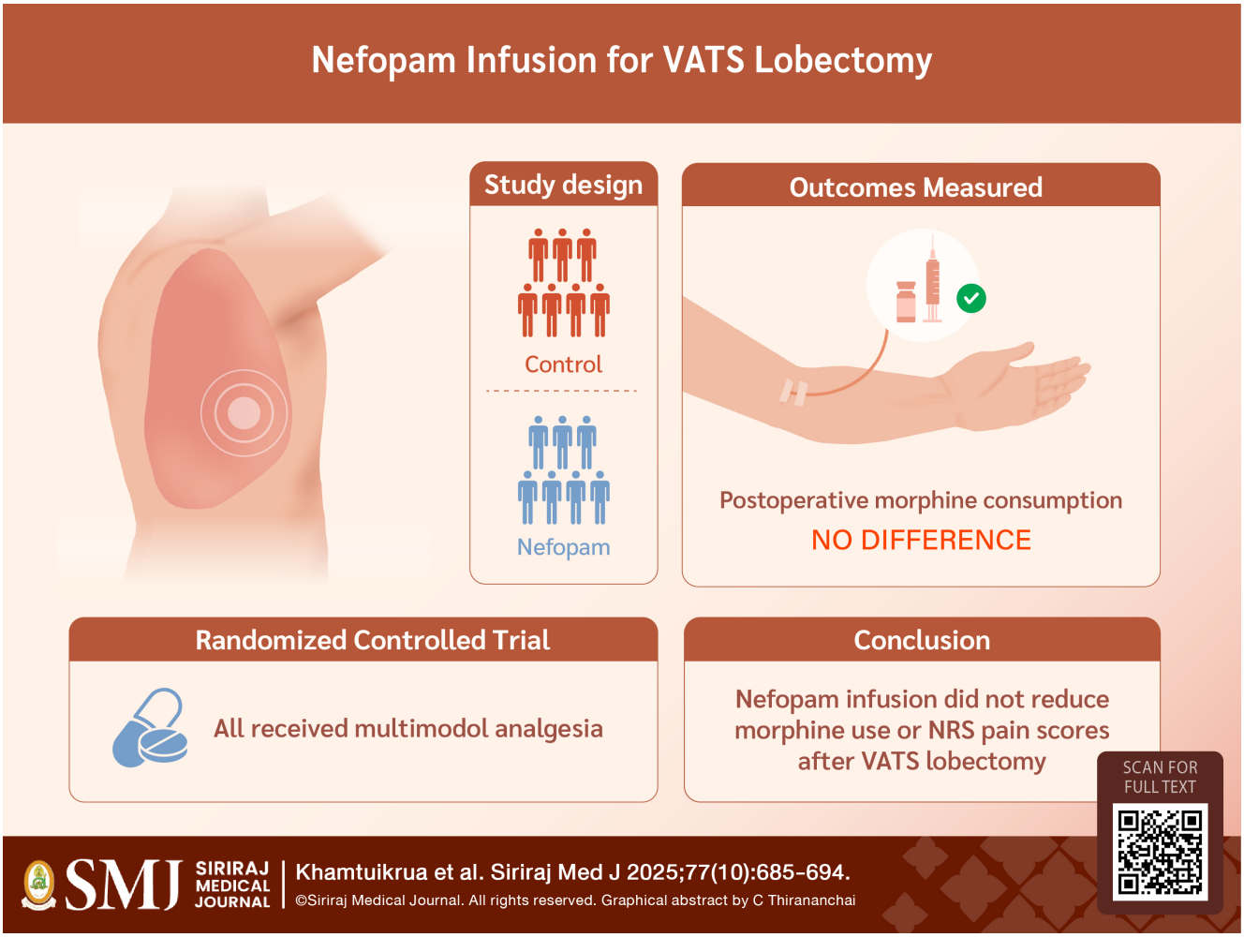
1. Lewis SR, Butler AR, Parker J, Cook TM, Schofield-Robinson OJ, Smith AF. Videolaryngoscopy versus direct laryngoscopy for adult patients requiring tracheal intubation: a Cochrane Systematic Review. Br J Anaesth. 2017;119(3):369-83.
2. Hansel J, Rogers AM, Lewis SR, Cook TM, Smith AF. Videolaryngoscopy versus direct laryngoscopy for adults undergoing tracheal intubation: a Cochrane systematic review and meta-analysis update. Br J Anaesth. 2022;129(4):612-23.
3. Ruderman BT, Mali M, Kaji AH, Kilgo R, Watts S, Wells R, et al. Direct vs Video Laryngoscopy for Difficult Airway Patients in the Emergency Department: A National Emergency Airway Registry Study. West J Emerg Med. 2022;23(5):706-15.
4. Apfelbaum JL, Hagberg CA, Connis RT, Abdelmalak BB, Agarkar M, Dutton RP, et al. 2022 American Society of Anesthesiologists Practice Guidelines for Management of the Difficult Airway. Anesthesiology. 2022;136(1):31-81.
5. Frerk C, Mitchell VS, McNarry AF, Mendonca C, Bhagrath R, Patel A, et al. Difficult Airway Society 2015 guidelines for management of unanticipated difficult intubation in adults. Br J Anaesth. 2015;115(6):827-48.
6. Najafi A, Imani F, Makarem J, Khajavi MR, Etezadi F, Habibi S, et al. Postoperative sore throat after laryngoscopy with macintosh or glide scope video laryngoscope blade in normal airway patients. Anesth Pain Med. 2014;4(1):e15136.
7. Kaplan MB, Hagberg CA, Ward DS, Brambrink A, Chhibber AK, Heidegger T, et al. Comparison of direct and video-assisted views of the larynx during routine intubation. J Clin Anesth. 2006; 18(5):357-62.
8. Schnittker R, Marshall S, Horberry T, Young KL. Human factors enablers and barriers for successful airway management - an in-depth interview study. Anaesthesia. 2018;73(8):980-9.
9. Kelly FE, Frerk C, Bailey CR, Cook TM, Ferguson K, Flin R, et al. Human factors in anaesthesia: a narrative review. Anaesthesia. 2023;78(4):479-90.
10. Kelly FE, Frerk C, Bailey CR, Cook TM, Ferguson K, Flin R, et al. Implementing human factors in anaesthesia: guidance for clinicians, departments and hospitals: Guidelines from the Difficult Airway Society and the Association of Anaesthetists: Guidelines from the Difficult Airway Society and the Association of Anaesthetists. Anaesthesia. 2023;78(4):458-78.
11. Fletcher G, Flin R, McGeorge P, Glavin R, Maran N, Patey R. Anaesthetists' Non-Technical Skills (ANTS): evaluation of a behavioural marker system. Br J Anaesth. 2003;90(5):580-8.
12. Flin R, Patey R. Non-technical skills for anaesthetists: developing and applying ANTS. Best Pract Res Clin Anaesthesiol. 2011; 25(2):215-27.
13. Cook TM, Woodall N, Harper J, Benger J, Fourth National Audit P. Major complications of airway management in the UK: results of the Fourth National Audit Project of the Royal College of Anaesthetists and the Difficult Airway Society. Part 2: intensive care and emergency departments. Br J Anaesth. 2011;106(5):632-42.
14. Jones CPL, Fawker-Corbett J, Groom P, Morton B, Lister C, Mercer SJ. Human factors in preventing complications in anaesthesia: a systematic review. Anaesthesia. 2018;73 Suppl 1:12-24.
15. Asanathong N, Jiamjira-anon N, Eiamcharoenwit J, Mantaga S, Thanakiattiwibun C, Siriussawakul A, et al. Incidence of adverse perioperative airway complications in obese non-pregnant and pregnant patients undergoing general anesthesia. Siriraj Med J. 2022;74(3):178-84.
16. Raksamani K, Jirativanont T, Sareenun P. Correlation of medical knowledge and non-technical skills assessment in anesthesia residents. Siriraj Med J. 2020;72(6):483-7.
17. Oofuvong M, Pattaravit N, Kanjanawanichkul O, Siripruekpong S, Nuanjun K, Suwannarat B. Are technical skills assessed using medical knowledge associated with non-technical skill knowledge in anaesthesia resident training? Siriraj Med J. 2022;74(12):844-56.
18. Flin R, Fioratou E, Frerk C, Trotter C, Cook TM. Human factors

in the development of complications of airway management: preliminary evaluation of an interview tool. Anaesthesia. 2013; 68(8):817-25.
19. Shruthi AH, Dinakara D, Chandrika YR. Role of videolaryngoscope in the management of difficult airway in adults: A survey. Indian J Anaesth. 2020;64(10):855-62.
20. Niven AS, Doerschug KC. Techniques for the difficult airway. Curr Opin Crit Care. 2013;19(1):9-15.
21. Hur M, Kim JY, Min SK, Lee K, Won YJ, Kim JE. Comparison of McGrath Videolaryngoscope and Macintosh Laryngoscope in Children with Torticollis: Randomized Controlled Trial. Children (Basel). 2021;8(12).
22. Jones L, Mulcahy K, Fox J, Cook TM, Kelly FE. C-MAC((c)) videolaryngoscopy: The anaesthetic assistant's view. J Perioper Pract. 2018;28(4):83-9.
23. Edelman DA, Perkins EJ, Brewster DJ. Difficult airway management algorithms: a directed review. Anaesthesia. 2019;74(9):1175-85.
24. De Jong A, Myatra SN, Roca O, Jaber S. How to improve intubation in the intensive care unit. Update on knowledge and devices. Intensive Care Med. 2022;48(10):1287-98.
25. Herbstreit F, Fassbender P, Haberl H, Kehren C, Peters J. Learning endotracheal intubation using a novel videolaryngoscope improves intubation skills of medical students. Anesth Analg. 2011;113(3): 586-90.
26. Malito ML, Mathias L, Kimura Junior A, Correa GH, Bardauil VR. The impact of introducing a videolaryngoscope in the initial training of laryngoscopy for undergraduate medical students: a simulation randomized trial. Braz J Anesthesiol. 2023;73(5): 532-8.
27. Gordon M, Darbyshire D, Baker P. Non-technical skills training to enhance patient safety: a systematic review. Med Educ. 2012;46(11):1042-54.
28. Arora S, Miskovic D, Hull L, Moorthy K, Aggarwal R, Johannsson H, et al. Self vs expert assessment of technical and non-technical skills in high fidelity simulation. Am J Surg. 2011;202(4):500-6.
29. Hernan MA, Hernandez-Diaz S, Robins JM. A structural approach to selection bias. Epidemiology. 2004;15(5):615-25.
30. Park HR, Lee JS. Induced interpretation bias affects free recall and episodic memory bias in social anxiety. PLoS One. 2023;18(11): e0289584.

Intraoperative and Postoperative Nefopam Administration for Video-assisted Thoracoscopic Lobectomy Pain: A Multicenter, Randomized, Controlled Trial

Chaowanan Khamtuikrua, M.D.[1], Sirilak Suksompong, M.D.[1], Punnarerk Thongcharoen, M.D.[2], Suparauk Geanphun, M.D.[2], Ratchaya Weerayutwattana, M.D.[3], Sira Laohathai, M.D.[4], Thanapat Vanichnatee, M.D.[1], Non Singpan, M.D.[1], Chompunoot Pathonsamit, M.D.[3,*]

[1]*Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand,* [2]*Division of Cardiothoracic Surgery, Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand,* [3]*Department of Anesthesiology, Faculty of Medicine, Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand,* [4]*Cardiothoracic Surgery Unit, Department of Surgery, Faculty of Medicine, Vajira Hospital, Navamindradhiraj University, Bangkok, Thailand.*



*Corresponding author: Chompunoot Pathonsamit
E-mail: chompunoot@nmu.ac.th
Received 17 March 2025 Revised 13 May 2025 Accepted 15 May 2025
ORCID ID:http://orcid.org/0000-0003-1722-8821
https://doi.org/10.33192/smj.v77i10.274325

ABSTRACT

Objective: Intraoperative nefopam infusion was documented as safe and viable for supplemental pain management, alongside opioids following surgery. Postoperative pain control with nefopam after video-assisted thoracoscopic surgery (VATS) is not well understood. This study assessed the effects of nefopam towards postoperative morphine requirements and pain intensity 24 hours after VATS lobectomies.

Materials and Methods: This multicenter, double-blind, randomized, controlled trial enrolled 18-70-year-old elective VATS lobectomy patients. Patients were randomized 1:1, receiving nefopam or normal saline solution (NSS) administered during the maintenance of anesthesia and 24-hour postoperative period. All received multimodal analgesia, including paracetamol, ibuprofen, and intercostal nerve blocks. Postoperative morphine was administered via patient-controlled analgesia (PCA) devices and recorded at 10 and 30 minutes, and 1, 2, 6, 12, 18 and 24 hours. Postoperative pain was graded at rest and during deep breathing using numeric rating scale (NRS) scores 1, 2, 12, and 24 hours.

Results: Of 72 enrolled patients, 70.8% were female, with a mean (± standard deviation) age of 56.5 ± 10.4 years. No significant postoperative difference was observed between groups for: total median (P_{25}, P_{75}) morphine amounts administered over 24 hours (nefopam, 14 [8, 24] mg; control, 8 [4.5, 19] mg; $p = 0.17$); NRS pain scores during rest ($p = 0.98$) or deep breathing ($p = 0.82$) 1, 2, 12, and 24 hours

Conclusion: Intraoperative and postoperative nefopam infusion, including multimodal analgesia, did not reduce morphine consumption or NRS pain scores in VATS lobectomy, but may have prolonged the duration of pain relief.

Keywords: Video-assisted thoracoscopic surgery; nefopam; postoperative pain; lobectomy (Siriraj Med J 2025; 77: 685-694)

INTRODUCTION

Open thoracotomy pulmonary resections require large surgical incisions and are linked to significant postoperative pain. Video-assisted thoracoscopic surgery (VATS) has recently emerged as a popular and effective surgical technique.[1,2] Compared to traditional thoracotomies, it is a minimally invasive surgical procedure for lung resections with smaller surgical incisions, better postoperative pulmonary function, and shorter hospital stays.[3,4] Hence, there is a growing preference for VATS as an alternative over open thoracotomies.[1,5-7]

Effective management of postoperative pain following thoracic surgery enables patients to ambulate early, contributing to a swift recovery and minimizing the risk of postoperative pulmonary complications.[4] Pain control for open thoracotomies in the past was mostly through opioids and local anesthetics administered by epidural catheter.[8,9] This technique is invasive and can cause many complications despite its effectiveness in controlling postoperative pain.[10] Less-invasive, non-opioid analgesics are alternatives that warrant further study to ensure safe and effective postoperative pain control in VATS lobectomy patients.[11]

Nefopam is a centrally acting, non-opioid, non-steroidal analgesic that is commonly prescribed worldwide to treat acute pain following surgery and has less severe adverse reactions (AEs) compared to opioids.[12] Its mechanism of action entails the inhibition of serotonin and norepinephrine reuptake. It also reduces glutamate release by modulating sodium and calcium channels.[13] Intraoperative nefopam infusions were found to reduce opioid requirements during laparoscopic cholecystectomies[14] and significantly reduce the amount of required morphine after orthopedic surgery.[15] It was also observed to lower pain scores during immediate[15] and early postoperative periods.[14] Nefopam performed notably better than paracetamol in reducing early postoperative morphine requirements.[16] It may serve as a valuable adjunct to morphine due to its significant analgesic effects, facilitating the management of severe postoperative pain in surgical procedures like upper abdominal surgery.[17]

Currently, postoperative pain control with nefopam after VATS is not well understood, Enhanced Recovery After Surgery (ERAS®) protocols recommended by the Society and the European Society of Thoracic Surgeons (ESTS) has not yet included nefopam use.[18] This study sought to clarify this issue. It assessed the clinical benefits of nefopam in postoperative pain control and morphine requirements in combination with an intraoperative intercostal nerve block (INB) as well as paracetamol and non-steroidal anti-inflammatory drug (NSAID) use immediately and 24-hours after VATS lobectomies.

We hypothesized that nefopam can decrease cumulative morphine consumption during the 24-hour postoperative period after VATS lobectomies.

MATERIALS AND METHODS

Study design and participants

This multicenter, double-blind, randomized clinical trial (RCT) was conducted between September 2020 and October 2021 across two hospitals: Siriraj and Vajira. Eighteen-to-seventy-year-old patients undergoing elective VATS lobectomies and capable of operating patient-controlled analgesia (PCA) devices were eligible for inclusion. Patients allergic to nefopam, paracetamol, ibuprofen, or bupivacaine; with nefopam contraindications; kidney disease(s) or disorders (estimated glomerular filtration rate [eGFR] <60 mL/min); a body mass index (BMI) >35 kg/m^2; with liver cirrhosis; or with chronic pain were excluded from the study. Patients observed to have a nefopam intolerance (i.e., tachycardia, dizziness, urinary retention) or who failed to use intravenous (IV) PCA were subject to withdrawal and termination criteria as determined at the researchers' discretion.

The study was approved by Institutional Ethics Committees (IECs) of each participating center (Siriraj Institute Review Board [SIRB] COA Si 489/2020 and Vajira Ethics Committee [EC] COA 155/2563). It was carried out in accordance with International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) Good Clinical Practice (GCP), the Belmont Report, and the Declaration of Helsinki. The study was registered under ClinicalTrials.gov on January 23, 2020 (NCT04241640). All patients provided written informed consent before enrollment.

Randomization and blinding

Patients were allocated 1:1 using computer-generated block randomization into two groups to receive nefopam or an infusion of normal saline solution (NSS) administered during anesthesia maintenance and the 24-hour postoperative period thereafter. Randomization numbers were distributed in opaque, sealed envelopes with running numbers of 1 to 72. Anesthesia was administered by an attending anesthesiologist unaffiliated with the research team and blinded from patients' allocations. The type of study drug administered to both nefopam and NSS patients was blinded (labeled as 100 mL and 500 mL study drugs) after formulation by anesthesia personnel (also unaffiliated with the research team). Patients in the control group would receive NSS infusions in bottles identical to those in the nefopam group.

Study procedures

During preoperative care, patients were educated on PCA and the numeric rating scale (NRS) scoring (where 0 = no pain and 10 = worst imaginable pain). Peak expiratory flow rate (PEFR) was measured in L/min using portable peak flow meters (MicroPeak®, CareFusion, San Diego, CA, USA). Preoperative PEFR was measured thrice to calculate a mean value. Anesthesia was induced with 1-2 mcg/kg fentanyl, 0.1 mg/kg cis-atracurium, and a continuous infusion of propofol controlled by a Schneider® model target control infusion (TCI) system (starting at 4 mcg/mL and subsequently adjusted by the attending anesthesiologist according to the patients' vital signs). Anesthesia was maintained with oxygen and air as well as a continuous infusion of propofol also controlled by the Schneider® model TCI system. Additional fentanyl may be administered if the patient's blood pressure and heart rate increase by more than 20% from their normal baseline, subject to the discretion of the anesthesiologist. 20 mg (2 mL) nefopam in 98 mL NSS was infused as 100 mL/hr at the beginning of surgery, then 80 mg (8 mL) nefopam in 492 mL NSS infused as 20 mL/hr for 24-hours in nefopam group patients. The same infusion procedures (100 mL/hr followed by 20 mL/hr) were performed for the control group using the blinded study drug (100 and 500 mL of NSS only). The number of surgical incisions were consistent across groups.

Before wound closure, direct vision INBs were performed by the attending surgeon using 0.5% bupivacaine. INBs were performed across three levels of the intercostal nerves, each administered 7 mL of 0.5% bupivacaine to ensure complete analgesia coverage of the wound and chest drain. When patients responded to verbal commands, opened their eyes, and had an appropriate tidal volume, they were extubated and moved to the post-anesthesia care unit (PACU). There, PCA devices were attached to patients for them to self-administer morphine. The PCA settings were fixed to PCA mode, 2 mg bolus doses (35 mg limit over a 4-hr period), and logout interval of five minutes.

Postoperative pain management and measured outcomes

Patients transferred to the PACU stayed for at least an hour. Each patient's pain level was assessed at rest and during deep breathing exercises using a NRS ranging from 0 (no pain) to 10 (most intense pain) upon arrival to the PACU as well as 1, 2, 12 and 24 hours thereafter. Respiratory rate was also monitored, with respiratory depression defined by a combination of a

respiratory rate (RR) <10 bpm and sedation score of 3. Patients were transferred to the general ward should no acute complications be observed. In the general ward, the cumulative dose of morphine administered postoperatively by PCA (primary outcome) was recorded 10 and 30 minutes after as well as 1, 2, 6, 12, 18, and 24 hours after surgery. Patients were also categorized by their NRS score into mild (0-3), moderate (4-6), and severe pain (7-10) groups. All patients received 500 mg paracetamol every six hours and 400 mg ibuprofen three times daily after meals for two days. PEFR were measured again at 24 hours after surgery. The difference in percentage between preoperative and postoperative PEFR was calculated as:

$$\left(\frac{Preoperative\ PEFR - Postoperative\ PEFR}{Preoperative\ PEFR}\right) \times 100$$

AEs were also recorded (specifically: nausea, vomiting, itching, urinary retention, drowsiness). Urinary retention was measured after the removal of Foley's catheters at least 24 hours after surgery.

Statistical analyses

Based on the estimated 6-hour post-operative fentanyl consumption in the nefopam and control groups (323.8 ± 119.3 mcg and 421.2 ± 151.6 mcg, respectively),[19] with a two-sided type I error of 0.05, 80% power, and 10% dropout, a sample size of 36 per group was required. Continuous data (age, weight, NRS score, and 24-hour morphine consumption) were presented as mean ± standard deviation (SD) or median (P_{25}, P_{75}). Demographic and perioperative data were compared using a Student's *t*-test or Mann-Whitney U test. NRS score at four time points and 24-hour morphine consumption at eight time points were compared using repeated measures ANOVA. Time to first PCA-trigger was analyzed using survival analysis and log-rank test for comparison of two survival curves. Categorical data (biological sex, and prevalence of AEs) were presented as number (%) and compared using a Chi-square test. Data were processed using SPSS® (v30.0; IBM® Corporation, Armonk, NY, USA). *P*-value ≤ 0.05 was considered statistically significant. To account for multiple comparisons, a Bonferroni correction was applied, to mitigate the false discovery rate, the adjusted *p*-values were used.

RESULTS

Seventy-two patients were enrolled in this study between September 2020 and October 2021, half received nefopam and half NSS (as a control) (Fig 1). 70.8% of patients were female (n = 51) with a mean ±

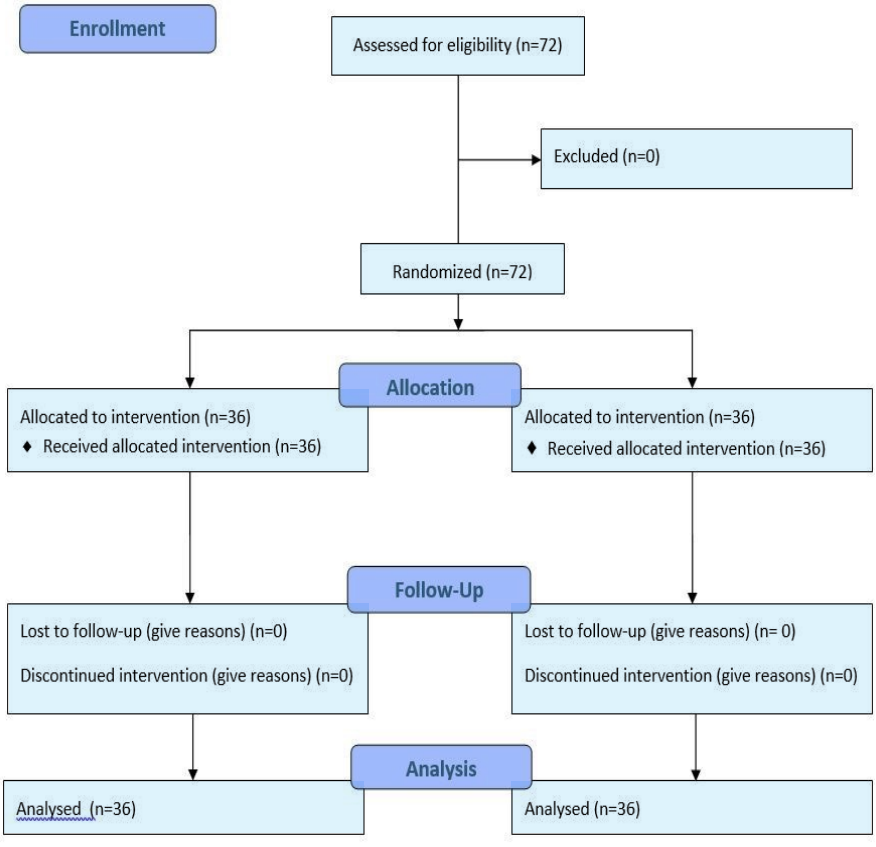


Fig 1. Consort diagram. Seventy-two participants were assessed for eligibility before 1:1 randomization into two study arms. All participants were enrolled and included during subsequent analyses.
Abbreviation: NSS = normal saline solution

standard deviation (SD) age of 56.5 ± 10.4 years. Baseline characteristics (age, body weight, biological sex, American Society of Anesthesiologists physical class [ASA-PS]) and demographics were similar and not statistically different across groups (Table 1). The number of surgical incisions (p = 0.13) as well as perioperative characteristics were also not statistically different across groups (Table 2). We additionally found no difference in time to first drink (p = 0.28), first eat (p = 0.42), sit (p = 0.60), and walk (p = 0.59) across both groups.

The postoperative morphine administered 24-hours after surgery was reported as median (P_{25}, P_{75}) because the data were non-normally distributed. No significant difference was observed in the median (P_{25}, P_{75}) cumulative postoperative morphine administered 24-hours after surgery between the nefopam and control groups (14 [8, 24] mg vs 8 [4.5, 19] mg, respectively, p = 0.17; Fig 2). Patients receiving nefopam had a longer mean pain-free duration than the control (75 min vs 70 min). This difference was not statistically significant (p = 0.79).

No difference in postoperative NRS scores or percentage of patients with moderate and severe pain 1, 2, 12, and 24 hours after surgery at rest and with deep breathing were observed as well (Figs 3 and 4, respectively). We also found no difference between preoperative and postoperative PEFR across both groups (25.4% ± 19.18% and 21.5% ± 30.0% for nefopam and control groups, respectively, P = 0.52).

TABLE 1. Demographics and characteristics of participants.

Characteristic	Nefopam (n = 36)	Control (n = 36)	*P*-value
Age (years)	58.4 ± 7.8	54.6 ± 12.2	0.12
Body weight (kg)	64.0 ± 10.1	60.8 ± 12.5	0.24
Biological sex (Female)	24 (66.7)	27 (75.0)	0.44
ASA-PS			
I	20 (55.6)	28 (77.8)	0.13
II	13 (36.1)	6 (16.7)	
III	3 (8.3)	2 (5.6)	

Data are presented as mean ± SD or n (%).
Abbreviation: ASA-PS = American society of anesthesiologists physical class

TABLE 2. Perioperative characteristics.

Variable	Nefopam (n = 36)	Control (n = 36)	*P*-value
Duration of anesthetic (min)	181.4 ± 46.5	186.8 ± 68.8	0.70
Duration of surgery (min)	131.8 ± 40.0	136.4 ± 62.9	0.71
Number of ports			
1	20 (55.6)	28 (77.8)	0.13
2	13 (36.1)	6 (16.7)	
3	3 (8.3)	2 (5.6)	
Intraoperative fentanyl use (mcg)	135.7 ± 47.9	126.3 ± 46.5	0.40
Postoperative 24-hour morphine consumption (hrs)	14 (8, 24)	8 (4.5, 19)	0.17
Difference between preoperative and 24-hour postoperative PEFR (%)	25.4 ± 19.1	21.5 ± 30.0	0.52

Data are presented as mean ± SD or n (%).
Abbreviation: PEFR = peak expiratory flow rate

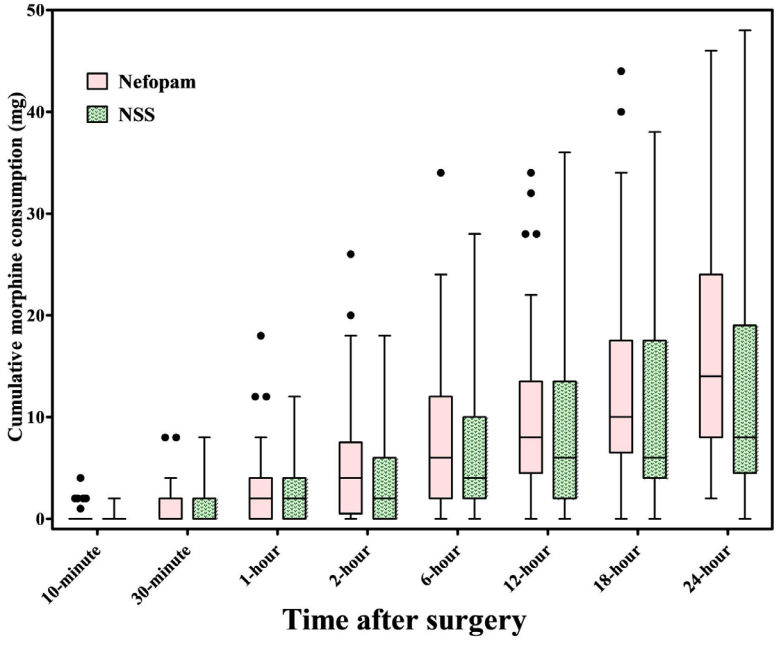


Fig 2. Boxplot (25th, 75th percentiles) of cumulative postoperative morphine consumption (mg) at each time point 24-hours after surgery. No statistically significant difference was observed between the two groups ($p = 0.17$).
Abbreviation: NSS = normal saline solution

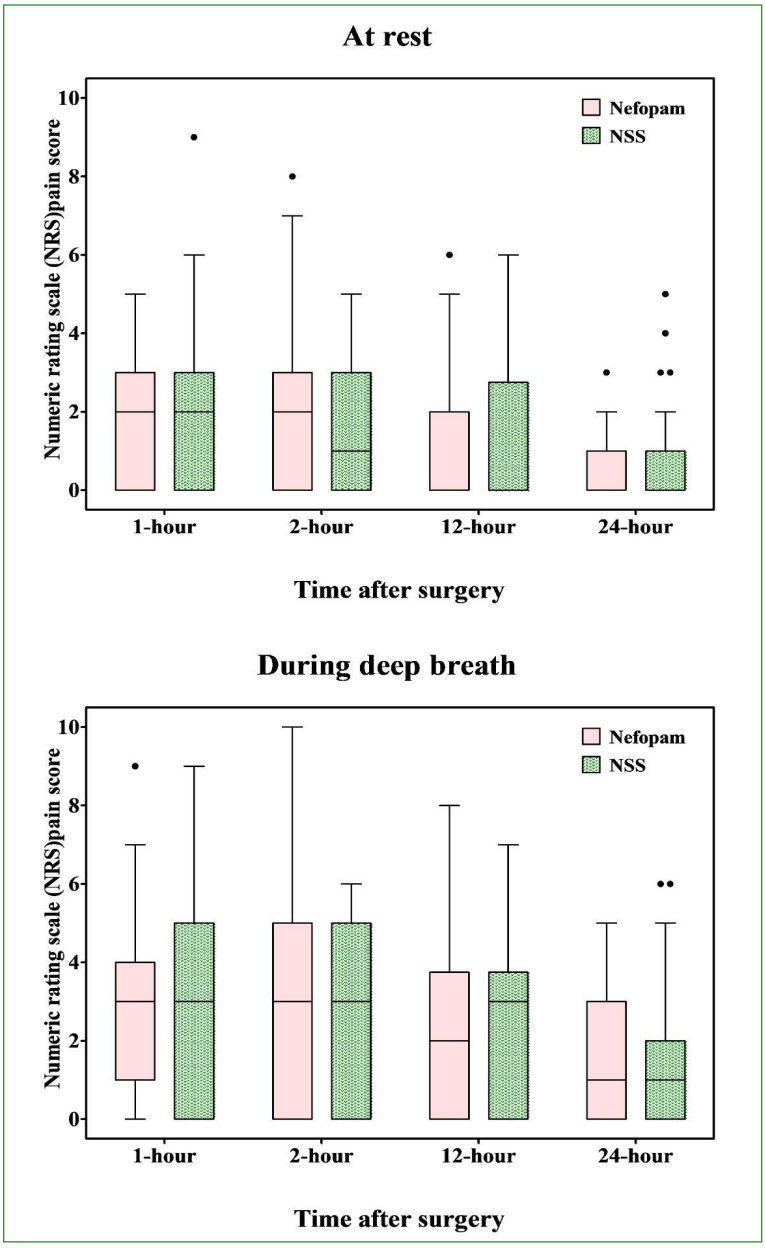


Fig 3. Boxplot (25th, 75th percentiles) of median numeric rating scale (NRS) scores at 1, 2, 12, and 24-hour postoperative at **(A)** rest ($p = 0.98$) and **(B)** during deep breathing ($p = 0.82$). NRS scores of 1-3 represent mild pain, 4-6 moderate pain, and 7-10 severe pain. Chi-square and Fisher's exact tests were used to assess statistical significance of postoperative NRS scores.
Abbreviations: NRS = numerical rating scale; NSS = normal saline solution

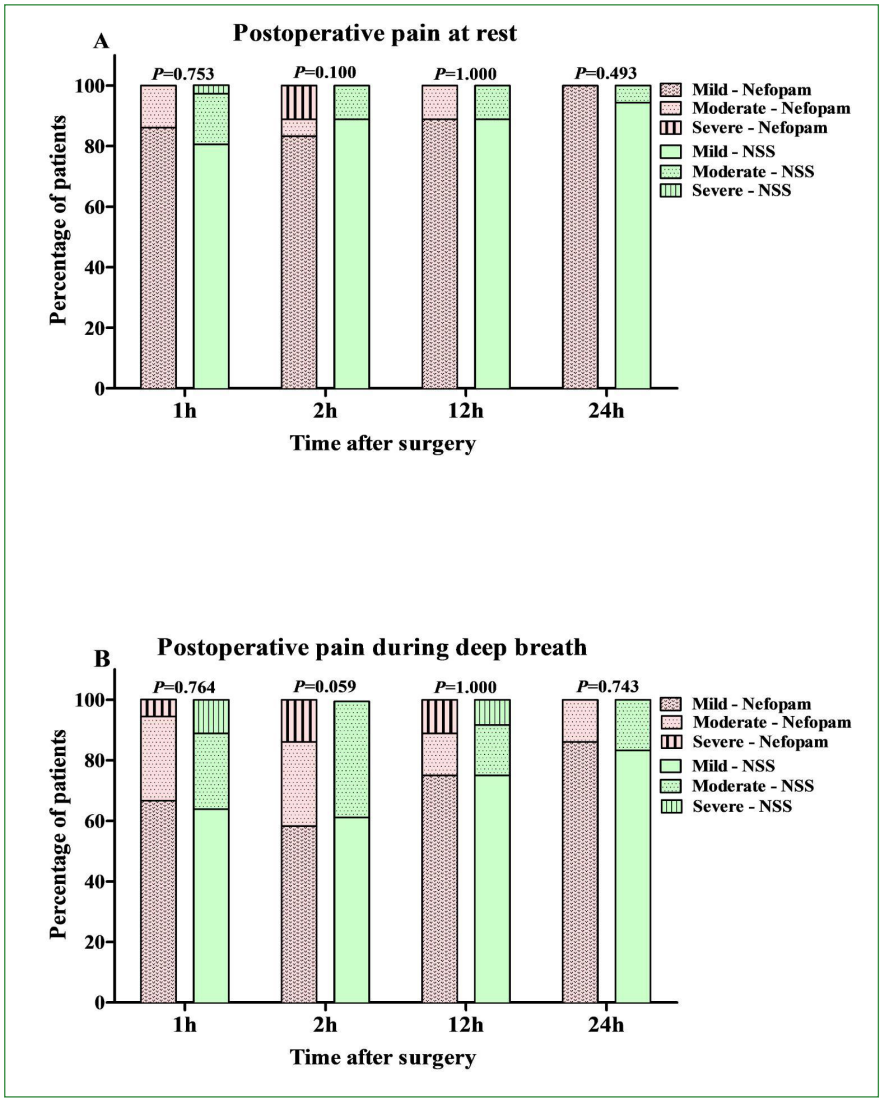


Fig 4. Percentage of patients with moderate and severe pain 1, 2, 12 and 24-hours postoperative at **(A)** rest and **(B)** during deep breathing.
Abbreviations: NRS = numerical rating scale; NSS = normal saline solution

Five patients from the nefopam group, and one from the control, reported feeling dizziness (Supplementary Table 1). However, the prevalence of the AE was not statistically significant across groups ($p = 0.12$). Patients from the Nefopam group also reported tachycardia (n = 1) and urinary retention (n = 1). Two patients from the control group also experienced urinary retention. Patients across both groups did not report sweating, respiratory depression, or delirium.

DISCUSSION

This study investigated the efficacy of nefopam infusion as a component of a multimodal analgesic approach in VATS lobectomy patients. We demonstrated that nefopam use as an adjunct to intra- and postoperative analgesic methods, as well as an INB, did not result in significant reductions in cumulative morphine requirements during the 24-hour postoperative period and postoperative NRS scores at rest and during deep breathing compared to the control group. Despite a lack of statistical significance, the nefopam group exhibited a longer time to the first analgesic requirement. Since the mean pain-free time differs by only a few minutes, it may not be clinically significant.

Several studies have investigated the efficacy of IV nefopam administration towards acute postoperative pain across many types of surgical operations. Kim *et al.* demonstrated that intraoperative nefopam infusions reduced opioid requirements and pain scores (graded by visual analogue scales [VAS]) in 60 patients with laparoscopic cholecystectomies during the early postoperative period after remifentanil-based anesthesia.[14] Na *et al.* found that nefopam decreased postoperative pain and opioid consumption during the acute postoperative period in patients that underwent laparoscopic gastrectomy.[19] Nefopam was also found to significantly reduce morphine use in orthopedic surgery patients with lower immediate postoperative pain scores.[15] While many studies reported that nefopam reduced opioid usage and significantly decreased postoperative pain, Lee *et al.* found no significant difference in the cumulative PCA-administered fentanyl between 135 patients that received nefopam only, fentanyl

only, or nefopam with fentanyl during laparoscopic gynecologic surgery.[20] This suggests that nefopam may not always be effective at reducing postoperative pain and opioid requirements for certain types of surgeries.

We found that cumulative morphine requirements and postoperative NRS scores were not statistically different between nefopam and control groups. This lack of statistical difference could be explained by the multimodal analgesia regimens for patients across both groups. Single-injection INB effectively reduces pain during the first 24 hours after thoracic surgery[21] and was found to be safe and effective at reducing immediate postoperative pain and analgesic requirements across 32 VATS bilateral sympathectomy patients.[22] One study also investigated VATS surgery with the use of nefopam but without performing an INB. The study found that nefopam effectively reduced the NRS score.[23] Therefore, this information may support the notion that INB can provide effective pain relief for patients without the need for nefopam. Moreover, all patients in our study received ibuprofen and paracetamol. Both drugs are effective adjuvant agents for postoperative pain.[24-26] Combinations of ibuprofen and paracetamol provided better acute postoperative pain control than either as a standalone, reducing the need for additional analgesia at least eight hours thereafter.[27] Nefopam may not have provided any additional analgesic benefits, hence the lack of statistical difference in the cumulative dose of morphine across groups.

The average morphine consumption across both groups was 15.08 ± 11.89 mg, similar to the amount reported by Suksompong *et al.* across 32 VATS patients (mean [interquartile range] morphine of 15 [5.5, 29.5] and 22.5 [15.3, 40.8] mg over 24 hours in the low dose ketamine group and NSS control, respectively, both with multimodal analgesia).[28] Na *et al.*'s[19] 60 laparoscopic gastrectomy patients required lower doses of fentanyl administered by IV PCA in the nefopam group (323.8 ± 119.3 mg) than the control (421.2 ± 151.6 mg) the first six hours after surgery. This is equivalent to 32.4 ± 11.9 mg and 42.1 ± 15.1 mg of morphine, respectively – 2.1-2.8 times greater than what was administered in our study. From this, we surmised that multimodal analgesia by INB, paracetamol, and ibuprofen may be sufficient for VATS lobectomies.

Postoperative nausea and vomiting (PONV) are prevalent AEs of drugs used in general anesthesia and opioids administered via IV PCA. This also applies to nefopam.[29] Tachycardia is another frequent AE associated with nefopam.[29] However, we observed none of patient experienced PONV across both groups, and only one patient in the nefopam group experienced tachycardia. However, this case did not present with significant hemodynamic changes and did not require immediate medical intervention. Other AEs like sweating, respiratory depression, or delirium were not reported by all participants. This aligns with previous studies that demonstrated nefopam's safety and reduced prevalence of AEs compared to other analgesic opioids.

The main limitation of this study was it only included VATS lobectomies. Our findings may not be generalizable to other VATS (e.g., thymectomies, wedge resections, etc.). This study did not explore the topic of prehabilitation, which is an area worth investigating in future research, as there is evidence supporting its benefits in enhancing postoperative recovery.[30] Further RCTs with large cohorts are warranted to assess nefopam use across other types of VATS.

CONCLUSION

To conclude, administering nefopam during and after VATS lobectomies did not appear to lower postoperative morphine usage or alleviate pain intensity. However, it could non-significantly prolong the duration of pain relief for patients undergoing this surgery.

Data Availability Statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

ACKNOWLEDGEMENTS

The authors would like to thank Assist. Prof. Dr. Chulaluk Komoltri for her contribution toward data interpretation and statistical analysis and Ms. Nachanita Luxnayingyong for her assistance with data collection.

DECLARATIONS

Grants and Funding Information

Faculty of Medicine Siriraj Hospital, Mahidol University (grant number: R016332022). The funder had no role in the conceptualization, design, data collection, analysis, decision to publish, or preparation of the manuscript.

Conflict of Interest

The authors declare that there is no conflict of interests.

Registration Number of Clinical Trial

The study was registered under ClinicalTrials.gov (NCT04241640).

Author Contributions

Conceptualization, Methodology, and Supervision, C.K., S.S., P.T. and C.P.; Data Curation and Investigation, C.P., S.G., R.W., S.L., T.V., N.S; Formal Analysis, C.K., T.V., N.S; Software and Visualization, C.K., T.V., N.S; Writing – Original Draft, C.K., T.V., N.S.; Writing – Review & Editing, all authors.

Use of Artificial Intelligence

The authors declare no use of artificial intelligence.

Ethics Approval and Consent to Participate

This study was approved by IECs of each participating center (SIRB COA Si 489/2020, Vajira EC COA 155/2563). All patients provided written informed consent before enrollment.

Consent for Publication

Not applicable.

Contributor's Publishing Agreement

List of Abbreviations

AE	Adverse event
ASA-PS	American Society of Anesthesiologists Physical Class
BMI	Body mass index
EC	Ethics committee
eGFR	Estimated glomerular filtration rate
ERAS	Enhanced recovery after surgery
ESTS	European Society of Thoracic Surgeons
IEC	Institutional ethics committees
INB	Intercostal nerve block
IV	Intravenous
NRS	Numeric rating scales
NSAID	Non-steroidal anti-inflammatory drug
NSS	Normal saline solution
PACU	Post-anesthesia care unit
PCA	Patient-controlled analgesia
PEFR	Peak expiratory flow rate
PONV	Postoperative nausea and vomiting
RCT	Randomized clinical trial
RR	Respiratory rate
SD	Standard deviation
SIRB	Siriraj institutional review board
TCI	Target control infusion
VAS	Visual analogue scale
VATS	Video-assisted thoracoscopic surgery

REFERENCES

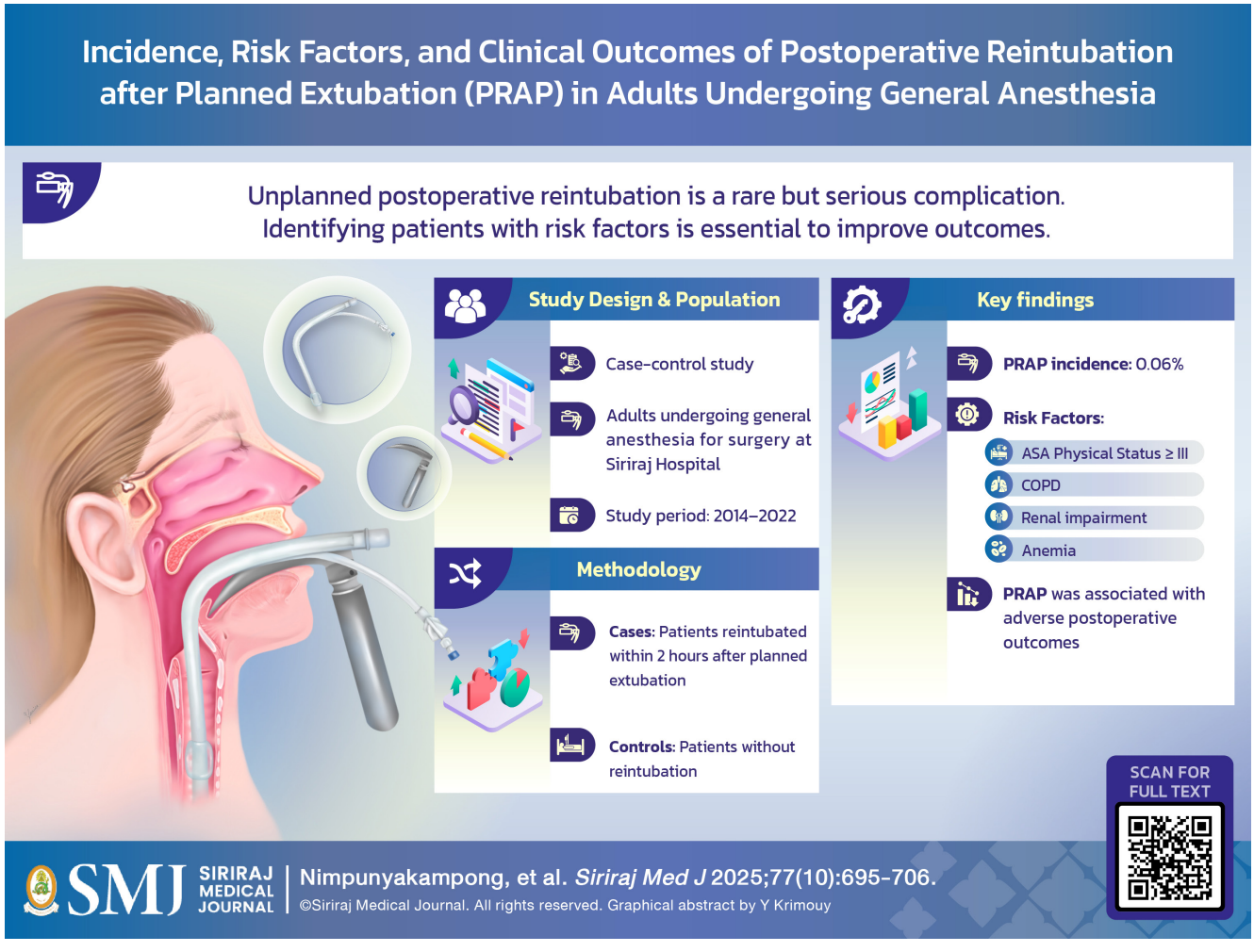
1. Sihoe ADL. Video-assisted thoracoscopic surgery as the gold standard for lung cancer surgery. Respirology. 2020;25(S2):49-60.
2. Bishnoi S, Puri HV, Asaf BB, Pulle MV, Parikh MBK, Patel MV, et al. Video-assisted thoracoscopic surgery: The preferred method to manage pulmonary sequestration. J Minim Access Surg. 2022;18(2):230-4.
3. Flores RM, Park BJ, Dycoco J, Aronova A, Hirth Y, Rizk NP, et al. Lobectomy by video-assisted thoracic surgery (VATS) versus thoracotomy for lung cancer. J Thorac Cardiovasc Surg. 2009;138(1):11-8.
4. Landreneau RJ, Hazelrigg SR, Mack MJ, Dowling RD, Burke D, Gavlick J, et al. Postoperative pain-related morbidity: video-assisted thoracic surgery versus thoracotomy. Ann Thorac Surg. 1993;56(6):1285-9.
5. Pan H, Chen H, Kong W, Ning J, Ge Z, Tian Y, et al. Video-assisted thoracoscopic surgery versus thoracotomy following neoadjuvant immunochemotherapy in resectable stage III non-small cell lung cancer among Chinese populations: a multi-center retrospective cohort study. Clin Lung Cancer. 2024;25(5):395-406.e5.
6. Zhang G, Fan J, Yu Z, Chai Y, Zhang S, Wu M, et al. Video-assisted thoracoscopic treatment as two-day surgery for lung neoplasms: a propensity-matched analysis. BMC Cancer. 2022;22(1):832.
7. Sabra MJ, Alwatari Y, Bierema C, Wolfe LG, Cassano AD, Shah RD. Five-year experience with VATS versus thoracotomy segmentectomy for lung tumor resection. Innovations. 2020;15(4):346-54.
8. Ng A, Swanevelder J. Pain relief after thoracotomy: is epidural analgesia the optimal technique? Br J Anaesth. 2007;98(2):159-62.
9. Goto T. What is the best pain control after thoracic surgery? J Thorac Dis. 2018;10(3):1335-8.
10. Soto RG, Fu ES. Acute pain management for patients undergoing thoracotomy. Ann Thorac Surg. 2003;75(4):1349-57.
11. Piccioni F, Segat M, Falini S, Umari M, Putina O, Cavaliere L, et al. Enhanced recovery pathways in thoracic surgery from Italian VATS Group: perioperative analgesia protocols. J Thorac Dis. 2018;10(Suppl 4):S555-S63.
12. Evans MS, Lysakowski C, Tramèr MR. Nefopam for the prevention of postoperative pain: quantitative systematic review. Br J Anaesth. 2008;101(5):610-7.
13. Heel RC, Brogden RN, Pakes GE, Speight TM, Avery GS. Nefopam: a review of its pharmacological properties and therapeutic efficacy. Drugs. 1980;19(4):249-67.
14. Kim EM, Jeon JH, Chung MH, Choi EM, Baek SH, Joen PH, et al. The Effect of Nefopam Infusion during Laparascopic Cholecystectomy on Postoperative Pain. Int J Med Sci. 2017;14(6):570-7.
15. Du Manoir B, Aubrun F, Langlois M, Guern ME, Alquier C, Chauvin M, et al. Randomized prospective study of the analgesic effect of nefopam after orthopaedic surgery. Br J Anaesth. 2003;91(6):836-41.
16. Mimoz O, Incagnoli P, Josse C, Gillon MC, Kuhlman L, Mirand A, et al. Analgesic efficacy and safety of nefopam vs. propacetamol following hepatic resection. Anaesthesia. 2001;56(6):520-5.
17. McLintock TTC, Kenny GNC, Howie JC, McArdle CS, Lawrie S,

Aitken H. Assessment of the analgesic efficacy of nefopam hydrochloride after upper abdominal surgery: A study using patient controlled analgesia. Br J Surg. 2005;75(8):779-81.
18. Batchelor TJP, Rasburn NJ, Abdelnour-Berchtold E, Brunelli A, Cerfolio RJ, Gonzalex M, et al. Guidelines for enhanced recovery after lung surgery: recommendations of the Enhanced Recovery After Surgery (ERAS®) Society and the European Society of Thoracic Surgeons (ESTS). Eur J Cardiothorac Surg. 2018;55(1):91-115.
19. Na HS, Oh AY, Ryu JH, Koo BW, Nam SW, Jo J, et al. Intraoperative Nefopam Reduces Acute Postoperative Pain after Laparoscopic Gastrectomy: a Prospective, Randomized Study. J Gastrointest Surg. 2018;22(5):771-7.
20. Lee S, Lee S, Kim H, Oh C, Park S, Kim Y, et al. The Analgesic Efficacy of Nefopam in Patient-Controlled Analgesia after Laparoscopic Gynecologic Surgery: A Randomized, Double-Blind, Non-Inferiority Study. J Clin Med. 2021;10(5):1043.
21. Guerra-Londono CE, Privorotskiy A, Cozowicz C, Hicklen RS, Memtsoudis SG, Mariano ER, et al. Assessment of Intercostal Nerve Block Analgesia for Thoracic Surgery: A Systematic Review and Meta-analysis. JAMA Netw Open. 2021;4(11):e2133394.
22. Bolotin G, Lazarovici H, Uretzky G, Zlotnick AY, Tamir A, Saute M. The efficacy of intraoperative internal intercostal nerve block during video-assisted thoracic surgery on postoperative pain. Ann Thorac Surg. 2000;70(6):1872-5.
23. Ki H-S, Shim J-G, Choi H-K, Ryu KH, Kang Dy, Park J, et al. Nefopam as a multimodal analgesia in thoracoscopic surgery: a randomized controlled trial. J Thorac Dis. 2024;16(6):3644-54.
24. Jahangiri Fard A, Farzanegan B, Khalili A, Ahmadabad NE, Kakhaki AD, Parsa T, et al. Paracetamol Instead of Ketorolac in Post-Video-Assisted Thoracic Surgery Pain Management: A Randomized Trial. Anesthe Pain Med. 2016;6(6):e39175.
25. Seers K. Review: single dose, oral paracetamol reduces moderate to severe postoperative pain. Evid Based Nurs. 2004;7(3):84.
26. Derry C, Derry S, Moore RA, McQuay HJ. Single dose oral ibuprofen for acute postoperative pain in adults. Cochrane Database Syst Rev. 2009;2009(3):CD001548.
27. Derry CJ, Derry S, Moore RA. Single dose oral ibuprofen plus paracetamol (acetaminophen) for acute postoperative pain. Cochrane Database Syst Rev. 2013;2013(6):CD010210.
28. Suksompong S, Chaikittisilpa N, Wanchiange S, Poolsuppasit S, Thongcharoen P, Limratana P. Low dose intraoperative ketamine infusion with multilevel paravertebral block for pain after video-assisted thoracic surgery: a randomized-controlled study. Ann Palliat Med. 2021;10(7):7258-69.
29. Alfonsi P, Adam F, Passard A, Guignard B, Sessler DI, Chauvin M. Nefopam, a nonsedative benzoxazocine analgesic, selectively reduces the shivering threshold in unanesthetized subjects. Anesthesiology. 2004;100(1):37-43.
30. Jirakulsawat A, Noocharoen N, Somnuke P. Prehabilitation in Clinical Practice: A Review of Concepts and Implementation in Enhancing Postoperative Outcomes. Siriraj Med J. 2024;76(9):646-54.

Incidence, Risk Factors, and Clinical Outcomes of Postoperative Reintubation after Planned Extubation in Adults Undergoing General Anesthesia: A Single-center Experience

Phonneeya Nimpunyakampong, M.D.[1,2], Manatsanan Denthet, M.D.[1], Aphichat Suphathamwit, M.D.[1], Wariya Vongchaiudomchoke, M.D., MSc.[1,*]

[1]Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [2]Department of Anesthesiology, Burirum Hospital, Burirum, Thailand.



**Corresponding author: Wariya Vongchaiudomchoke*
Email: wariya.von@mahidol.ac.th
Received 25 March 2025 Revised 21 May 2025 Accepted 21 May 2025
ORCID ID:http://orcid.org/0000-0001-9235-513X
https://doi.org/10.33192/smj.v77i10.274468

ABSTRACT

Objective: Postoperative reintubation after planned extubation (PRAP) is a complication following general anesthesia. This study aimed to determine the incidence, risk factors, and outcomes in a tertiary-care university hospital.

Materials and Methods: A retrospective case-control study was conducted between 2014 and 2022. The PRAP group included patients requiring reintubation within 2 h after planned extubation following general anesthesia, while the control group included patients who did not require reintubation. Cases and controls were matched in a 1:3 ratio, with time-matched controls randomly selected within 2 weeks. Descriptive statistics and logistic regression were utilized for analysis.

Results: Of 139,103 patients, 88 PRAP cases were identified, yielding an incidence of 0.06% (95% Confidence Interval [CI], 0.05–0.08). Multivariate analysis revealed independent risk factors associated with PRAP: the American Society of Anesthesiologists Physical Status (ASA) ≥ III (adjusted odds ratio [aOR], 2.72; 95% CI, 1.58–4.66; $P < 0.001$), hemoglobin < 12 g/dL (aOR, 1.76; 95% CI, 1.02–3.01; $P = 0.041$), creatinine clearance < 60 mL/min (aOR, 3.38; 95% CI, 2.16–5.30; $P < 0.001$), and chronic obstructive pulmonary disease (COPD) (aOR, 18.73; 95% CI, 1.60–219.22; $P = 0.020$). PRAP was associated with increased 30-day mortality, cardiac arrest, and prolonged length of hospital and intensive care unit stay (all, $P < 0.001$).

Conclusion: The incidence of PRAP was 0.06%. Independent risk factors associated with PRAP were ASA, hemoglobin, creatinine clearance, and COPD. PRAP is associated with adverse postoperative outcomes, highlighting the need for preventive strategies and careful perioperative management.

Keywords: Anesthesia complication; extubation; mortality; postoperative complication; postoperative reintubation; risk factors (Siriraj Med J 2025; 77: 695-706)

INTRODUCTION

Postoperative reintubation after planned extubation (PRAP) is a severe complication of general anesthesia involving endotracheal intubation. PRAP is associated with significantly higher rates of postoperative complications—such as cardiac and pulmonary complications, prolonged hospital stays, and increased mortality.[1-3] Despite established extubation protocols and preventive strategies, PRAP remains a persistent issue.[4]

Reported PRAP incidence rates vary widely, ranging from 0.06% to 14.8%.[5-11] This variability may stem from differences in study populations and definitions of PRAP. While some studies define PRAP occurrences within the post-anesthesia care unit (PACU),[5-7,10,11] others consider later events in surgical wards.[8,9] In Thailand, two-decade-old studies reported PRAP incidences of 0.14% and 0.27% in PACU settings,[7,10] but these findings may not reflect current anesthesia practices. Updated data on PRAP incidence is crucial, as it serves as an indicator of anesthesia service quality and aligns with patient safety goals.[12]

Several risk factors for PRAP have been identified, including extreme age, chronic obstructive pulmonary disease (COPD), prolonged surgical duration, a higher American Society of Anesthesiologists (ASA) physical status, and the use of certain neuromuscular blocking agents.[13] However, findings vary across studies, likely due to differences in patient populations, surgical types, and institutional practices. Furthermore, most of these identified risk factors are non-modifiable, either patient-related or surgery-related. Understanding the risk factors within a specific institution and exploring potentially modifiable anesthesia-related factors is crucial for optimizing perioperative care and anesthetic management to reduce the occurrence of PRAP.[14]

This study aimed to evaluate the incidence of PRAP in a tertiary-care university hospital in Thailand. Additionally, it aimed to identify associated risk factors for and adverse outcomes. The focus was on immediate PRAP occurring within the first two postoperative hours, as such events are typically related to anesthetic management.[15] While PRAP may also occur later during hospitalization, these later cases are often influenced by factors unrelated to anesthesia.[9,16] The study sought to explore modifiable anesthesia-related risk factors that could be implemented in future anesthesia practices to reduce the occurrence of PRAP.

MATERIALS AND METHODS

A retrospective case-control study was conducted at Siriraj Hospital, a tertiary-care center in Bangkok, Thailand. The study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines and was approved by the Siriraj

Institutional Review Board (COA no. Si 621/2022). Informed consent was not required due to the retrospective nature and anonymization of data. Data was extracted from electronic records spanning January 1, 2014, and August 24, 2022.

Study participants

This study included adult patients aged ≥ 18 yr undergoing any types of surgery under general anesthesia with endotracheal intubation. The total number of these patients during the study period was obtained from the anesthesiology department's records. Anesthetic records at the study site comprised three components: preoperative, intraoperative, and postoperative data. Reintubation events were retrieved through the Anesthesiology's department postoperative dataset and considered as potential PRAP cases. PRAP was defined as reintubation occurring within 2 h following planned extubation. All potential PRAP cases were reviewed by anesthesiologists to exclude patients who were intubated before surgery, remained intubated postoperatively, had tracheostomies, or experienced accidental extubation. For the control group, patients who underwent postoperative extubation without reintubation were included. Cases and controls were matched at a 1:3 ratio, with controls randomly selected and time-matched within 2 weeks to minimize potential bias from temporal changes. Exclusion criteria for controls were similar to the cases. Anesthesiologists reviewed electronic medical records for both groups to collect data on preoperative, intraoperative, and anesthetic-related risk factors and postoperative outcomes.

Definitions of the variables

Preoperative variables included demographics (age, sex, and body mass index [BMI]), ASA physical status[17], comorbidities, and laboratory results. Respiratory conditions included COPD, asthma, obstructive sleep apnea, pleural effusion, and current smoking (defined as active smoking or cessation within 6 weeks before surgery). Recent pneumonia (within 30 days) and recent upper respiratory tract infections, characterized by symptoms such as cough, rhinorrhea, or sore throat within 2 weeks, were recorded.[18] Preoperative desaturation was defined as oxygen saturation < 95% on room air.[19] Cardiovascular conditions included congestive heart failure (CHF)[20] and myocardial infarction (MI).[21] Renal diseases encompass chronic kidney disease (CKD) and end-stage renal disease.[22] Central nervous system disorders included dementia, neuromuscular diseases, and altered consciousness (Glasgow Coma Score < 15). Hepatic disorders included ascites and cirrhosis. Systemic inflammatory response syndrome (SIRS), sepsis, and septic shock were noted.[23] Hematologic risk factors included bleeding disorders and recent blood transfusions (within 72 h before surgery). Laboratory parameters included preoperative serum creatinine, creatinine clearance, hemoglobin, white blood cell (WBC) count, and serum albumin levels. Elevated WBC or leukocytosis was classified when WBC count was ≥ 11,000 cells/μL.[24]

Operative variables included emergency surgery, operative duration, and surgical type (head and neck, airway, thoracic, cardiac, vascular, abdominal, orthopedic, neurosurgical, urological, and obstetric/gynecologic).

Anesthetic variables included the type and dosage of the last neuromuscular blocking agent (NMBA) and opioid, the reversal agent used, and the intervals between the last administration of NMBA or opioid and reversal. At our institution, atracurium, cisatracurium, and rocuronium are the primary NMBAs, with a typical clinical duration of 30–45 minutes.[25] Since neuromuscular blockade monitoring is not routinely used, reversal agents are administered based on clinical signs of recovery and the elapsed time since the last NMBA dose. For this study, early reversal was defined as the administration of a reversal agent within 45 minutes of the last NMBA dose.[26,27] We recognize that multiple factors, such as dose, duration, and renal clearance, influence the clinical duration of opioids, which in turn affect postoperative respiratory function and the risk of PRAP. To standardize our analysis, we applied a 45-minute cutoff for the last opioid dose before NMBA reversal.[27] Although this approach does not account for individual pharmacokinetic and pharmacodynamic variations, it provides a consistent reference for evaluating potential associations between opioid administration timing and PRAP.

Postoperative outcomes included 30-day mortality, cardiac arrest, hospital length of stay, intensive care unit (ICU) length of stay, and postoperative complications, such as pulmonary complications (pneumonia[28], mechanical ventilation > 48 h, and tracheostomy), cardiac complications (MI[29] and CHF[20]), renal complications (acute renal failure[30] and urinary tract infection[31]), neurologic complications (cerebrovascular accidents), thromboembolic events (deep vein thrombosis and pulmonary embolism), infections (wound infections[32], SIRS, sepsis, and septic shock[23]), and blood transfusions.

Sample size calculation

The primary outcome of PRAP incidence was used for sample size calculation. Based on a reported PRAP incidence of 0.14%[7] and using a two-sided significance level of 0.05 (type I error) and 90% power (type II error

= 10%), the minimum required sample size was 65,640 patients. An additional 10% was included to account for data loss.

For risk factor analysis, the sample size followed the rule of 10 events per variable. Based on seven previously identified risk factors,[5,6,33] the case group required at least 70 cases. Using a 3:1 control-to-case ratio, the final sample comprised 70 cases and 210 controls.

Statistical analysis

Patients were divided into PRAP and control groups. Continuous variables were presented as mean ± standard deviation or median (interquartile range [IQR]), depending on the data distribution, while categorical variables were reported as frequency (percentage). The Shapiro-Wilk test was used to assess the normality of continuous data. Univariable analysis was conducted to compare preoperative, intraoperative, anesthetic, and outcome variables. Continuous variables were compared using the Student's t test or Mann–Whitney U test depending on the distribution of data, while categorical variables were analyzed using the chi-square test or Fisher's exact test. Univariable logistic regression was conducted to estimate odds ratios for each variable. Pairwise exclusion was applied, whereby cases with missing data for a given variable were excluded only from the analysis of that specific variable. Variables with p values < 0.1 in univariable analysis were included in a stepwise backward multivariable logistic regression model to identify independent risk factors for PRAP. Collinearity was assessed using Variance Inflation Factor (VIF) and a correlation matrix, and only non-collinear variables were included in the model. A P value <0.05 was considered statistically significant. Data analysis was performed using Stata® statistics version 14 (StataCorp, College Station, Texas, USA).

RESULTS

Among 139,103 patients undergoing general anesthesia with endotracheal intubation at Siriraj Hospital between January 1, 2014, and August 24, 2022, 88 PRAP cases were identified, yielding an incidence rate of 0.06% (95% Confidence Interval [CI], 0.05–0.08). The control group comprised 264 randomly selected patients without PRAP. Fig 1 illustrates the study flow.

Univariable analysis revealed several preoperative risk factors for PRAP, including ASA physical status ≥ III, recent pneumonia, desaturation, CKD, altered consciousness, neuromuscular disease, cirrhosis, SIRS/sepsis, recent blood transfusions, creatinine clearance < 60 mL/min, hemoglobin < 12 g/dL, and WBC ≥ 11,000 cells/μL (Table 1). Intraoperative risk factors included emergency surgery, cardiovascular/thoracic surgery, neurosurgery, use of steroidal NMBAs, and time from last opioid administration to reversal < 45 min (Table 2). Multivariable analysis identified ASA physical status ≥ III, COPD, creatinine clearance < 60 mL/min, and hemoglobin < 12 g/dL as independent risk factors for PRAP (Table 3).

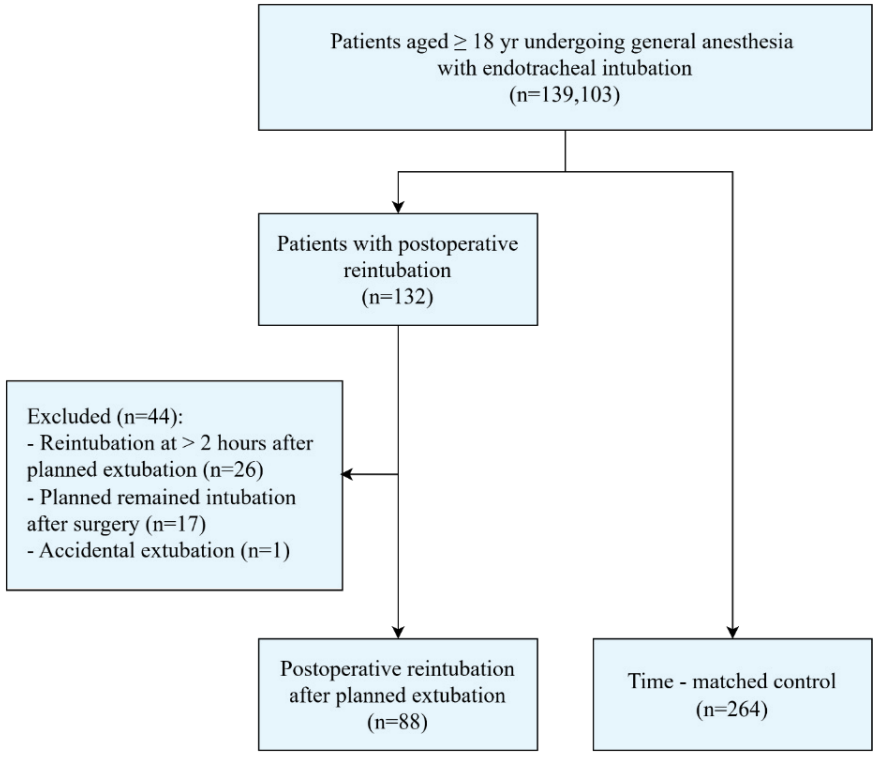


Fig 1. Study flow diagram.

TABLE 1. Univariate analysis of preoperative risk factors associated with postoperative reintubation after planned extubation (n = 352).

Variables	PRAP (n=88)	Control (n=264)	Crude OR (95% CI)	*P*-value
Demographic data				
Age, year, mean ± SD	62 ± 16	55 ± 19	-	**0.003**
< 65, n (%)	49 (55.7%)	184 (69.7%)	Reference	
≥ 65, n (%)	39 (44.3%)	80 (30.3%)	1.83 (1.11–3.01)	**0.017**
Gender (male), n (%)	46 (52.3%)	107 (40.5%)	1.61 (0.99–2.61)	0.055
ASA, n (%)				
I-II	38 (43.2%)	193 (73.1%)	Reference	
≥ III	50 (56.8%)	71 (26.9%)	3.58 (2.17–5.91)	**< 0.001**
BMI, kg/m^2, mean ± SD	23.5 ± 5.2	23.6 ± 5.1	1.00 (0.95–1.04)	0.851
Comorbidities, n (%)				
COPD	4 (4.5%)	3 (1.1%)	4.14 (0.91–18.89)	0.066
Asthma	4 (4.5%)	4 (1.5%)	3.10 (0.75–12.65)	0.116
OSA	1 (1.1%)	9 (3.4%)	0.33 (0.04–2.61)	0.291
Pleural effusion	8 (9.1%)	1 (0.4%)	26.30 (3.24–213.46)	**0.002**
Recent pneumonia	5 (5.7%)	1 (0.4%)	15.84 (1.83–137.54)	0.012
URI	2 (2.3%)	4 (1.5%)	1.51 (0.27–8.40)	0.637
Desaturation	8 (9.1%)	3 (1.1%)	8.70 (2.25–33.57)	**0.002**
Smoker	7 (8.0%)	8 (3.0%)	2.77 (0.97–7.86)	0.056
CHF	2 (2.3%)	4 (1.5%)	1.51 (0.27–8.40)	0.637
MI	6 (6.8%)	22 (8.3%)	0.8 (0.32–2.05)	0.650
CKD	14 (15.9%)	9 (3.4%)	5.36 (2.23–12.88)	**< 0.001**
ESRD	4 (4.5%)	6 (2.3%)	2.05 (0.56–7.43)	0.276
Dementia	4 (4.5%)	4 (1.5%)	3.1 (0.76–12.65)	0.116
GCS < 15	10 (11.4%)	1 (0.4%)	33.72 (4.25–267.5)	**0.001**
Neuromuscular disease	4 (4.5%)	1 (0.4%)	12.52 (1.38–113.6)	**0.025**
Cirrhosis	6 (6.8%)	4 (1.5%)	4.76 (1.31–17.27)	**0.018**
Ascites	2 (2.3%)	1 (0.4%)	6.12 (0.55–68.29)	0.141
SIRS/Sepsis	17 (19.3%)	16 (6.1%)	3.71 (1.79–7.72)	**< 0.001**
Septic shock	1 (1.1%)	2 (0.8%)	1.51 (0.13–16.8)	0.740
Recent blood transfusion	12 (13.6%)	15 (5.7%)	2.62 (1.18–5.84)	**0.018**
Laboratory values, n (%)				
Creatinine clearance (mL/min)				
≥ 60	47 (53.4%)	182 (68.9%)	Reference	
< 60	41 (46.6%)	70 (26.5%)	2.27 (1.37–3.74)	**0.001**
No test	0 (0.0%)	12 (4.5%)		

TABLE 1. Univariate analysis of preoperative risk factors associated with postoperative reintubation after planned extubation (n = 352). (Continue)

Variables	PRAP (n=88)	Control (n=264)	Crude OR (95% CI)	*P*-value
Hemoglobin (g/dL)				
≥ 12	42 (47.7%)	165 (62.5%)	Reference	
< 12	46 (52.3%)	96 (36.4%)	1.67 (1.05–2.66)	**0.031**
No test	0 (0.0%)	3 (1.1%)		
WBC count (cells/μL)				
< 11,000	63 (71.6%)	216 (81.8%)	Reference	
≥ 11,000	25 (28.4%)	45 (17.0%)	1.9 (1.08–3.35)	**0.025**
No test	0 (0.0%)	3 (1.1%)		
Serum albumin (g/dL)				
≥ 4	15 (17.0%)	28 (10.6%)	Reference	
< 4	51 (58.0%)	56 (21.2%)	1.7 (0.82–3.54)	0.156
No test	22 (25.0%)	180 (68.2%)		

P values < 0.05 indicate the statistical significance of the crude odds ratios.

Abbreviations: 95% CI, 95% Confidence Interval; ASA, ASA physical status; BMI, body mass index; CHF, congestive heart failure; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ESRD, end-stage renal disease; GCS, Glasgow Coma Scale; MI, myocardial infarction; OR, odds ratio; OSA, obstructive sleep apnea; PRAP, postoperative reintubation after planned extubation; SIRS, systemic inflammatory response syndrome; URI, upper respiratory tract infection; WBC, white blood cell.

TABLE 2. Univariate analysis of operative and anesthetic risk factors associated with postoperative reintubation after planned extubation (n = 352).

Variables	PRAP (n=88)	Control (n=264)	Crude OR (95% CI)	*P*-value
Type of surgery, n (%)				
Head and Neck	12 (13.6%)	33 (12.5%)	Reference	
Airway	0 (0.0%)	22 (8.3%)	NA†	
Cardiothoracic	10 (11.4%)	6 (2.3%)	4.58 (1.37–15.35)	**0.014**
Vascular	2 (2.3%)	3 (1.1%)	1.83 (0.27–12.35)	0.533
Abdominal	12 (13.6%)	41 (15.5%)	0.8 (0.32–2.02)	0.645
Orthopedic	8 (9.1%)	36 (13.6%)	0.61 (0.22–1.68)	0.340
Neurologic	15 (17.0%)	11 (4.2%)	3.75 (1.35–10.41)	**0.011**
Urological	8 (9.1%)	18 (6.8%)	1.22 (0.42–3.54)	0.711
Obstetric and gynecologic	3 (3.4%)	25 (9.5%)	0.33 (0.08–1.3)	0.112
Others	18 (20.5%)	69 (26.1%)	0.72 (0.31–1.66)	0.438

TABLE 2. Univariate analysis of operative and anesthetic risk factors associated with postoperative reintubation after planned extubation (n = 352). (Continue)

Variables	PRAP (n=88)	Control (n=264)	Crude OR (95% CI)	*P*-value
Emergency surgery, n (%)	24 (27.3%)	46 (17.4%)	1.78 (0.05–1.01)	**0.047**
Duration of operation, n (%)				
< 1 hour	30 (34.1%)	81 (30.7%)	Reference	
1–3 hours	41 (46.6%)	133 (50.4%)	0.83 (0.48–1.44)	0.510
> 3 hours	17 (19.3%)	50 (18.9%)	0.92 (0.24–0.56)	0.808
Last NMBA, n (%)				
None/Succinylcholine	3 (3.4%)	12 (4.5%)	Reference	
Benzylisoquinoline (Atra/Cis)	71 (80.7%)	246 (93.2%)	1.15 (0.32–4.2)	0.828
Steroidal (Roc/Pan/Vec)	14 (15.9%)	6 (2.3%)	9.33 (1.91–45.58)	**0.006**
Last opioid, n (%)				
No opioid	1 (1.1%)	1 (0.4%)	Reference	
Fentanyl	65 (73.9%)	147 (55.7%)	0.44 (0.03–7.18)	0.566
Morphine	19 (21.6%)	114 (43.2%)	0.17 (0.01–2.78)	0.212
Meperidine	3 (3.4%)	2 (0.8%)	1.5 (0.06–40.63)	0.560
Time from last NMBA administration to reversal, n (%)				
No reversal	37 (42.0%)	114 (43.2%)	Reference	
< 45 mins	46 (52.3%)	130 (49.2%)	1.09 (0.66–1.80)	0.735
≥ 45 mins	5 (5.7%)	15 (5.7%)	1.03 (0.35–3.02)	0.961
Missing	0 (0.0%)	5 (1.9%)		
Time from last opioid administration to reversal, n (%)				
No reversal	18 (20.7%)	93 (35.4%)	Reference	
< 45 mins	64 (73.6%)	150 (57.0%)	2.20 (1.23–3.95)	**0.008**
≥ 45 mins	5 (5.7%)	15 (5.7%)	1.72 (0.56–5.34)	0.346
Missing	0 (0.0%)	5 (1.9%)		

P values < 0.05 indicate the statistical significance of the crude odds ratios.

† The odds ratio could not be calculated because no event occurred in the PRAP group.

Abbreviations: 95% CI, 95% Confidence Interval; Atra, atracurium; Cis, cisatracurium; NMBA, neuromuscular blocking agent; OR, odds ratio; Pan, pancuronium; PRAP, postoperative reintubation after planned extubation; Roc, rocuronium; Vec, vecuronium.

Patients with PRAP experienced significantly longer hospital and ICU stays, higher mortality rates, and an increased incidence of cardiac arrest. Additionally, PRAP was associated with a greater frequency of postoperative complications and blood transfusions. Detailed comparisons of postoperative outcomes between the PRAP and control groups are presented in Table 4.

TABLE 3. Final multivariable regression model showing risk factors associated with postoperative reintubation after planned extubation.

Variables	Adjusted OR (95% CI)	*P* value
ASA ≥ III	2.72 (1.58–4.66)	< 0.001
COPD	18.73 (1.60–219.22)	0.020
Creatinine clearance < 60 mL/min	3.38 (2.16–5.3)	< 0.001
Hemoglobin < 12 g/dL	1.76 (1.02–3.01)	0.041

P values < 0.05 indicate the statistical significance of the adjusted odds ratios.
Abbreviations: ASA, ASA physical status; COPD, chronic obstructive pulmonary disease; OR, odds ratio; PRAP, postoperative reintubation after planned extubation; WBC, white blood cell.

TABLE 4. Postoperative outcomes of the PRAP and the control groups (n = 352).

Postoperative outcomes	PRAP (n = 88)	Control (n = 264)	*P*-value
Length of hospital stay, day, median [IQR]	12.5 [7.5–22.0]	5.0 [3.0–10.0]	**< 0.001**
Length of ICU stay, day, median [IQR]	3.0 [0.0–6.0]	0.0 [0.0–0.0]	**< 0.001**
30-day mortality, n (%)	7 (8.0%)	4 (1.5%)	**0.007**
Cardiac arrest, n (%)	10 (11.4%)	3 (1.1%)	**< 0.001**
Blood transfusion, n (%)	38 (43.2%)	36 (13.6%)	**< 0.001**
Pulmonary complications, n (%)			
Pneumonia	12 (13.6%)	7 (2.7%)	**< 0.001**
On ventilator > 48 hour	38 (43.2%)	6 (2.3%)	**< 0.001**
Tracheostomy	5 (5.7%)	0 (0.0%)	**< 0.001**
Cardiac complications, n (%)			
Myocardial infarction	2 (2.3%)	2 (0.8%)	0.261
Heart failure	6 (6.8%)	0 (0.0%)	**< 0.001**
Renal complications, n (%)			
Acute renal failure	17 (19.3%)	10 (3.8%)	**< 0.001**
Urinary tract infection	10 (11.4%)	9 (3.4%)	**0.011**
Neurological complications, n (%)			
Cerebrovascular accident	4 (4.5%)	2 (0.8%)	**0.036**
Thromboembolic complications, n (%)			
Deep vein thrombosis	1 (1.1%)	1 (0.4%)	0.438
Pulmonary embolism	1 (1.1%)	1 (0.4%)	0.438
Infectious complications, n (%)			
Wound infection	1 (1.1%)	13 (4.9%)	0.204
SIRS/Sepsis	23 (26.1%)	20 (7.6%)	**< 0.001**
Septic shock	13 (14.8%)	7 (2.7%)	**< 0.001**

P values < 0.05 indicate the significance of the difference between the PRAP and control groups.
Abbreviations: ICU, intensive care unit; IQR, interquartile range; OR, odds ratio; PRAP, postoperative reintubation after planned extubation; SIRS, systemic inflammatory response syndrome. Postoperative outcomes were expressed as frequency (percentage) unless otherwise specified.

DISCUSSION

This study identified an incidence of PRAP of 0.06 % at Siriraj Hospital. Independent risk factors for PRAP included ASA physical status ≥ III, COPD, preoperative creatinine clearance < 60 mL/min, and hemoglobin < 12 g/dL. Furthermore, PRAP was significantly correlated with increased postoperative morbidity and mortality.

The observed PRAP incidence aligns with some previous studies[5,6,11]; however, it was lower than rates reported in Thailand two decades ago.[7,10] This reduction may reflect advancements in identifying patients requiring postoperative airway protection or positive pressure ventilation, leading to increased rates of postoperative intubation in high-risk cases. Changes in anesthetic practices, such as the greater adoption of short-acting anesthetic agents and neuromuscular blockade monitoring, likely contributed to this trend.[34,35] Improvements in surgical techniques may also be relevant; notably, none of the PRAP patients in this study underwent airway surgery, a procedure traditionally linked to higher risks of airway obstruction during extubation.[4]

Our findings differ from those of a previous study on patients undergoing elective intracranial surgery, which reported a higher incidence of PRAP.[8] This discrepancy may be explained by the high prevalence of consciousness disturbances in that patient population. Similarly, a prior study on orthotopic liver transplantation reported a significantly higher PRAP incidence than observed in our study.[9] This difference could be attributed to the inclusion of all reintubations occurring throughout the postoperative hospitalization period in the earlier study, thereby capturing PRAP cases related to later surgical and medical complications. Additionally, the higher PRAP incidence in liver transplant patients may reflect their greater burden of comorbidities and the increased surgical complexity associated with the procedure.

Our findings revealed that preoperative risk factors were the sole contributors to PRAP. ASA physical status ≥ III emerged as an independent risk factor, aligning with previous studies.[13] The ASA physical status classification system is a widely recognized tool for assessing preoperative comorbidities and has been shown to correlate with postoperative morbidity and mortality.[36] Despite its subjective nature and lack of surgical specificity, the ASA classification system remains valuable in predicting PRAP.[37]

COPD was also identified as a significant risk factor for PRAP. COPD is a chronic respiratory condition characterized by excessive mucus production and airway hyper-reactivity, which can result in postoperative airway obstruction, thus necessitating reintubation.[38] Notably, COPD is included under ASA physical status III.[17] Preoperative optimization strategies, such as bronchodilator and corticosteroid use and addressing modifiable factors like recent exacerbations, may reduce this risk.[39] Intraoperative management, including avoiding bronchospasm-inducing drugs and favoring bronchodilators, also mitigates risk.[38] Regional anesthesia can be considered for some procedures to minimize airway manipulation and the associated risks of endotracheal intubation.[40]

Preoperative low creatinine clearance and anemia were additional independent risk factors for PRAP, consistent with prior findings.[1,41] Impaired renal functions may alter drug metabolism, leading to the accumulation of renally excreted anesthetic agents, such as morphine and meperidine, thereby prolonging their effects.[42] Although a creatinine clearance < 60 mL/min is classified as early-stage CKD, it significantly increased PRAP risk in this study.[22] Anemia, by reducing oxygen delivery, can lead to hypoxemia and respiratory failure, necessitating reintubation and mechanical ventilation.[43] Given the high prevalence of preoperative anemia and its association with adverse outcomes,[44] identifying and addressing anemia preoperatively is essential.

Conversely, intraoperative and anesthetic factors were not significantly associated with PRAP in our multivariable regression model. Procedures such as airway, head and neck, and thoracic surgeries—previously identified as significant PRAP risk factors[6,7]—were not significant in this study. This discrepancy may reflect the high quality of surgical and anesthetic practices at our institution, delivered at our high-volume, tertiary care university hospital by experienced providers. Effective perioperative communication, multidisciplinary collaboration, and the adoption of a lower threshold for delaying extubation in high-risk patients may have contributed to this finding. Additionally, the use of steroidal NMBAs was not associated with PRAP, in contrast to findings from previous studies,[45,46] likely due to their infrequent use at our facility (5.7% of total study participants). Residual neuromuscular blockade is recognized as a contributor to postoperative reintubation.[47] However, neuromuscular monitoring was not routinely implemented at our institution; therefore, we lacked objective data on the degree of neuromuscular recovery before extubation. To address this limitation, we used the early reversal as a proxy indicator. This approach was based on prior literature suggesting that premature administration of reversal agents may reduce their predictability, potentially leading to residual blockade.[47] In our analysis, this timing variable was not significantly associated with PRAP. However, we acknowledge the limitation of using timing alone, as it

does not account for interindividual variability in drug metabolism and sensitivity, nor does it reflect whether adequate neuromuscular function was achieved prior to extubation.

The negative postoperative outcomes linked to PRAP, including higher mortality and increased postoperative complications, align with existing literature.[1-3] Endotracheal intubation increases the risk of hemodynamic instability such as hypertension and pulmonary complications such as hypoxia.[48] Additionally, reintubation presents a greater risk of difficult airway management and airway injury, as patients may develop airway edema due to prior intubation, intraoperative fluid resuscitation, or prolonged surgical positioning, such as the prone position.[49,50] These risks underscore the need for effective perioperative strategies to prevent PRAP.[1,2] Identifying high-risk patients along with addressing modifiable risk factors may help reduce PRAP incidence. In selected cases, delaying extubation to allow for hemodynamic stabilization or respiratory weaning may be a safer alternative.[4,51] However, the interpretation of these results should be approached with caution, as critical confounding factors—such as patient age, comorbidities, and surgical type—were not adjusted for in this analysis. Older age, a higher prevalence of comorbidities, and differences in surgical procedures may also contribute to the observed variations in postoperative outcomes between the PRAP and the control group.

Strengths and limitations

This study has notable strengths. First, it included patients undergoing diverse surgical procedures, enhancing the generalizability of the findings. Comprehensive data on preoperative, intraoperative, and anesthetic risk factors were collected, and time-matched control selection minimized potential biases arising from temporal changes in clinical practices. The use of multivariable regression analysis strengthened the reliability of the results. Additionally, the study evaluated postoperative outcomes associated with PRAP, providing a complete picture of the perioperative trajectory. Our findings confirm the significance of preoperative factors on the occurrence of PRAP, thus underscoring the importance of preoperative optimization, such as the optimal control of COPD and the correction of preoperative anemia. Future research is warranted to determine the effectiveness and magnitude of these strategies in reducing PRAP incidence and improving postoperative outcomes. Moreover, the identified risk factors can help perioperative healthcare professionals assess the necessity of delayed extubation in high-risk patients.

However, the study also has limitations. First, some preoperative laboratory test data were missing, particularly for younger and healthier patients, which may have introduced bias.[52] Second, the clinical indications for reintubation were not explored, limiting the understanding and the critical assessment of the decision-making process underlying reintubation. Thirdly, the absence of routine neuromuscular monitoring in our institution limited the ability to objectively assess residual neuromuscular blockade, which could be a contributing factor to PRAP. Lastly, the retrospective study design precludes causal inferences, and the findings should therefore be interpreted with caution.

CONCLUSION

The incidence of PRAP in this study was 0.06%. Independent risk factors for PRAP included ASA physical status ≥ III, COPD, creatinine clearance < 60 mL/min, and hemoglobin < 12 g/dL. PRAP was significantly associated with adverse postoperative outcomes, underscoring the need for preventive strategies and careful perioperative management.

Data Availability Statement

The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.

ACKNOWLEDGMENTS

The authors thank Chusana Rungjindamai, Research Assistant, Department of Anesthesiology, for her assistance in summarizing the documents. The authors also extend their thanks to Dr. Orawan Suppapueng, Faculty of Medicine Siriraj Hospital, Division of Clinical Epidemiology, Department of Research, Mahidol University, for conducting statistical analyses.

DECLARATIONS

Grants and Funding Information

This research project is supported by Siriraj research development fund, Grant number (IO) R016531078, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand. The funders had no role in study design, data collection, and analysis, decision to publish, or preparation of the manuscript.

Conflict of Interest

The authors declared no conflict of interest.

Registration Number of Clinical Trial

Not applicable.

Author Contributions

Conceptualization and methodology, P.N., M.D., A.S., and W.V.; Investigation, P.N. and M.D.; Formal analysis, M.D. and W.V.; Visualization and writing – original draft, M.D.; Writing – review and editing, W.V. and A.S.; Funding acquisition, P.N. and A.S.; Supervision, A.S. All authors have read and agreed to the final version of the manuscript.

Use of Artificial Intelligence

Not applicable.

REFERENCES

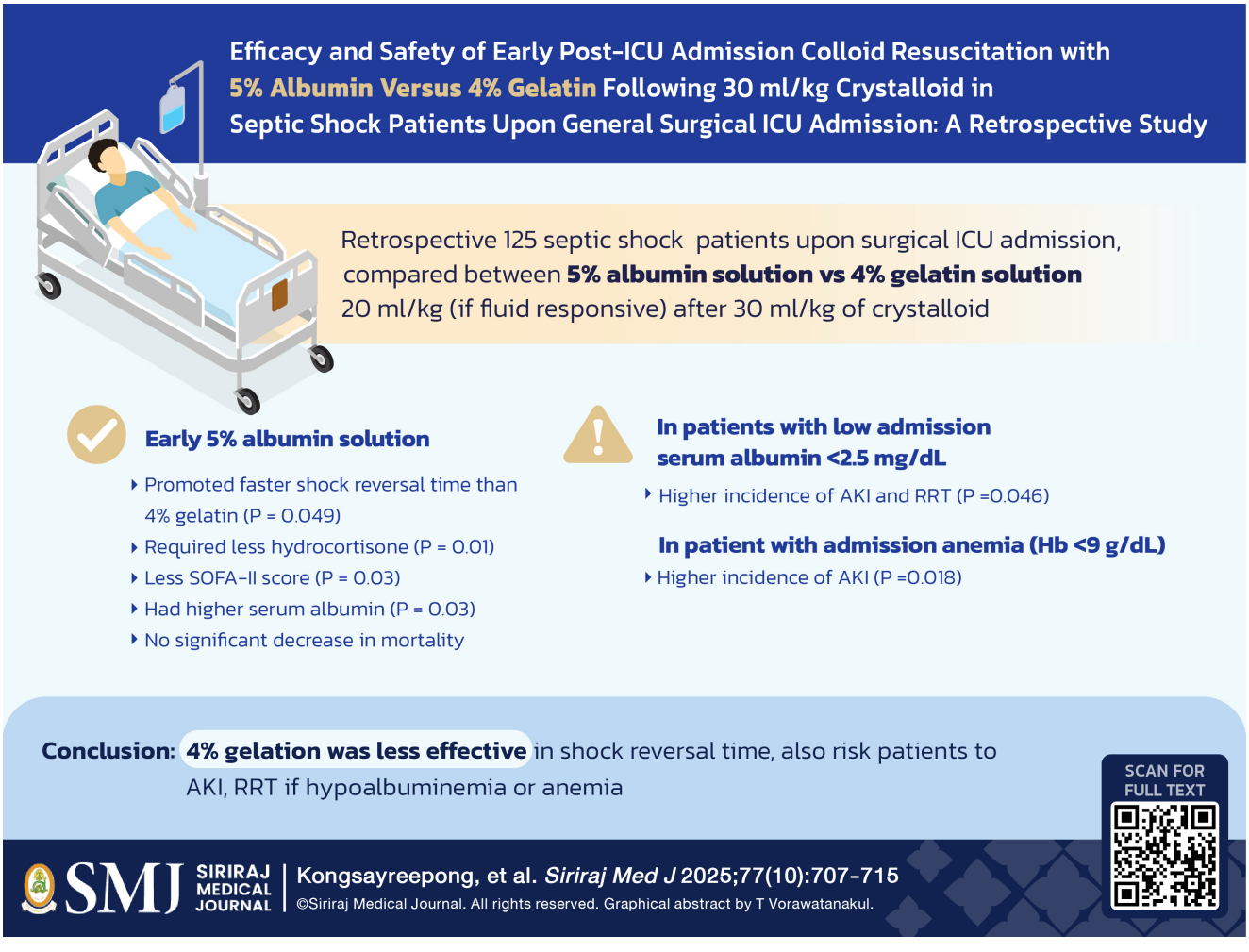
1. Acheampong D, Guerrier S, Lavarias V, Pechman D, Mills C, Inabnet W, et al. Unplanned postoperative reintubation following general and vascular surgical procedures: Outcomes and risk factors. Ann Med Surg (Lond). 2018;33:40-3.
2. Liu S, Dong Y, Wan L, Luo A, Chen H, Xu H. Incidence and outcome of reintubation in the postanesthesia care unit: A single-center, retrospective, observational matched cohort study in China. J Perianesth Nurs. 2023;38(6):912-7.e1.
3. Ramachandran SK, Nafiu OO, Ghaferi A, Tremper KK, Shanks A, Kheterpal S. Independent predictors and outcomes of unanticipated early postoperative tracheal intubation after nonemergent, noncardiac surgery. Anesthesiology. 2011;115(1):44-53.
4. Benham-Hermetz J, Mitchell V. Safe tracheal extubation after general anaesthesia. BJA Educ. 2021;21(12):446-54.
5. Ting PC, Chou AH, Yang MW, Ho AC, Chang CJ, Chang SC. Postoperative reintubation after planned extubation: a review of 137,866 general anesthetics from 2005 to 2007 in a Medical Center of Taiwan. Acta Anaesthesiol Taiwan. 2010;48(4):167-71.
6. Tillquist MN, Gabriel RA. Incidence and risk factor for early postoperative reintubation. J Clin Anesth. 2016;31:80-9.
7. Rujirojindakul P, Geater AF, Mcneil EB, Vasinanukorn P, Prathep S, Asim W, et al. Risk factors for reintubation in the post-anaesthetic care unit: a case-control study. Br J Anaesth. 2012;109(4):636-42.
8. Hayashi LY, Gazzotti MR, Vidotto MC, Jardim JR. Incidence, indication and complications of postoperative reintubation after elective intracranial surgery. Sao Paulo Med J. 2013;131(3):158-65.
9. Glanemann M, Kaisers U, Langrehr JM, Schenk R, Stange BJ, Muller AR, et al. Incidence and indications for reintubation during postoperative care following orthotopic liver transplantation. J Clin Anesth. 2001;13(5):377-82.
10. Chinachoti T, Chau-In W, Suraseranivongse S, Kitsampanwong W, Kongrit P. Postoperative reintubation after planned extubation in Thai Anesthesia Incidents Study (THAI Study). J Med Assoc Thai. 2005;88 Suppl 7:S84-94.
11. Banik RK, Honeyfield K, Qureshi S, Reddy SG. Incidence and mortality rate of perioperative reintubation: Case series of 196 patients. Aana J. 2021;89(6):476-9.
12. Ramsay DP, Quinn P, Gin V, Starkie TD, Fry RA, Grummitt S. National quality improvement indicators project: an initial descriptive study. Anaesth Intensive Care. 2021;49(6):455-67.
13. Xie Z, Liu J, Yang Z, Tang L, Wang S, Du Y, et al. Risk factors for post-operative planned reintubation in patients after general anesthesia: a systematic review and meta-analysis. Front Med (Lausanne). 2022;9:839070.
14. Popat M, Mitchell V, Dravid R, Patel A, Swampillai C, Higgs A. Difficult Airway Society Guidelines for the management of tracheal extubation. Anaesthesia. 2012;67(3):318-40.
15. Sofjan I, Vazquez S, Dominguez J, Sekhri N, Wecksell M, Samuel BM, et al. Risk factors for postoperative unplanned reintubation in a cohort of patients undergoing general anesthesia. Cureus. 2023;15(5):e38949.
16. Marquez-Lara A, Nandyala SV, Fineberg SJ, Singh K. Incidence, outcomes, and mortality of reintubation after anterior cervical fusion. Spine (Phila Pa 1976). 2014;39(2):134-9.
17. American Society of Anesthesiologists. Statement on ASA Physical Status Classification System 2020 [cited 2023 December 29]. Available from: https://www.asahq.org/standards-and-practice-parameters/statement-on-asa-physical-status-classification-system.
18. Lee HJ, Woo JH, Cho S, Oh HW, Joo H, Baik HJ. Risk Factors for Perioperative Respiratory Adverse Events in Children with Recent Upper Respiratory Tract Infection: A Single-Center-Based Retrospective Study. Ther Clin Risk Manag. 2020;16:1227-34.
19. Hafen BB, Sharma S. Oxygen Saturation. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Available from: https://www.ncbi.nlm.nih.gov/books/NBK525974/.
20. Ho KKL, Pinsky JL, Kannel WB, Levy D. The epidemiology of heart failure: The Framingham Study. Journal of the American College of Cardiology. 1993;22(4, Supplement 1):A6-A13.
21. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth Universal Definition of Myocardial Infarction (2018). Circulation. 2018;138(20):e618-e51.
22. Cheung AK, Chang TI, Cushman WC, Furth SL, Hou FF, Ix JH, et al. KDIGO 2021 Clinical practice guideline for the management of blood pressure in chronic kidney disease. Kidney Int. 2021;99(3):S1-S87.
23. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801-10.
24. Widick P, Winer ES. Leukocytosis and Leukemia. Primary Care: Clinics in Office Practice. 2016;43(4):575-87.
25. Appiah-Ankam J, Hunter JM. Pharmacology of neuromuscular blocking drugs. Continuing Education in Anaesthesia Critical Care & Pain. 2004;4(1):2-7.
26. Santos FNC, Braga AdFdA, Ribeiro CJBdL, Braga FSdS, Carvalho VH, Junqueira FEF. Use of protocol and evaluation of postoperative residual curarization incidence in the absence of intraoperative acceleromyography – Randomized clinical trial. Brazilian Journal of Anesthesiology (English Edition). 2017;67(6):592-9.
27. Ting P-C, Chou A-H, Yang M-W, Ho AC-Y, Chang C-J, Chang S-C. Postoperative reintubation after planned extubation: A review of 137,866 general anesthetics from 2005 to 2007 in a Medical Center of Taiwan. Acta Anaesthesiologica Taiwanica. 2010;48(4):167-71.
28. Miskovic A, Lumb AB. Postoperative pulmonary complications. British Journal of Anaesthesia. 2017;118(3):317-34.
29. Ruetzler K, Smilowitz NR, Berger JS, Devereaux PJ, Maron BA, Newby LK, et al. Diagnosis and Management of Patients With Myocardial Injury After Noncardiac Surgery: A Scientific

Statement From the American Heart Association. Circulation. 2021;144(19):e287-e305.
30. Mehta RL, Kellum JA, Shah SV, Molitoris BA, Ronco C, Warnock DG, et al. Acute Kidney Injury Network: report of an initiative to improve outcomes in acute kidney injury. Critical Care. 2007;11(2):R31.
31. Rowe TA, Juthani-Mehta M. Diagnosis and management of urinary tract infection in older adults. Infect Dis Clin North Am. 2014;28(1):75-89.
32. Owens CD, Stoessel K. Surgical site infections: epidemiology, microbiology and prevention. Journal of Hospital Infection. 2008;70:3-10.
33. Chen S, Zhang Y, Che L, Shen L, Huang Y. Risk factors for unplanned reintubation caused by acute airway compromise after general anesthesia: a case-control study. BMC Anesthesiol. 2021;21(1):17.
34. Moon JS, Cannesson M. A century of technology in anesthesia & analgesia. Anesth Analg. 2022;135(2S Suppl 1):S48-S61.
35. Murphy GS, Brull SJ. Quantitative neuromuscular monitoring and postoperative outcomes: A narrative review. Anesthesiology. 2022;136(2):345-61.
36. Hackett NJ, De Oliveira GS, Jain UK, Kim JYS. ASA class is a reliable independent predictor of medical complications and mortality following surgery. Int J Surg. 2015;18:184-90.
37. Mayhew D, Mendonca V, Murthy BVS. A review of ASA physical status – historical perspectives and modern developments. Anaesthesia. 2019;74(3):373-9.
38. Duggappa DR, Rao GV, Kannan S. Anaesthesia for patient with chronic obstructive pulmonary disease. Indian J Anaesth. 2015;59(9):574-83.
39. Lee AHY, Snowden CP, Hopkinson NS, Pattinson KTS. Pre-operative optimisation for chronic obstructive pulmonary disease: a narrative review. Anaesthesia. 2021;76(5):681-94.
40. Khetarpal R, Bali K, Chatrath V, Bansal D. Anesthetic considerations in the patients of chronic obstructive pulmonary disease undergoing laparoscopic surgeries. Anesth Essays Res. 2016;10(1):7-12.
41. Riveros C, Ranganathan S, Shah YB, Huang E, Xu J, Hsu E, et al. Association of chronic kidney disease with postoperative outcomes: a national surgical quality improvement program (NSQIP) multi-specialty surgical cohort analysis. BMC Nephrol. 2024;25(1):305.
42. Chowdhury SR, Mclure HA. Chronic kidney disease and anaesthesia. BJA Educ. 2022;22(8):321-8.
43. Khamiees M, Raju P, Degirolamo A, Amoateng-Adjepong Y, Manthous CA. Predictors of extubation outcome in patients who have successfully completed a spontaneous breathing trial. Chest. 2001;120(4):1262-70.
44. Hawkins T, Agarwal S, Evans CR. Centre for Perioperative Care anaemia guideline: Implications for anaesthesia. Br J Anaesth. 2023;130(2):115-9.
45. Greco KM, Conti BM, Bucci CJ, Galvagno SM, Jr. Rocuronium is associated with an increased risk of reintubation in patients with soft tissue infections. J Clin Anesth. 2016;34:186-91.
46. Lin HT, Ting PC, Chang WY, Yang MW, Chang CJ, Chou AH. Predictive risk index and prognosis of postoperative reintubation after planned extubation during general anesthesia: a single-center retrospective case-controlled study in Taiwan from 2005 to 2009. Acta Anaesthesiol Taiwan. 2013;51(1):3-9.
47. Cammu G. Residual Neuromuscular Blockade and Postoperative Pulmonary Complications: What Does the Recent Evidence Demonstrate? Curr Anesthesiol Rep. 2020;10(2):131-6.
48. Russotto V, Myatra SN, Laffey JG, Tassistro E, Antolini L, Bauer P, et al. Intubation Practices and Adverse Peri-intubation Events in Critically Ill Patients From 29 Countries. JAMA. 2021;325(12):1164-72.
49. Higgs A, Mcgrath BA, Goddard C, Rangasami J, Suntharalingam G, Gale R, et al. Guidelines for the management of tracheal intubation in critically ill adults. Br J Anaesth. 2018;120(2):323-52.
50. Mantaga S, Thanakiattiwibun C, Siriussawakul A, Mantaga S, Asanathong N, Jiamjira-Anon N, et al. Incidence of Adverse Perioperative Airway Complications in Obese Non-Pregnant and Pregnant Patients Undergoing General Anesthesia. Siriraj Med J. 2022;74(3):178-84.
51. Pangthipampai P, Chinachoti T, Halilamien P, Jirativanont T, Nivatpumin P, Jalayanavin S, et al. Factors Contributing to Delayed Extubation After Cervical Spine Surgery in Siriraj Hospital. Siriraj Med J. 2020;63(4):123-7.
52. National Guideline Centre. Preoperative tests (update): Routine preoperative tests for elective surgery. 2016. London: National Institute for Health and Care Excellence (NICE).

Efficacy and Safety of Early Post-ICU Admission Colloid Resuscitation with 5% Albumin Versus 4% Gelatin Following 30 mL/kg Crystalloid in Septic Shock Patients Upon General Surgical ICU Admission: A Retrospective Study

Suneerat Kongsayreepong, M.D.[1,*], Nuntiya Phaetthayanan, M.D.[2], Surat Tongyoo, M.D.[3]

[1]Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [2]Division of Anesthesia, Nakhon Pathom Hospital, Nakhon Pathom, Thailand, [3]Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.



**Corresponding author: Suneerat Kongsayreepong*
E-mail: suneeratkong@gmail.com
Received 19 May 2025 Revised 19 August 2025 Accepted 19 August 2025
ORCID ID:http://orcid.org/0000-0003-1432-3006
https://doi.org/10.33192/smj.v77i10.275519

ABSTRACT

Objective: To compare the efficacy and safety of early post-ICU admission colloid resuscitation with 5% albumin versus 4% gelatin after 30 ml/kg crystalloid solution in septic shock patients upon general surgical ICU admission at Thailand's largest tertiary reference center.

Materials and Methods: This retrospective study included 125 adults with septic shock admitted to the ICU (September 2017-July 2018). After 30 mL/kg crystalloid, patients received 20 mL/kg of either 4% gelatin (Group G) or 5% albumin (Group A) if fluid responsive. The main efficacy was time to vasopressor discontinuation, and the main safety outcome was the incidence of acute kidney injury (AKI) per KDIGO criteria, within 72 hours of ICU admission. Other safety endpoints included allergic reactions, the need for renal replacement therapy (RRT), and 90-day mortality.

Results: Of 125 patients, 62 received gelatin and 63 albumin. Despite being older, having more severe baseline illness, higher proportion undergoing surgical drainage prior to ICU admission, and a greater incidence of intra-abdominal infections, Group A achieved faster vasopressor discontinuation (48 vs. 60 h; p=0.049), required less hydrocortisone (p=0.01), had lower SOFA-II scores (p=0.03), and higher serum albumin (p=0.03). In patients with hypoalbuminemia (<2.5 g/dL) or anemia (<9 g/dL), Group G was associated with higher AKI and RRT rates (p<0.05). No allergic reactions occurred, and ICU stay, hospital stay, and 90-day mortality were not different.

Conclusion: Early 4% gelatin was associated with slower shock reversal and higher AKI risk compared with 5% albumin in critically ill surgical patients, while hospital stay and 90-day mortality were not different.

Keywords: Early Colloid Resuscitation; 5% Albumin; 4% Gelatin; 30 mL/kg Crystalloid Solution; Surgical Septic Shock (Siriraj Med J 2025; 77: 707-715)

INTRODUCTION

Septic shock is the main etiology of mortality among critically ill surgical patients undergoing noncardiac procedures. This condition is characterized by peripheral vasodilation, vasoplegia, and hypovolemia. Fluid resuscitation is a principal intervention for septic shock.[1,2] Delayed or inadequate fluid therapy can result in severe microvascular alterations, heightened expression of pro-inflammatory mediators, and profound mitochondrial dysfunction, particularly within the first 3 hours of treatment.[3,4] In contrast, excessive fluid administration leading to a positive fluid balance has been correlated with poor outcomes.[5,6]

Human albumin solution is generally regarded as a safe colloid with multiple physiological benefits.[7] It tends to remain in circulation despite capillary leak during septic shock[8], making it a promising option for rescue after substantial crystalloid resuscitation. External albumin replacement, targeted to keep a serum albumin level of 3.0 mg/dL in patients with septic shock, has been shown to lower 90-day mortality, decrease daily net fluid balance, and reduce organ dysfunction.[8] However, its role in early septic shock resuscitation remains uncertain, especially concerning shock reversal time and mortality in surgical septic shock patients who often experience greater fluid losses.

A 4% gelatin solution, a synthetic colloid, offers a more cost-effective resuscitation fluid compared with albumin-based solutions and has been used for septic shock. Although it possesses a lower molecular weight, it carries a higher incidence of anaphylaxis, and some studies showed a higher likelihood of developing acute kidney injury (AKI).[9,10] Given the limited data on the safety and efficacy of gelatin in septic shock patients, it is still uncertain whether this solution should be advised for surgical patients with this condition.

The purpose of this study was to evaluate the effectiveness and safety of 5% albumin (Group A) compared with 4% gelatin (Group G) for early colloid resuscitation following 30 ml/kg of crystalloid resuscitation in septic shock patients upon admission to the general surgical intensive care unit (SICU). The main efficacy was time to vasopressor discontinuation, and the main safety outcome was the incidence of acute kidney injury (AKI) per KDIGO criteria, within 72 hours of ICU admission. Other safety endpoints included allergic reactions, the need for renal replacement therapy (RRT) and 90-day mortality.

MATERIALS AND METHODS

Study design and participants

This retrospective study, approved by the Siriraj

Ethics Committee (COA no. Si 500/2017), involved 125 consecutive surgical patients over 18 years old diagnosed with septic shock upon admission to the general surgical ICU. (ICU Siamitra and ICU Salad-Sumang, Department of Anesthesiology, Siriraj Hospital, Mahidol University, Bangkok, Thailand; Thailand's largest national tertiary referral center from September 2017 to July 2018. All patients obtained blood cultures and cultures from infection sites and received appropriate antibiotics. Each patient received an initial fluid resuscitation of 30 mL/kg of crystalloids before receiving either a 5% albumin solution (Group A) or a 4% gelatin solution (Group G) at a dose of 20 mL/kg. Patients were included only if they remained fluid responsive. The attending physician managed subsequent fluid administration after the colloid infusion as per the septic shock protocol practice in our ICU. Norepinephrine (NE) was the primary vasopressor used, which was initiated after 30 mL/kg crystalloid if MAP remained <65 mmHg and titrated to maintain MAP >65 mmHg. Shock reversal time was defined as the duration (in hours) from NE initiation to discontinuation.

Inclusion and exclusion criteria

Patients were included in this study if they were over 18 years old, diagnosed with septic shock upon general surgical ICU admission. The exclusion criteria were patients who underwent cardiothoracic, neurosurgical, traumatic, or transplant procedures. Additional exclusion criteria included prior administration of fresh frozen plasma or other synthetic colloids or received both 5% albumin and 4% gelatin, chronic kidney disease stage IV or V, end-stage renal disease, requirement of RRT before ICU admission, use of hemoperfusion or extracorporeal membrane oxygenation (ECMO), or an ICU stay shorter 3 days.

Collected data

Baseline data included demographics, comorbidities (stroke, hypertension, coronary artery disease, chronic obstructive pulmonary disease, diabetes mellitus, chronic kidney disease, immunocompromised status, and cancer), and initial laboratory results (hemoglobin, serum creatinine, albumin, and lactate levels). The use of potentially nephrotoxic medications (gentamicin, vancomycin, amphotericin B, polymyxin, cyclosporine A, intravenous contrast dye, nonsteroidal anti-inflammatory drugs, and COX-2 inhibitors) was recorded. Surgical details (type of procedure) and infection sites were also documented.

Over the first 3 ICU days, hemoglobin, serum creatinine, albumin, lactate, and liver function tests were measured. Fluid administration (including type and amount), blood or blood component use, total intake and output, and fluid balance were recorded. The type and duration of vasopressor or inotropic support were noted, along with APACHE II and SOFA II scores. RRT use, ventilator support, duration of stay in the ICU and hospital, and all-cause mortality in 28 and 90 days were likewise collected.

Operational definitions

Septic shock was diagnosed according to the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis–3).[11] Chronic kidney disease and AKI were classified based on KDIGO criteria.[12,13] Time to reverse shock was measured in hours, from the initiation of vasopressors until they were discontinued. Fluid balance was the total fluid intake minus the total fluid output.

Statistical analysis

According to previous reports, the incidence of AKI was 69%[10] in 4% gelatin solution and 44% in 5% albumin solution.[14] Based on these data, we calculated a required sample size of 62 patients per group, presuming a two-sided type I error of 0.05 and a power of 80%. For univariate analysis, the chi-square test was used to assess associations between categorical variables and the outcome of interest. We reported crude odds ratios with 95% confidence intervals to show the strength of these associations. An unpaired t-test was employed for normally distributed quantitative data, and a Mann-Whitney test for non-normally distributed data. For multivariable analysis, we performed an unconditional multiple logistic regression to assess the independent effect of each risk factor, adjusting for potential confounders. We then reported adjusted odds ratios with 95% confidence intervals, along with the *p*-value for statistical significance. All statistical analyses were conducted using IBM SPSS Statistics, version 21 (IBM Corp, Armonk, NY, USA). A two-sided *p*-value of < 0.05 was considered statistically significant.

RESULTS

Baseline characteristics

We enrolled 63 patients in Group A and 62 patients in Group G. Demographic data and ICU information are summarized in Table 1. Group G was significantly younger and had higher rates of pneumonia as the primary infection. These patients also demonstrated more frequent use of hydrocortisone (77.4% vs 57.1%, $p=0.01$) and higher SOFA-II scores on day 1 (8.8±3.0 vs 7.7±2.6, $p=0.03$). In contrast, Group A had a significantly higher

TABLE 1. Demographic and baseline characteristics of the patients in the albumin and gelatin groups.

	Albumin group (n=63)	Gelatin group (n=62)	*p*-value
Age (years) (mean ± SD)	68 ± 12	57 ± 15	< 0.01*
Male (n%)	36 (57.1)	32 (51.6)	0.59
Body mass index (kg/m^2) (mean ± SD)	23.1 ± 5.2	23.0 ± 4.2	0.94
Diabetes mellitus, n (%)	16 (25.4)	20 (32.3)	0.43
Previous stroke, n (%)	13 (20.6)	4 (6.5)	0.03*
Hypertension, n (%)	32 (51.6)	25 (40.3)	0.28
Coronary artery disease, n (%)	8 (12.7)	6 (9.7)	0.78
Chronic obstructive pulmonary disease, n (%)	2 (3.2)	2 (3.2)	0.98
Chronic kidney disease (eGFR<60 mL/min/1.73 m^2), n (%)	14 (22.2)	10 (16.1)	0.49
Immunocompromised, n (%)	12 (19.0)	18 (29.0)	0.21
Cancer, n (%)	18 (28.6)	12 (19.4)	0.29
Received nephrotoxic drug, n (%)	13 (20.6)	12 (19.4)	0.99
Received radio contrast, n (%)	14 (22.2)	7 (11.3)	0.15
Baseline serum creatinine (mg/dL) (in the past 3 months) (mean ± SD)	0.91 ± 0.32	0.86 ± 0.28	0.43
Had an operation for infection drainage before admission to the ICU, n (%)	33 (52.4%)	12 (19.4%)	<0.01*
Source of infection			
Intra-abdominal infection, n (%)	33 (52.4)	16 (25.8)	0.03*
Pneumonia, n (%)	9 (14.3)	16 (25.8)	0.02*
Urinary tract infection (n%)	8 (12.7)	10 (16.1)	0.53

Data are presented as the frequency of n (%), mean ± standard deviation (SD). * $p<0.05$ is considered significant.
Abbreviations: Kg, kilogram; m, meter; eGFR, estimated glomerular filtration rate; mg, milligram; dL, deciliter; ICU, Intensive care unit.

rate of underlying stroke and more intra-abdominal infections. More patients in Group A underwent surgery for infection source control and required higher volumes of packed red blood cell transfusions. Additionally, Group A had a significantly higher average albumin level during the first 72 hours (2.60 ± 0.45 vs 2.35 ± 0.53 mg/dL, $p = 0.03$) (Table 2).

Primary outcome

As shown in Table 3, Group A had a significantly faster shock reversal time than Group G. The median time was 48 hours (range 30-84) for Group A versus 60 hours (range 42-99) for Group G ($p = 0.049$).

Secondary outcomes

No allergic reactions were observed in both groups. Additionally, no statistically significant differences were noted between groups in the incidence of AKI, requirement for RRT, SOFA scores at 72 hours, respiratory support-free days, duration of stay in the ICU, and all-cause mortality in 90 days (Table 3).

TABLE 2. Intensive care unit admission characteristics and clinical parameters in the first 72 hours in albumin and gelatin groups.

	Albumin group (n=63)	Gelatin group (n=62)	*p*-value
Admitted hemoglobin (g/dL) (mean ± SD)	10.7 ± 2.4	10.7 ± 2.5	0.90
Admitted serum albumin (mg/dL) (mean ± SD)	2.6 ± 0.6	2.5 ± 0.6	0.26
Admitted serum creatinine (mg/dL) (median [interquartile range])	1.5 (1.0 - 2.1)	1.6 (0.9 - 2.3)	0.89
Average serum albumin (in the first 72 hours) (mg/dL) (mean ± SD)	2.60 ± 0.45	2.35 ± 0.53	0.03*
Average serum lactate (in the first 72 hours) (mg/dL) (median [interquartile range])	3.9 (2.9 - 5.7)	4.5 (2.75 - 8.5)	0.41
Need ventilator support, n (%)	55 (87.3)	48 (77.4)	0.16
Received hydrocortisone, n (%)	36 (57.1)	48 (77.4)	0.01*
APCHE II score day 1 (mean ± SD)	20.6 ± 6.0	21.4 ± 6.2	0.31
SOFA II score day 1 (mean ± SD)	7.7 ± 2.6	8.8 ± 3.0	0.03*
SOFA II score day 3 (median [interquartile range])	6 (0 - 18)	6 (0 - 18)	0.81
Fluid balance			
Fluid balance day 1 (liter) (mean ± SD)	5.3 ± 2.4	5.2 ± 1.6	0.65
Fluid balance day 2 (liter) (mean ± SD)	2.3 ± 1.7	2.3 ± 1.9	0.98
Fluid balance day 3 (liter) (mean ± SD)	1.0 (-2.3 - 1.87)	2.1 (0.4 - 2.0)	0.28
Net fluid in 3 days (liters) (mean ± SD)	8.5 ± 3.7	8.9 ± 3.9	0.56
Transfusion in the first 3 days			
Pack red cell (ml) (median [interquartile range])	366 (0 - 849)	254 (0 - 605)	0.07
Fresh frozen plasma (ml) (median [interquartile range])	303 (0 - 933)	438 (0 - 963)	0.90
Platelet (ml) (median [interquartile range])	0 (0 - 209)	0 (0 - 257)	0.22

Data are presented as the frequency of n (%), mean ± standard deviation (SD), and median (interquartile range). * $p<0.05$ is considered significant.

Abbreviations: g, gram; mg, milligram; dL, deciliter; ml, milliliter

Subgroup analysis

In the subgroup analysis (Table 4), based on admission serum albumin <2.5, ≥2.5 mg/dL) revealed that Group G resulted in a statistically higher percentage of AKI (KDIGO-1, p=0.046; KDIGO-2, p=0.046; KDIGO-3, p=0.045) and RRT (p=0.048). Similarly, based on admission hemoglobin levels, the G group also revealed a statistically significantly higher percentage of AKI (KDIGO-1, p=0.018) when compared to those with levels<9 g/dL. Also, Group G tended to be a predictor of AKI from multivariable logistic regression analysis for factors independently associated with acute kidney injury (Table 5). However, the result did not reach a statistically significant.

TABLE 3. Primary and secondary outcomes of this study.

	Albumin group (n=63)	Gelatin group (n=62)	*p*-value
Shock reversal time (hours) (median [interquartile range])	48 (30-84)	60 (42-99)	0.049*
AKI within 72 hours, n (%)	31 (49.2)	32 (51.6)	0.78
KDIGO I, n (%)	10 (15.9)	7 (11.3)	0.45
KDIGO II, n (%)	6 (9.5)	6 (9.7)	0.97
KDIGO III, n (%)	15 (23.8)	19 (30.6)	0.39
RRT, n (%)	10 (15.9)	13 (21.0)	0.46
RRT free day (days) (median [interquartile range])	28 (15 - 28)	28 (20.5 - 28)	0.68
90-day mortality, n (%)	17 (27.0)	17 (27.4)	0.95
SOFA II score day 3 (median [interquartile range])	6 (0 - 18)	6 (0 - 18)	0.81
Ventilator-free day (days) (median [interquartile range])	20 (0 - 25)	21 (3 - 26.5)	0.17
ICU length of stay (days) (median [interquartile range])	8 (5 - 13)	7 (4 - 12)	0.11
Hospital length of stay (days) (median [interquartile range])	15 (10 - 29)	15 (9.7 - 28.2)	0.54

Data are presented as the frequency of n (%), median [interquartile range]; *$p<0.05$ is considered significant.
Abbreviations: AKI, acute kidney injury; ICU, intensive care unit; RRT, renal replacement therapy

TABLE 4. Relationship between serum albumin and hemoglobin levels on day-1, and acute kidney injury and renal replacement therapy in the first 72 hours.

	Type	n	KDIGO-1 n (%)	*p*-value	KDIGO-2 n (%)	*p*-value	KDIGO-3 n (%)	*p*-value	RRT n (%)	*p*-value
Serum albumin d-1 < 2.5 mg/dL	Gr. A Gr. G	23 30	9 (39.1) 20 (66.7)	**0.046***	6 (26.1) 16 (53.3)	**0.046***	4 (17.4) 13 (43.3)	**0.045***	4 (17.4) 10 (33.3)	**0.048***
Serum albumin d-1 ≥ 2.5 mg/dL	Gr. A Gr. G	40 32	22 (55.0) 12 (37.5)	0.139	15 (37.5) 9 (28.1)	0.402	11 (27.5) 6 (18.8)	0.385	6 (15.0) 3 (9.4)	0.548
Hemoglobin d-1 < 9 g/dL	Gr. A Gr. G	15 16	6 (40.0) 13 (81.3)	**0.018***	5 (33.3) 56.3%	0.200	5 (33.3) 43.8%	0.552	5 (33.3) 6 (37.5	0.201
Hemoglobin d-1 ≥ 9 g/dL	Gr. A Gr G	48 46	52.1% 41.3%	0.295	33.3% 34.8%	0.882	20.8% 26.1%	0.548	5 (10.4) 7 (15.2)	0.158

Data are presented as n (%); * $p<0.05$ is considered significant.
Abbreviations: g, gram; mg, milligram; dL, deciliter; ml, milliliter; Gr. A, albumin group; Gr. G, gelatin group; RRT, Renal Replacement Therapy; d-1, day one after day of admission in the intensive care unit

TABLE 5. Multivariable logistic regression analysis for factors independently associated with acute kidney injury.

	Adj OR (95% CI)	*p*-value
BMI	1.12 (1.02, 1.24)	0.019
APACHE II day 1	1.17 (1.07, 1.28)	0.001
CKD	1.64 (0.54, 4.96)	0.379
Amount of fluid/kg	1.00 (1.00, 1.01)	0.450
Gelatin	1.19 (0.50, 2.81)	0.700
Admitted serum albumin	0.69 (0.34, 1.37)	0.284
Average Hemoglobin in the first 72 hours	0.81 (0.60, 1.09)	0.160

Data are presented as adjusted odds ratios with 95% confidence intervals; $p<0.05$ is considered significant.

Abbreviations: mg, milligram; dL, deciliter; g, gram; adj OR, Gr A., group A; Gr G., group G; adj OR, adjusted odds ratio; BMI, body mass index; CKD, chronic kidney disease; Hb, hemoglobin; day 1, day after day of admission in the intensive care unit

DISCUSSION

Given the goal of early septic shock resuscitation is to reduce time to shock reversal, prevent organ dysfunction, and improve survival, a key challenge lies in identifying a safe and effective colloid that can minimize reliance on high-dose crystalloid fluid, particularly in surgical septic shock patients who typically sustain greater fluid losses. Gelatin is one of the colloids used for fluid resuscitation; however, previous studies have suggested a higher risk of AKI[9,10], and data on its safety and efficacy in surgical septic shock patients remain limited. Despite the study by Tongyoo S et al., which showed a significantly higher 28-day mortality rate in critically ill medical patients with refractory septic shock.[15]

Findings from this study indicate that a 4% gelatin solution is less effective than a 5% albumin solution. Patients receiving the gelatin solution had a significantly longer shock reversal time (60 [42-99] vs 48 [30-84], p=0.049). This reduced effectiveness may stem from gelatin's lower molecular weight of approximately 4,000 Da, in contrast to albumin's much higher molecular weight (commonly cited as approximately 66 kDa). The smaller molecular size of gelatin leads to lower oncotic pressure and diminished volume expansion.[9,14] By comparison, albumin exerts higher oncotic pressure and appears to remain longer in the circulation during septic shock. The ALBIOS trial[8] supports the use of albumin by demonstrating higher serum albumin levels in patients receiving exogenous albumin, similar to this study, where Group A had higher average serum albumin in the first 72 hours (p=0.03).

Despite the higher incidence of intra-abdominal infections and greater need for surgical interventions in the albumin group, these patients required less hydrocortisone, had lower SOFA scores on day 1, and showed a trend toward lower fluid balance by day 3. In addition, the higher efficacy of 5% albumin was also observed, even with the lesser use of hydrocortisone compared to the gelatin solution in this study.

Regarding secondary outcomes, no allergic reactions were observed in this study. There was no statistically significant difference in AKI, RRT, or duration of stay in the ICU and hospital between groups. In the subgroup analysis (Table 4) based on admission serum albumin levels (<2.5, ≥2.5 mg/dL), it was shown that Group G, who were admitted with serum albumin levels <2.5 mg/dL had a significantly higher percentage of AKI (KDIGO 1-3) and RRT. Similarly, Group G patients who were admitted with hemoglobin levels <9 g/dL showed a significantly higher percentage of AKI (KDIGO-1). This result was different from Tongyoo S, et al study that showed more RRT incidence[15], however our result was analyzed from subgroup analysis and, given the small sample size in both Group A and Group B, this result should be interpreted with caution, as it is only for exploratory analysis. A larger sample size is needed to confirm this finding. We can use the data to develop a new multivariable logistic regression analysis model by adding the admission albumin group (<2.5, ≥2.5 mg/dL) and the admission hemoglobin group (<9 g/dL, ≥9 g/dL), as well as the interaction between Group G and AKI. This will give a more precise answer about gelatin

as a predictor of AKI. Unfortunately, the final version of this data is unavailable.

In septic shock patients with low serum albumin levels (<2.5 mg/dL), indicating reduced oncotic pressure, this study found that resuscitation with 4% gelatin was associated with a significantly higher incidence of AKI across KDIGO stages 1-3, as well as an increased need for RRT. Furthermore, patients who developed hemodilution (hemoglobin <9 g/dL) also showed a significantly higher incidence of AKI (KDIGO stage 1) when treated with gelatin. These findings align with previous research by Bayer et al.[10], which identified 4% gelatin as a risk factor for AKI and increased RRT use in septic patients compared to crystalloids. Similarly, a meta-analysis by Moeller et al[9]. reported an association between gelatin use and AKI, with a risk ratio of 1.35 (95% CI: 0.58–3.14) in the context of hypovolemia resuscitation. Therefore, the use of gelatin should be approached with caution in patients with sepsis and septic shock, particularly those presenting with hypoalbuminemia or significant hemodilution.

The results of this study showed that the albumin group required more packed red blood cell (PRC) transfusions due to a higher number of surgeries. Nevertheless, there were no significant differences in the volumes of transfused fresh frozen plasma (FFP) and platelets when compared to the 5% albumin solution. Therefore, despite the presence of surgical septic shock, our study found that 4% gelatin did not demonstrate any difference in bleeding complications compared to the 5% albumin solution.

This study did give significant information of the lower effectiveness of 4% gelatin as a resuscitation colloid in addition to crystalloid in surgical septic shock. This gelatin potentially adds the risk of AKI and the need for RRT in patients with low serum albumin levels and hemodilution. This study had several limitations, including being a retrospective study, a small sample size, and unbalanced baseline characteristics (Group A was significantly older, and more patients underwent operations for infection drainage before admission to the ICU, and a higher incidence of intraabdominal infections that led to greater fluid loss).

CONCLUSION

This observational study suggests that early administration of 4% gelatin is less effective for shock resuscitation than the 5% albumin solution. Moreover, 4% gelatin is linked to a greater incidence of AKI and RRT in patients with low oncotic pressure, as well as a higher incidence of AKI in cases of hemodilution. No allergic reactions or bleeding complications were significantly associated with the use of the colloid solutions studied. A large, randomized controlled trial is needed to determine the effectiveness and safety of 4% gelatin in treating surgical septic shock.

Data availability statement

This study's information came from ICU Siamitra and ICU Salad–Sumang of the Department of Anesthesiology, Siriraj Hospital, Mahidol University database from September 2017 to July 2018. However, the ICU's confidential information cannot be shared openly; instead, the detailed data were kept in the researcher's pool data file with a security code. This manuscript was also edited with CHT GPT 4 Pro for more concise reporting of the information.

ACKNOWLEDGMENTS

The study team sincerely thanks Assistant Professor Dr. Chulaluk Komoltri, Ph.D., for her significant contribution to the statistical analysis of this study. Also a great thanks to Mr. David Park for the excellent manuscript edition and Ms. Nachanita Luxnayingyong for manuscript submission.

DECLARATIONS

Grants and Funding Information

This study is not supported by any grants.

Conflict of Interest

The authors do not have any conflict of interest associated with this study.

Registration Number of Clinical Trial

This study was registered to the US clinical number NCT01363635 and NCT01361477.

Author Contributions

Conceptualization and methodology, S.K., S.T.; Investigation, S.K., N.P., and S.T.; Formal analysis, S.K., N.P.; Visualization and writing – original draft, S.K., N.P.; Writing –review and editing, S.K.; Funding acquisition, S.K.; Supervision, S.K., S.T.

All authors have read and agreed to the final version of the manuscript.

Use of Artificial Intelligence

This manuscript was also edited by Mr. David Park and ChatGPT-4 Pro for more concise reporting of the information.

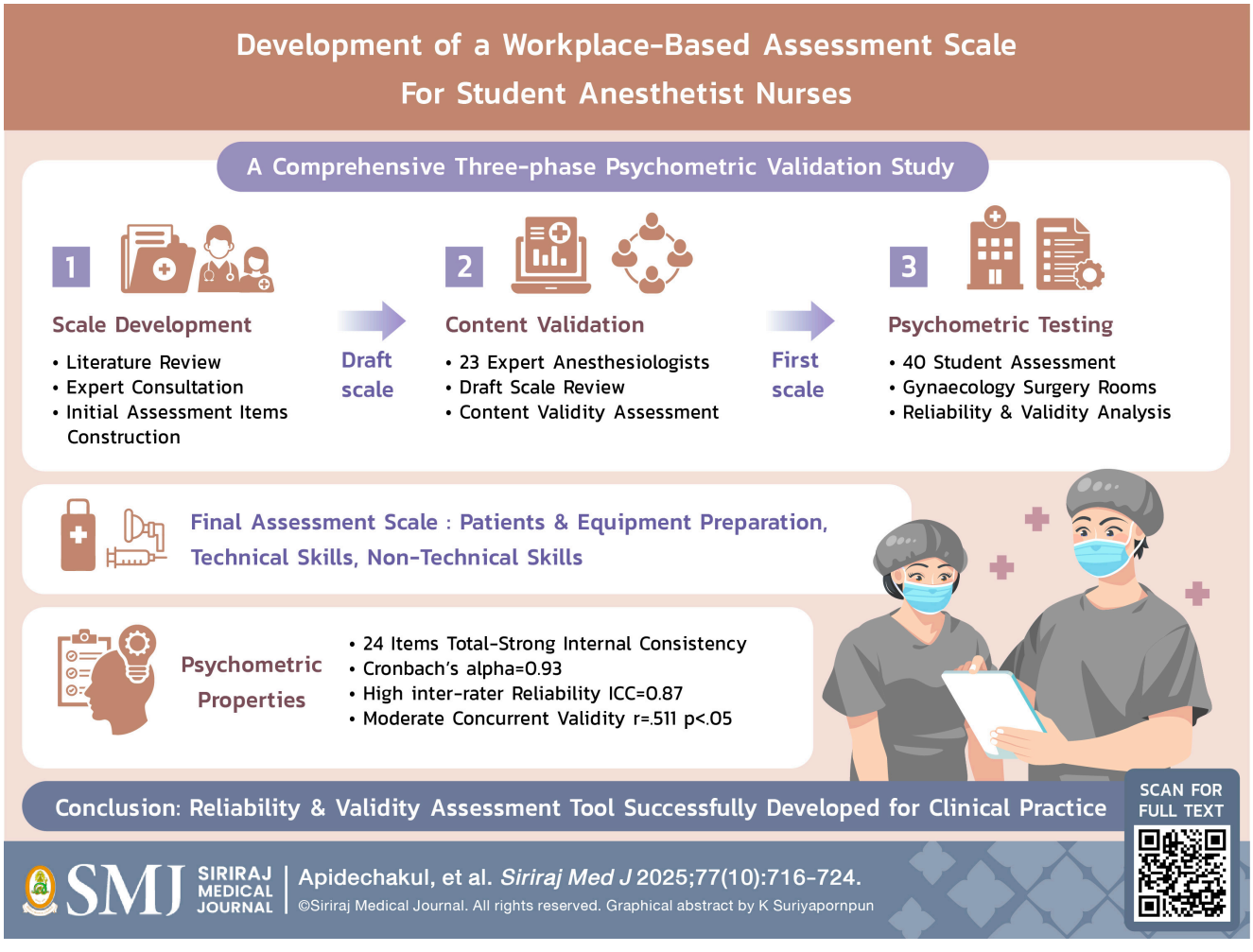
REFERENCES

1. Vincent JL, De Backer D. Circulatory shock. N Engl J Med. 2013;369(18):1726-34.
2. Cecconi M, De Backer D, Antonelli M, Beale R, Bakker J, Hofer C, et al. Consensus on circulatory shock and hemodynamic monitoring. Task force of the European Society of Intensive Care Medicine. Intensive Care Med. 2014;40(12):1795-815.
3. Legrand M, Bezemer R, Kandil A, Demirci C, Payen D, Ince C. The role of renal hypoperfusion in development of renal microcirculatory dysfunction in endotoxemic rats. Intensive Care Med. 2011;37(9):1534-42.
4. Corrêa TD, Vuda M, Blaser AR, Takala J, Djafarzadeh S, Dünser MW, et al. Effect of treatment delay on disease severity and need for resuscitation in porcine fecal peritonitis. Crit Care Med. 2012;40(10):2841-9.
5. Vincent JL, Sakr Y, Sprung CL, Ranieri VM, Reinhart K, Gerlach H, et al. Sepsis in European intensive care units: results of the SOAP study. Crit Care Med. 2006;34(2):344-53.
6. Boyd JH, Forbes J, Nakada TA, Walley KR, Russell JA. Fluid resuscitation in septic shock: a positive fluid balance and elevated central venous pressure are associated with increased mortality. Crit Care Med. 2011;39(2):259-65.
7. Vincent JL, De Backer D, Wiedermann CJ. Fluid management in sepsis: The potential beneficial effects of albumin. J Crit Care. 2016;35:161-7.
8. Caironi P, Tognoni G, Masson S, Fumagalli R, Pesenti A, Romero M, et al. Albumin replacement in patients with severe sepsis or septic shock. N Engl J Med. 2014;370(15):1412-21.
9. Moeller C, Fleischmann C, Thomas-Rueddel D, Vlasakov V, Rochwerg B, Theurer P, et al. How safe is gelatin? A systematic review and meta-analysis of gelatin-containing plasma expanders vs crystalloids and albumin. J Crit Care. 2016;35:75-83.
10. Bayer O, Reinhart K, Sakr Y, Kabisch B, Kohl M, Riedemann NC, et al. Renal effects of synthetic colloids and crystalloids in patients with severe sepsis: a prospective sequential comparison. Crit Care Med. 2011;39(6):1335-42.
11. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801-10.
12. Levey AS. Defining AKD: The Spectrum of AKI, AKD, and CKD. Nephron. 2022;146(3):302-5.
13. Lameire NH, Levin A, Kellum JA, Cheung M, Jadoul M, Winkelmayer WC, et al. Harmonizing acute and chronic kidney disease definition and classification: report of a Kidney Disease: Improving Global Outcomes (KDIGO) Consensus Conference. Kidney Int. 2021;100(3):516-26.
14. Finfer S, Bellomo R, Boyce N, French J, Myburgh J, Norton R. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. N Engl J Med. 2004;350(22):2247-56.
15. Tongyoo S, Chayakul C, Kanoknatsiwattana S, Permpikul C. Albumin Versus Gelatin Solution for the Treatment of Refractory Septic Shock: A Patient Baseline-Matched-Cohort Study. Siriraj Med J. 2020;72(6):451-61.

Development of a Workplace-based Assessment Scale for Student Anesthetist Nurses

Parichad Apidechakul, Ph.D.[1], Namtip Triyasunant, M.D.[2], Ladda Permpolprasert, B.Sc.[2], Wiruntri Punchuklang, B.Sc.[2], Phongthara Vichitvejpaisal, M.D., Ph.D.[2,*]

[1]*Siriraj Health Science Education Excellence Center, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand,* [2]*Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.*



*Corresponding author: Phongthara Vichitvejpaisal
E-mail: phongthara@gmail.com
Received 24 June 2025 Revised 8 August 2025 Accepted 8 August 2025
ORCID ID:http://orcid.org/0000-0003-2656-6718
https://doi.org/10.33192/smj.v77i10.276186

ABSTRACT

Objective: To develop and validate a skills assessment tool for evaluating the workplace performance of student anesthetist nurses through a psychometric analysis of its reliability and validity.

Materials and Methods: The study was conducted in three sequential phases: Scale Development: A comprehensive literature review and expert consultations were undertaken to construct the initial assessment items. Content Validation: Three expert anesthetists reviewed the draft scale for content validity. Psychometric Testing: The final scale was evaluated using data from 40 student anesthetist nurse assessments in 2023-2024. Recruitment was conducted in the gynecology surgery rooms.

Results: The finalized workplace-based assessment scale consisted of 24 items spanning three key domains: patient and equipment preparation, technical skills, and non-technical skills. The psychometric analysis demonstrated strong internal consistency (Cronbach's $\alpha = 0.93$), high inter-rater reliability (The Intraclass Correlation Coefficient (ICC) = 0.87), and moderate concurrent validity, as evidenced by Pearson's correlation analysis ($r=.511$, $p<.05$, $N=40$).

Conclusion: The newly developed workplace-based assessment scale exhibits strong psychometric properties, providing a reliable and comprehensive tool for evaluating the clinical competencies of student anesthetist nurses in practice settings.

Keywords: Medical education; scale; student anesthetist nurses; workplace-based assessment (Siriraj Med J 2025; 77: 716-724)

INTRODUCTION

Healthcare professionals prioritize patient safety in their practice. The Ministry of Public Health and the Institute for Healthcare Quality Accreditation jointly considered the criteria of the Institute for Healthcare Improvement (IHI) and the Joint Commission on Accreditation of Healthcare Organizations (JCAHO) to select safety issues that are consistent with the Thai context and to put these ideas into practice for drafting policies (Patient and Personnel Safety, 2P Safety Goals), with the primary objective of fostering the potential and safety consciousness of healthcare personnel. The policy covers anesthesiology duties, ensuring anesthesia is provided safely. Training sessions focus on risk management, guided by the Royal College of Anesthesiologists of Thailand (RCAT), emphasizing non-technical skills through lectures and hands-on training for student anesthetist nurses.[1]

Professional nurses in the anesthesia nurse program receive comprehensive training focused on patient safety. They learn cognitive processes, patient monitoring, and procedural skills under the supervision of anesthesiologists during training. Over the one-year course, knowledge, skills, and attitudes are taught and evaluated in theory and practice. Additionally, the curriculum consists of practical exams with real-life patients in operating theaters and simulated crisis scenarios using high-fidelity manikins. In actuality, intubating patients under general anesthesia is the responsibility of most student anesthetist nurses during training. Furthermore, when they graduate as anesthetist nurses, general anesthesia is the primary task nurses must complete. Thailand still has a dearth of anesthesiologists and an increased general anesthesia workload, with nearly 1 million cases yearly handled by anesthetist nurses.[2] Student anesthetist nurses in our training institute located in Thailand stated their opinions after taking a practical exam in emergency general anesthesia situations with obstetric simulated patients. More than 70 percent did not meet the passing criteria. This may happen due to real-life training sessions within the operating room; nursing students do not have the opportunity to make their own decisions. Routine work must be performed closely under the supervision of the anesthesia staff. As a result, nursing students may not recognize their decision-making abilities. In training, nursing students also have limited opportunities to perform general anesthesia on cesarean section patients due to patient safety concerns. Regarding the primary obligation of nurse anesthetists in performing intubation, the process requires vigilance in maintaining airway patency, preventing aspiration, and preventing gastric contents from entering the lungs.

This anesthesia technique requires skilled anesthesia staff to evaluate patients before the procedure, especially in emergency surgical situations, to prevent complications and unintended events. Appropriate intubation and anesthesia administration skills enable a quick recovery after the procedure, allowing for endotracheal tube removal.[3] Therefore, anesthetist nurses play a crucial

role in patient care and assist doctors during the pre-anesthesia, intra-anesthesia, and post-anesthesia periods.

Anesthesiology includes teams of anesthesiologists crucial for delivering anesthesia services, ensuring patient safety and comfort during procedures. The Nursing and Midwifery Council's competency framework for anesthetist nurses has been collated and summarized into a list of anesthesia nurse competencies,[4] which include: 1) Preoperative planning; 2) Intraoperative management and patient monitoring; 3) Anesthesia nursing practice during the recovery period; 4) Decision-making during crises; 5) Clinical pharmacology of drugs used in anesthesia; 6) Airway management in an unconscious patient; 7) Knowledge management and using technology and information in evidence-based practice, and 8) Communicating with the anesthesiologist or surgeons. Practical tools to assess student anesthetist nurse competencies in general anesthesia are rare.

Clinical skills are considered the most critical aspect of patient care.[5] The assessment of clinical competence is challenging and complex. There is a trend toward a competency-based training process that emphasizes formative assessment over summative assessment. Workplace-based Assessment (WPBA) scale is an essential part of the evaluation that involves direct observation of clinical and non-clinical skills with actual patients in a particular workplace to provide constructive feedback for the trainees.[6] Mini-clinical examination exercise (mini-CEX) is a form of on-the-job assessment where a specialist or instructor observes the trainee performing on-site work with patients. Students are graded on history taking, physical exam skills, counseling, and feedback. The mini-CEX has been developed for use in anesthesia training in many countries.[7-9] Applying these assessment methods in accordance with the nurse anesthetist competency framework to student anesthetist nurses sounds interesting, especially in real practice settings with actual patients.

Non-technical skills have been utilized in industry and other agencies for some time. A majority of anesthesia incidents occur during work. Investigations of adverse events have shown that up to 80% of cases are caused by human error factors such as ineffective communication, inadequate patient supervision, and a failure to inspect medications and equipment. This is not just a lack of technical knowledge. The Anesthesiologist Non-Technical Skills (ANTS) is a system developed by industrial psychologists and anesthesiologists, covering topics like task management, teamwork, situational awareness, and decision-making. Combining non-technical skills with medical knowledge and clinical skills supports safe and effective performance in daily work and emergencies. ANTS can be observed in good anesthesia practice.[10] The performance assessment tools used to guide evaluation should be clear and transparent. These tools can assess individual behavior, provide information for the training process, and constructive feedback on skill development. Non-clinical skills can be identified through observable behaviors.

The general anesthesia practical skills assessment form of the anesthesia nurse training program at Siriraj Hospital was originally a rubric assessment with four levels of performance in the workplace. The scores were weighted according to the importance of the workload before, during, and after general anesthesia, which lasted for 6 months. The scores that appear on the form are complicated in that they must be calculated in terms of decimal points for each level of the score. The original form was developed and used for more than 5 years for formal evaluation. Behavioral observation in real-world settings has patient context, location, and complexity variability. The researcher is thus interested in developing a new form to assess the practical skills of nursing students in preoperative, intraoperative, and post-anesthesia evaluation for the ability to perform airway opening and intubation and incorporate elements of the ANTS System in assessment. As such, this new form will provide feedback on both technical and non-technical skills to student anesthetist nurses, resulting in the daily development of anesthesia nurse competencies. This study aims to develop and validate a skills assessment tool for evaluating the workplace performance of student anesthetist nurses through a psychometric analysis of its reliability and validity.

MATERIALS AND METHODS

Setting and design

This is a descriptive cross-sectional study conducted from July to October 2024. The study population were student anesthetist nurses, training in the Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand.

Ethical approval

The study received ethical approval from the Human Research Ethics Committee of Siriraj Institutional Review Board (SIRB) at the Faculty of Medicine Siriraj Hospital Certificate of Approval No. Si 522/2024. It was based on the Declaration of Helsinki,[11] the Belmont Report, the International Conference on Harmonization in Good Clinical Practice (ICH-GCP), and the International Guidelines for Human Research, along with Thai laws and regulations.

Sampling criteria

The sample size for a bivariate correlation was determined using power analysis. The power analysis was conducted in a software program as G*Power[12], using an alpha of 0.05, a power of 0.95, and a medium effect size (0.05); the required sample size was 38. The Faculty of Medicine at Siriraj Hospital trains 40 anesthetist nurses each year. This demonstrates the program's dedication to maintaining a focused cohort size because of the limited number of students accepted annually. Therefore, the researcher determined that the final sample size for this research would be 40 individuals in the academic year 2023-2024. Recruitment was conducted in the gynecology surgery rooms. The inclusion criteria of nurse students and patients were: 1) Being a student anesthetist nurse at an accredited training center by the Royal College of Anesthesia of Thailand; 2) Having completed theoretical and practical training in general anesthesia for patients over 18; and for patients 3) Gynecologic patients aged > 18 years with American Society of Anesthesiologists (ASA) physical status 1-2. The exclusion criteria were: 1) Student anesthetist nurses without experience or training in general anesthesia; and for patients 2) Patients with ASA classification ≥ 3 or those younger than 18.

Data collection

Anesthesia training program chairpersons were contacted to share the study's background and gauge their willingness to participate. Posters were distributed via student groups for recruitment assistance. After participants were recruited for additional assessments beyond standard evaluations, explicit, informed consent was provided for their participation. All eligible participants had consented beforehand, understanding they could withdraw at any time. They were assured of data confidentiality and anonymity. Valid clinical and non-clinical competency assessments in authentic practice settings are considered crucial for student anesthetist nurses. The research was comprised of three steps, as shown in Fig 1.

Step 1: Scale development	
• Item generation	• Literature review • Previous research
24 draft items	
Step 2: Content validation	
Expert opinion: A panel of two anesthesiologists and one expert in measurement and evaluation in education.	• Item-Objective Congruence (IOC) calculated - 1st round - 2nd round
Drafted scale (24 items)	
• Field test 40 student anesthetist nurses	• Student anesthetist nurses performed general anesthesia to patients undergoing gynecological surgery with a risk assessment score of no more than level 2. • Two trained raters observed the same student for a duration of 1 to 4 hours
Final draft scale (24 items)	
Step 2: Psychometric testing	
• Criterion-related validity	• Pearson's correlation test (n=40) • Correlated with existing 6-month clinical rotation competency scores before, during, and after administering evaluations that utilized standard practical examination methods
• Reliability	• Internal consistency (n=40) Cronbach's alpha for the scale is >0.70
• Inter-rater reliability	• Intraclass correlation coefficients (ICC) >0.80
The workplace-based assessment scale for student anesthetist nurses has 24 items and 3 subscales.	

Fig 1. A workplace-based assessment scale for student anesthetist nurses

Step 1: Scale development

The goal was to create practical assessment tools to evaluate the student anesthetist nurses' clinical and non-technical skills, foster their development, and enhance the quality of their training. The technical and non-technical skills items were developed based on the competency framework for anesthetist nurses as determined by the Nursing and Midwifery Council of Thailand and the Anesthetists' Non-Technical Skills (ANTS). Subsequently, psychometric tests were performed to establish the reliability and validity of the scale.

Step 2: Content validation

Specific performance indicators were carefully formulated, and their congruence with conceptual definitions was evaluated by two anesthesiologists and one expert in measurement and evaluation in education using the Item-Objective Congruence index (IOC). IOC of < 0.50 were modified.[13] This rigorous process established the content validity of the newly developed workplace assessment tools. Then, a total of 24 items were prepared to assess anesthetist nurse competencies in the workplace with a sample group.

Step 3: Psychometric testing

Psychometric testing involves implementing and validating these workplace-based assessments. Preliminary items were scored on a four-point scale, ranging from 1 (fair) to 4 (excellent). The newly developed instruments underwent field testing to assess the competencies of student anesthetist nurses who provided general anesthesia to patients undergoing gynecological surgery with a risk assessment score of no more than level 2 according to the American Society of Anesthesiologist guidelines under the supervision of the attending anesthesiologist throughout the general anesthesia period, following the standard procedures for general anesthesia of the Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, in the gynecology surgery room, (approximately 2-4 hours). Two trained raters observed the same student before, during, and after the administration of general anesthesia. Assessment results from the workplace-based assessment tools were analyzed against existing 6-month clinical rotation competency scores before, during, and after administering evaluations that utilized standard practical examination methods. This comprehensive two-phase study provided an evidence-based approach to developing valid and reliable workplace-based assessment tools for anesthesia nurse competencies.

Statistical analysis

IBM SPSS statistics, version 29 (IBM Corp, Armonk, NY, USA) was used to analyze the collected data. The student demographic data were presented using descriptive statistics. The criterion-related validity of the new workplace assessments was analyzed by comparing their results to those from the established examination process at a statistical significance level of 0.05, using Pearson's correlation coefficient to check validity. Validity coefficient values above 0.35 were interpreted as very beneficial.[14] Additionally, the internal consistency reliability of the workplace assessment instruments was calculated using the Cronbach's alpha coefficient, and a Cronbach's α of > 0.70 was indicated to be acceptable.[15] The intra-class correlation coefficient was calculated as inter-rater reliability. The student competencies were assessed by two trained anesthetist nurse raters simultaneously. Intra-class correlation coefficients ranging from 0.75 to 1.00 show consistent inter-rater scoring from good to very good.[15]

RESULTS

The present study gathered data on students' age, sex, and work experience with general anesthesia.

General characteristics of the sample

A total of 40 nurse anesthetist students participated in the study. Most participants were women (95%); the mean age was 28.7 ± 1.9 years. The average number of cases experienced in general anesthesia was 142.7 ± 10.2 cases, as shown in Table 1.

TABLE 1. Demographic data and details regarding the participants (N=40).

Demographic characteristics	Value
Sex: Female	38 (95%)
Age	28.7 ± 1.9
Number of cases experiences in general anesthesia	142.7 ± 10.2

Data presented as a number (percentage) or mean ± SD

Step 1: Scale development

A comprehensive literature review and expert consultations were undertaken to construct the initial assessment items. The new WPBA scale had 24 items spanning three key domains: patient and equipment preparation (10 items), technical skills (10 items), and non-technical skills (4 items). Preliminary items were scored on a four-point scale, ranging from 1 (fair) to 4 (excellent).

Rating Scale:

Excellent: Demonstrates outstanding behavior and fully meets expectations.

Good: Shows appropriate behavior with minor areas for improvement.

Fair: Displays acceptable behavior but with occasional inconsistencies.

Poor: Exhibits behavior that is below the expected standard and considered unacceptable.

Responses marked as "N/A" (Not Available) required evaluation for validity, reliability, and alignment with the research objectives. In this study, listwise deletion was applied to remove entire cases containing "N/A" responses when the rate was below 5–10% and the missingness appeared to be random. This approach helped maintain data quality and prevent score inflation.[16]

The Nursing and Midwifery Council's competency framework for anesthetist nurses has been collated and summarized into a list of anesthesia nurse competencies4 and elements of the ANTS System in assessment.[9] (Supplementary file 1)

Step 2: Content validation

Three experts reviewed the content validity of the scale, and the scale achieved an index of Item-Objective Congruence (IOC) ranging between 0.67 and 1.0. Two items did not fulfill the criteria due to unclear content, so the researcher revised them (IOC<0.5).

Step 3: Psychometric testing

The final scale was evaluated using data from 40 student anesthetist nurse assessments. To further check the quality of the new scale, we used Pearson's correlation coefficient, and the criterion-related validity of the workplace scale was investigated against those from the established examination process with a prior scale at a statistical significance level of 0.05. The correlation coefficient for the new scale compared to the old formal scale was 0.511. ($r=0.511$, $p<0.05$, $n=40$) As shown by Pearson's correlation analysis, in Fig 2, moderate concurrent validity was indicated.

Furthermore, the internal consistency reliability of the workplace assessment instruments was calculated using the Cronbach's alpha coefficient. The psychometric analysis demonstrated strong internal consistency (Cronbach's $\alpha = 0.93$).

The intra-class correlation coefficient was calculated as inter-rater reliability. Two trained anesthetist nurse raters assessed student competencies simultaneously—intra-class correlation coefficients ranging from 0.75 to 1.00 show consistent inter-rater scoring from good to very good.[17] This study, the reliability of scoring consistency between the two raters, as the Intraclass Correlation Coefficient (ICC), was calculated for their evaluations at the 95% confidence level. The type of ICC used includes the model (2-way mixed effects), type (mean of multiple raters), and the definition (consistency or agreement). An ICC (3, 2) where "3" signifies a two-way mixed-effects

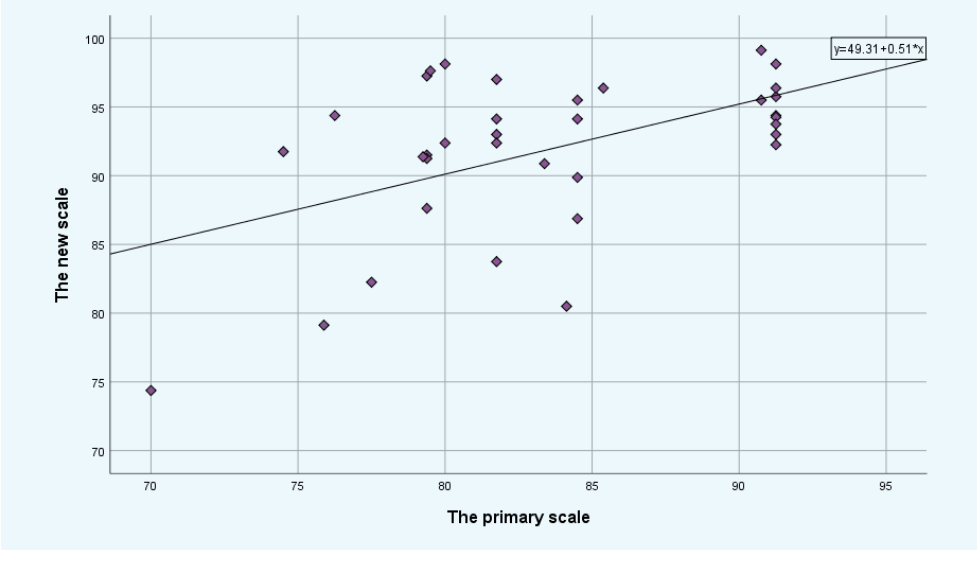


Fig 2. Correlation for the new scale and the primary scale scores

model where raters are considered fixed, and reliability is assessed based on the mean of multiple two raters or measurements.[18] The new assessment scale has an average two-way mixed effects model ICC (3,2) value of 0.93 (0.87 - 0.97), indicating high dependability as in Table 2.

DISCUSSION

The finalized WPBA scale consisted of 24 items spanning three key domains: patient and equipment preparation and technical and non-technical skills. The psychometric analysis demonstrated strong internal consistency (Cronbach's α = 0.93), high inter-rater reliability (ICC = 0.93), and moderate concurrent validity, as evidenced by Pearson's correlation analysis. These findings affirm the scale's robustness in reliably assessing clinical performance.

The development and validation of WPBA scales for student anesthetist nurses addresses a significant gap in competency assessment within anesthesia education. This study contributes to the existing literature by developing a context-specific assessment tool capturing the unique competencies required in anesthesia nurse practice. Our findings provide insights regarding the psychometric properties of the developed scale, with notable strengths and limitations.

Validity Evidence: This WPBA scale demonstrates strong content validity established through expert review and alignment with professional frameworks. WPBA instruments should be grounded in professional standards while remaining sensitive to specific educational contexts.[19] Examination of the professional judgment and decision-making of strength and conditioning coaches' workplace assessments evaluates competence dimensions beyond cognitive knowledge, including contextual judgment and professional behaviors.[20] This WPBA scale is aimed at assessing the practical skills of nursing students in preoperative, intraoperative, and post-anesthesia phases and incorporates elements of the ANTS System in assessment. The anesthetist experts reviewed the draft scale (IOC<0.5) for content validity, and finally, the Item-Objective Congruence (IOC) was over 0.66. The criterion-related validity was evidenced by moderate to strong correlations with existing performance measures, similar to findings regarding anesthesia technical skills assessment.[21]

The improved framework and updated items of the new scale are likely to capture additional dimensions, which may account for the moderate—rather than high—correlation observed.

The psychometric analysis of the new scale demonstrated strong internal consistency (Cronbach's alpha = 0.93), in line with the results of similar studies; previous studies reported this amount for the whole instrument in the range of 0.916 to 0.975.[22] Similar challenges have been reported in achieving high reliability when assessing rarely encountered clinical scenarios.[23]

The inter-rater reliability of two trained anesthetist nurses showed high dependability. The high inter-rater reliability shows that the WPBA scale yields consistent measurements across various evaluators, which is essential for establishing the scale's psychometric properties. This consistency indicates that the assessment criteria are clear and objective enough for trained evaluators to reach similar conclusions when evaluating the same performance. Delfino AE et al. (2023)[24] documented similar challenges in achieving consistent ratings of non-technical skills. Structured rater training improved ICC values by approximately 0.12 across domains. Therefore, training enhances assessment reliability but cannot eliminate subjective judgment elements.[25] It is recommended that other institutions offering training, including those in Thailand, adopt this approach. Consequently, an appendix should be appended to the evaluation form utilized, enabling all individuals who review it to consider its further application.

TABLE 2. Intraclass Correlation Coefficient (ICC).

Measures	Intraclass Correlation Coefficient: ICC (95% CI)	p
One rater	0.88 (0.77 - 0.94)	p< 0.001
Average value from 2 raters	0.93 (0.87 - 0.97)	p< 0.001

Two-way random effects model where both people effects and measures effects are random

Limitation

A primary limitation is the lack of longitudinal validity evidence demonstrating the scale's predictive relationship with post-graduation performance,[26] documented correlations between simulation-based assessments, and subsequent practice. However, the relationship between WPBA scores and practice outcomes requires further research.

The initially planned effect size of r = 0.05 was too small for this study; a more appropriate effect size would have been in the range of r = 0.30–0.50.[27] Additionally, a post-hoc power analysis revealed that, with n = 40 and an observed effect size of r = 0.511, the study achieved approximately 99% power (α = 0.05, two-tailed)—well above the conventional 0.80 threshold. This significant observed effect suggests a meaningful relationship, despite the study's sample size limitations. Future research should employ larger sample sizes to enhance generalizability and improve the precision of effect size estimates.

The scale emphasizes observable behaviors but may not fully capture the cognitive processes underlying clinical decisions. Incorporating cognitive assessment methods could improve this. The think-aloud protocols could enhance clinical reasoning evaluation in future iterations.[28] Several assessment domains remain inherently subjective despite structured rating scales.[29]

CONCLUSION

The workplace assessment scale for student anesthetist nurses shows strong psychometric properties in validity and reliability. Its strengths include content validity, internal consistency, and educational impact, while challenges exist in inter-rater reliability for non-technical skills and feasibility in complex clinical scenarios. Future refinement should aim at technology integration for improved assessment efficiency, longitudinal validation for predictive validity, and adaptation to enhance generalizability across various contexts.[30] These improvements would boost the effectiveness of workplace assessments in anesthesia nurse education, ultimately promoting better patient care through efficient competency evaluation.

Data Availability Statement

Dataset 1. Raw response data of participants to each item of the new workplace-based assessment scale.

Dataset 2. Raw response data of participants to each item of the primary workplace-based assessment scale.

ACKNOWLEDGEMENTS

The authors thank the Siriraj Health Science Education Excellence Center, Faculty of Medicine Siriraj Hospital, for funding our research.

DECLARATIONS

Grants and Funding Information

This study was funded by Siriraj Health Science Education Excellence Center, Faculty of Medicine Siriraj Hospital, Mahidol University, Thailand, under grant number R016861009.

Conflict of Interest

The authors declare no conflict of interest.

Registration Number of Clinical Trial

None.

Author Contributions

Conceptualization and methodology, P.A., N.T., and P.V.; Investigation, L.P., W.P.; Formal analysis, P.A. and P.V.; Visualization and writing – original draft, P.A.; Writing – review and editing, P.A., N.T., and P.V.; Funding acquisition, P.A., L.P., W.P.; Supervision, P.V. All authors have read and agreed to the final version of the manuscript.

Use of Artificial Intelligence

The authors used Grammarly AI to assist with grammar correction and sentence refinement. The authors thoroughly validated and approved all AI-assisted content to ensure accuracy and compliance with academic and ethical standards.

REFERENCES

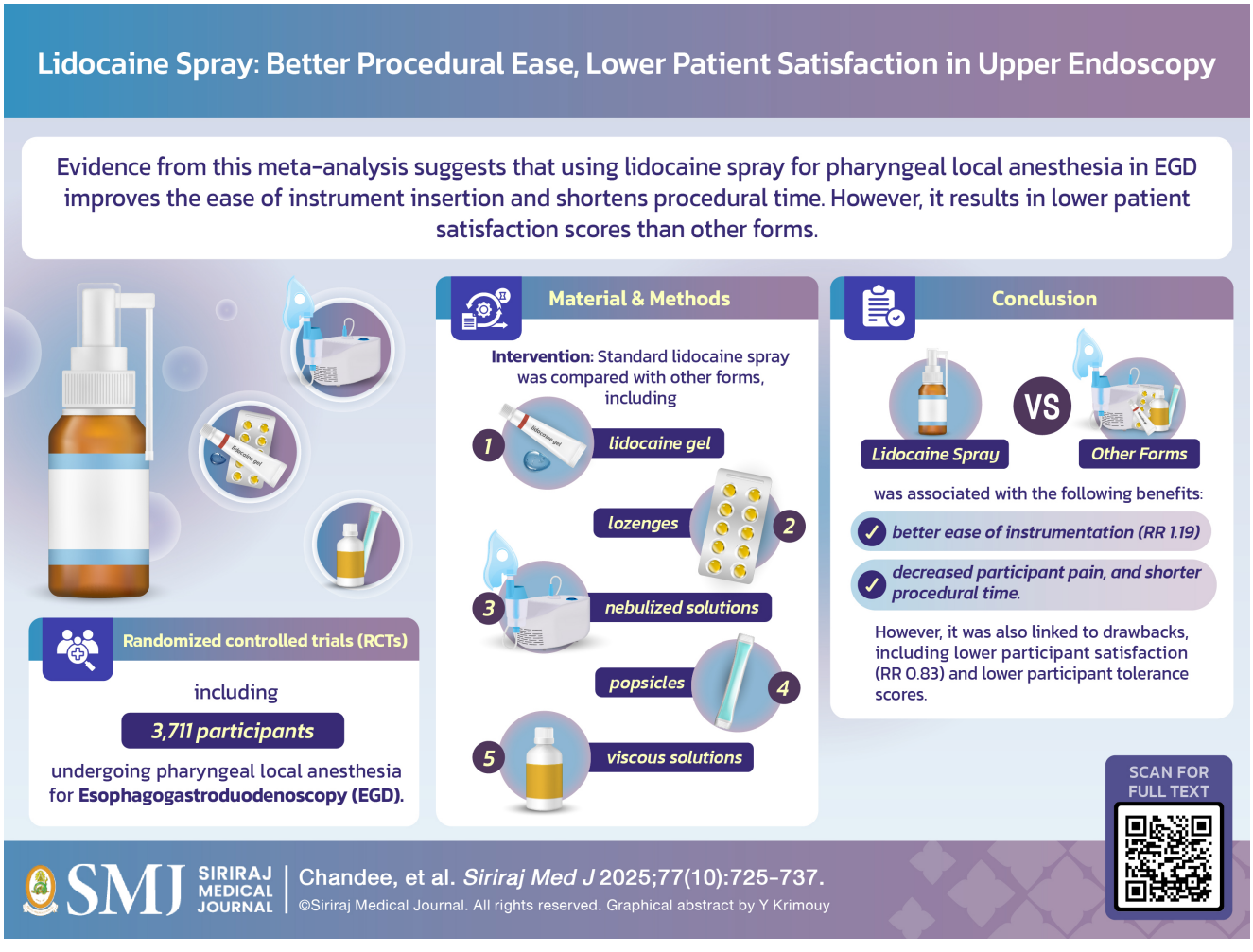
1. Antonsen KN, Hofstad JK. Simulating preoperative preparations with focus on non-technical skills in an OR nursing education program in Norway. In: Springer International Publishing; 2022. p. 37–52.
2. Ratanasuwan P, Sriraj W, Punjasawadwong Y, Choorat J, Charuluxananan S, Pravitharangul T. The Perioperative and Anesthetic Adverse Events in Thailand (PAAd Thai) study of anesthetic equipment malfunction or failure: An analysis of 2206 incident reports. J Med Assoc Thai. 2021;104:286–92.
3. Smedley P, Nicholas-Holley J. Recovery of patients from anaesthesia and surgery. In: Rodger D, Henshaw K, Rawling P, Miller S, editors. Fundamentals of Operating Department Practice. Cambridge: Cambridge University Press; 2022. p. 384–406.
4. Nucharoenkul S. Competencies and certification of knowledge and specialized expertise for advanced practice nurses. 1st ed. Bangkok: Siriyod Printing; 2010.
5. Matlhaba K. Essential clinical skills. In: Enhancing Clinical Competence of Graduate Nurses. Cham: Springer Nature Switzerland; 2025. p. 113–34.
6. Boker AM. Toward competency-based curriculum: Application of workplace-based assessment tools in the National Saudi Arabian Anesthesia Training Program. Saudi J Anaesth. 2016;10(4):417–22.
7. Khalafi A, Sharbatdar Y, Khajeali N, Haghighizadeh MH, Vaziri M. Improvement of the clinical skills of nurse anesthesia

students using mini-clinical evaluation exercises in Iran: A randomized controlled study. J Educ Eval Health Prof. 2023;20:12.
8. Mortaz Hejri S, Jalili M, Masoomi R, Shirazi M, Nedjat S, Norcini J. The utility of mini-clinical evaluation exercise in undergraduate and postgraduate medical education: A BEME review: BEME Guide No. 59. Med Teach. 2020;42(2):125–42.
9. Kurdi MS, Hungund BR. Evaluation of mini-clinical evaluation exercise (mini-CEX) as a method for assessing clinical skills in anaesthesia postgraduate education. Indian J Anaesth. 2021; 65(3):248–52.
10. Flin R, Fletcher G, Glavin R, Maran N, Patey R. Anaesthetists' Non-Technical Skills (ANTS) System Handbook. Aberdeen: University of Aberdeen; 2003.
11. World Medical Association. World Medical Association Declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA. 2013;310:2191–4.
12. 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.
13. Kanjanawasee S. Classical test theory. 7th ed. Bangkok: Chulalongkorn University Press; 2013.
14. Saad S, Carter GW, Rothenberg M, Israelson E. Testing and assessment: An employer's guide to good practices. Washington, DC: U.S. Department of Labor; 1999.
15. Taber KS. The use of Cronbach's alpha when developing and reporting research instruments in science education. Res Sci Educ. 2018;48:1273–96.
16. Popovich D. How to treat missing data in survey research. J Mark Theory Pract. 2025;33(1):43-59.
17. Koo TK, Li MY. A guideline of selecting and reporting intraclass correlation coefficients for reliability research. J Chiropr Med. 2016;15(2):155–63.
18. Senthil Kumar VS, Shahraz S. Intraclass correlation for reliability assessment: The introduction of a validated program in SAS (ICC6). Health Serv Outcomes Res Methodol. 2024;24(1): 1–3.
19. Chin M, Pack R, Cristancho S. "A whole other competence story": Exploring faculty perspectives on the process of workplace-based assessment of entrustable professional activities. Adv Health Sci Educ Theory Pract. 2023;28(2):369–85.
20. Slabbert B, Hoole C. A competency framework for coaches working in coaching development centres. SA J Ind Psychol. 2021;47(1):1–10.
21. Wingate TG, Bourdage JS, Steel P. Evaluating interview criterion-related validity for distinct constructs: A meta-analysis. Int J Sel Assess. 2025;33(1):1–21.
22. Gümüş MM, Kukul V. Developing a digital competence scale for teachers: Validity and reliability study. Educ Inf Technol. 2023;28(3):2747–65.
23. Maj M, van Os J, De Hert M, Gaebel W, Galderisi S, Green MF, et al. The clinical characterization of the patient with primary psychosis aimed at personalization of management. World J Psychiatry. 2021;20(1):4–33.
24. Delfino AE, Fuentes-López EA, de la Fuente RF, Altermatt FR. Cross-cultural adaptation and validation of the Spanish version of the Anesthetists' Non-Technical Skills (ANTS) assessment tool. J Clin Anesth. 2023;84:1-5.
25. Yeates P, Maluf A, Kinston R, Cope N, Cullen K, Cole A, et al. A realist evaluation of how, why and when objective structured clinical exams (OSCEs) are experienced as an authentic assessment of clinical preparedness. Med Teach. 2025;47(3):458–66.
26. Yi L, Shuai T, Zhou J, Cheng L, Jiménez-Herrera MF, Tian X. Development and validation of a machine learning-based predictive model for compassion fatigue in Chinese nursing interns: A cross-sectional study utilizing latent profile analysis. BMC Med Educ. 2024;24(1):1–20.
27. Martin EL, Martinez DA. The effect size in scientific publication. Educ. XXI.2023;26(1):9-17.
28. Gamborg ML, Mehlsen M, Paltved C, Vetter SS, Musaeus P. Clinical decision-making and adaptive expertise in residency: A think-aloud study. BMC Med Educ. 2023;23(1):1–20.
29. McIntosh TR, Liu T, Susnjak T, Watters P, Halgamuge MN. A reasoning and value alignment test to assess advanced GPT reasoning. ACM Trans Interact Intell Syst. 2024;14(3):1–37.
30. Chudapongse R, Sangpetngam B, Chankaew E, Aurboonyawat T, Churojana A, Withayasuk P. Comparative Evaluation of Imaging Modalities for Eligibility in Endovascular Treatment of Delayed Onset Acute Anterior Circulation Ischemic Stroke in Siriraj Hospital: A Retrospective Analysis. Siriraj Med J. 2024; 76(9):573-80.

Lidocaine Spray versus Other Forms for Local Anesthesia in Upper Gastrointestinal Endoscopy: A Systematic Review and Meta-analysis

Theerada Chandee, M.D.[1], Saritphat Orrapin, M.D.[2,3], Prasit Mahawongkajit, M.D.[2,3], Neranchala Soonthornkes, M.D.[1], Chuleerat Suptongchai, M.D.[1], Thanatcha Luangmaneerat, M.D.[1], Sudsayam Manuwong, M.D.[1,*]

[1]Department of Anesthesiology, Faculty of Medicine, Thammasat University, Pathumthani, Thailand, [2]Department of Surgery, Faculty of Medicine, Thammasat University, Pathumthani, Thailand, [3]Research Group in Surgery, Faculty of Medicine, Thammasat University, Pathumthani, Thailand.



*Corresponding author: Sudsayam Manuwong
E-mail: Ohmtu@yahoo.com
Received 21 July 2025 Revised 4 September 2025 Accepted 4 September 2025
ORCID ID:http://orcid.org/ 0000-0003-3338-2036
https://doi.org/10.33192/smj.v77i10.276670

ABSTRACT

Objective: To evaluate the effectiveness of various lidocaine forms compared to the traditional spray during esophagogastroduodenoscopy (EGD).

Materials and Methods: We searched PubMed, Scopus, EMBASE, the Cochrane Central Register of Controlled Trials, CENTRAL, Web of Science Core Collection, World Health Organization, International Clinical Trials Registry Platform, and ClinicalTrials.gov databases in December 2022. Selection criteria were randomized controlled trials comparing lidocaine spray with other forms of pharyngeal anesthesia. Outcomes of interest included ease of instrumentation, participants' satisfaction scores, tolerance scores, pain, endoscopist's satisfaction scores, and procedural time.

Results: We included 13 trials with 3,711 participants. The quality of trials was poor. Lidocaine spray provided better ease of instrumentation (risk ratio (RR) 1.19, 95% confidence intervals (CI)1.06,1.34; I^2 = 66%; very low certainty of evidence), decreased participants' pain (mean difference (MD) 0.38, 95% CI 0.25,0.5; I^2 = 92%; very low certainty of evidence), and shorter procedural time (MD 0.22, 95% CI 0.10,0.35; I^2 = 13%; low certainty of evidence). However, spray had lower participants' highest satisfaction scores (RR 0.83, 95% CI 0.76,0.92; I^2 = 62%; very low certainty of evidence), participants' mean satisfaction scores (MD -0.61, 95% CI -0.29,-0.04; I^2 = 92%; very low certainty of evidence), participants' tolerance scores (RR 0.83, 95% CI 0.71,0.97; I^2 = 0%; low certainty of evidence), and endoscopist's satisfaction scores (MD -0.33, 95% CI -0.45,-0.21; I^2 = 94%; very low certainty of evidence).

Conclusion: Evidence suggests that lidocaine spray may improve the ease of EGD instrumentation, although limitations in trial quality warrant cautious interpretation.

Keywords: Anesthesia; esophagogastroduodenoscopy; lidocaine (Siriraj Med J 2025; 77: 725-737)

INTRODUCTION

EGD is a widely used procedure for screening, diagnosing, and treating upper gastrointestinal diseases. It can be performed with no sedation, mild sedation, or moderate/conscious sedation with or without the use of topical pharyngeal anesthesia.[1] During the procedure, an endoscope is inserted through the oral cavity into the upper gastrointestinal tract, which often causes discomfort or pain, particularly in patients with a strong gag reflex.[2] Sedation during EGD may also lead to adverse events, including cardiopulmonary complications such as hypoxia, respiratory depression, hypertension or hypotension, arrhythmias (tachycardia or bradycardia), pulmonary edema, cardiovascular collapse, and vasovagal reactions.[3]

Topical anesthesia with lidocaine reduces cough, suppresses the gag reflex, and mitigates overall airway hyperreactivity. This improves patient compliance and enhances operator satisfaction during endoscopic procedures.[4] Performing EGD under topical lidocaine, with or without sedation, decreases adverse events, reduces the gag reflex, and increases patient comfort, especially in patients at higher risk of complications, such as those with cardiopulmonary disease, high ASA physical status, advanced age, or obesity.[5-7]

Lidocaine spray is a commonly used local anesthetic for EGD in Thailand due to its convenience and safety. However, it has some drawbacks, including a bitter taste and the potential to provoke a gag reflex.[8] Recent studies have compared lidocaine spray with alternative delivery methods, such as gel, viscous solutions, lozenges, popsicles, and nebulized forms, by evaluating ease of procedure, pain levels, gag reflex intensity, procedure duration, patient tolerance, and satisfaction among both patients and endoscopists.[7,9-12] Despite this, no study has yet comprehensively assessed the effectiveness of these alternative forms of local anesthesia compared to conventional topical spray during EGD.

MATERIALS AND METHODS

The protocol was developed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines for reporting systematic reviews and meta-analyses[13,14] as well as the PRISMA Extension Statement for Systematic Reviews Incorporating Network Meta-analyses of Health Care Interventions.[15]

Search strategy

We searched the PubMed, Scopus, EMBASE, Cochrane Central Register of Controlled Trials (CENTRAL), Web of Science Core Collection, World Health Organization (WHO) International Clinical Trials Registry Platform (ICTRP), and ClinicalTrials.gov databases up through 31 December 2022. The search used the following medical

search terms: 'gastroscope' [Mesh] OR 'gastroenteroscopy' [Mesh] OR 'esophagogastroduodenoscopy' [Mesh] OR 'upper gastrointestinal scope' [Mesh] NOT colonoscope NOT lower; lidocaine spray OR local anesthesia OR lidocaine nebulizer OR lidocaine solution OR lidocaine. These terms were combined using AND and were limited to clinical trials involving human participants. We also reviewed reference lists from previous meta-analyses and research for additional relevant studies.

Study selection

Two authors (SO, TC) independently screened the titles and abstracts of the studies retrieved from the electronic searches. Full texts were reviewed when eligibility could not be determined based on the title and abstract alone. The remaining studies were read in full by the same authors, whose eligibility was assessed according to predefined criteria. Disagreements were resolved through discussion with other authors [SM, NS]. Duplicated publications were combined into a single study for analysis.

Inclusion criteria

Randomized controlled trials (RCTs) were eligible if they involved patients undergoing EGD and compared lidocaine spray with at least one of the following interventions: viscous lidocaine solution, lidocaine nebulizer, popsicle, gel, or lozenge. Studies had to report at least one of the following outcomes: ease of instrumentation, endoscopist satisfaction, participant satisfaction, tolerance, pain or discomfort, or procedural time. Studies were excluded if they lacked usable data.

Intervention and control groups

Lidocaine blocks sensations in the glossopharyngeal and superior laryngeal nerves in the upper airway. It is commonly used for pharyngeal anesthesia prior to EGD. Lidocaine is available in various forms, including spray, gel, viscous solution, and lozenges, with spray being the most frequently used. This study compared the standard lidocaine spray with other forms, specifically lidocaine gel, lozenges, nebulized lidocaine, popsicles, and viscous solutions.

Outcomes

The primary objective was to compare the effectiveness of conventional lidocaine spray with other forms of local anesthesia during EGD, without compromising the success of the endoscopic procedure. The outcomes assessed in the study included:

Primary outcome:

Ease of procedure (defined as no gag reflex)

Secondary outcomes:

- Participants' highest satisfaction score
- Participants' mean satisfaction score (NRS 0-10)
- Participants' tolerance score
- Participants' pain or discomfort (NRS 0-10)
- Endoscopist's satisfaction score (NRS 0-10)
- Procedural time (minutes)

Data extraction

Two independent authors (SO and TC) extracted data using standardized forms. The extracted data included study characteristics and interventions, including type of lidocaine administration, composition and preparation of lidocaine, and primary outcome. Data on outcomes, including means, standard deviations (SDs), and frequencies, were extracted for statistical pooling. When summary data were unavailable, we used the mean difference (MD) or risk ratio (RR) for analysis. Any inconsistencies in data were resolved by consulting a third author. We contacted corresponding authors twice for missing data, which were used to explore sources of heterogeneity.

Risk of bias assessment

We assessed the risk of bias using the Cochrane 'Risk of Bias' tool, as described in the Cochrane Handbook for Systematic Reviews of Interventions. Risks were classified as high, low, or unclear for the following areas: random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding outcome assessment (detection bias), and incomplete outcome data (attrition bias). Two independent researchers (TC and SM) performed the risk assessments, and disagreements were resolved by discussion with other review authors (NS, PM).

Dealing with missing data

If data were missing, we contacted the corresponding author, first author, or coauthor for clarification. If contact information was unavailable, we attempted to locate the study group through the internet.

Assessment of heterogeneity

Heterogeneity between studies was assessed using the I^2 statistic and the Q test. A value of $I^2 \geq 25\%$ or a significant Q test $p<0.10$ indicated substantial heterogeneity, and a random-effects model was applied.[16]

Grading evidence

The quality of evidence for each outcome was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach.[17] Evidence was downgraded if there were serious or very serious concerns in any of the following domains: limitations in study design, inconsistency of results, indirectness of evidence, imprecision, or publication bias. We summarized the findings using GRADE Profiler 3.6, and presented the results and the certainty of the evidence (high, moderate, low, or very low).[19]

Statistical analysis

We pooled data directly when at least three studies were available for each comparison. The Mantel-Haenszel method (fixed-effects model) was used for the final analysis of results from the original trials included in the combined analysis. Relative risks with 95% confidence intervals (CIs) were estimated for dichotomous outcomes. For continuous outcomes, we estimated unstandardized or standardized MDs with 95% CIs, depending on whether the studies used the same or different measurement scales, respectively. When a study did not report the mean and standard deviation (SD), we estimated them from the median and range or interquartile range.

We performed subgroup or sensitivity analyses based on factors that could affect heterogeneity. A funnel plot was used to assess publication bias.

All analyses of the intervention's effect were conducted on an intention-to-treat basis, using randomized treatment allocation. Significant differences between treatment groups were assessed with the log rank test, stratified by study. Absolute treatment effects and their 95% CIs were estimated. Differences in baseline data between trials and treatment groups were tested using the Chi^2 test or Student's t-test, as appropriate.

All analyses were performed using RevMan 5 and STATA version 16.0 for Mac. A fixed-effects model was used for meta-analysis if clinical, methodological, or statistical heterogeneity were lacking. Statistical significance was defined as $p<0.05$, except for the heterogeneity test, where $p<0.10$ was used. A random-effects model was applied to determine whether the conclusions differed, and any differences were noted. A narrative summary was planned if data pooling was not possible or appropriate.

RESULTS

We identified a total of 722 records through database searches in January 2023. After duplication and exclusion of studies with unclear outcome data, 13 RCTs[7,9,12,20-29] comprising 3,711 participants were included in the quantitative synthesis comparing lidocaine spray with other forms (gel, viscous solutions, lozenges, popsicles, or nebulized lidocaine) (Fig 1).

Risk of bias in the included studies

There were several significant biases in most of the included trials (Figs 2 and 3).

Eight trials had adequate random sequence generation.[7,9,12, 22,23,26-28]

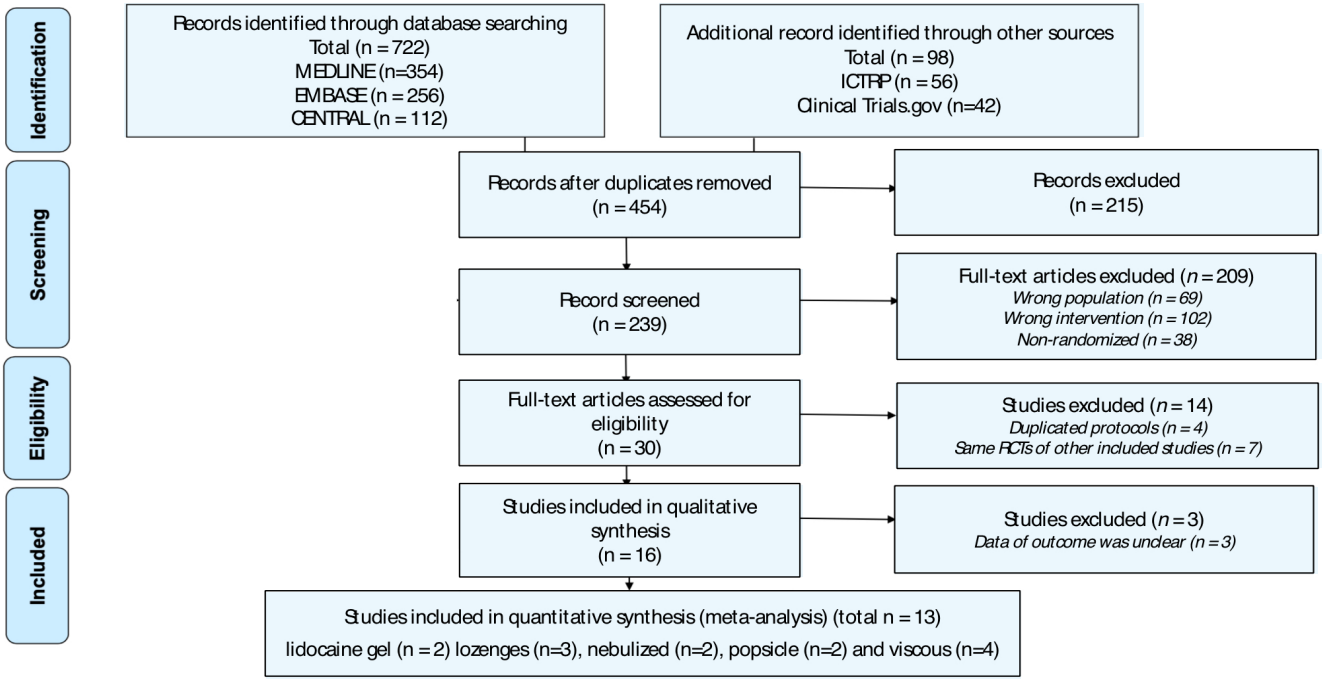


Fig 1. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) flow diagram of the literature search results.

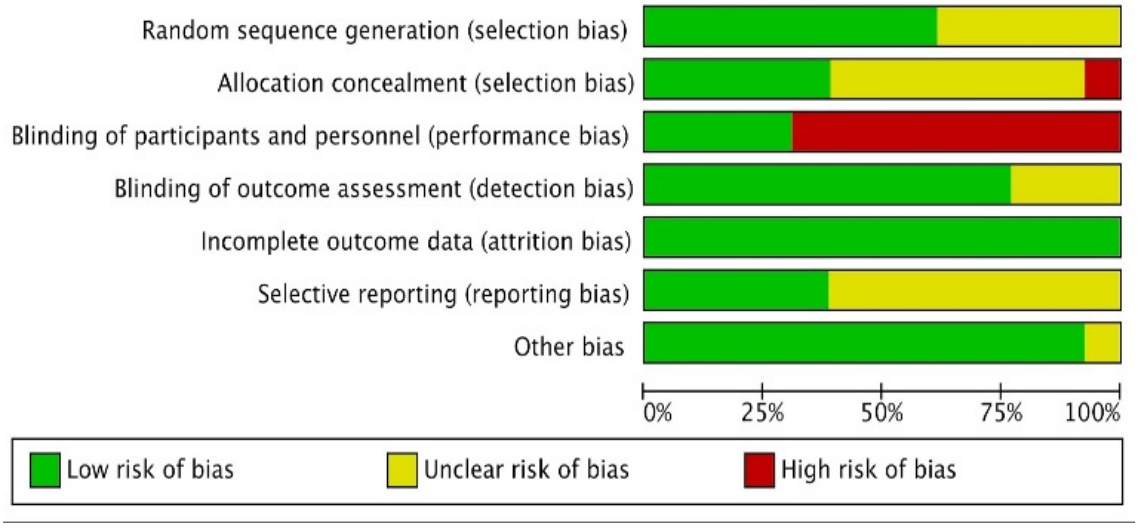


Fig 2. Risk of bias graph.

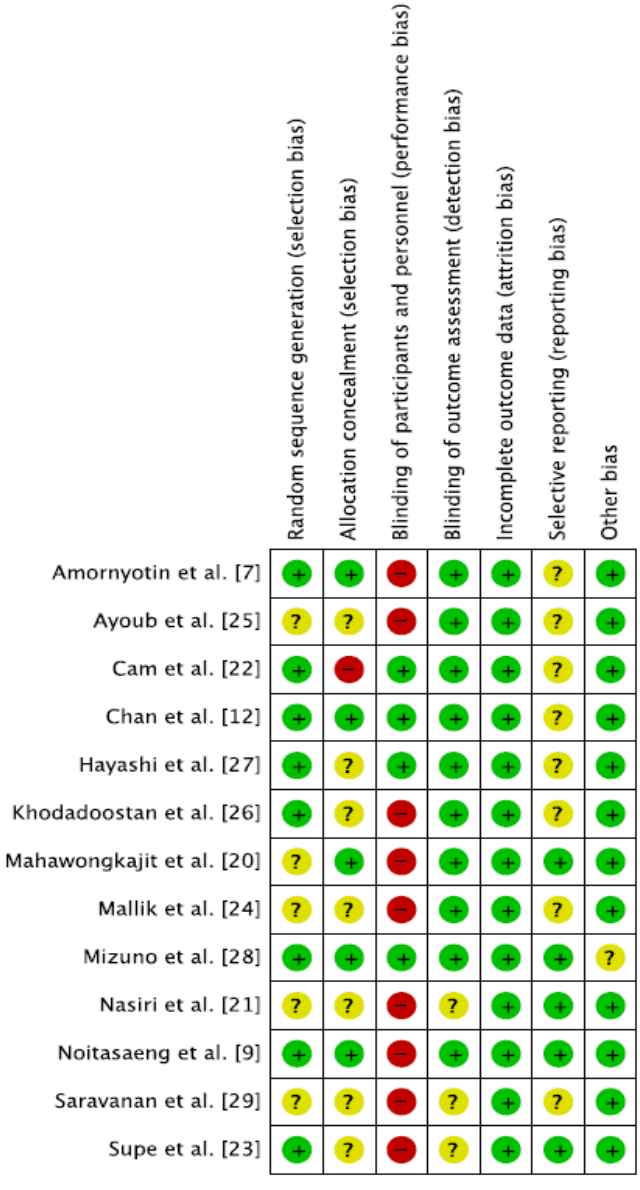


Fig 3. Risk of bias table.

Allocation concealment was adequate in only five trials[7,12,9,20,28], which used numbered, sealed, opaque envelopes as the randomization method.

Blinding is crucial to reduce bias in outcome assessment. Only four trials successfully blinded the interventions[12,22,27,28], while ten trials reported blinding of clinical assessors.[7,9,12,20,22,24-28] No trial reported incomplete outcome data. However, only five trials published results for all planned outcomes.[9,20,21,23,28] Most studies were judged to be at low risk of 'other' bias, with the exception of Mizuno et al.[28]

Outcomes

A summary of the findings is presented in Table 1. Lidocaine spray was associated with greater ease of instrumentation (risk ratio (RR) 1.19, 95% confidence interval (CI) 1.06, 1.34; I^2 = 66%; very low certainty of evidence) (Fig 4), reduced participant-reported pain or discomfort (mean difference (MD) 0.38, 95% CI 0.25, 0.5; I^2 = 92%; very low certainty of evidence) (Fig 5), and shorter procedural time (MD 0.22, 95% CI 0.10, 0.35; I^2= 13%; low certainty of evidence) (Fig 6).

However, lidocaine spray was associated with lower participant-reported highest satisfaction scores (RR 0.83, 95% CI 0.76,0.92; I^2 = 62%; very low certainty of evidence) (Fig 7), mean satisfaction scores (MD -0.61, 95% CI -0.29, 0.04; I^2 = 92%; very low certainty of evidence) (Fig 8), tolerance scores (RR 0.83, 95% CI 0.71,0.97; I^2= 0%; low certainty of evidence) (Fig 9), and satisfaction scores (MD -0.33, 95% CI -0.45, 0.21; I^2 = 94%; very low certainty of evidence) (Fig 10).

TABLE 1. Summary of findings.

Lidocaine spray versus other forms of local anesthesia in EGD.

Patient or population: participants undergoing EGD with pharyngeal local anesthesia

Settings: In Esophagogastroduodenoscopy

Intervention: Lidocaine spray

Comparison: Other forms e.g. lidocaine gel, lozenges, nebulized, popsicle, and viscous

Outcomes	Anticipated absolute effects (95% CI)		Relative effect (95%CI)	No. of participants (Studies)	Certainty of the evidence (GRADE)	Comments
	Risk with others	Risk with spray				
Ease of instrument	28 per 100	36 per 100	RR 1.19 (1.06,1.34)	2460 (5 RCTs)	⊕⊖⊖⊖ Very low ◆,‡,§	No studies could be blinded participants due to the types of anesthetics used
Participants' pain/discomfort	-	MD 0.38 (0.25-0.50)	- (6 RCTs)	2786	⊕⊖⊖⊖ Very low ◆,‡,§	Some studies could be blinded participants due to the types of anesthetics used
Participants' highest satisfaction score	34 per 100	41 per 100	RR 0.83 (0.76,092)	2817 (7 RCTs)	⊕⊖⊖⊖ Very low ◆,‡,§	Some studies could be blinded participants due to the types of anesthetics used
Participants' mean satisfaction score	-	MD -0.16 (-0.29, -0.04)	-	2504 (6 RCTs)	⊕⊖⊖⊖ Very low ◆,‡,§	Some studies could be blinded participants due to the types of anesthetics used
Participants' tolerance score	22 per 100	27 per 100	RR 0.83 (0.71-0.97)	1926 (2 RCTs)	⊕⊕⊖⊖ Low ◆,‡	No studies could be blinded participants due to the types of anesthetics used
Endoscopist's satisfaction score	-	MD -0.33 (-0.45, -0.21)	-	2301 (4 RCTs)	⊕⊖⊖⊖ Very low ◆,‡,§	Some studies could be blinded participants due to the types of anesthetics used
Procedural time	-	MD 0.22 (0.10,0.35)	- (4 RCTs)	565	⊕⊕⊖⊖ Low ◆,‡	Some studies could be blinded participants due to the types of anesthetics used

◆ Downgraded one level for risk of bias concerns, as studies did not blind participants[7,9,20,21,23-26,29], selective reporting[7,22,24-27,29,30], inadequate allocation concealment[21-27,29] and random sequence generation.[20,21,24,25,29]

‡ Downgraded one level for imprecision owing to wide confidence intervals.

§ Downgraded one level for inconsistency due to true heterogeneity according to I^2 statistics and P values, confidence interval overlap, difference in point estimates, and between-study variance.

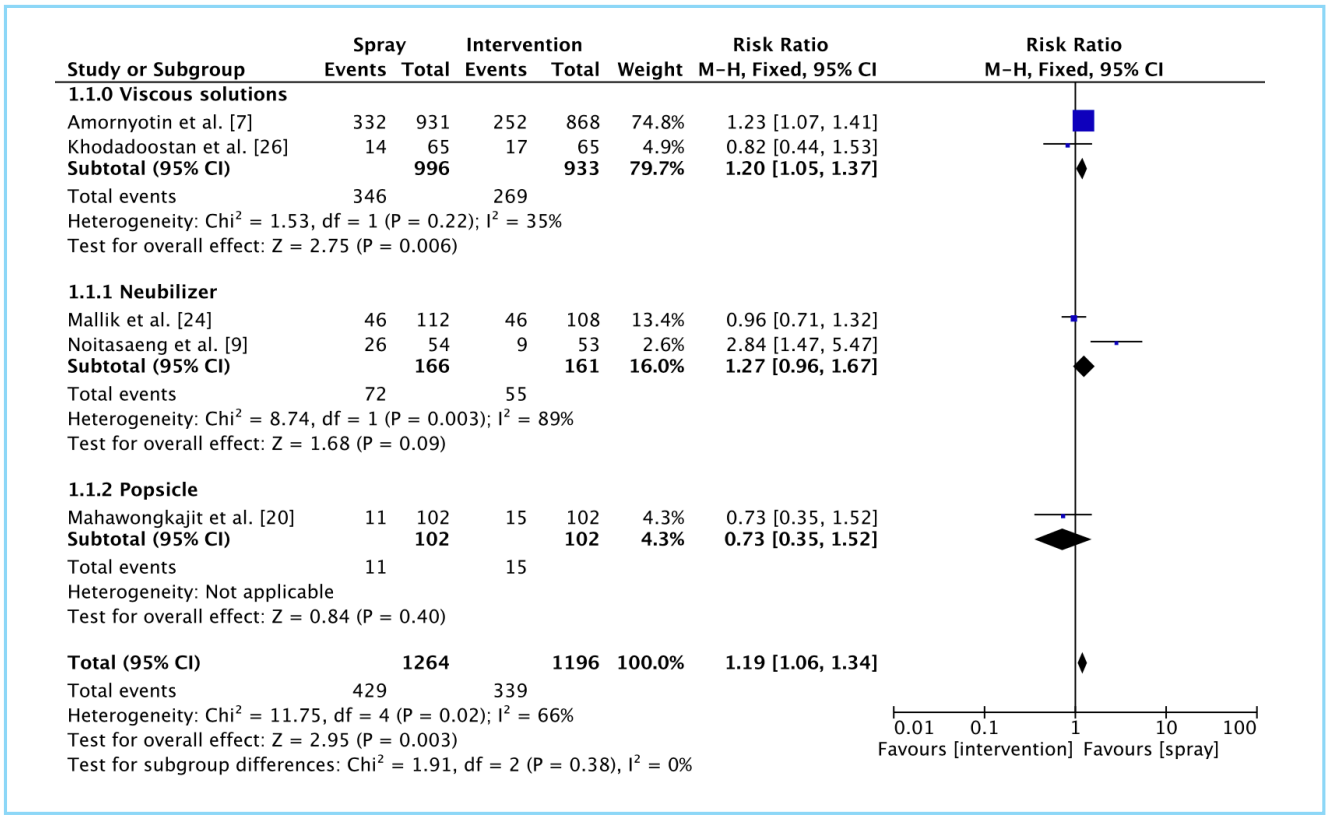


Fig 4. Forest plot of studies comparing the ease of instrumentation between intervention and spray groups, with subgroups of intervention for viscous solution, nebulizer, and popsicle.

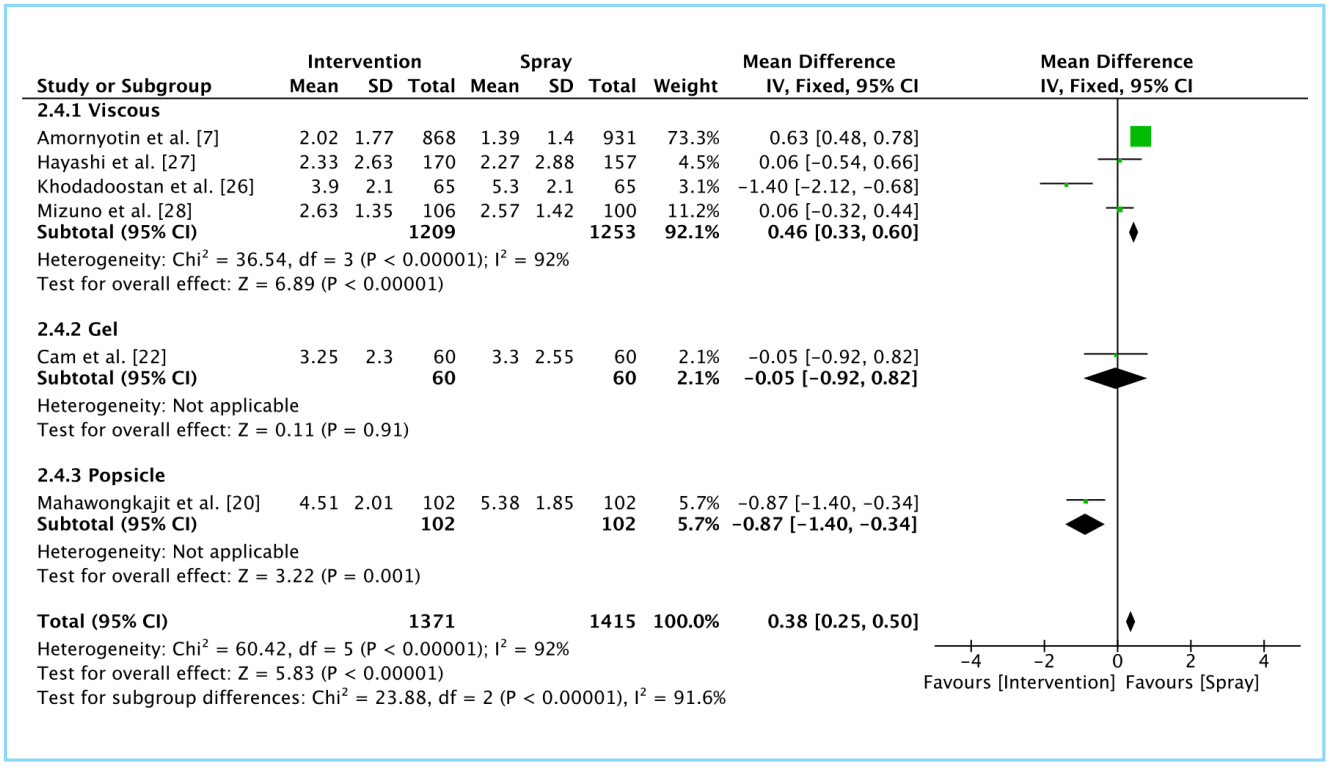


Fig 5. Forest plot of studies comparing the mean score of numeric rating scale for participants' pain/discomfort (0-10) between intervention and spray groups, with subgroups of intervention for viscous, gel, and popsicle.

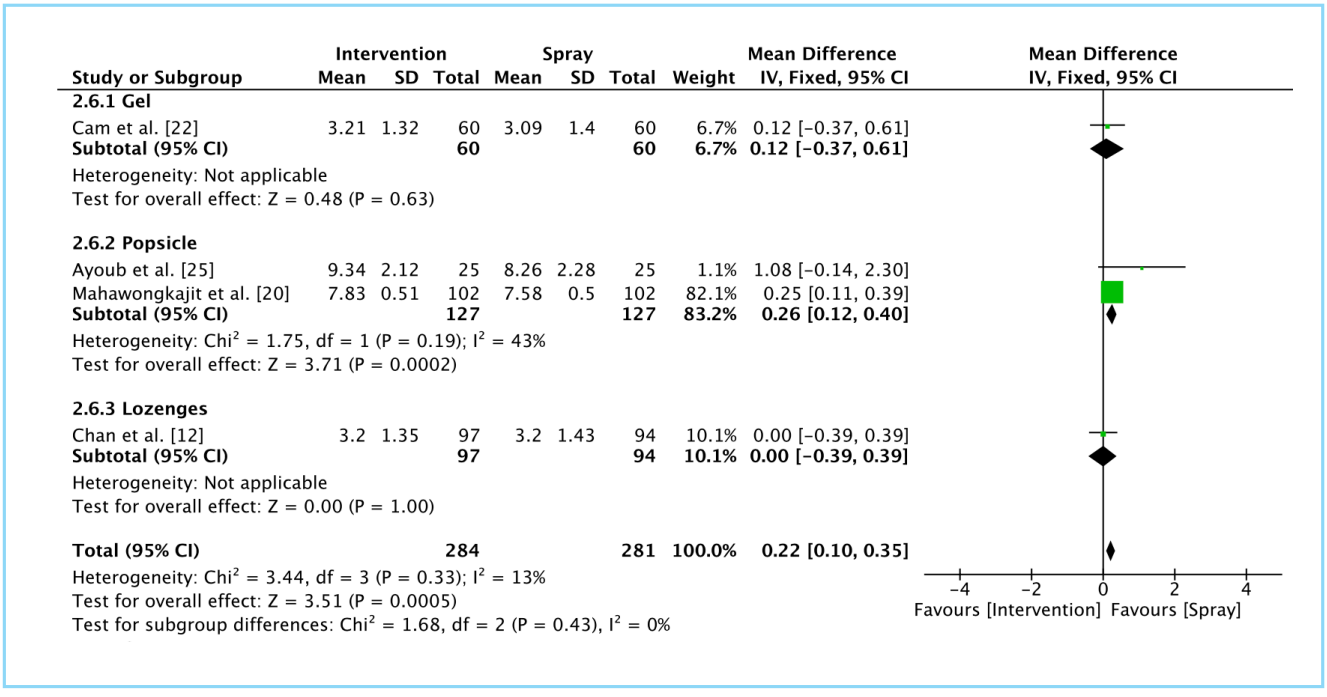


Fig 6. Forest plot of studies comparing procedural time of EGD between intervention and spray groups, with subgroups of intervention for gel, popsicle, and lozenges.

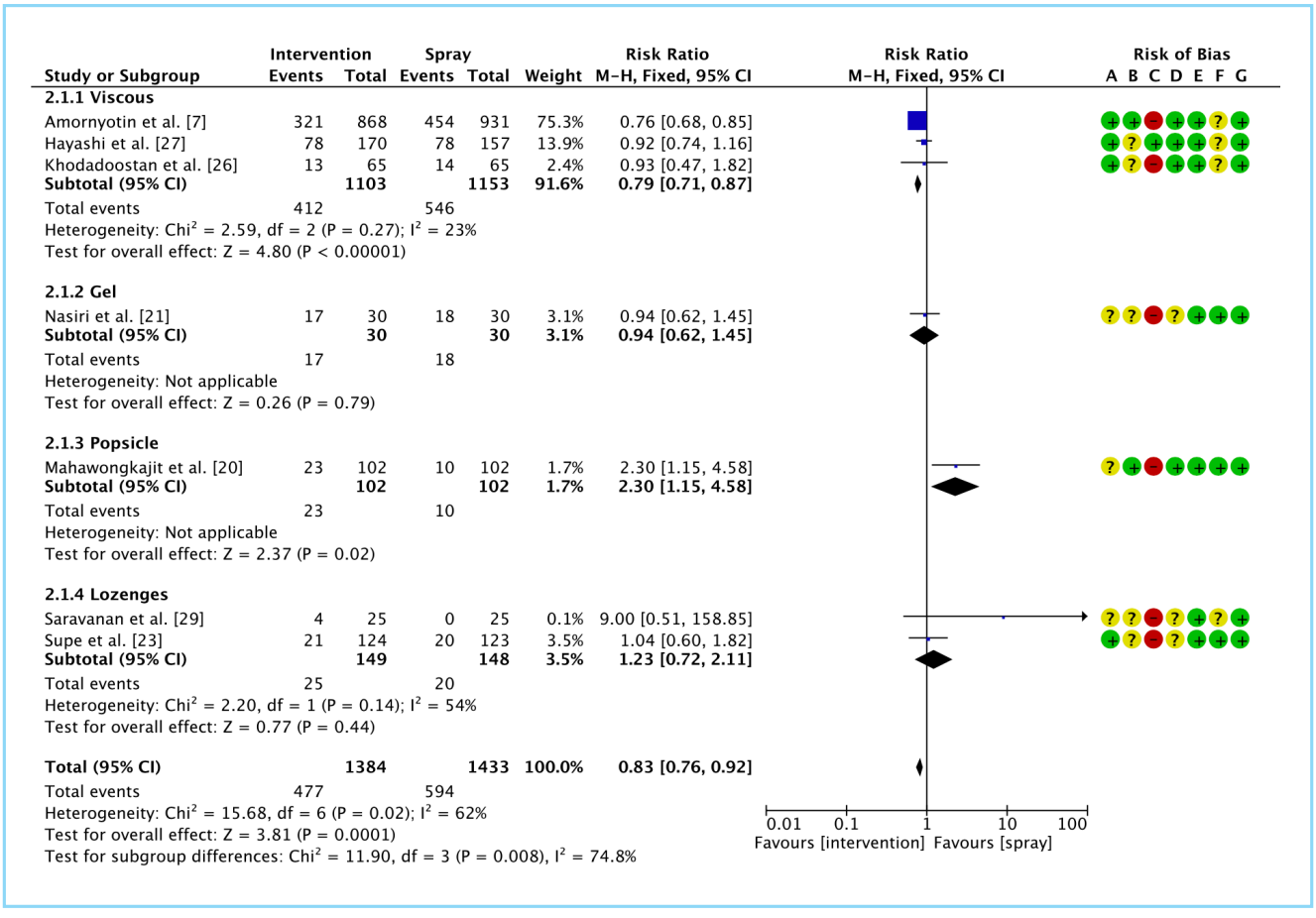


Fig 7. Forest plot of studies comparing the proportion of participants who reported the highest satisfaction score between intervention and spray groups, with subgroups of intervention for viscous, gel, popsicle, and lozenges.

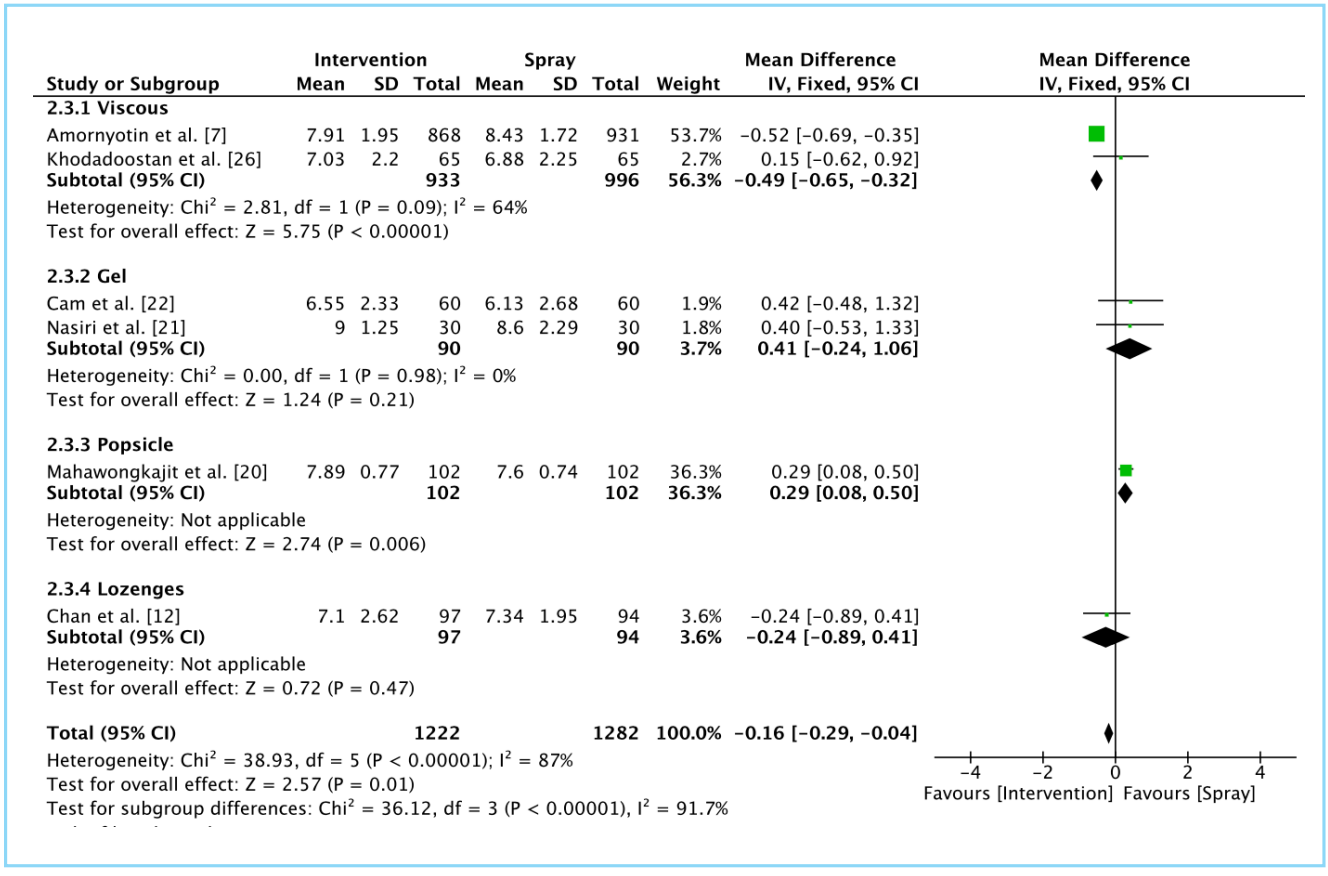


Fig 8. Forest plot of studies comparing the mean participants' satisfaction score (0–10) between intervention and spray groups, with subgroups of intervention for viscous, gel, popsicle, and lozenges.

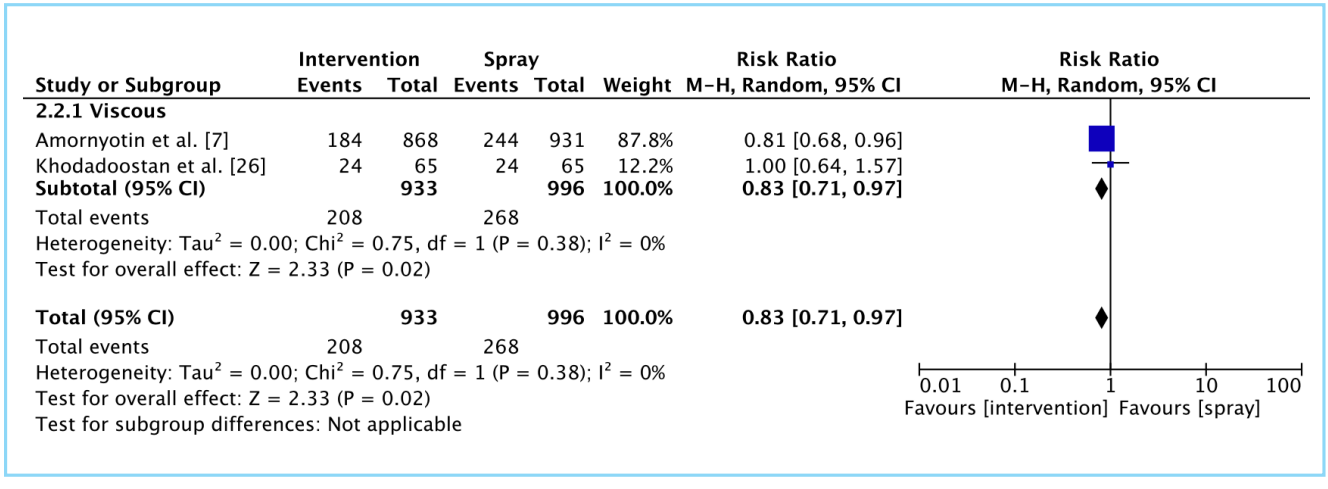


Fig 9. Forest plot of studies comparing the proportion of participants who achieved the highest tolerance score between intervention (Viscous) and spray groups.

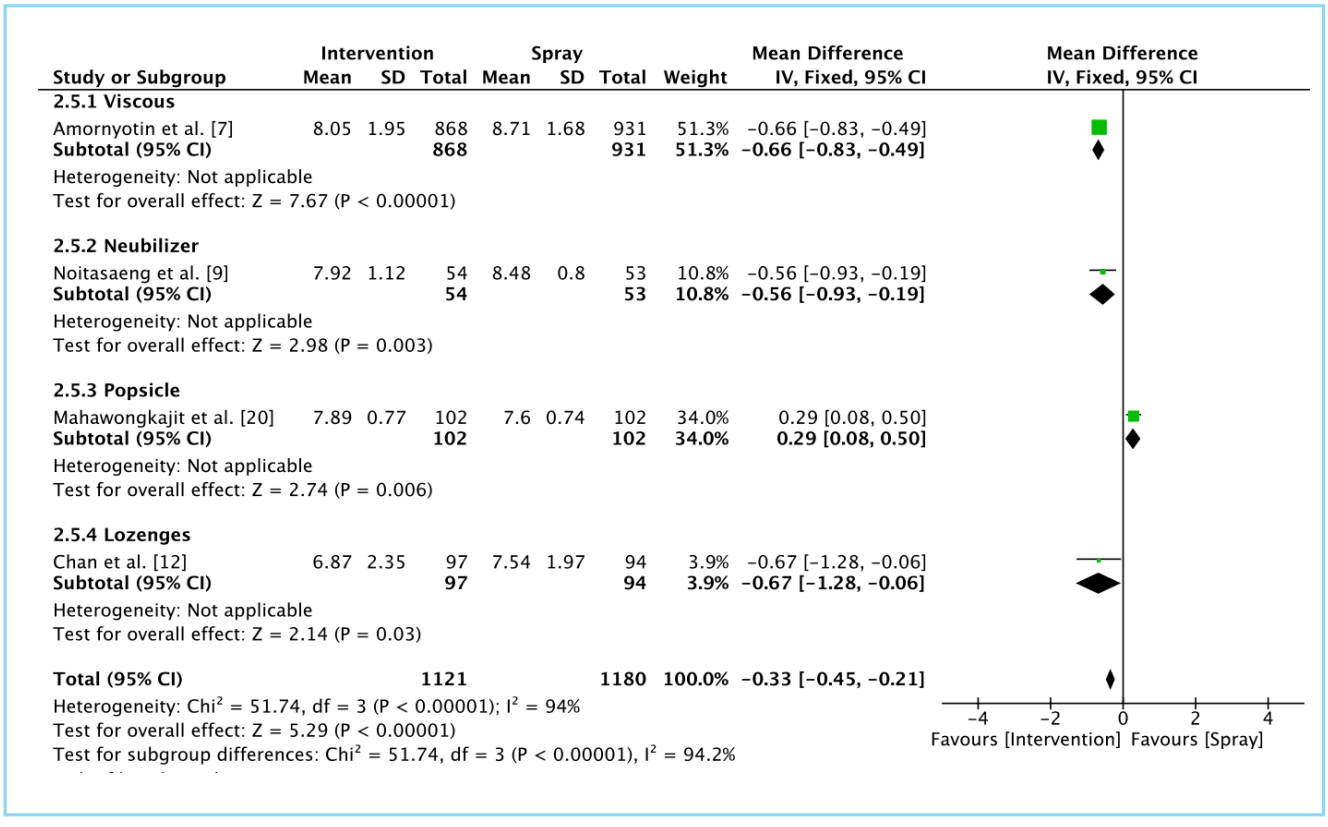


Fig 10. Forest plot of studies comparing the mean endoscopist satisfaction score (0–10) between intervention and spray groups, with subgroups of intervention for viscous, nebulizer, popsicle, and lozenges.

DISCUSSION

This systematic review, which included 13 RCTs involving 3,711 participants, found that lidocaine spray, compared to other forms of lidocaine, provided better ease of instrumentation, reduced pain or discomfort, and shorter procedural time. However, it was associated with lower participants' highest satisfaction scores, mean satisfaction scores, tolerance scores, and overall satisfaction. Most RCTs in this review had low or very low certainty of evidence, based on GRADE methodology. These studies revealed design issues, inconsistent results, imprecise effect estimates, and potential publication bias. These issues seriously limit the reliability of our findings.

Topical lidocaine spray typically uses a water-oil emulsion, which enhances tissue penetration and nerve access. It is rapidly absorbed across the mucous membrane and provides effective anesthesia.

In the spray group, ease of instrumentation improved due to more accurate anesthesia of the posterior pharynx. Using a tongue blade further exposed this region. Lidocaine spray offered more effective topical pharyngeal anesthesia, contributing to a higher procedure success rate. In contrast, viscous lidocaine is rinsed in the oral cavity, where it mixes with saliva and is retained in the mouth, leading to inadequate pharyngeal anesthesia.[7] Our analysis suggests that lidocaine spray eases instrument insertion; however, the low certainty of evidence means that these results require caution.

Over 7 million people undergo EGD annually in the United States. EGD procedures in Thailand have also increased significantly over the past decade, reflecting improved healthcare accessibility and diagnostic capacity[30,31], with approximately 12% concerned about pain during the procedure.[32] Inserting instruments through the oral cavity into the digestive tract may trigger a gag reflex, leading to pain or discomfort.[2] Lidocaine spray helped suppress or eliminate the gag reflex, improving ease of instrumentation, reducing procedural time, and alleviating pain and discomfort.

The lower satisfaction scores in the lidocaine spray group likely stemmed from its bitter taste and the discomfort associated with administration.[33] Some patients swallowed the drug immediately, and the plastic applicator—being weak, thin, and short—sometimes failed to direct the spray accurately to the posterior pharynx, leading to incomplete anesthesia.[34] Additionally, lidocaine itself can trigger a gag reflex. In a study by Mogensen et al.[35] patients preferred lidocaine lozenges, which had a better taste during EGD. Similarly, lidocaine ice popsicles provided higher satisfaction, possibly due

to their gradual melting, which prolonged anesthetic exposure to the pharynx.[20] Lidocaine nebulizers were also well accepted and increased satisfaction during airway and GI endoscopy.[9,36]

Patient satisfaction may also be influenced by multiple factors, such as the operator's manner and skill, patient preparation, age, gender, gag reflex sensitivity, and baseline anxiety.[21] Campo et al.[2] identified factors reducing EGD tolerance, including a strong gag reflex, apprehension, female sex, younger age, and high anxiety. While some studies show that suppressing the gag reflex increases tolerability[37-39], others report no significant difference.[40,41] In our review, tolerance was higher in the non-spray group. This may be due to the more pleasant taste of lozenges or popsicles, or to baseline patient factors such as anxiety, age, or sex.

Interestingly, endoscopist satisfaction in our study was higher in the non-spray group. Previous research found that endoscopist satisfaction was influenced by ease of instrumentation, lower gag reflex, shorter preparation time, less secretion, and overall effortlessness.[9] Although our findings showed better ease of instrumentation and shorter procedural time with lidocaine spray, endoscopist satisfaction appeared to align more closely with patient tolerance—suggesting that endoscopists may value patient comfort and cooperation as much as procedural efficiency.

Our findings show that while lidocaine spray makes instrumentation easier and procedures shorter, it leads to lower patient tolerance and less endoscopist satisfaction than non-spray methods. This disconnect is unexpected. Technical efficiency does not automatically lead to a better experience for patients or providers. The sensory discomfort of the spray likely outweighs its procedural benefits. Endoscopists seem to value patient comfort as much as ease of the procedure. In practice, this suggests we should balance technical efficiency with patient experience. The best anesthetic approach may be the one offering the best overall experience, not just the easiest instrumentation.

Pain and satisfaction outcomes showed considerable heterogeneity ($I^2 > 90\%$), so the results should be interpreted with caution. This heterogeneity comes from several sources. There are differences in lidocaine formulations and how it is applied. Patient characteristics also play a part, such as age, baseline pain, and anxiety about the procedure. Differences in study methods, such as the timing of outcomes assessment and measurement tools, make direct comparisons more challenging. Still, most studies found that lidocaine had a positive effect in different situations.

Limitations

Our study has several limitations. First, eight of the thirteen included studies had a risk of bias in outcome reporting, potentially affecting the validity of the findings. Second, data extraction was challenging due to incomplete outcome reporting in several studies. We attempted to mitigate this by contacting the study authors to retrieve missing data. Lastly, low and very low certainty evidence in this review limits our ability to draw firm conclusions. We need more rigorous, well-designed studies with larger samples, standardized protocols, and comprehensive reporting to establish more reliable evidence on the efficacy of lidocaine spray in EGD procedures.

CONCLUSIONS

Compared with other forms of lidocaine used for local anesthesia, lidocaine sprays may improve ease of instrumentation, reduce pain and discomfort, and shorten procedural time during EGD. However, it is associated with lower patient satisfaction and tolerance scores. Given the variability in study quality and outcome reporting, further studies are needed to determine the most effective form of pharyngeal anesthesia for EGD with high-quality RCTs.

Data Availability Statement

The data generated and analyzed for this study are available in the databases where individual articles were searched. Upon reasonable request, this information can be provided by the corresponding author.

ACKNOWLEDGEMENTS

The authors would like to acknowledge Michael Jan Everts, from the Clinical Research Center, Faculty of Medicine, Thammasat University, for English editorial assistance.

DECLARATIONS

Grants and Funding Information

This study was approved by Thammasat University's Ethic Committee (MTU-EC-AN-0-035/66).

Conflict of Interest

The authors declare that they have no conflict of interest.

Registration Number of Clinical Trial

Not applicable.

Author Contributions

TC: Conceptualization, Methodology, Investigation,

Writing - Original draft preparation, Writing - Reviewing and Editing., SO: Conceptualization, Investigation, Formal analysis, Data curation, Writing - Reviewing and Editing, Visualization., PM: Conceptualization, Formal analysis, Data curation, Writing - Reviewing and Editing, Visualization., NS: Conceptualization, Supervision., CS: Conceptualization, Writing - Original draft preparation., TL: Conceptualization, Methodology, Writing - Original draft preparation., SM: Conceptualization, Writing - Reviewing and Editing, Supervision.

Use of Artificial Intelligence

Not applicable.

REFERENCES

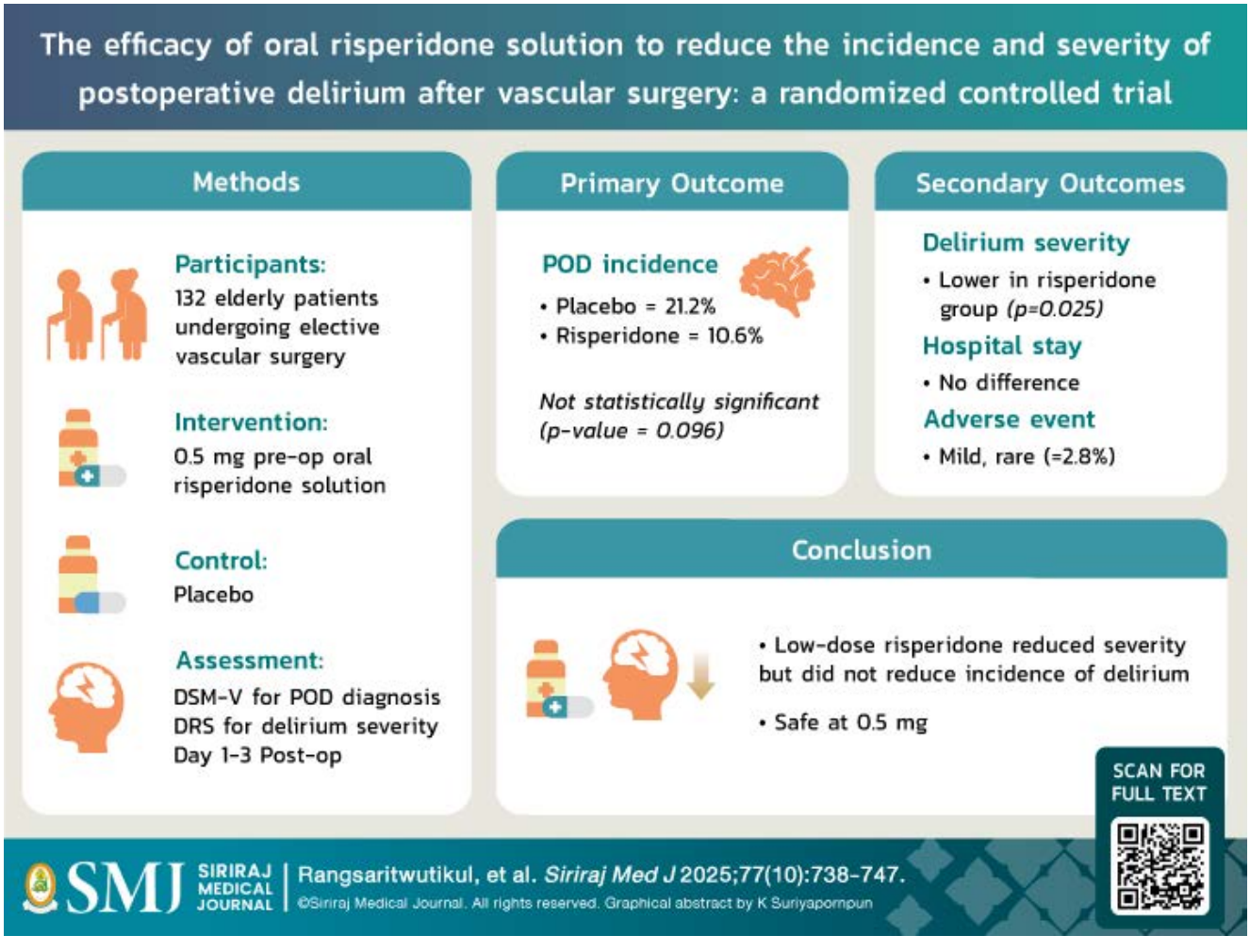
1. ASGE Standards of Practice Committee, Early DS, Lightdale JR, Vargo JJ, Acosta RD, Chandrasekhara V, et al. Guidelines for sedation and anesthesia in GI endoscopy. Gastrointest Endosc. 2018;87:327-37.
2. Campo R, Brullet E, Montserrat A, Calvet X, Moix J, Rué M, et al. Identification of factors that influence tolerance of upper gastrointestinal endoscopy. Eur J Gastroenterol Hepatol. 1999;11:201-4.
3. Sharma VK, Nguyen CC, Crowell MD, Lieberman DA, De Garmo P, Fleischer DE. A national study of cardiopulmonary unplanned events after GI endoscopy. Gastrointest Endosc. 2007;66:27-34.
4. VHA Pharmacy Benefits Management Strategic Healthcare Group. A guidance on the use of topical anesthetics for Naso/oropharyngeal and laryngotracheal procedures [Internet]. Ucm.es. [cited 2024 Mar 15]. Available from: https://www.ucm.es/data/cont/docs/107-2016-07-20-DEPRESORES43.pdf
5. Kollmann CM, Schmiegel W, Brechmann T. Gastrointestinal endoscopy under sedation is associated with pneumonia in older inpatients-results of a retrospective case-control study. United European Gastroenterol J. 2018;6:382-90.
6. Jirapinyo P, Thompson CC. Sedation challenges: obesity and sleep apnea. Gastrointest Endosc Clin N Am. 2016;26:527-37.
7. Amornyotin S, Srikureja W, Chalayonnavin W, Kongphlay S, Chatchawankitkul S. Topical viscous lidocaine solution versus lidocaine spray for pharyngeal anesthesia in unsedated esophagogastroduodenoscopy. Endoscopy. 2009;41:581-6.
8. Asante MA, Northfield TC. Variation in taste of topical lignocaine anaesthesia for gastroscopy. Aliment Pharmacol Ther. 1998;12:685-6.
9. Noitasaeng P, Vichitvejpaisal P, Kaosombatwattana U, Tassanee J, Suwannee S. Comparison of spraying and nebulized lidocaine in patients undergoing esophago-gastro-duodenoscopy: a randomized trial. J Med Assoc Thai. 2016;99:462-8.
10. Soweid AM, Yaghi SR, Jamali FR, Kobeissy AA, Mallat ME, Hussein R, et al. Posterior lingual lidocaine: a novel method to improve tolerance in upper gastrointestinal endoscopy. World J Gastroenterol. 2011;17:5191-6.
11. Salale N, Treldal C, Mogensen S, Rasmussen M, Petersen J, Andersen O, et al. Bupivacaine lozenge compared with lidocaine spray as topical pharyngeal anesthetic before unsedated upper gastrointestinal endoscopy: a randomized, controlled trial. Clin Med Insights Gastroenterol. 2014;7:55-9.
12. Chan CK, Fok KL, Poon CM. Flavored anesthetic lozenge versus xylocaine spray used as topical pharyngeal anesthesia for unsedated esophagogastroduodenoscopy: a randomized placebo-controlled trial. Surg Endosc. 2010;24:897-901.
13. Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JP, et al. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. BMJ. 2009;339:B2700.
14. 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. Syst Rev. 2021;10:89.
15. 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;162:777-84.
16. Higgins JPT, Savović J, Page MJ, Elbers RG, Sterne JAC. Assessing risk of bias in a randomized trial. In: Higgins JPT, Thomas J, Chandler J, Cumpston M, Li T, Page MJ, Welch VA, editors. Cochrane handbook for systematic reviews of interventions: assessing risk of bias in a randomized trial. Chichester UK: Wiley-Blackwell; 2019. p. 205-28.
17. Schünemann H, Brożek J, Guyatt G, Oxman A, editors. GRADE handbook for grading quality of evidence and strength of recommendations. Updated October 2013. The GRADE Working Group, 2013. Available from guidelinedevelopment.org/handbook.
18. Nordic Cochrane Center. The cochrane collaboration review manager 5 (RevMan 5). Version 5.4. Copenhagen: Nordic Cochrane Center, The Cochrane Collaboration; 2020.
19. Schünemann HJ, Vist GE, Higgins JPT, Santesso N, Deeks JJ, Glasziou P, et al. Interpreting results and drawing conclusions. In: Higgins JP, Green S, editors. Cochrane handbook for systematic reviews of interventions. Chichester UK: Wiley-Blackwell; 2019. p. 403-31.
20. Mahawongkajit P, Talalak N, Soonthornkes N. Comparison of lidocaine spray and lidocaine ice popsicle in patients undergoing unsedated esophagogastroduodenoscopy: a single center prospective randomized controlled trial. Clin Exp Gastroenterol. 2021;14:209-16.
21. Nasiri J, Amin A, Ganji F. The effect of eutectic mixture of local anesthesia cream (EMLA) on satisfaction, pain, and nausea/vomiting of patients undergoing gastro-intestinal endoscopy-a randomized clinical trial comparing EMLA cream and gel, lidocaine gel and spray, and placebo. Glob J Health Sci. 2024;9:273-9.
22. Çam H, Pehlivan S, Dağ MS, Yılmaz N, Demir U, Gülşen MT. Study of ideal topical pharyngeal anesthesia in upper gastrointestinal system endoscopy: a double-blind, randomized, controlled trial. Turk J Gastroenterol. 2016;27:103-7.
23. Supe A, Haribhakti SP, Ali M, Rathnaswami A, Ulla TZ, Maroo SH, et al. Lidocaine lozenges for pharyngeal anesthesia during upper gastrointestinal endoscopy: a randomized controlled trial. J Dig Endosc. 2014;5:58-63.
24. Mallik D, Singh A, Narayan J. Study on nebulized or sprayed lidocaine as anesthesia for esophago-gastro duodenoscopy (EGD). Int J Appl Res. 2019;5:125-8.
25. Ayoub C, Skoury A, Abdul-Baki H, Nasr V, Soweid A. Lidocaine lollipop as single-agent anesthesia in upper GI endoscopy.

Gastrointest Endosc. 2007;66:786-93.
26. Khodadoostan M, Sadeghian S, Safaei A, Shavakhi AR, Shavakhi A. Viscous lidocaine solution versus lidocaine spray for pharyngeal local anesthesia in upper gastroesophageal endoscopy. J Res Med Sci. 2018;23:102.
27. Hayashi T, Asahina Y, Waseda Y, Kitamura K, Kagaya T, Seike T, et al. Lidocaine spray alone is similar to spray plus viscous solution for pharyngeal observation during transoral endoscopy: a clinical randomized trial. Endosc Int Open. 2017;5:E47-53.
28. Mizuno Y, Hikichi T, Itabashi M. A comparative study of the effect and discomfort produced by pharyngeal anesthesia with viscous lidocaine solution and with lidocaine spray in esophagogastroduodenoscopy. Fukushima Med J. 2011;61:12-7.
29. Saravanan RB, Malarvizhi M, Hemamala, Safique, Radha, Arvind J, et al. An open label comparative study between xylocaine lozenges and xylocaine spray in patients undergoing upper gastrointestinal endoscopy in a tertiary care center. Indian J Gastroenterol. 2011;30:A101-5.
30. Rerknimitr R, Akaraviputh T, Ratanachu-Ek T, Kongkam P, Pausawasdi N, Pisespongsa P. Current Status of GI Endoscopy in Thailand and Thai Association of Gastrointestinal Endoscopy (TAGE). Siriraj Med J [internet]. 2018 Oct. 31 [cited 2025 Sep. 4];70(5):476-8. available from: https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/152789
31. Kongkam P, Mekaroonkamol P, Pausawasdi APN, Ratanachu-ek T, Rerknimitr PR, Taweerutchana V, et al. Endoscopic Sleeve Gastroplasty in the Armamentarium of Bariatric Treatment in Thailand: A TAGE-TSMBS Joint Addendum Statement to TSMBS Consensus Guideline. Siriraj Med J [internet]. 2021 Mar. 31 [cited 2025 Sep. 4];73(5):289-92. available from: https://he02.tci-thaijo.org/index.php/sirirajmedj/article/view/250280
32. Peery AF, Dellon ES, Lund J, Crockett SD, McGowan CE, Bulsiewicz WJ, et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology. 2012;143:1179-87.e3.
33. Tsai HI, Tsai YF, Liou SC, Su MY, Lin CC, Chang CJ, et al. The questionable efficacy of topical pharyngeal anesthesia in combination with propofol sedation in gastroscopy. Dig Dis Sci. 2012;57:2519-26.
34. Smith JL, Opekun A, Graham DY. Controlled comparison of topical anesthetic agents in flexible upper gastrointestinal endoscopy. Gastrointest Endosc. 1985;31:255-8.
35. Mogensen S, Treldal C, Feldager E, Pulis S, Jacobsen J, Andersen O, et al. New lidocaine lozenge as topical anesthesia compared to lidocaine viscous oral solution before upper gastrointestinal endoscopy. Local Reg Anesth. 2012;5:17-22.
36. Korttila K, Tarkkanen J, Tarkkanen L. Comparison of laryngotracheal and ultrasonic nebulizer administration of lidocaine in local anaesthesia for bronchoscopy. Acta Anaesthesiol Scand. 1981;25:161-5.
37. Davies AE, Kidd D, Stone SP, MacMahon J. Pharyngeal sensation and gag reflex in healthy subjects. Lancet. 1995;345:487-8.
38. Pound DC, O'Connor KW, Brown ED, Weddle R, McHenry R, Crabb D, et al. Oral medications for upper gastrointestinal endoscopy using a small diameter endoscope. Gastrointest Endosc. 1988;34:327-31.
39. Ladas SD, Raptis SA. Selection of patients for upper gastrointestinal endoscopy without sedation-the finger-throat test. Ital J Gastroenterol. 1986;18:162-5.
40. Pereira S, Hussaini SH, Hanson PJ, Wilkinson ML, Sladen GE. Endoscopy: throat spray or sedation? J R Coll Physicians Lond. 1994;28:411-4.
41. Hedenbro JL, Ekelund M, Aberg T, Lindblom A. Oral sedation for diagnostic upper endoscopy. Endoscopy. 1991;23:8-1.

The Efficacy of Oral Risperidone Solution to Reduce the Incidence and Severity of Postoperative Delirium After Vascular Surgery: A Randomized Controlled Trial

Varit Rangsaritwutikul, M.D.[1], Panate Pukrittayakamee, M.D.[2], Tachawan Jirativanont, M.D.[1], Aphichat Suphathamwit, M.D.[1], Tanamate Chaibanjongwat, M.D.[1], Orawan Pongraweewan, M.D.[1,*]

[1]Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [2]Department of Psychiatry, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.



*Corresponding author: Orawan Pongraweewan
E-mail: o.pongraweewan@gmail.com
Received 28 July 2025 Revised 17 September 2025 Accepted 19 September 2025
ORCID ID:http://orcid.org/0009-0007-4817-536X
https://doi.org/10.33192/smj.v77i10.276806

ABSTRACT

Objective: To determine the efficacy of the preoperative oral solution of risperidone in preventing Postoperative delirium (POD) and reducing the severity of POD in patients with geriatric vascular disease.

Materials and Methods: Randomized, double-blind, placebo-controlled trial. A total of 140 elderly patients scheduled for vascular surgery were enrolled and randomly assigned to either the risperidone group (0.5 mg oral solution of risperidone within 1 hour before surgery) or the placebo group.

Results: POD was assessed daily using the DSM-5 criteria, and its severity was measured with the Delirium Rating Scale (DRS) for the first three days after surgery. The incidence and severity of POD were compared between the two groups. Potential side effects of risperidone, and the length of hospital stay were also recorded. There were no statistical differences in demographic data between the two groups. The incidence of POD was 10.6% compared to 21.2 % in the intervention group without statistical significance (p-value=0.096). However, the severity of POD, measured by the DRS, was significantly lower in the risperidone group (2.0 vs. 6.0, p-value=0.025). The length of hospital stay did not show significant differences between the two groups.

Conclusions: The overall incidence of POD in this study without intervention was 21.2%. Preoperative administration of oral risperidone (0.5mg) reduced the severity of POD, but did not affect the incidence of POD or the length of hospital stay in this population.

Keywords: Vascular surgery; postoperative delirium; risperidone (Siriraj Med J 2025; 77: 738-747)

INTRODUCTION

Postoperative delirium (POD) is a form of delirium that occurs in patients who received surgical procedures and anesthesia. It is common among geriatric surgical patients, and its etiology is not fully understood. For vascular surgical patients alone, the incidence of POD ranges from 33 to 54 %.[1-3] Since this world is becoming an aging society, more geriatric patients undergo surgeries each year. The impact of POD is becoming more significant for perioperative care.

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the diagnosis of delirium includes an acute disturbance in attention, cognition, and / or awareness that is not explained by another medical condition or substance intoxication or toxin.[1] Unlike dementia, POD has an acute onset and fluctuates throughout the day. It typically appears during the first three postoperative days.[2] Common risk factors for postoperative delirium include the elderly, preexisting cognitive impairment, history of prior delirium, hip surgery, cardiac surgery, vascular surgery, use of benzodiazepine, alcohol withdrawal, etc.[3]

POD is associated with significant morbidities, increased length of hospitalization, worse surgical outcome, and higher healthcare costs.[4-6] Prevention of POD in this patient group can enhance patient recovery, reduce morbidity and mortality, and hospital fee. The proposed preventive methods include the identification of patients who are at higher risk, the prevention of risk factors, and pharmacological management. Previous studies have found that some medications show benefits for delirium prevention, including some antipsychotic agents and dexmedetomidine.[7,8] However, frail elderly patients can develop significant side effects, including hypotension, hypertension, and bradycardia due to dexmedetomidine.[9]

Antipsychotic agents that were studied for the prevention of POD include haloperidol and risperidone. Haloperidol, a typical antipsychotic, showed conflicting results for postoperative delirium prevention in previous studies.[10-13] Risperidone is an atypical antipsychotic agent with less extrapyramidal side effects such as dyskinesia, dystonia, or Parkinsonism compared to typical antipsychotics. It is also cheap and very accessible and does not have interactions with anesthetic agents. Previous studies showed promising results in preventing POD in patients undergoing elective cardiac surgery with cardiopulmonary bypass.[14,15]

The study by Prakanrattana et al. found that 1 mg of risperidone administered sublingually after awakening on the postoperative ward reduced the incidence of postoperative delirium from 31.7% in the placebo group to 11.1% in the intervention group.[14] Another study by Hakin et al. showed the effectiveness of 0.5 mg of risperidone when given orally every 12 hours in patients with subsyndromal delirium after on-pump cardiac surgery reduced the incidence of delirium from 34% to 13.7%.[15] An adverse effect of risperidone was reported as a mild extrapyramidal syndrome in two patients of the intervention group (3.9%).

We decided to give risperidone preoperatively,

contrary to previous studies, due to its long duration of action and ease of administration. When given at a low dose of 0.5 mg, we expected risperidone to have minimal side effects, while still being effective.[16]

Objectives

The primary objective of this study is to determine the efficacy of preoperative oral risperidone solution 0.5mg for reducing the incidence of POD in surgical vascular patients compared to placebo.

Secondary objectives include demonstrating the incidence of POD in vascular surgical patients, its efficacy in reducing delirium severity and length of hospital stay, and reporting adverse side effects observed in this study.

MATERIALS AND METHODS

Study design

This study is a prospective, double-blind, randomized, placebo-controlled trial conducted at the tertiary-care university hospital. After the study was authorized by the institutional review board. All patients signed an informed consent before enrollment.

Study population

Patients more than 60 years-old who were admitted for an elective aorta, carotid or peripheral vascular surgery and were expected to be under anesthesia for more than 2 hours were included in the study. Exclusion criteria were patients with delirium prior to surgery positive Confusion Assessment for Intensive Care Unit (CAM-ICU) (Thai version) or severe cognitive impairment Thai Mental State Examination (TMSE less than 10)[17,18] history of alcoholic abuse or alcohol ingestion within the 14-day period preceding surgery, history of psychiatric illness, receiving antipsychotic drugs, physical disabilities that limit the evaluation of delirium such as blindness, deafness or mute, liver impairment with Child-Turcotte-Pugh score more than or equal to 10, history of allergy to risperidone, risk of adverse effects from risperidone such as history of neuroleptic malignant syndrome, Parkinson's disease, Parkinsonism or prolongation of QTc, and patients who refused to participate. This study withdrawal or termination criteria included patients who developed cardiac arrest during surgery and patients who received dexmedetomidine or benzodiazepine during the perioperative period.

Sample size calculation

The formula used to calculate the sample size of this study was made with n4 studies program. The formula used is as follow.

$$n = \frac{(Z_1 - \alpha/2\sqrt{2\bar{p}(1-\bar{p})} + Z_1 - \beta\sqrt{p_1(1-p_2) + p_2(1-p_2)})^2}{(p1-p2)^2}$$

Assumptions: we used a two-sided $\alpha = 0.05$ and 80% power ($\beta = 0.2$)

Incidence rates: According to previous studies, the incidence of postoperative delirium in patients undergoing vascular surgery was between 33-54%; we assumed P1 (control incidence) =48% as a mid-range estimate.

Expected effect size: From the study by Prakanrattana et al., risperidone reduced the incidence of postoperative delirium in cardiac surgery patients from 31.7% to 11% compared to placebo. In this study, we hypothesized a 50% relative reduction (P2=24%) with prophylactic risperidone. This estimate was based on prior trials that show a substantial risk reduction. While the dose, timing and population differences might influence effect size; we chose this conservative but clinically meaningful reduction to ensure adequate study power.

The calculated sample size is equal to 62 for each group. Allowing for 10% dropout for protocol deviation and loss to follow-up, we increase the sample size to: treatments = 70, controls = 70. Therefore, the sample size for this study was 70 in each group. The total sample size was 140.

The study outcomes

The primary outcome of this study is the efficacy of risperidone in reducing the incidence of POD in elderly vascular surgical patients. Secondary outcomes include the incidence of POD in this group of patients, the delirium rating scale, and the length of hospital stay.

Study process

Participants who met the inclusion criteria will be recruited from the surgical ward by anesthesiology residents. After written informed consent was obtained from eligible participants, they were screened for severe cognitive impairment and delirium by trained anesthesiology residents using TMSE and CAM-ICU screening tools.

All participants received a preanesthetic evaluation the day before surgery and were premedicated based on their underlying disease. Benzodiazepines were omitted during the perioperative period. The participants were randomized into a 1:1 ratio to the intervention or the control group using simple randomization. A random sequence was generated in advance, and allocation was concealed using sequentially numbered, sealed, and opaque envelopes. A research assistant, who was not involved in patient care or outcome assessment, opened the next enveloped in sequence to assign each participant after

enrollment. The risperidone group received a 0.5ml solution containing 0.5 mg of risperidone while the control group received 0.5 ml of sterile water within 1 hour before surgery (Fig 1). The risperidone and sterile water were prepared by a pharmacist and the solution were labeled by trial name and participations' randomization number. A nurse anesthetist, who did not participate in this study and blinded to the randomization, was assigned to administer these per oral solutions according to the participant's randomization number. Both risperidone and sterile water were matched in volume, color and transparency. However, a blinding test for both solutions was not conducted. Non-invasive blood pressure, EKG and oxygen saturation were monitored before the operation. The attending anesthesiologist selected the type of anesthesia, including general anesthesia (GA), intravenous sedation, regional or local anesthesia.

For the GA technique, participants received fentanyl (1-2 µg/kg) and propofol (1-2 mg/kg) intravenously. Endotracheal intubations were facilitated with cis-atracurium (0.15 mg/kg) when the train-of-four count was equal to 0. The level of anesthesia was maintained with desflurane, fentanyl (1-2 µg/kg/h) and cis-atracurium (1-3 µg/kg/min). The TOF count was maintained between 1 and 2 during the surgery. The anesthesiologist adjusted the concentration of desflurane with the air : oxygen

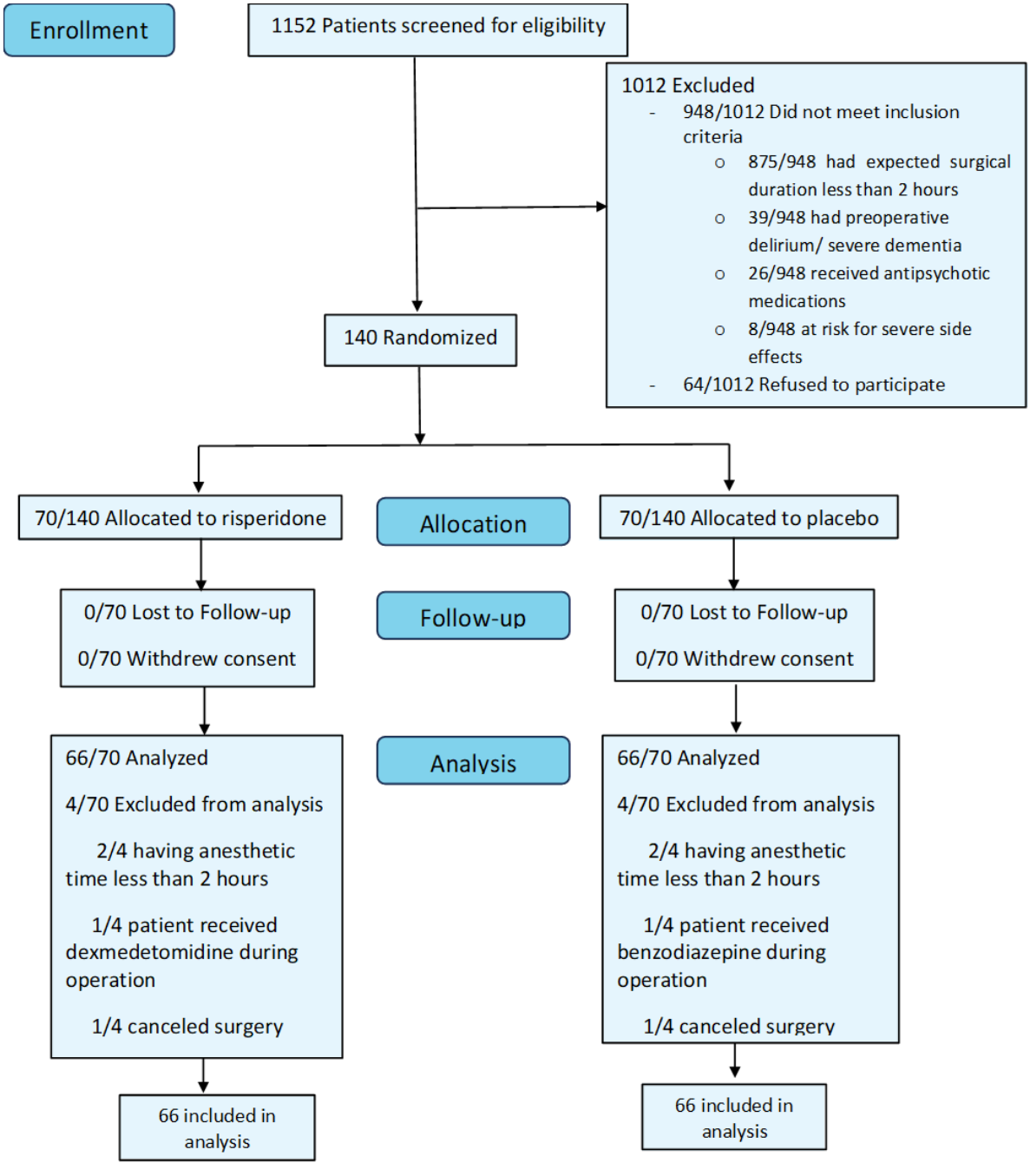


Fig 1. Consort flow diagram.

mixture. Ventilator settings were set for low tidal volume (6-8 ml/kg, PEEP 5 cm H_2O). The respiratory rate was adjusted to keep the end tidal CO_2 between 35 and 40 mmHg during surgery. At the end of the surgery, 2.5 mg of neostigmine and 0.4 mg of glycopyrrolate were administered and extubation was performed when the TOF ratio was greater than 90%.

Fentanyl infusion (1-2 μg/kg) and/or propofol was used to sedate the patients. 25 μg of fentanyl could be added during the operation when the pain score was greater than or equal to 5 or the patient was agitated. The patients received oxygen by cannula or mask. Benzodiazepines were avoided during the operation. The anesthesiologist determined the dose of anesthetic drugs and sedation drugs for regional anesthesia and the surgeon determined the concentration and volume of drugs for local anesthesia.

During surgery, noninvasive blood pressure or direct arterial pressure, electrocardiogram, pulse oximetry, end-tidal concentration of CO_2 and desflurane, body temperature, and neuromuscular monitoring were monitored and recorded. After the operation, the patients were transferred to the ward or the surgical critical care unit. They were assessed for postoperative delirium using the DSM-5 criteria by a psychiatrist who was blinded by allocation. They were reassessed for the first three days postoperatively by the same psychiatrist.

If postoperative delirium was detected, the severity of delirium would be further assessed using the Delirium Rating Scale.[19] Treatments for postoperative delirium were provided by the psychiatrist team. The researchers recorded all physical examination, treatment, and complication during the postoperative period.

Data collection

Preoperative data include general demographic characteristics, TMSE score, and preoperative laboratory results. Intraoperative data include anesthetic technique, surgical and anesthetic duration, amount of each medication administered, number of episodes of intraoperative hypotension, number of episodes of hypoxemia, amount of fluid and blood products administered, urine output, and estimated blood loss. Postoperative data include pain score in the recovery room or intensive care unit, adverse effects of risperidone, DSM-5 evaluation, and delirium rating scale in delirious patient.

Statistical analysis

All randomized patients who met the protocol eligibility criteria were included in the analysis with a modified intention-to-treat (mITT) approach. Patients who were excluded post-randomization due to protocol deviations were not included in the analysis.

Continuous variables were reported according to data distribution. Normally distributed data are presented as mean ± SD and compared using the student's *t*-test. Skewed data are reported as median (interquartile range [IQR]) and compared using the Mann–Whitney U test. Categorical variables were expressed as frequency and percentage and were compared using Chi-square test. A two-sided $p < 0.05$ was considered statistically significant.

The primary analysis followed a modified intention-to-treat approach, excluding patients who were randomized but not treated due to protocol-related reasons. A total of 140 patients were randomized, of whom 132 patients were included in the modified intention-to-treat analysis (Intervention =66, Control = 66).

Delirium Rating Scale (DRS) was compared among patients who developed POD and was reported as median with IQR. Comparison was conducted using Mann-Whitney U test.

Subgroup analyses based on TMSE scoring and hypotensive events were conducted as post-hoc exploratory analyses.

Statistical analysis was conducted using IBM Statistic SPSS for Windows version 21.0.

RESULTS

The recruitment took place from September 2020 to January 2023. During the study period, 1,152 elective vascular patients were evaluated for eligibility, 1,012 patients were excluded mainly due to expected anesthesia time less than 2 hours, followed by preoperative delirium, receiving antipsychotic medications preoperatively, age less than 60 years, having a prolonged QT interval in preoperative ECG, and declining participation.

A total of one hundred and forty participants were eligible and were randomized to the placebo group (n=70) and the risperidone group (n=70). After exclusions for protocol deviations (n=8), 132 patients were included in the modified intention-to-treat (mITT) analysis. In each group, two patients (2.8%) had anesthetic time less than 2 hours, and a patient had her operation cancelled by the surgeon. A patient in the placebo group received benzodiazepine during the operation and was excluded from the analysis. A patient in the risperidone group received dexmedetomidine and was withdrawn from the analysis (Fig 1).

The baseline clinical characteristics and intraoperative variables were balanced between the two groups and were demonstrated in Tables 1 and 2. Clinical outcomes are demonstrated in Table 3.

TABLE 1. Baseline patient characteristics.

Characteristics	Placebo Group (n=66)	Risperidone Group (n=66)	P value
Age, mean (SD), y	72.6 (7.4)	71.5 (7.3)	0.374
Gender			0.434
Female, No., %	16 (24.2%)	20 (30.3%)	
Male, No., %	50 (75.8%)	46 (69.7%)	
Body mass index, mean (SD)	22.8 (4.3)	23.8 (3.8)	0.165
Hematocrit, mean, %	34.0 (6.5)	36.0 (6.6)	0.076
eGFR, mean (SD)	58.5 (28.7)	58.4 (31.5)	0.993
Sodium level, mean (SD)	137.1 (4.3)	136.5 (4.0)	0.343
Comorbidity			
Stroke	10 (15.2%)	14 (21.2%)	0.367
Coronary artery disease	23 (34.8%)	24 (36.4%)	0.856
Diabetes	25 (37.9%)	36 (54.5%)	0.055
ASA classification			0.637
II	7 (10.6%)	7 (10.6%)	
III	55 (83.3%)	52 (78.8%)	
IV	4 (6.1%)	7 (10.6%)	

Abbreviations: eGFR: Estimated glomerular filtration rate, ASA: American Society of Anesthesiologists physical status classification.

TABLE 2. Intraoperative variables.

Intraoperative variables	Placebo Group (n=66)	Risperidone Group (n=66)	P value
Anesthesia techniques			0.186
GA or iv sedation	45 (68.1%)	52 (78.7%)	
RA or MAC	21 (31.8%)	14 (21.2%)	
Estimated blood loss, ml, IQR	125 (50-285)	100 (50-250)	0.532
Hypotensive events >5minutes, times, IQR	1 (0-4)	2 (0-4)	0.561
Supra-inguinal operation, no., %	36 (54.5%)	33 (50%)	0.601
Operative time, mean (SD), min	207.8 (123.5)	181.5 (98.9)	0.179
Anesthesia time, mean (SD), min	265.0 (141.3)	243.8 (120.1)	0.356

Abbreviations: *GA*: General anesthesia, *RA*: Regional anesthesia, *MAC*: Monitored anesthesia care, *IQR*: Interquartile range, *SD*: Standard deviation.

TABLE 3. Clinical outcomes during study drug administration.

Outcomes	Placebo Group (n=66)	Risperidone Group (n=66)	P value
Delirium, No., %	14 (21.2%)	7 (10.6%)	0.096
Subtype of delirium			0.174
Hypoactive, No, %	7 (50%)	6 (85.7%)	
Hyperactive, No, %	7 (50%)	1 (14.2%)	
Delirium rating scale. Median, IQR	6.0 (5.0-8.25)	2.0 (2.0-5.0)	0.025
Length of hospital stay. Median, IQR	5.0 (4.0-14.25)	7.0 (3.0-15.25)	0.922

Abbreviation: *IQR*: Interquartile range.

The incidence of postoperative delirium in the risperidone group was 10.6% compared to the control group 21.2% with no statistical significance (p = 0.096). In patients who developed postoperative delirium of each group, the incidence of hyperactive delirium in the risperidone group (14.2%) vs the placebo group (50%) was also not statistically different (p = 0.174). However, the DRS in the risperidone group was statistically lower at median of 2 (2-5) compared to the control group at median of 6 (5-8.25) (p = 0.025). There was no difference in hospital stay between the two groups (5.0 (4.0-14.25) vs 7.0 (3.0-15.25), p = 0.922).

In a subgroup analysis, we found that the risperidone group had a lower incidence of postoperative delirium in patients with hypotensive events (defined by mean arterial blood pressure < 20% of the baseline value or systolic blood pressure <90 mmHg) less than 3 times. We found no difference in postoperative delirium in patients with hypotensive events more than 3 times. We found no statistical differences between patients with mild cognitive impairment (TMSE scores <22) compared to patients with TMSE scores ≥ 22 (Table 4).

The side effects of risperidone included mild extrapyramidal symptoms (cogwheel rigidity) in one patient (1.4%) that resolved spontaneously and asymptomatic QT prolongation in one patient (1.4%). A patient developed cardiac arrest on postoperative day 3 due to acute heart failure and hypoxemia. We believe that this is unlikely to be due to risperidone which was administered 3 days prior to the event. After the incident, the patient's randomization to the risperidone group was quickly disclosed and reported to the IRB.

TABLE 4. Subgroup analysis of clinical outcomes.

Subgroup	Outcome	Placebo group (n=66)	Risperidone Group (n=66)	P value
Hypotension < 15 min	Delirium, No., %	11 (24.4%)	3 (7%)	0.025
Hypotension ≥ 15 min	Delirium, No., %	3 (14.3%)	4 (17.4%)	0.778
Preoperative TMSE score < 22	Delirium, No. %	5 (35.7%)	2 (18.2%)	0.332
Preoperative TMSE score ≥ 22	Delirium, No. %	9 (17.3%)	5 (9.1%)	0.258

Abbreviation: *TMSE*: Thai Mental State Examination.

DISCUSSION

We found that 0.5 mg of oral risperidone solution, when administered preoperatively, reduced the severity of delirium, but not the incidence of POD or the length of stay in the hospital. In a subgroup analysis, risperidone showed a benefit in reducing POD in patients with less than three hypotensive events.

In contrast to our hypothesis, this randomized controlled trial showed that 0.5 mg of risperidone oral solution administered preoperatively did not reduce the incidence of POD in elderly vascular patients (21.2% VS 10.6%, p=0.096). We believe that this may be due to several factors.

First, the incidence of postoperative delirium in our placebo group (21.2%) was much lower than the incidence used for the calculation of the sample size (48%). This discrepancy may be due several factors including differences in patient characteristics, surgical techniques, perioperative practices, and intraoperative hemodynamic control. Our study also used DSM-5 criteria for diagnosis of delirium, which are highly specific but less sensitive than CAM-ICU, potentially missing milder or transient cases. Protocol related exclusions including patients with severe cognitive impairment, sedative use and patients having pre-operative delirium may resulted in a lower risk population.

Second, a single dose of 0.5 mg of risperidone used in this study may not be enough to reduce the incidence of POD. Previous studies used a higher dose (1 mg) or higher frequency (every 12 hours).[17,18]

The choice of a single 0.5 mg preoperative dose of risperidone in this study was based on concerns regarding tolerability and safety in elderly vascular patients, who often have multiple comorbidities and polypharmacy. Risperidone at low doses has been shown to treat postoperative delirium in elderly orthopedic patients with minimal side effects.[22] Pharmacokinetically, oral risperidone reaches peak plasma concentrations within 1–2 hours, with a mean elimination half-life of approximately 20 hours, and its active metabolite, 9-hydroxyrisperidone, has a half-life of 20–30 hours.[23] Therefore, we hypothesized that a single preoperative dose would provide an effect for least 48–72 hours, which is the period with the highest risk of POD. However, compared with prior studies using 1 mg or repeated dosing schedules, a single low dose regimen was insufficient in preventing POD. Future studies should explore the optimal dosing that balance efficacy with safety in this vulnerable population.

It is also important to consider some potential confounding factors that could influenced POD risk. Variables such as site of surgery (supra-inguinal surgery vs infra-inguinal surgery), duration of anesthesia and surgery, intraoperative hypotension, opioid exposure and baseline cognitive function (TMSE score) may affect delirium incidence and severity. Although randomization was intended to balance these factors, residual differences may contribute to variability in outcomes.

Regarding our secondary outcomes, risperidone showed a reduction in the severity of postoperative delirium defined by the Delirium Rating Scale (6 VS 2, p=0.025) but not hospital stay (5 VS 7, p=0.922). In contrast to a previous study[20], the reduced delirium severity found in risperidone group was not associated with a reduction in the length of hospital stay. Other worse clinical outcomes including higher 1-year mortality rate, greater in-hospital costs[20] and long-term cognitive decline[21] was also linked with delirium severity but were not studied in this research. There were few reported side effects of risperidone.

The external validity of our findings is limited. This was a single-center study focusing on elderly patients undergoing elective vascular surgery, with a benzodiazepine-avoidant anesthetic protocol. Therefore, results may not fully apply to other surgical populations, including non-vascular geriatric patients, or to centers with different perioperative practices. Future multicenter studies across diverse surgical settings are needed to determine the broader applicability of these findings.

Strengths of this study include the use of DSM-5 criteria for the diagnosis of delirium, a gold standard for the diagnosis of delirium, compared to previous studies using CAM-ICU. Assessment of all participants was done by only one psychiatrist and the assessment period is three consecutive days, which are the period with the highest incidence of delirium. All participants, researchers, and psychiatrists were blinded to the groups of patient allocation.

Limitations

Our study had some limitations. The assessment of delirium was performed once each day, which may have missed some cases of delirium due to its fluctuating course. The sample size was calculated using the incidence of delirium, which was the primary outcome. This may have reduced the power of our study to detect a statistically significant difference in the primary and secondary outcomes.

CONCLUSIONS

In this RCT, we observed that surgical vascular patients receiving 0.5 mg of risperidone before surgery

showed a reduction in severity but not incidence of POD compared to placebo. There were no differences in hospital stay between the two groups. Risperidone has low side effects.

Suggestions for future research include determining the proper sample size for other research outcomes, increasing the frequency of delirium assessment, and considering the appropriate dose of risperidone for effective postoperative delirium prevention.

Data Availability Statement

De-identified data were available from the corresponding author upon reasonable request.

ACKNOWLEDGMENTS

The authors acknowledge Ms. Julaporn Pooliam for her assistance with statistical analyzes and Mrs. Nipaporn Sangarunakul for her assistance in study coordination and documentation. Finally, the authors gratefully acknowledge the professional editing of this paper by Mr. James Mark Simmerman.

DECLARATIONS

Grants and Funding Information

This research was funded by the Faculty of Medicine Siriraj Hospital, Bangkok, Thailand, under grant number R016333024. The funder had no role in the study's design, data collection or analysis, decision to publish, or manuscript preparation.

Conflict of Interest

The authors assert that they have no conflicts of interest to declare.

Registration Number of Clinical Trial

Registered at the Thai Clinical Trials Registry (TCTR ID: TCTR20190704003) on 4 July 2019.

Author Contributions

Conceptualization: O.P., P.P.; Data curation: V.R., T.C.; Formal analysis: V.R., T.C.; Methodology: O.P., P.P.; Supervision: O.P.; Writing – original draft: V.R., T.C.; Writing – review & editing: V.R., T.C., O.P., P.P., T.J., A.S. All authors have read and agreed to the final version of the manuscript.

Use of Artificial Intelligence

AI-based tools (ChatGPT, OpenAI) were used for language editing under author supervision.

Ethics Approval Statement

This study was authorized by the Siriraj Institutional Review Board (approval number: COA no. Si 381/2019), Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

REFERENCES

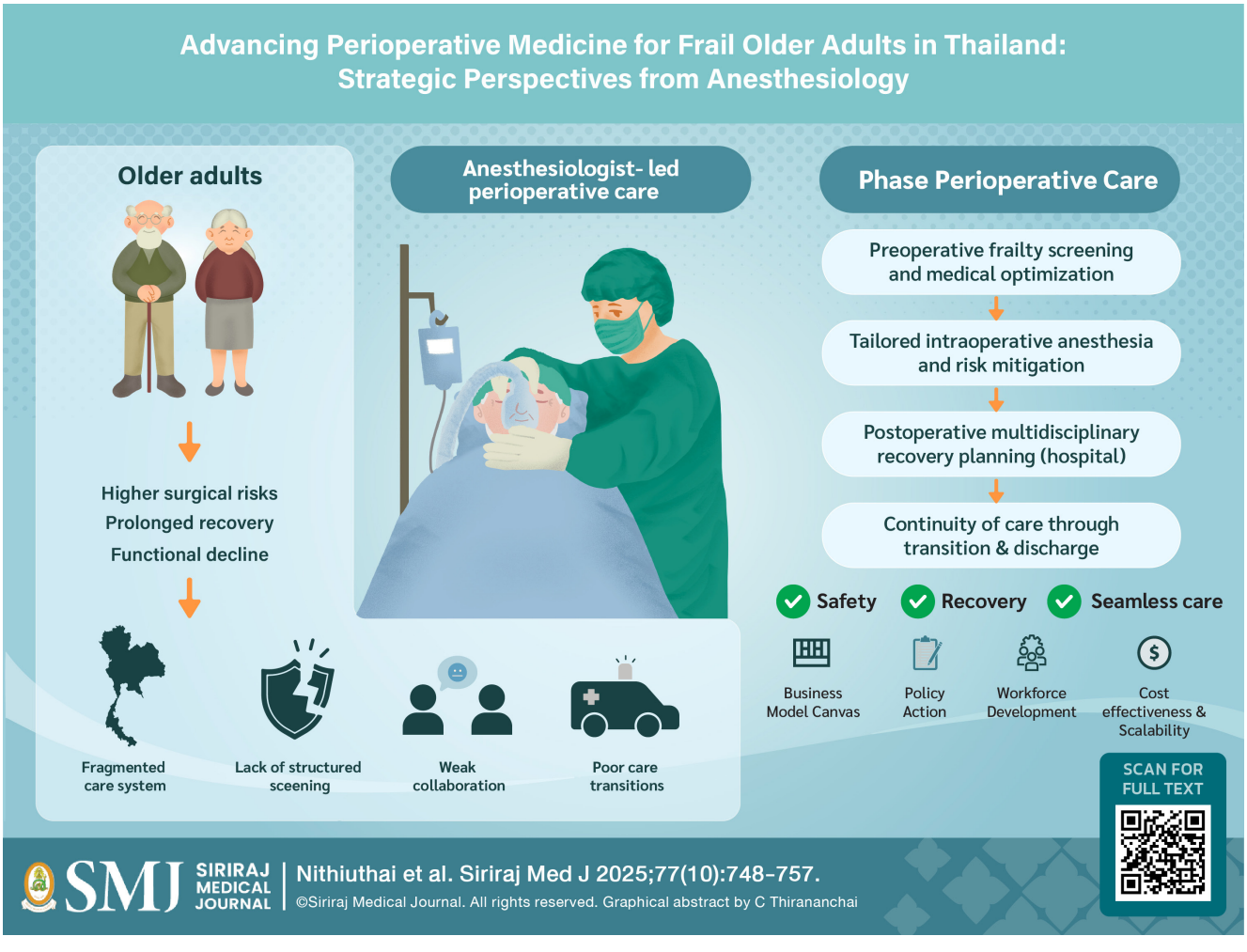
1. Baril DT, Ghosh K, Rosen AB. Trends in the incidence, treatment, and outcomes of acute lower extremity ischemia in the United States Medicare population. J Vasc Surg. 2014;60(3):669-77.e2.
2. Whitlock EL, Vannucci A, Avidan MS. Postoperative delirium. Minerva Anestesiol. 2011;77(4):448-56.
3. Oh ST, Park JY. Postoperative delirium. Korean J Anesthesiol. 2019;72(1):4-12.
4. Ha A, Krasnow RE, Mossanen M, Nagle R, Hshieh TT, Rudolph JL, et al. A contemporary population-based analysis of the incidence, cost, and outcomes of postoperative delirium following major urologic cancer surgeries. Urol Oncol. 2018;36(7):341.e15-e22.
5. Aitken SJ, Blyth FM, Naganathan V. Incidence, prognostic factors and impact of postoperative delirium after major vascular surgery: A meta-analysis and systematic review. Vasc Med. 2017;22(5):387-97.
6. Brown CHt, Laflam A, Max L, Lymar D, Neufeld KJ, Tian J, et al. The Impact of Delirium After Cardiac Surgical Procedures on Postoperative Resource Use. Ann Thorac Surg. 2016;101(5):1663-9.
7. Wang Y, Bu X, Zhao N, Wang S, Wang X, Ge Y, et al. Dexmedetomidine effect on delirium in elderly patients undergoing general anesthesia: A protocol for systematic review and meta-analysis. Medicine (Baltimore). 2021;100(48):e27782.
8. Pluta MP, Dziech M, Czempik PF, Szczepańska AJ, Krzych Ł J. Antipsychotic Drugs in Prevention of Postoperative Delirium-What Is Known in 2020? Int J Environ Res Public Health. 2020;17(17).
9. Naaz S, Ozair E. Dexmedetomidine in current anaesthesia practice- a review. J Clin Diagn Res. 2014;8(10):GE01-4.
10. Kaneko T, Cai J, Ishikura T, Kobayashi M, Naka T, Kaibara N. Prophylactic consecutive administration of haloperidol can reduce the occurrence of postoperative delirium in gastrointestinal surgery. Yonago Acta Med. 1999;42(3):179-84.
11. Kalisvaart KJ, de Jonghe JF, Bogaards MJ, Vreeswijk R, Egberts TC, Burger BJ, et al. Haloperidol prophylaxis for elderly hip-surgery patients at risk for delirium: a randomized placebo-controlled study. J Am Geriatr Soc. 2005;53(10):1658-66.
12. Vochteloo AJ, Moerman S, van der Burg BL, de Boo M, de Vries MR, Niesten DD, et al. Delirium risk screening and haloperidol prophylaxis program in hip fracture patients is a helpful tool in identifying high-risk patients, but does not reduce the incidence of delirium. BMC Geriatr. 2011;11:39.
13. Wang W, Li HL, Wang DX, Zhu X, Li SL, Yao GQ, et al. Haloperidol prophylaxis decreases delirium incidence in elderly patients after noncardiac surgery: a randomized controlled trial*. Crit Care Med. 2012;40(3):731-9.
14. Prakanrattana U, Prapaitrakool S. Efficacy of risperidone for prevention of postoperative delirium in cardiac surgery. Anaesth Intensive Care. 2007;35(5):714-9.

15. Hakim SM, Othman AI, Naoum DO. Early treatment with risperidone for subsyndromal delirium after on-pump cardiac surgery in the elderly: a randomized trial. Anesthesiology. 2012;116(5):987-97.
16. Chaput AJ, Bryson GL. Postoperative delirium: risk factors and management: Continuing Professional Development. Can J Anesth. 2012;59(3):304-20.
17. Phannarus H, Muangpaisan W, Siritipakorn P, Pianchob S, Supapueng O. Development of a Thai tool for assessing behavioral and psychological symptoms of dementia: A confirmatory factor analysis. Brain Behav. 2020;10(11):e01816.
18. Perneczky R, Wagenpfeil S, Komossa K, Grimmer T, Diehl J, Kurz A. Mapping scores onto stages: mini-mental state examination and clinical dementia rating. Am J Geriatr Psychiatry. 2006;14(2):139-44.
19. Trzepacz PT, Dew MA. Further analyses of the Delirium Rating Scale. Gen Hosp Psychiatry. 1995;17(2):75-9.
20. Vasunilashorn SM, Fong TG, Helfand BKI, Hshieh TT, Marcantonio ER, Metzger ED, et al. Psychometric Properties of a Delirium Severity Score for Older Adults and Association With Hospital and Posthospital Outcomes. JAMA Netw Open. 2022;5(3):e226129.
21. Vasunilashorn SM, Fong TG, Albuquerque A, Marcantonio ER, Schmitt EM, Tommet D, et al. Delirium Severity Post-Surgery and its Relationship with Long-Term Cognitive Decline in a Cohort of Patients without Dementia. J Alzheimers Dis. 2018;61(1):347-58.
22. Raphael L, Edna E, Irina K, Oded H. The Efficacy of Low-Dose Risperidone Treatment for Post-Surgical Delirium in Elderly Orthopedic Patients. Medicina (Kaunas). 2023;59(6):1052.
23. Heykants J, Huang ML, Mannens G, Meuldermans W, Snoeck E, Van Beijsterveldt L, et al. The pharmacokinetics of risperidone in humans: a summary. J Clin Psychiatry. 1994;55 Suppl:13-7.

Advancing Perioperative Medicine for Frail Older Adults in Thailand: A Strategic Perspective from Anesthesiology

Jitsupa Nithiuthai, M.D.[1], Arunotai Siriussawakul, M.D., Ph.D.[1,*], Patchareya Nivatpumin, M.D.[1], Orawan Pongraweewan, M.D.[1], Weerasak Muangpaisan, M.D.[2], Thammawat Parakonthun, M.D.[3], Piyapat Dajpratham, M.D.[4], Varalak Srinonprasert, M.D., MM[5]

[1]Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [2]Department of Preventive and Social Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [3]Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [4]Department of Rehabilitation Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand, [5]Division of Geriatric Medicine, Department of Medicine, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.



*Corresponding author: Arunotai Siriussawakul
E-mail: arunotai.sir@mahidol.ac.th
Received 7 July 2025 Revised 6 August 2025 Accepted 8 August 2025
ORCID ID:http://orcid.org/0000-0003-0848-6546
https://doi.org/10.33192/smj.v77i10.276435

ABSTRACT

Thailand has officially entered an aged-society phase: people ≥ 65 years already constitute > 14% of the population. This demographic transition strains surgical services; frail older adults face disproportionately high perioperative morbidity, prolonged recovery, and functional decline. Yet, perioperative care delivery in Thailand remains fragmented, with sporadic frailty screening, inconsistent multidisciplinary collaboration, and rudimentary transitional care pathways.

Using the Business Model Canvas to map current service gaps, this review delineates strategic levers for reform. At high-volume centers such as Siriraj Hospital, nearly 40% of surgical patients are aged ≥ 65 years, positioning anesthesiologists to champion frailty screening, preoperative risk optimization, and postoperative recovery planning.

Inspired by models from Singapore, the UK, and the US, we propose a four-phase, anesthesiologist-led perioperative care model spanning pre- to post-surgery. Prioritizing safety, recovery, and continuity of care, it is supported by workforce development and policy action. To manage implementation costs, a Business Model Canvas is recommended. This scalable strategy aims to enhance perioperative care for Thailand's aging population.

Keywords: Anesthesiologist; frail; elderly; perioperative care; prehabilitation (Siriraj Med J 2025; 77: 748-757)

INTRODUCTION

Official 2024 registration data show that Thailand has crossed the threshold into an aged society; people ≥ 65 years already represent a substantial proportion of the population. The consequent surge in older surgical candidates is clinically complex because multimorbidity, polypharmacy, cognitive impairment, and frailty are common.[1] Frailty—a multidimensional syndrome marked by depleted physiologic reserve and heightened vulnerability to stressors—is linked to postoperative complications, extended hospital stays, loss of independence, and mortality.[2-6] Local evidence from Siriraj Hospital—Thailand's oldest and largest tertiary academic medical center, with over 2,000 beds, more than 3 million outpatient visits, and around 80,000 inpatient admissions annually—supports these concerns. Among patients undergoing gastrectomy for gastric or esophagogastric junction cancer, advanced age is associated with increased postoperative complications and adverse events.[7,8] Those aged ≥ 80 years exhibited a significantly higher in-hospital mortality risk.

Internationally, perioperative medicine for older adults with frailty is a fully integrated discipline that unites surgeons, anesthesiologists, geriatricians, and structured recovery planning. In Thailand, however, implementation is nascent. Routine frailty screening and comprehensive geriatric assessment (CGA) are rare, multidisciplinary collaboration is inconsistent, and postoperative plans often overlook functional and cognitive endpoints. At Siriraj Hospital, older adults constitute almost 40% of the facility's 50 000 annual surgical cases. The national shortage of geriatricians therefore creates a strategic window for anesthesiologists to lead system redesign. Expanded duties could include frailty screening, orchestration of prehabilitation services, and delivery of frailty-adapted anesthesia. Over time, anesthesiologists might also coordinate discharge planning and recovery optimization.

This review applies the Business Model Canvas (BMC) to critically evaluate the existing perioperative care model for frail older adults in Thailand. Comparative exemplars from Singapore, the United Kingdom, and the United States are used to identify transferable service innovations. On the basis of this analysis, we propose a 4-phase, anesthesiologist-led model aligned with the surgical timeline to advance perioperative medicine in Thailand's aging society.

Business Model Canvas Analysis

The Business Model Canvas (BMC) is a strategic framework comprising nine interrelated domains that analyze how a service creates, delivers, and captures value. We selected the BMC as a tool to integrate clinical innovation with sustainable service delivery. In contrast to purely clinical models that focus primarily on patient outcomes, the BMC facilitates a systematic examination of value creation, resource allocation, and cost structure—key considerations in the design of perioperative services for older adults, whose care is often complex and resource-intensive. Employing the BMC framework supports not only improved clinical outcomes but also long-term financial sustainability and potential alignment with reimbursement mechanisms within the Thai healthcare system.

Our adapted design envisions a 24-week continuum—

12 weeks pre- and 12 weeks post-operation—led or co-led by anesthesiologists to address the physiologic and functional needs of frail patients. The preoperative block enables prehabilitation that enhances nutrition, physical resilience through targeted exercise, and comorbidity optimization, whereas the postoperative block emphasizes complication surveillance, rehabilitation, and readmission prevention. This extended arc enables proactive, personalized care that traditional surgical timelines often overlook, especially in frail or high-risk populations.

Each domain of the BMC was developed through a narrative synthesis of institutional insights, clinical experience at Siriraj Hospital, and comparative review of international models. These domains collectively informed the service redesign summarized in Table 1. This approach allowed us to structure a frailty-focused perioperative model that addresses Thailand's system-level challenges.

1. Customer Segments were defined based on demographic data and clinical trends indicating a growing proportion of surgical patients who are frail older adults. The role of family members and caregivers was also emphasized, as they are central to decision-making and transitions across care settings.

2. Value Proposition emerged from clear unmet clinical needs in this population—specifically, the need for safer surgery, fewer complications (e.g., delirium, postoperative cognitive dysfunction or postoperative pulmonary complication), better functional recovery, and long-term independence. Additional value lies in interdisciplinary teamwork and alignment with educational and routine service activities.

3. Channels were identified by examining current points of care delivery (e.g., pre-anesthesia clinics) and by integrating feasible innovations such as prehabilitation units, digital frailty screening tools, and telemedicine follow-up.

4. Customer Relationships reflected the need for longitudinal patient-family engagement, including preoperative counseling, shared decision-making, education, expectation setting, and continuity through discharge planning.

5. Revenue Streams were shaped by the economic challenges of elderly care, with potential cost savings from fewer complications and shorter length of stay. Future revenue may also come from reimbursement of comprehensive geriatric assessment (CGA), prehabilitation, and telehealth-supported postoperative care.

6. Key Resources included both degree and non-degree–trained anesthesiologists in geriatrics or perioperative medicine, interdisciplinary teams, validated screening instruments, clinical practice guidelines, and digital platforms to support service delivery and monitoring.

7. Key Activities were drawn from evidence-based perioperative practices, including frailty screening and CGA, interdisciplinary prehabilitation, geriatric-informed anesthesia, delirium prevention, early mobilization, and structured transitional care with follow-up.

8. Key Partnerships were identified across multiple levels: clinical (e.g., anesthesiologists, geriatricians), institutional (e.g., medical societies), policy and payers (e.g., National Health Security Office; NHSO, Social Security Scheme; SSS), care continuum (e.g., transitional and home-based services), academic (e.g., university centers), and technology providers supporting digital health integration.

9. Cost Structure was based on the initial investment required for workforce development and IT systems, balanced by long-term savings through reduced postoperative complications, readmissions, and functional decline.

Within this review, the BMC is first applied to map the current Thai perioperative ecosystem and then used to prioritize service innovations. The resulting blueprint supports strategic alignment by integrating interdisciplinary teamwork, shared decision-making among providers, patients, and families, and coordinated transitions to consistently deliver a value-based care model. This approach ensures that every component contributes to function-targeted, person-centered surgical outcomes.

Comparative Analysis (Thailand vs Singapore, UK, US)[10-12]

The Start-to-Finish model at Khoo Teck Puat Hospital (KTPH) in Singapore is a pioneering example of integrated perioperative care for frail older adults. This phase-based, transdisciplinary pathway couples structured prehabilitation, early family engagement, and coordinated rehabilitation stretching from initial assessment to community re-entry.

Guy's and St Thomas' NHS Foundation Trust in the United Kingdom developed Proactive Care of Older People Undergoing Surgery (POPS). This geriatrician-led model provides CGA across elective and emergency pathways, with ward-based multidisciplinary team meetings and structured discharge planning.

Duke University's Perioperative Optimization of Senior Health (POSH) in the United States is an interdisciplinary pathway for high-risk older adults that, through early CGA, shared decision-making, and coordinated perioperative planning, lowers postoperative complications, length of stay, and costs. POSH aligns with

TABLE 1. Anesthesiologist-Led Model for Perioperative Geriatric Care in Frailty using Business Model Canvas

BMC Domain	Targeted Redesign for Frailty-Focused Perioperative Model
1. Customer Segments	1. Frail older adults scheduled for elective or high-risk procedure 2. Families or caregivers involved in decision-making and supporting transitions across care settings
2. Value Proposition	1. Provide safe and person-centered surgical care for frail older adults by using frailty-based decision-making, aiming to reduce complications such as delirium, support functional recovery, and help patients maintain independence. 2. Working as an interdisciplinary team and planning for care transitions. 3. Integration with education and routine service activity such as interdisciplinary case conferences or postoperative care pathways
3. Channels	1. Pre-anesthesia clinic 2. Prehabilitation units 3. Digital screening platforms and telemedicine follow-up
4. Customer Relationships	Longitudinal engagement with older patients and families through preoperative counselling, shared decision-making, education, and expectation setting, with continuity of care extended through discharge planning
5. Revenue Streams	Cost savings from fewer complications and shorter hospital stays, with future revenue potential from value-based payment for the comprehensive geriatric assessment (CGA) and interventions, prehabilitation and post-operative care through telehealth
6. Key Resources	1. Anesthesiologists trained in geriatric medicine, gerontology, or perioperative medicine (formal degree programs such as diplomas, master's, or PhDs.) 2. Frontline specialists, including attending geriatricians and anesthesiologists (non-degree programs such as short courses, workshops, or certificate programs) 3.Human resources to support coordinated and interdisciplinary care such as nurses, psychologists and rehabilitation specialists 4. National and international clinical practice guidelines 5. Validated frailty screening tools and CGA instruments 6. Digital platforms and telehealth/ telemedicine
7. Key Activities	1. Systematic frailty screening and CGA 2. Interdisciplinary prehabilitation interventions including medication review, nutrition counselling, exercise prescribing, and psychological preparation 3. Geriatric-informed anesthesia and pain management; delirium prevention protocols; early mobilization and rehabilitation 4. Coordination of transitional care with structured postoperative follow-up
8. Key Partnerships	Multilevel coordination: • *Clinical Partners:* Anesthesiologists, geriatricians, surgeons, rehabilitation specialists, family medicine, nutritionists, pharmacists, mental health providers, social workers and educators • *Institutional Partners:* Ministry of Public Health, Royal College of Anesthesiologists of Thailand, Royal College of Surgeons of Thailand, Thai Gerontology and Geriatric Medicine Society and Royal College of Physicians of Thailand • *Payers and Policy Stakeholders:* Universal Coverage Scheme (UCS), Social Security Scheme (SSS) and Civil Servant Medical Benefit Scheme (CSMBS) for reimbursement and coverage alignment • *Care Continuum Partners:* Community-based facilities such as Primary Health Care (PHC), transitional care teams, intermediate care (IMC) and home healthcare services • *Academic and Training Institutions:* University hospitals and academic centers for workforce development, research, and innovation pilots • *Technology Partners:* Digital health providers and information technology (IT) platforms supporting frailty screening, CGA documentation, and outcome tracking
9. Cost Structure	1. Initial investment in workforce upskilling, care coordination 2. IT infrastructure 3. Long-term savings through improved outcomes such as reduced readmission, fewer complications, and sustained independence post-surgery

national quality programs—most notably, the American College of Surgeons (ACS) Geriatric Surgery Verification Program—and provides a scalable template for high-value, personalized surgery.

Thailand's perioperative services remain fragmented: CGA access is limited, prehabilitation infrastructure underdeveloped, and postoperative rehabilitation and discharge coordination inconsistent. This is consistent with findings from national data and local studies, including those at Siriraj Hospital, which highlight the high prevalence of geriatric syndromes and gaps in service coordination in older populations.[13] Pilot testing a hybrid Thai model that fuses best-practice elements is warranted. Essential pillars include early CGA led by geriatricians or trained anesthesiologists, structured prehabilitation embedded in tertiary centers, and postoperative discharge pathways linking surgical wards to rehabilitation units and community health services.

Adopting the POSH framework would permit phased scaling according to workforce capacity and existing resources. Alignment with the National Elderly Health Strategic Plan could enhance surgical safety, curb delirium, and accelerate functional recovery. Implementation should start within tertiary or university hospitals, harness workforce-development programs, and synchronize with the Thai Elderly Health Policy. Subsequent collaboration with the National Health Security Office could embed the model in the Universal Coverage Scheme (a government health insurance program) and secure equitable, value-based surgical care for older adults nationwide.

The expanding role of anesthesiologists in perioperative geriatric care

Anesthesiologists are moving beyond intraoperative management to oversee the entire perioperative continuum for frail older adults, a population whose surgical courses are increasingly complex. Their deep expertise in physiology, pharmacology, and perioperative risk positions them to coordinate multidisciplinary strategies that reduce surgical risk and enhance functional resilience. In models such as Start-to-Finish in Singapore, POPS in the United Kingdom, and POSH in the United States, anesthesiologists collaborate with geriatricians and interdisciplinary teams to implement frailty-adapted protocols—among them EEG-guided anesthesia, opioid-sparing analgesia, and intraoperative hemodynamic optimization. They also contribute to early frailty screening and CGA, customizing perioperative trajectories to each patient's cognitive, nutritional, and functional profiles.

Postoperatively, anesthesiologists maintain continuity by translating intraoperative events into recovery targets and discharge plans. Their participation in transitional-care pathways, along with coordination with primary-care or community rehabilitation services, facilitates safe reintegration and sustained functional independence. Positioning anesthesiologists as perioperative leaders enhances patient safety, preserves independence, and advances patient-centered outcomes. Their active involvement throughout the perioperative timeline supports a proactive model of care—one urgently needed as Thailand enters an aged society with rising demand for integrated, frailty-informed surgical services.

System-Level Implications for Thailand

To embed anesthesiologists as perioperative geriatric leaders, Thailand must pair workforce up-skilling with structural redesign of surgical services. Training curricula for anesthesiology residents and continuing professional education should be updated to include core competencies in geriatrics, frailty assessment, prehabilitation planning, and postoperative recovery management. Institutions such as Siriraj Hospital and other academic medical centers can pilot collaborative perioperative care for frail patients, generate local data, and provide interprofessional training that bridges anesthesiology with geriatric principles. National adoption of this integrated framework would improve outcomes for older adults and redefine the role of anesthesiologists as clinical leaders in perioperative geriatric care, aligning surgery with broader aging and surgical-safety initiatives. Embedding anesthesiology within broader geriatric and surgical-safety initiatives would shift the system toward proactive, efficient, patient-centered care.

Proposed 4-phase continuum of perioperative care for frailty

Their expertise in risk stratification, intraoperative management, and postoperative recovery positions anesthesiologists to coordinate multidisciplinary efforts tailored to frail older adults. We propose a 4-phase, 24-week continuum—12 weeks preoperative and 12 weeks postoperative—that builds physiologic reserve, forestalls complications, and restores cognitive and physical function. This approach aligns with evidence-based practices that emphasize early identification of frailty and targeted interventions. Roles for anesthesiologists within each phase are depicted in Fig 1.[14-16]

Phase 1 — Preoperative optimization

Anesthesiologists lead comprehensive risk stratification for older surgical candidates, incorporating frailty screening, multimorbidity profiling, polypharmacy review, and

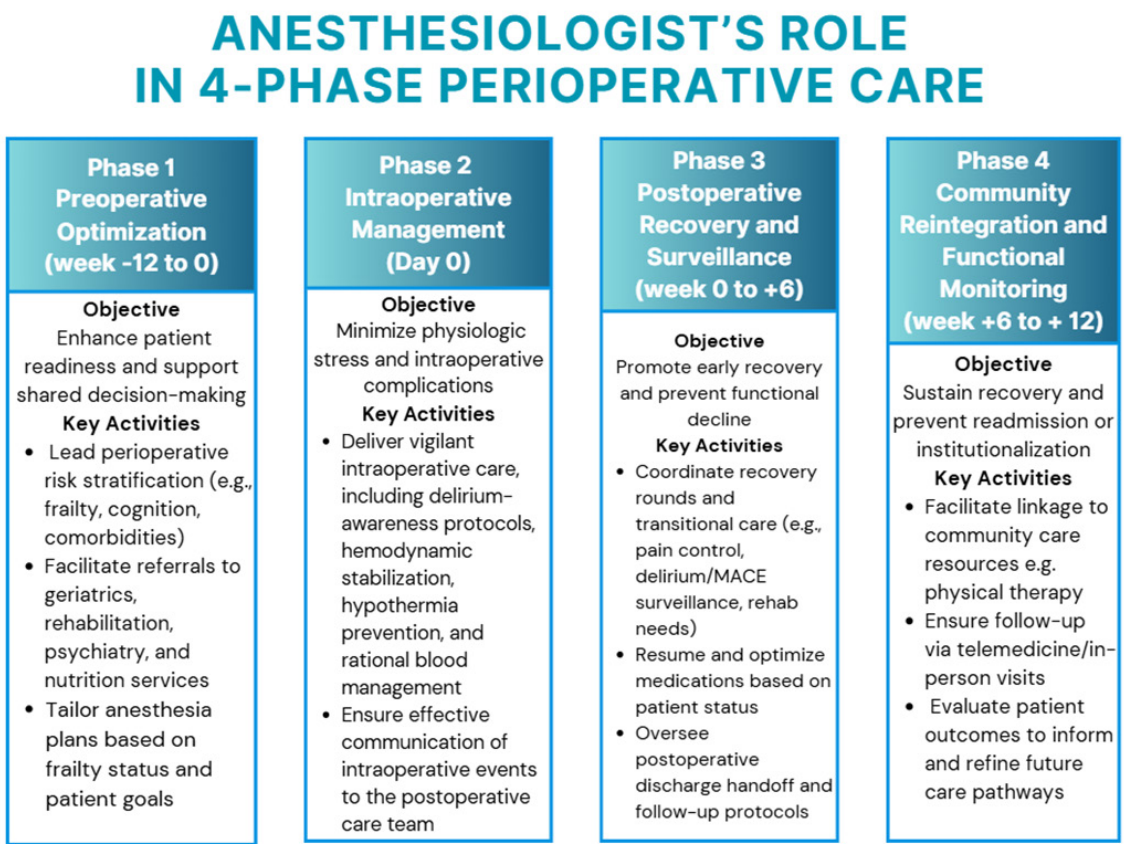


Fig 1. The proposed 4-phases of the anesthesiologist-led model of integrated perioperative care.
Abbreviation: MACE, major adverse cardiac event

functional–cognitive appraisal to craft patient-specific perioperative plans. Early referral to a comprehensive prehabilitation clinic is pivotal; nutrition screening and supplementation, tailored exercise programs, and physiotherapy strengthen functional reserve and reduce postoperative complications. Optimization also requires identification and management of anemia, because both anemia and perioperative transfusion are associated with increased morbidity and mortality. For procedures expected to lose > 500 mL of blood, patients must undergo preoperative hemoglobin evaluation; iron-deficiency cases should receive prompt replacement therapy. In older orthopedic populations, maintaining preoperative hemoglobin > 12.0 g/dL reduces transfusion requirements and improves outcomes. This integrated, anesthesiologist-driven approach advances perioperative safety and recovery for frail older adults.[17,18]

Phase 2 — Intraoperative management for frailty[19,20]

In frail older adults, intraoperative care must attenuate physiologic stress and forestall complications. First, apply delirium-mitigation protocols: avoid benzodiazepines, correct anemia or electrolyte derangements, maintain normotension and normoxia, and use processed electroencephalography monitoring, which lowers postoperative delirium rates and shortens length of stay. Second, sustain hemodynamic stability to preserve organ perfusion and minimize the risk of organ dysfunction in patients with limited physiologic reserve. Third, apply continuous active warming throughout the perioperative period because impaired thermoregulation increases vulnerability to cold-related complications. Together, these targeted interventions safeguard cognition and protect end-organ function.

Phase 3 — Recovery and surveillance

During the immediate postoperative period, anesthesiologists contribute significantly to recovery and surveillance, particularly for frail older adults at elevated risk for complications. They monitor for geriatric syndromes—such as postoperative delirium, pain-related agitation, and functional decline—to guide individualized care. Collaboration with surgeons, nurses, and geriatricians enables anesthesiologists to deliver multimodal, opioid-sparing analgesia that minimizes adverse effects and supports early mobilization. By tracking clinical trajectories and adjusting goals of care, they identify patients who may benefit from step-down geriatric co-management or

extended rehabilitation in intermediate-care settings. Early detection of deterioration permits timely interventions that support safe recovery.

Phase 4 — Community reintegration and functional monitoring

Following hospital discharge, anesthesiologists trained in perioperative medicine can extend their role into the post-acute phase by supporting coordinated transitions and ongoing functional recovery. Their responsibilities include reviewing postoperative progress, identifying residual impairments, and facilitating connections to community rehabilitation, home-based services, and primary care providers. Functional reassessment—conducted through structured in-person visits or telemedicine—enables anesthesiologists to monitor key recovery milestones and support sustained mobility, cognitive health, and independence. In collaboration with multidisciplinary teams, they contribute to individualized recovery plans that bridge the transition from hospital to home. Implementing this phase requires substantial resources, infrastructure, and coordinated networks—elements still developing in Thailand's health system—but it remains critical to lowering readmissions and promoting long-term functional outcomes for frail older adults.

When should anesthesiologists involve other specialists in geriatric surgical care?

Timely, coordinated specialist involvement is essential to mitigate perioperative risk and optimize recovery in frail older adults. Table 2 outlines key scenarios in which anesthesiologists should involve multidisciplinary partners to deliver personalized, evidence-informed care for older adults undergoing surgery, based on vulnerabilities identified during preoperative assessment.

Referral should ideally be placed 4–12 weeks before surgery, allowing sufficient time for nutrition-centered and exercise-based prehabilitation. A positive

TABLE 2. Multidisciplinary partner consultations: triggers and expected roles.

Specialists	Timing of Involvement	Key Triggers / Indications	Primary Role in Perioperative Care
Geriatrician	≥4 weeks preop (immediately after frailty is identified)	Frailty, cognitive impairment, multimorbidity, polypharmacy	Conduct CGA, optimize comorbidities, lead shared decision-making, support goal-of-care alignment
Cardiologist	Preop clinic (if cardiac risk is high or unstable)	Heart failure, valvular disease, ischemic heart disease, arrhythmias, poor functional capacity	Stratify cardiac risk, adjust medications, guide perioperative monitoring
Nutritionist/ Dietitian	≥2–4 weeks preop	Malnutrition (e.g., low BMI, weight loss), sarcopenia, hypoalbuminemia	Nutritional screening, oral supplementation, dietary planning for recovery
Rehabilitation Specialists	≥4 weeks preop	Poor mobility, slow gait speed, falls, ADL/IADL dependence, oromotor problems	Prescribe exercise and mobility plan, enhance endurance and strength, prevent functional decline, swallowing intervention
Pharmacist	During CGA or preop medication review	Polypharmacy (>5 meds), potentially inappropriate medications (e.g., benzodiazepines, anticholinergics)	Reconcile medications, deprescribe as needed, optimize drug regimens for changes in age-related physiology
Mental Health Provider / Psychologist	Preop if concern arises	Depression, anxiety, fear of surgery, baseline cognition,	Supportive counselling, optimize mental health, assist in delirium risk reduction

Abbreviations: ADL, activities of daily living; CGA, comprehensive geriatric assessment; IADL, instrumental activities of daily living; OT, occupational therapy; PT, physical therapy

frailty screen serves as an automatic trigger for prompt consultation with geriatrics, rehabilitation, nutrition, and allied-health teams. Finally, anesthesiologists must align intraoperative strategies with each patient's functional capacity, comorbidity profile, care goals, and discharge plan to ensure seamless, goal-concordant management.

System-level strategy and support for Thailand

Embedding a geriatric-sensitive perioperative model in Thailand demands synchronized system reform and targeted workforce development. Academic flagships—for example, Siriraj Hospital—should pioneer dedicated perioperative geriatric-anesthesia tracks that teach frailty-based decision making, interdisciplinary collaboration, and transition-of-care design. Integrating these competencies into residency curricula and buttressing them with purpose-built multidisciplinary teams will create the infrastructure for durable change.

Thai health systems should prioritize 4 actions:

- Provide foundational geriatric training for anesthesiologists through short courses, workshops, certificate programs, or formal diploma, master's, or PhD pathways covering frailty syndromes, cognitive vulnerability, pharmacologic sensitivity, and collaborative care models.
- Embed cross-disciplinary expertise in preoperative optimization and postoperative recovery by routinely involving geriatricians, rehabilitation specialists, psychiatrists, dietitians, pharmacists, psychologists, and case managers.
- Elevate anesthesiologists to co-lead development of postoperative pathways centered on delirium prevention, early mobilization, and age-appropriate analgesia.
- Forge formal partnerships with transitional-care services to synchronize discharge planning and link surgical wards to intermediate-care facilities and community or primary-care networks.

At the policy level, the Ministry of Public Health should promulgate national guidelines and reimbursement levers for systematic frailty screening, comprehensive geriatric assessment (CGA), and structured prehabilitation. In parallel, tertiary academic centers such as Siriraj Hospital can act as national demonstration sites to pilot and scale these innovations, enabling Thailand to deliver high-quality, function-preserving surgical care to its aging population.

Strategic policy recommendations

Thailand's entry into an aged society necessitates urgent reform of perioperative care systems, especially for frail older adults. Existing procedure-centric models are fragmented and ill equipped to handle the intertwined biologic, cognitive, and social vulnerabilities of frailty. Using the Business Model Canvas and comparative analysis of international models—such as Start-to-Finish in Singapore, POPS in the United Kingdom, and POSH in the United States—this review identified the absence of structured prehabilitation, limited multidisciplinary coordination, and insufficient continuity of care.

Anesthesiologists are strategically positioned to drive this transformation. Their role across the perioperative continuum—from preoperative risk stratification to intraoperative management and postoperative planning—places them at the intersection of clinical decision-making and system redesign. With geriatric up-skilling and expanded leadership, they can institute frailty screening, steer shared decision making, and coordinate the 24-week, 4-phase pathway proposed herein. The proposed 4-phase integrated model provides a clear roadmap for redesigning surgical services around function preservation, patient-centered goals, and seamless care transitions.

A Step-by-step approach to strategic deployment

- *Develop National Guidelines for Perioperative Frailty Care*

Standardize validated screening instruments—Clinical Frailty Scale, FRAIL Scale, Frailty Index—and make frailty assessment mandatory for every surgical candidate ≥ 65 years during preoperative evaluation.[21,22]

- *Establish Prehabilitation and Postoperative Recovery Clinics*

Create multidisciplinary prehabilitation units in tertiary centers to optimize functional status preoperatively, then integrate preoperative optimization with postoperative rehabilitation and home-reintegration pathways.[23,24]

- *Create a Perioperative Medicine Track Within Anesthesiology*

Embed geriatrics, comprehensive geriatric assessment (CGA), and transition-of-care design in residency and continuing-education curricula; define anesthesiologist-led pathways tailored to frail surgical populations.

- *Incentivize Multidisciplinary, Longitudinal Care*

Implement reimbursement mechanisms for CGA, multidisciplinary-team conferences, and structured post-discharge follow-up; fund pilot programs linking surgical wards to intermediate-care and community-based services.

• *Invest in Digital Infrastructure and Outcome Tracking*

Build electronic-health-record–integrated frailty registries and real-time surgical risk dashboards that track postoperative mobility, cognition, independence, and 30-day readmissions.

To evaluate this model in practice, pilot testing in tertiary hospitals is recommended. Key outcomes could include rates of complications (such as delirium), hospital length of stay, 30-day readmissions, and patients' functional recovery. Process measures—like how often frailty screening or CGA are completed—can help monitor how well the model is applied. To test whether the model is reliable and appropriate for wider use, methods such as expert reviews, small-scale feasibility studies, and real-world feedback from healthcare teams can be used.

CONCLUSION

A Vision Forward

Transforming perioperative care for frail older adults requires sustained system redesign, not a single intervention. With anesthesiologist leadership aligned to Thailand's aging-health agenda, the nation can become a regional exemplar of safe, function-preserving, and person-centered surgery. The evidence is compelling, the models are validated, and the imperative is immediate.

Data Availability Statement

No new data were generated or analyzed in this study.

ACKNOWLEDGMENTS

This review was developed in recognition of the 60th anniversary of the Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, and reflects the department's continued commitment to advancing perioperative care for Thailand's aging population. We thank Mr. David William Park for his assistance with English language editing.

DECLARATIONS

Grants and Funding Information

This article received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors declare no conflict of interest.

Author Contributions

Conceptualization and methodology: J.N., A.S., and O.P.; Visualization and writing – original draft: J.N., A.S.; Writing – review and editing: J.N., A.S., P.N., O.P., W.M., T.P., P.D., and V.S.; Supervision: O.P., A.S. All authors have read and agreed to the final version of the manuscript.

Use of Artificial Intelligence

We acknowledge the use of ChatGPT (OpenAI) for language support and grammar suggestions during the preparation of this review article

REFERENCES

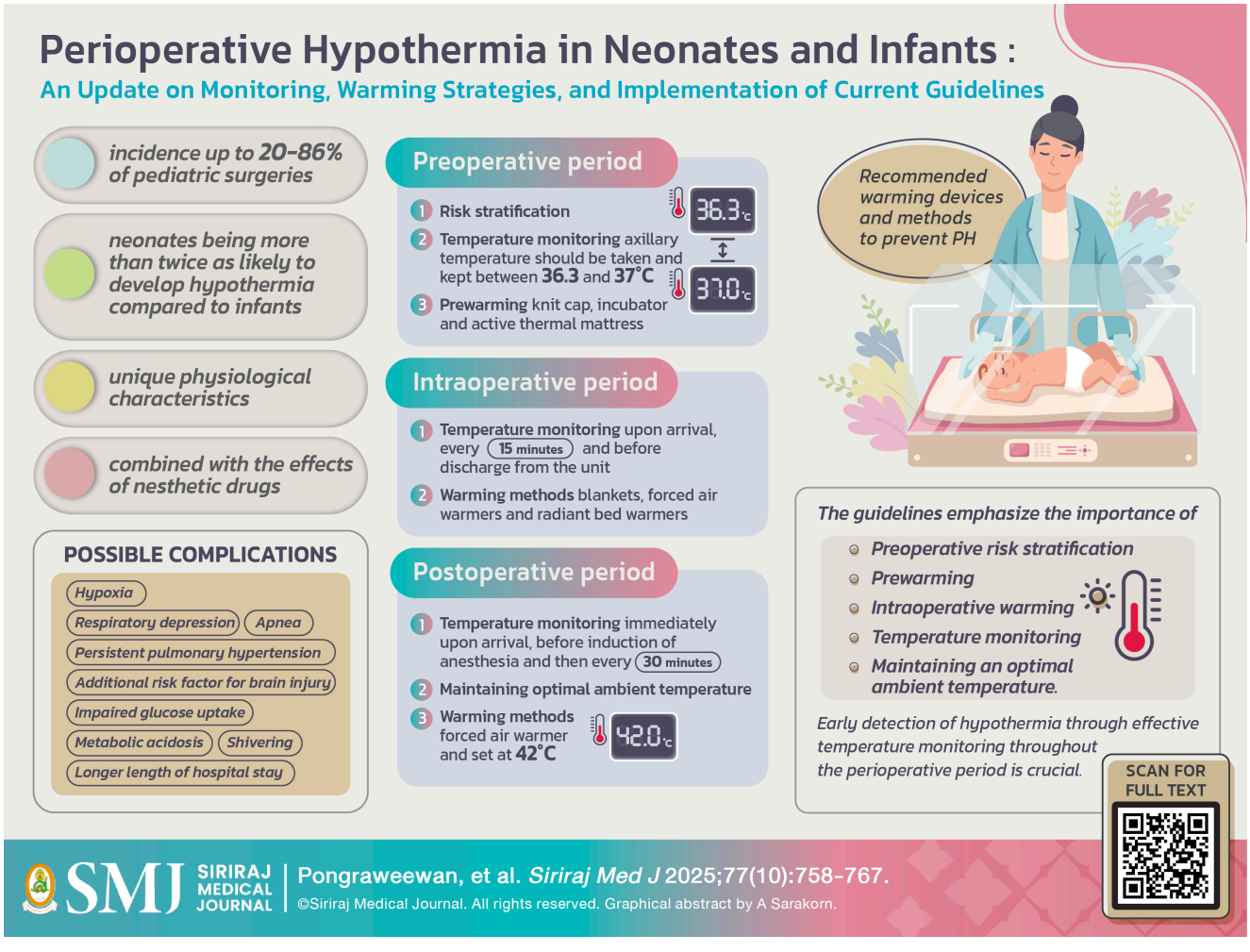
1. Lertkovit S, Siriussawakul A, Suraarunsumrit P, Lertpipopmetha W, Manomaiwong N, Wivatdechakul W, et al. Polypharmacy in Older Adults Undergoing Major Surgery: Prevalence, Association With Postoperative Cognitive Dysfunction and Potential Associated Anesthetic Agents. Front Med (Lausanne). 2022;9:811954.
2. Makary MA, Segev DL, Pronovost PJ, Syin D, Bandeen-Roche K, Patel P, et al. Frailty as a predictor of surgical outcomes in older patients. J Am Coll Surg. 2010;210(6):901-8.
3. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K. Frailty in elderly people. Lancet. 2013;381(9868):752-62.
4. Robinson TN, Walston JD, Brummel NE, Deiner S, Brown CHt, Kennedy M, et al. Frailty for Surgeons: Review of a National Institute on Aging Conference on Frailty for Specialists. J Am Coll Surg. 2015;221(6):1083-92.
5. George EL, Hall DE, Youk A, Chen R, Kashikar A, Trickey AW, et al. Association Between Patient Frailty and Postoperative Mortality Across Multiple Noncardiac Surgical Specialties. JAMA Surg. 2021;156(1):e205152.
6. Deiner SG, Marcantonio ER, Trivedi S, Inouye SK, Travison TG, Schmitt EM, et al. Comparison of the frailty index and frailty phenotype and their associations with postoperative delirium incidence and severity. J Am Geriatr Soc. 2024;72(6):1781-92.
7. Parakonthun T, Sirisut B, Nampoolsuksan C, Gonggetyai G, Swangsri J, Methasate A. Factors associated with complication after gastrectomy for gastric or esophagogastric cancer compared among surgical purpose, surgical extent, and patient age: Retrospective study from a high volume center in Thailand. Ann Med Surg (Lond). 2022;78:103902.
8. Parakonthun T, Nampoolsuksan C, Swangsri J, Yiengpruksawan A, Methasate A. Retrospective analysis of the outcomes in elderly patients with adenocarcinoma of the stomach and esophagogastric junction following three different treatments. Siriraj Med J. 2019;71(6):457-65.
9. Osterwalder A, Pigneur Y. Business model generation: a handbook for visionaries, game changers, and challengers. John Wiley & Sons; 2010.
10. Chia CLK, Mantoo SK, Tan KY. 'Start to finish trans-institutional transdisciplinary care': a novel approach improves colorectal surgical results in frail elderly patients. Colorectal Dis. 2016;18(1):O43-50.
11. Lodge ME, Dhesi J, Shipway DJ, Braude P, Meilak C, Partridge J, et al. Core elements of the perioperative medicine for older people undergoing surgery (POPS) model of care. Eur Geriatr Med. 2025;16(2):435-46.
12. Wingfield SA, McDonald SR. Geriatric Models of Care:

Perioperative Optimization of Senior Health (POSH). In: Malone ML, Boltz M, Macias Tejada J, White H, editors. Geriatrics Models of Care: Bringing 'Best Practice' to an Aging America. Cham: Springer International Publishing; 2024. p. 377-82.
13. Phannarus H, Chansaengpetch S, Virojskulchai T, Pengsorn N, Chaopanitwet P, Wong-ekkabut J, et al. Prevalence of Geriatric Syndromes and Satisfaction of Service in Older People Receiving Annual Health Screening at the Check-up Clinic, Siriraj Hospital. Siriraj Med J. 2025;77(1):51-63.
14. Wolfe JD, Wolfe NK, Rich MW. Perioperative care of the geriatric patient for noncardiac surgery. Clin Cardiol. 2020;43(2): 127-36.
15. Thillainadesan J, Hilmer SN, Fleury AM, Naganathan V. New horizons in the perioperative care of older adults. Age Ageing. 2022;51(2):afab245.
16. Olotu C, Weimann A, Bahrs C, Schwenk W, Scherer M, Kiefmann R. The perioperative care of older patients: time for a new, interdisciplinary approach. Deutsch Ärztebl Int. 2019;116(5): 63-69.
17. Aceto P, Antonelli Incalzi R, Bettelli G, Carron M, Chiumiento F, Corcione A, et al. Perioperative Management of Elderly patients (PriME): recommendations from an Italian intersociety consensus. Aging Clin Exp Res. 2020;32(9):1647-73.
18. Lasocki S, Krauspe R, Von Heymann C, Mezzacasa A, Chainey S, Spahn DR. PREPARE: the prevalence of perioperative anaemia and need for patient blood management in elective orthopaedic surgery: a multicentre, observational study. Eur J Anaesthesiol. 2015;32(3):160-7.
19. Somnuke P, Pongraweewan O, Siriussawakul A. Optimizing Perioperative Care for Elderly Surgical Patients: A Review of Strategies and Evidence-Based Practices. Siriraj Med J. 2024; 76(7):465-72.
20. Sieber F, McIsaac DI, Deiner S, Azefor T, Berger M, Hughes C, et al. 2025 American Society of Anesthesiologists Practice Advisory for Perioperative Care of Older Adults Scheduled for Inpatient Surgery. Anesthesiology. 2025;142(1):22-51.
21. Centre for Perioperative Care BGS, and Royal College of Anaesthetists. Guideline for perioperative care for people living with frailty undergoing elective and emergency surgery. London: Centre for Perioperative Care; 2021.
22. Thompson A, Fleischmann KE, Smilowitz NR, de Las Fuentes L, Mukherjee D, Aggarwal NR, et al. 2024 AHA/ACC/ACS/ASNC/HRS/SCA/SCCT/SCMR/SVM guideline for perioperative cardiovascular management for noncardiac surgery: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. J Am Coll Cardiol. 2024;84(19):1869-969.
23. Jirakulsawat A, Noocharoen N, Somnuke P. Prehabilitation in Clinical Practice: A Review of Concepts and Implementation in Enhancing Postoperative Outcomes. Siriraj Med J. 2024;76(9): 646-54.
24. Wong HMK, Qi D, Ma BHM, Hou PY, Kwong CKW, Lee A, et al. Multidisciplinary prehabilitation to improve frailty and functional capacity in high-risk elective surgical patients: a retrospective pilot study. Perioper Med (Lond). 2024;13(1):6.

Perioperative Hypothermia in Neonates and Infants: An Update on Monitoring, Warming Strategies, and Implementation of Current Guidelines

Panithi Pongraweewan, M.D., Ornin Chintabanyat, M.D., Sahatsa Mandee, M.D.*

Department of Anesthesiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, Thailand.



*Corresponding author: Sahatsa Mandee
E-mail: Sahatsa.mandee@gmail.com
Received 14 July 2025 Revised 14 August 2025 Accepted 17 August 2025
ORCID ID:http://orcid.org/0009-0001-3271-7706
https://doi.org/10.33192/smj.v77i10.276540

ABSTRACT

Perioperative hypothermia (PH) is a common concern in neonates and infants, and neonates are more than twice as likely to develop hypothermia due to their unique physiological characteristics. Combined with the effects of anesthetic drugs, these factors make them particularly susceptible to heat loss. Despite the implementation of effective warming methods, maintaining normothermia in this vulnerable population remains challenging.

Several guidelines tailored to specific hospitals and institutions aimed to emphasize the importance of preoperative risk stratification, prewarming, intraoperative warming, temperature monitoring, and maintaining an optimal ambient temperature. Early detection of hypothermia through effective temperature monitoring throughout the perioperative period is crucial. Combining the use of warming devices with specific techniques is more effective in reducing perioperative hypothermia.

This article highlights recent updates in monitoring and warming strategies, comparing the advantages and disadvantages of different approaches, and reviews the guidelines designed to prevent perioperative hypothermia in neonates and infants in order to optimize surgical outcomes.

Keywords: Perioperative hypothermia; pediatric; anesthesia; guideline; warming methods (Siriraj Med J 2025; 77: 758-767)

INTRODUCTION

Perioperative hypothermia, defined as a core body temperature below 36.5°C in children up to five years of age and below 36°C for children older than five years during the perioperative period[1], is a common concern among neonates and infants, as these age groups are particularly susceptible due to their unique physiological and anatomical features. Compared to older children and adults, they are at a significantly higher risk of developing perioperative hypothermia.

The incidence of perioperative hypothermia was reported in 82.83% of neonates and 38.31% of infants[2], while intraoperative hypothermia occurred in 54%[3] of patients. Despite efforts to monitor, detect, and implement interventions, the incidence of neonates and young children developing perioperative hypothermia remains high. This article highlights recent updates on monitoring, warming strategies, and the implementation of guidelines to prevent perioperative hypothermia in neonates and infants in order to optimize surgical outcomes.

Complications of perioperative hypothermia

Perioperative hypothermia in neonates and infants can ultimately lead to serious complications across multiple systems, as reported in Table 1.

Pathophysiology

Pediatric patients are particularly prone to developing perioperative hypothermia due to their unique physiological characteristics. Compared to adults, they have a larger body surface area-to-weight ratio, immature thermoregulation, and lower thermal insulation due to reduced subcutaneous fat. As a result, they lose heat primarily through conduction and radiation. In infants, **non-shivering thermogenesis** plays a dominant role in heat production, defined as an increase in metabolic heat production regardless of associated muscle activity. Brown fat, commonly located at the nape of the neck, interscapular region, axillae, and groin and around the kidneys and adrenals, results in double heat production in children up to 2 years of age.

Heat is produced from the aerobic metabolism of body cells, with skeletal muscles and the heart being the primary sources during physical activity. At rest, heat production comes mainly from the kidneys, brain, and liver. In response to exposure to cold, the body typically increases heat production through physical activity and shivering.

Effects of anesthesia on thermoregulation

General anesthesia

General anesthesia commonly causes hypothermia by increasing heat loss and suppressing heat production, resulting in significantly impaired thermoregulation which leads to an imbalance between heat gain and heat loss. Radiation is the most significant source of heat loss in pediatric patients (40%), followed by convection (30%), evaporation (25%), and conduction (5%).[4] The overall physiological changes during general anesthesia include: **(1) Abolition of behavioral responses,** leaving only autonomic defenses. **(2) Expansion of the interthreshold range,** the temperature difference between the onset of vasoconstriction and the initiation of shivering, from 0.4°C

TABLE 1. Complications of perioperative hypothermia.

Systems	Complications
Respiratory system	Hypoxia, respiratory depression and apnea, decreased surfactant synthesis
Cardiovascular system	Persistent pulmonary hypertension, right-to-left shunting
Central nervous system	Additional risk factor for brain injury
Endocrine system	Impaired glucose uptake, hypoglycemia, increased noradrenaline release, and metabolic acidosis
Other	Thermal discomfort, shivering, decreased tissue perfusion leading to increased risk of surgical site infection, increased transfusion requirement, and longer length of hospital stay

to 4°C, combined with an immature thermoregulatory center in neonates and infants, increases their susceptibility to develop hypothermia during anesthesia.[4] **(3) Reduction in vasoconstriction and shivering thresholds,** consequently, these thermoregulatory responses are triggered at higher core temperatures than usual, and may disrupt normal temperature regulation. **(4) Alteration of the sweating threshold,** most anesthetics increase the sweating threshold in a concentration-dependent manner. Conversely, midazolam tends to decrease the sweating threshold and reduces the vasoconstriction threshold.[5] **(5) Systemic vasodilation and (6) Catecholamine reduction**. However, sufficient stress levels can still activate autonomic defenses.

Neuraxial anesthesia effects on thermoregulation

Regional anesthesia affects thermoregulation by inhibiting peripheral vasoconstriction and shivering in blocked areas below the level of the blockade[3], which prevents patients from achieving a steady thermal state. Compared to general anesthesia, patients undergoing general or regional anesthesia face an equally significant risk of developing hypothermia[6] and the combination of both anesthetic techniques results in the most heat loss.[4]

Risk factors for developing PH

(1) Age Neonates experience hypothermia significantly more often than older infants as they have an increased body surface-to-weight ratio. ***(2) Lower body weight (3) Prematurity (4) Longer duration of surgery*** Temperature decrease during the redistribution phase to linear phase, taking up to 3 hours before continuing steadily in the plateau phase in the next hours after induction.[4] ***(5) Lower baseline temperature*** Temperature before induction of anesthesia lower than 36.5°C is known to have greater risk of perioperative hypothermia.[4] ***(6) Greater blood loss[7] and transfusion rate[7] (7) More fluid administered*** Infusion of a volume of fluid greater than half a liter contributes to intraoperative hypothermia ***(8) Lack of prewarming measures (9) Major surgery*** Invasive procedures, i.e. major surgery, were at greater risk compared to non-invasive procedures. Some specific types of surgery are also associated with a greater risk of developing hypothermia, including bronchoscopy, burn surgery, cystoscopy, hypospadias, mastoidectomy, neurosurgery, thoracic, squint surgery, esophagoduodenoscopy, and colonoscopy.[8] ***(10) Choice of anesthesia*** Patients are at an equal risk of developing hypothermia in both general anesthesia and regional anesthesia, with combined techniques accounting for the greatest heat loss. ***(11) Lower operating room temperature***

Updates in monitoring sites and devices

The optimal period for perioperative temperature monitoring, together with the appropriate sites and devices, plays a key role in determining whether patients develop hypothermia or hyperthermia, which could possibly lead to serious events.

Sites

- Core temperature monitoring sites include the nasopharynx, distal esophagus, tympanic membrane, pulmonary artery, and rectum.
- The esophageal temperature has limitations, as it has been shown to increase significantly during ventilation with warmed and /or humidified respiratory gases.[9]
- For all patients 2 years and under and those at high risk for hypothermia, temperature should only be monitored via **rectal probe**, to a maximum depth of 2 cm, or by **esophageal probe or nasopharyngeal probe**.[10]
- Skin temperature is ***not*** an acceptable means of measuring temperature and should only be used in specific cases determined by the anesthesiologist.[9,10]

TABLE 2. Active warming devices.

Active warming devices	Details
Forced air warmer	**Advantages** Rapid distribution of heat Easy to use Does not require direct skin contact Disposable blanket More effective than a water-circulating mattress Reduces the incidence of post-anesthetic shivering **Disadvantages** Loud noise Bacteria could potentially be introduced into the surgical field Still a limited supply in some specific countries Could be unsuitable for young, awake children **Suggestion** Should be considered only for pediatric patients with a baseline temperature below 36°C with the presence of a caregiver in the induction room
Water-circulating mattress	Requires significantly less time to warm hypothermic patients, compared with forced air warmer Inferior to both resistive heating blanket and forced air warmer
Intravenous blood-fluid warming	As effective as forced air warmers in adults Combined with the warming blankets, showed the shortest rewarming time
Overhead radiant heater	Inexpensive and effective Significantly increase insensible water loss
Resistive heating blanket	As effective as the forced air warmer Non-inferior to radiant warmer in short-term use

TABLE 3. Passive warming devices.

Passive warming devices	Details
Head caps and thermal hats	Plastic caps are more effective than cotton caps Combined with overhead warmers, can effectively reduce hypothermia in neonates
Warm blankets	Reduce conductive heat loss to the operating table Patients should be covered during sterile prep and exposed for the minimum time as necessary
Heat-moisture exchangers	Lightweight Easy-to-use Cost-effective Provide sufficient humidity to prevent tracheal damage Increase dead space Increase airway resistance results in greater inspiratory workload Increase intrinsic PEEP Limited in patients with secretions, variable minute ventilation, have large air leaks, and increased airway resistance
Warm irrigation fluids	Prevent conductive heat loss Should be warmed to 37°- 38°C, or 38°C-40°C and no more than 50°C

Abbreviation: PEEP; Positive end-expiratory pressure

• Axillary temperature is close to core temperature and appears to be an acceptable alternative to rectal/oral temperature measurements in children[11] possibly minimizing discomfort, potential risk of perforation[12] and can reasonably be used for most patients recovering from anesthesia. However, some studies revealed that it does not accurately represent the oral/rectal temperatures and should therefore be interpreted with caution.[13]

Timing

• Generally, if the operative time is expected to last 30 minutes or longer, the patient's temperature should be documented, and her temperature should be monitored preoperatively before induction as a baseline temperature[8,10], specifically, 1 hour before surgery and then every 30 minutes until the end of the surgery.[14,15] Patients 2 years and younger and those at risk for hypothermia should have the core temperature documented every 15 minutes.[10]

• If the preoperative baseline temperature is below 36°C, the temperature should be checked every 15 minutes until the temperature reaches 36°C or greater.[10]

• *Continuous intraoperative monitoring* should be considered, especially in surgeries that exceed 60 minutes. In children at risk, they should also receive intraoperative active warming in conjunction with continuous temperature monitoring.[8]

Devices

Thermistors and Thermocouples

Both thermistors and thermocouples are temperature-sensing devices. However, thermistors are more sensitive and capable of detecting smaller temperature changes, whereas thermocouples have a wider temperature range. Both devices produce a continuous, rapid response, are sufficiently accurate for clinical use, and are inexpensive enough to be disposable. However, thermistors require calibration and may not be reproducible, and thermocouples could be too complicated.[16]

Infrared

Infrared thermometers offer rapid and noninvasive usage, application of the device to temporal and mid-forehead sites causes only minimal disturbance in neonates. They are most commonly used to measure temperature through the tympanic membrane or forehead, but they can be used on any part of the body surface.[16] However, infrared thermometers are subject to variable accuracy as environmental factors can interfere with measurement[1], require calibration during thermometer use, and could also be expensive.[16] Whether infrared signals obtained from the tympanic membrane truly reflect core temperature remains debatable. Earphone-type infrared tympanic thermometers have been proposed for reliable, continuous intraoperative core temperature monitoring.[17] However, "tympanic membrane" systems essentially measure aural canal skin temperature and often provide poor estimates of core temperature, as none of the tested devices has demonstrated sufficient accuracy or precision for perioperative use.[18] This limitation may stem from the anatomical challenge of reaching the tympanic membrane.[1] In practice, probes are frequently not inserted deeply enough, resulting in measurement of the canal's skin temperature rather than the membrane's.[19] Notably, current data in pediatric populations remain scarce.

Zero-Heat-Flux

Zero-heat-flux thermometers provide continuous, noninvasive, and reliable core temperature monitoring under hypothermic and normothermic conditions.[20] Sang et al. reported that the 3M™ SpotOn™ sensor was closely correlated with esophageal temperatures in pediatric patients and could serve as a noninvasive alternative to pulmonary catheter monitoring.[21]

Recommended warming devices and methods to prevent PH in each perioperative

Period-- based on guidelines

The physiological characteristics of children make them particularly vulnerable to heat loss and more susceptible to hypothermia. Therefore, the implementation of effective hypothermia prevention methods is crucial from preoperative care to postoperative recovery on the wards. In this section, we review and summarize guidelines from multiple studies that focused on patient temperature during the perioperative period.

Preoperative period

Before and during transport to the operating theater

During transportation, heat supply and maintenance should be provided. Premature infants should be nursed in an incubator (4) and infants less than 6 months of age should wear a hat, preferably a plastic cap. Furthermore, combining an incubator or overhead warmer with a thermal hat provides greater effectiveness.[22] All patients should be kept warm with blankets and older children should be encouraged to walk to the operating theater if possible.[4,10,15]

1. Risk stratification should be applied to all patients undergoing surgery and anesthesia in order to identify

patients at increased risk of developing hypothermia using the following criteria:

- Expected duration of the procedure of more than 1 hour
- Age of 1 year or younger

Several types of surgery in pediatric patients were found to be associated with the occurrence of PH, including angiography, arthroscopic knee repair, anterior cruciate ligament (ACL) reconstruction, bronchoscopy, burn surgery, cystoscopy, hypospadias, mastoidectomy, neurosurgery, thoracic, squint surgery, esophagoduodenoscopy, and colonoscopy.[8]

According to the National Institute for Health and Care Excellence (NICE) prevention of hypothermia in adults guideline[15], these criteria could possibly be adapted in the pediatric age group and in adults. Two or more of the following should be considered high risk of developing PH;

- American Society of Anesthesiologists (ASA) grades 2 to 5
- Preoperative temperature below 36.0°C with inadequate warming (could be due to clinical urgency or emergency)
- Undergoing combined general and regional anesthesia
- Undergoing major or intermediate surgery
- At risk of cardiovascular complications

Following risk stratification, pediatric patients at risk should receive intraoperative active warming and continuous temperature monitoring.[8,14]

2. Prewarming

Passive warming should be considered in all patients undergoing anesthesia for more than 30 minutes.[14] Place a knit cap on the patient's head and place the patient in the OR warmer.

An incubator should be applied, but an active thermal mattress should only be applied if the patient's temperature is below 37°C.[23]

3. Temperature monitoring

- Before transport from the ward, the axillary temperature should be taken and kept between 36.3 and 37°C.[23]
- Baseline temperatures should be taken in all patients preoperatively, specifically 1 hour before surgery[14,15], and if the temperature is found to be below 36°C, it should be checked every 15 minutes until the patient reaches 36 degrees Celsius or greater[10] then active warming measures should be initiated in the ward and continued throughout the surgical procedure.[8,14]

Intraoperative period

Intraoperative hypothermia, primarily occurring after the induction period[3], accounts for more than half of perioperative hypothermia cases. The patient's baseline temperature should be maintained above 36°C before the induction of anesthesia. If not, an active warming should be applied for at least 30 minutes before induction of anesthesia until achieving the desired temperature at above 36°C, unless there is a need to expedite surgery because of clinical urgency.[14,15] Proper use of warming devices is also crucial, and clinicians should be trained to use the monitoring device properly and be aware of any possible chance of developing complications. Optimal operating room temperature should be maintained above 26°C, as an increase in operating room temperature by 1°C results in up to 10% reduction in heat loss.[23]

Temperature monitoring

The axillary temperature should be taken immediately upon arrival, before induction of anesthesia and then every 30 minutes[15], at the end of the operation, and before transport back to the NICU.[23] Additionally, *Continuous intraoperative monitoring* should only be considered in surgeries that exceed 60 minutes or in high-risk surgeries.[8]

Maintaining optimal ambient temperature

The maintenance of the ambient temperature plays a crucial role in keeping patients in an optimal temperature range. The ambient temperature in the operating room should be maintained above 23°C[8] when the patient is not draped. Specifically, for patients aged 1 year or younger, the ambient temperature should be set at higher levels: 25°C for infants, 27°C for full-term newborns, and 29°C for premature newborns.[8,10]

Operating room temperature should not be adjusted unless instructed by the anesthesiologist or surgeon.[10] However, if the ambient temperature cannot be determined or falls below 21°C, active warming should be considered.[8]

Warming methods

- Upon arrival in the OR, the patient should be placed in the **forced air warmer** (3M™ Bair Hugger™) and set at 42 degrees Celsius.[10]
- A thermal mattress or warming blanket should be placed on the operating table. All irrigation fluids should be warmed and plans to minimize fluid pooling should be discussed before the start of the procedure.[10]
- After surgery, before removing the drapes, room temperature should be readjusted to 85°F (29.44 °C) and the patient should be placed on OR warmer or Giraffe

Omni-bed with shuttle, with a knit cap placed on the patient's head in conjunction with active warming.[10]

- Sultana et al. at KK Women's and Children's Hospital in Singapore demonstrated the following guidelines:
  - For temperatures below 36.0°C, forced air warming will be applied.
  - For temperatures between 36.0°C and 36.2°C, warm blankets will be used for children, and radiant warmers will be used for neonates and infants.
  - For temperatures above 36.2°C, the patient can proceed to surgery.[8]

Postoperative period

Warming methods

- Before transfer to PACU, patients should be warmed with blankets, forced air warmers, and, if needed, radiant bed warmers for patients 8 kg or less.[10]
- The incubator or warmer should be plugged in immediately and then switched to baby control mode. The thermal mattress should be removed immediately, unless axillary temperature is below 36.3°C.[10]
- Passive warming using blankets and cotton sheets or a duvet should be provided to keep the patient comfortably warm.[10,14,15]
- Moreover, if the patient's temperature is below 36°C, active warming using a forced-air warmer should be applied until discharging from the recovery room or until they are comfortably warm along with temperature documented at least every 30 minutes during warming.[10,14,15]
- Ambient room temperature in the PACU should be maintained at 24°C or higher at all times.[10]

Temperature monitoring

- In the PACU, the patient's temperature should be recorded upon arrival, every 15 minutes, and before discharge from the unit.[10,14,15]
- Axillary temperature should be documented immediately upon arrival at the ward or NICU, and kept between 36.3-37°C[23], if it falls below 36.3°C, or above 37°C, rectal temperature should be monitored every 30 minutes until normothermic, and incubator temperature should also be recorded.[23]
- Only discharge the patient from the PACU if the patient's temperature is above 36°C.[14,15]

Pros, Cons, Comparison and Recommendations on Warming Devices

Active warming devices

Forced air warmer (3M™Bair Hugger™)

Forced air warmer offers various advantages. It distributes heat quickly, has disposable blankets, and does not require direct skin contact. Compared to a **water-circulating mattress, a forced air warmer** was found to be more effective in preventing neonatal hypothermia during intraabdominal operations[24] and in reducing postanesthetic shivering.[25]

However, the use of a forced air warmer may introduce bacteria into the surgical field, potentially increasing the risk of surgical wound infection.[26] However, another study reported that using a forced air warmer does not cause nosocomial infections.[27] Moreover, this method could be inappropriate for young, awake children; thus, it should only be considered for pediatric patients with a baseline temperature below 36°C with the presence of a caregiver in the induction room.[8]

Water-circulating mattress

A Water-filled mattress warms the patient through conduction with thermostatic control. Water-circulating systems required significantly less time to warm hypothermic patients compared to **forced-air systems**.[28]

Intravenous blood-fluid warming

Rapid infusion of cold intravenous (I.V.) fluids could induce hypothermia; therefore, it is recommended **to apply** intravenous blood-fluid warming if not contraindicated.[10] In adults, intravenous fluids (500 ml or more) and blood products should be warmed to 37°C[15], but the optimal temperature is still unclear in small children. Compared to **forced air warmers**, no statistically significant differences were reported in terms of body temperature.[29] Furthermore, the combination of warming blankets and pre-warmed intravenous infusion showed the shortest rewarming time.[30]

Incubators

Incubators offer effective temperature control and reduce metabolic demand as much as **heated water-filled mattresses**.[31]

Overhead radiant heaters

A radiant heater uses infrared radiation to warm the patient. Although this method appeared to be inexpensive and effective, a significant increase in insensible water loss in neonates has been reported.[23] The patient should be closely monitored for signs of overheating and burns.

Resistive heating blanket

The resistive heating blanket consists of a polymer fiber sheet that produces heat through and warms the patient through conduction. It is as effective as the **forced-air warming system** to maintain the core temperature of the patient, and both are reported to be superior to the circulating water mattress.[32] The short-term use of conductive thermal mattresses is not inferior to radiant warmers to maintain body temperature.[3]

Passive warming devices

Head caps and thermal hats

Especially in premature and newborn infants, **plastic caps** should be considered as they are proven to be more effective to prevent heat loss, compared to **cotton caps**.[33] The combined use of **thermal hats** and **overhead warmers** was also proven to be effective in reducing perioperative hypothermia in neonatal patients.[22]

Warm blankets

Simple, affordable, and effective warming blankets reduce conductive heat loss to the operating table. Patients should also be covered with warm blankets. During the sterile preparation, the patient should be exposed for the minimum necessary time.[10] For infants undergoing open abdominal surgery, **waterproof draping** is also recommended.

Heat-moisture exchangers filters

Heat-moisture exchanger filters (HMEFs) are used during general anesthesia to humidify and warm inspired gases and to filtrate bacteria. These devices are lightweight, easy to use, and cost-effective. Passive humidification helps minimize body temperature loss, while active humidification can increase the core temperature.[34]

However, HMEFs, also known as artificial noses, can increase dead space, airway resistance, and intrinsic positive end-expiratory pressure (PEEP), leading to increased breathing work, particularly in infants.[35]

Warm irrigation fluids

Large amounts of irrigation fluids could potentially cause conductive heat loss.[23] Therefore, all intraoperative irrigation fluids should be warmed in a thermostatically controlled cabinet to 37° - 38°C[23], or 38°C to 40°C[14,15] but should not exceed 50°C.[10]

After the implementation

Following their own guidelines, Sultana et al reported that the incidence of PH decreased to 213 cases out of 1,766 patients analyzed (12.1%).[8] This rate was significantly lower compared to the findings of Pearce et al. study in 2010, which illustrated that out of 530 patients, 278 developed PH (52%).[5]

This suggests that tailored guidelines may effectively reduce the occurrence of perioperative hypothermia in neonates and infants. However, further analysis of the results and effectiveness of other guidelines is needed.

CONCLUSIONS

Perioperative hypothermia occurs in 20 to 86% of pediatric surgeries, with neonates being more than twice as likely to develop hypothermia compared to infants. Despite the availability of effective warming methods, their unique physiological characteristics, combined with the effects of anesthetic drugs, make them particularly susceptible to temperature loss.

The guidelines emphasize the importance of preoperative risk stratification, prewarming, intraoperative warming, temperature monitoring, and maintaining an optimal ambient temperature. Early detection of hypothermia through effective temperature monitoring throughout the perioperative period is crucial. Combining warming devices and techniques is more effective than using a single method to reduce PH.

Finally, the development of local guidelines tailored to the available resources and cost effectiveness in different countries and hospitals can help prevent perioperative hypothermia and its complications, thus optimizing postoperative outcomes.

Reflective questions

1. In the context of your hospital or institution, what tailored guidelines can be implemented to effectively reduce the incidence of perioperative hypothermia in neonates and infants?
2. What is the optimal combination of anesthetic agents to minimize the risk of intraoperative hypothermia?
3. How can monitoring techniques be enhanced to detect early signs of perioperative hypothermia in neonates and infants during surgery?

ACKNOWLEDGMENTS

The authors thank Ms. Arporn Pimthong for her assistance with editorial support and submission. We are also indebted to Dr. James Mark Simmerman for editing the English language of this manuscript.

DECLARATIONS

Grants and Funding Information

This article received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of Interest

The authors declare that they have no conflicts of interest.

Author Contributions

Conceptualization and methodology : P.P., S.M. and O.C.; Visualization and writing – original draft: P.P., S.M.; Writing – review and editing : S.M. and O.C.; Supervision : S.M. and O.C. All authors have read and agreed to the final version of the manuscript.

Use of Artificial Intelligence

We acknowledge the use of ChatGPT (OpenAI) for the language support and grammar suggestions during the preparation of this review article.

REFERENCES

1. Nemeth M, Miller C, Brauer A. Perioperative Hypothermia in Children. Int J Environ Res Public Health. 2021;18(14).
2. Zhao J, Le Z, Chu L, Gao Y, Zhang M, Fan J, et al. Risk factors and outcomes of intraoperative hypothermia in neonatal and infant patients undergoing general anesthesia and surgery. Front Pediatr. 2023;11:1113627.
3. Eltun Guliyev CŞ, Canan Bor, Meltem Uyar. Newborns are Prone to More Hypothermia in the Low Temperature of Operating Rooms. J Pediatr Res. 2024;11(1):30-7.
4. Riley C, Andrzejowski J. Inadvertent perioperative hypothermia. BJA Educ. 2018;18(8):227-33.
5. Kurz A, Sessler DI, Annadata R, Dechert M, Christensen R, Bjorksten AR. Midazolam Minimally Impairs Thermoregulatory Control. Anesthesia & Analgesia. 1995;81(2):393-8.
6. Frank SM, Beattie C, Christopherson R, Norris EJ, Rock P, Parker S, et al. Epidural versus general anesthesia, ambient operating room temperature, and patient age as predictors of inadvertent hypothermia. Anesthesiology. 1992;77(2):252-7.
7. Pearce B, Christensen R, Voepel-Lewis T. Perioperative Hypothermia in the Pediatric Population: Prevalence, Risk Factors and Outcomes. Journal of Anesthesia & Clinical Research. 2010;01.
8. Sultana R, Allen JC, Siow YN, Bong CL, Lee SY. Development of local guidelines to prevent perioperative hypothermia in children: a prospective observational cohort study. Canadian Journal of Anesthesia/Journal canadien d'anesthésie. 2022;69(11):1360-74.
9. Bissonnette B, Sessler DI, LaFlamme P. Intraoperative Temperature Monitoring Sites in Infants and Children and the Effect of Inspired Gas Warming on Esophageal Temperature. Anesthesia & Analgesia. 1989;69(2):192-6.
10. Grant Geissler M, FACS, FAAP, Thomas Moroney, MD, Perioperative Thermoregulation. 2022.
11. Lodha R, Mukerji N, Sinha N, Pandey RM, Jain Y. Is axillary temperature an appropriate surrogate for core temperature? Indian J Pediatr. 2000;67(8):571-4.
12. Friedrichs J, Staffileno BA, Fogg L, Jegier B, Hunter R, Portugal D, et al. Axillary Temperatures in Full-Term Newborn Infants: Using Evidence to Guide Safe and Effective Practice. Advances in Neonatal Care. 2013;13(5):361-8.
13. Falzon A, Grech V, Caruana B, Magro A, Attard-Montalto S. How reliable is axillary temperature measurement? Acta Paediatrica. 2003;92(3):309-13.
14. Wongsripuemtet P, LR, T, S., VP, KC, KO, et al. Clinical guideline for prevention and management of perioperative hypothermia by the Royal College of Anesthesiologists of Thailand. Thai Journal of Anesthesiology. 2024;50(4):288-300.
15. NICE. Hypothermia: prevention and management in adults having surgery2008.
16. Sullivan G, Spencer M. Heat and temperature. BJA Education. 2022;22(9):350-6.
17. Kiya T, Yamakage M, Hayase T, Satoh J-I, Namiki A. The Usefulness of an Earphone-Type Infrared Tympanic Thermometer for Intraoperative Core Temperature Monitoring. Anesthesia & Analgesia. 2007;105(6):1688-92.
18. Imamura M, Matsukawa T, Ozaki M, Sessler DI, Nishiyama T, Kumazawa T. The accuracy and precision of four infrared aural canal thermometers during cardiac surgery. Acta Anaesthesiologica Scandinavica. 1998;42(10):1222-6.
19. Sessler DI. Perioperative Temperature Monitoring. Anesthesiology. 2021;134(1):111-8.
20. Pedersen C, Munch P, Kjaergaard J, Grønlykke L, Bräuer A. Accuracy of a zero-heat-flux thermometer in cardiac surgery, a prospective, multicentre, method comparison study. Scientific Reports. 2024;14(1):3169.
21. Sang B-H, Lee C, Lee DY. Prospective comparative analysis of noninvasive body temperature monitoring using zero heat flux technology (SpotOn sensor) compared with esophageal temperature monitoring during pediatric surgery. PLOS ONE. 2022;17(8):e0272720.
22. Ramjist JK, Sutthatarn P, Elliott C, Lee KS, Fecteau A. Introduction of a Warming Bundle to Reduce Hypothermia in Neonatal Surgical Patients. J Pediatr Surg. 2024;59(5):858-62.
23. Luginbuehl I, Bissonnette B, Davis P. Thermoregulation: Physiology and Perioperative Disturbances. 2006. p. 153-76.
24. Buisson P, Bach V, Elabbassi EB, Chardon K, Delanaud S, Canarelli JP, et al. Assessment of the efficiency of warming devices during neonatal surgery. European Journal of Applied Physiology. 2004;92(6):694-7.
25. Kim HY, Lee KC, Lee MJ, Kim MN, Kim JS, Lee WS, et al. Comparison of the efficacy of a forced-air warming system and circulating-water mattress on core temperature and post-anesthesia shivering in elderly patients undergoing total knee arthroplasty under spinal anesthesia. Korean J Anesthesiol. 2014;66(5):352-7.
26. Albrecht M, Gauthier RL, Belani K, Litchy M, Leaper D. Forced-air warming blowers: An evaluation of filtration adequacy and airborne contamination emissions in the operating room. Am J Infect Control. 2011;39(4):321-8.
27. Moretti B, Larocca AMV, Napoli C, Martinelli D, Paolillo L, Cassano M, et al. Active warming systems to maintain perioperative normothermia in hip replacement surgery: a therapeutic aid or a vector of infection? Journal of Hospital Infection. 2009;73(1):58-63.
28. Wadhwa A, Komatsu R, Orhan-Sungur M, Barnes P, In J, Sessler DI, et al. New Circulating-Water Devices Warm More Quickly than Forced-Air in Volunteers. Anesthesia & Analgesia. 2007;105(6):1681-7.
29. Erdoğan H, Işıl C, Türk H, Ergen G, Oba S. The Comparison of Forced-air Warming Systems and Intravenous Fluid Warmers in the Prevention of Pediatric Perioperative Hypothermia. Medical Bulletin of Haseki. 2019;57.
30. Shen J, Wang Q, Zhang Y, Wang X, Shi P. Combination of warming blanket and prewarmed intravenous infusion is effective for rewarming in infants with postoperative hypothermia in China. Paediatr Anaesth. 2015;25(11):1139-43.
31. Gray PH, Flenady V. Cot-nursing versus incubator care for preterm infants. Cochrane Database Syst Rev. 2003(1):Cd003062.
32. Matsuzaki Y, Matsukawa T, Ohki K, Yamamoto Y, Nakamura M, Oshibuchi T. Warming by resistive heating maintains perioperative normothermia as well as forced air heating. Br J Anaesth. 2003;90(5):689-91.
33. McCall EM, Alderdice F, Halliday HL, Vohra S, Johnston L.

Interventions to prevent hypothermia at birth in preterm and/or low birth weight infants. Cochrane Database Syst Rev. 2018;2(2):Cd004210.

34. Bissonnette B, Sessler Daniel I, LaFlamme P. Passive and Active Inspired Gas Humidification in Infants and Children. Anesthesiology. 1989;71(3):350-4.

35. Bell GT, Martin KM, Beaton S. Work of breathing in anesthetized infants increases when a breathing system filter is used. Paediatr Anaesth. 2006;16(9):939-43.