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Orthostatic intolerance during early mobilization following thoracoscopic lung resection: a prospective observational study

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Abstract

Background Early postoperative mobilization is important for enhanced recovery but can be hindered by orthostatic intolerance. However, study on postoperative orthostatic intolerance in thoracoscopic lung resection is limited. Thus, this investigation aims to examine the prevalence and variables contributing to orthostatic intolerance on the first day following thoracoscopic lung cancer resection.

Methods A prospective observational study was conducted from February 01 to May 05, 2023, at the First Affiliated Hospital of Chongqing Medical University. Typically, 215 subjects subjected to thoracoscopic lung resection were enrolled in this study. Their general information, disease, and treatment information were collected, and the occurrence of orthostatic intolerance was recorded.

Results Typically, 64 patients (29.77%) demonstrated orthostatic intolerance during early mobilization, and 43.75% failed to walk. The prevalence of nausea, dizziness, and impaired vision was 60.94%, 92.19%, and 25.00%, respectively, and no patient experienced syncope. The factors shown to be independently linked with orthostatic intolerance were being female (OR = 2.98, 1.53 to 5.82) and high pain level during sitting (OR = 2.69, 1.79 to 4.04). Individuals with orthostatic intolerance had a longer postoperative hospital stay with a mean of 5.42 days against 4.25 days ($p = 0.003$).

Conclusions Orthostatic intolerance was prevalent following thoracoscopic lung cancer resection and affected patients' capability to mobilize and prolonged postoperative hospitalization. Being female and having high pain levels during sitting were identified as independent factors for orthostatic intolerance. This suggests that more emphasis should be given to risky patients, and for these groups, we may optimize pain management to adjust the risk of emerging orthostatic intolerance, facilitating early mobilization and early postoperative rehabilitation.

Keywords Lung resection, Postoperative, Orthostatic intolerance, Early mobilization, Factors

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Background

Cancer of the lungs is the most often detected cancer globally and continues to be the primary cause of death from cancer [1], as well as it is the predominant cancer in terms of both morbidity and death rates in China [2]. At present, video-assisted thoracoscopic surgery (VATS) is the most effective treatment for lung cancer and has been widely used, which is the key link to enhanced recovery after surgery (ERAS) [3]. Directions for enhanced recovery after lung surgery emphasize that early mobilization after the surgical procedure is an important measure for quick recovery postoperatively, which can effectively counteract the postoperative decline in endurance and muscle strength caused by bed rest and promote the recovery of multiple system functions such as respiratory, gastrointestinal, and skeletal muscles [3–5].

However, during out-of-bed activities, some patients may experience orthostatic intolerance (OI) symptoms, such as blurred vision, nausea, dizziness, and even syncope [6], which can hinder early postoperative mobilization. It has also been shown [7] that OI and its associated symptoms are a major contributor to in-hospital falls and prolonged hospital stays. Therefore, OI is gaining attention as a safety issue in nursing care that affects patients' early postoperative recovery and as a pressing issue in advancing ERAS.

Investigations have demonstrated that postoperatively OI is a prevalent medical issue with 22–65% incidence after major elective surgery, such as orthopedic joint replacement [8, 9], laparoscopic radical surgery [7, 10], thoracoscopic radical surgery [11, 12], and gynecological surgery [6]. Investigations assessing possible risk factors for OI are restricted, and the current studies have suggested that OI may be related to factors such as age, gender, American Society of Anesthesiologist (ASA) physical status, surgical blood loss, nutritional status, postoperative bedtime, postoperative opioid use, and pain level [6, 11–14]. However, studies on postoperative OI in thoracoscopic lung cancer resection patients are relatively few and mostly retrospective [11], and the occurrence and risk factors of OI have not been well clarified.

This investigation aims to examine the incidence and cardiovascular response of OI within the early mobilization after thoracoscopic lung cancer resection and to analyze the potential factors associated with postoperative OI through a prospective observational study design to provide references for clinical nursing.

Methods and materials

Study design

The present investigation was a prospective observational single-center study conducted in the Department of Thoracic Surgery at the First Affiliated Hospital of Chongqing Medical University.

Participants

Two hundred fifteen consecutive patients who were scheduled for thoracoscopic lung cancer resection at the First Affiliated Hospital of Chongqing Medical University were included in the investigation between February and May 2023. Inclusion criteria were: (1) proposed selective thoracoscopic lung cancer resection, (2) age ≥ 18 years, (3) normal cognitive and mental state, and (4) informed permission, both orally and in writing. Exclusion criteria were: (1) debilitating illnesses or impaired mobility (e.g., cerebrovascular accident or femoral hip fracture), (2) severe cardiovascular and surgical history, (3) intraoperative surgical changes (e.g., total lung resection, open thoracic exploration or combined with other excision surgeries), (4) unable to correctly express dizziness, nausea, or double vision, and (5) intraoperative or postoperative complications preventing the early ambulation.

Anesthesia, analgesia, and surgery

All patients received standard anesthetic, analgetic, and operative approaches that adhered to a standardized ERAS strategy. Anesthesia was induced utilizing sufentanil, propofol, and rocuronium, and then double-lumen endobronchial intubation was performed. Anaesthesia was maintained with propofol pumped intravenously. Different surgical accesses were chosen for the patients' lesion sites, all single-port thoracoscopies with indwelling thoracic drainage tubes. A prophylactic paroxysmal pain regimen of subcutaneous analgesic pumps combined with intravenous infusion of non-steroidal anti-inflammatory analgesics was given postoperatively. For acute pain, weak opioids (e.g., dizocin injection 20 mg, tramadol injection 50–100 mg) were given for moderate pain, and strong opioids (e.g., morphine injection 10 mg) were given for severe pain. Metoclopomide is routinely administered or combined with a 5-hydroxytryptamine receptor antagonist to prevent nausea and vomiting.

Orthostatic challenge

Mobilization was conducted per a predetermined protocol for a day after the operation. Recommendations for improved recovery after pulmonary operation [15] recommend that patients can be out of bed 24 h postoperatively. Furthermore, prior research has demonstrated a contradictory change toward heightened vagal activity when OI patients transition from lying down to standing up, both 6 and 24 h after surgery [16]. It is probable that during the initial postoperative duration, there may be deficient cardiovascular control and malfunction in the autonomic nervous system, which can negatively impact the capacity to maintain an upright position [12]. So, we defined the measurement time as 24 h after surgery. Before mobilization, two dedicated investigators assessed all patients' vital signs and conditions [17]. The mobilization technique consisted of the patient lying down for 3 min, then sitting on the bed with their feet on the floor for 3 min, followed by standing for 3 min. During the standing phase, the patient was vocally encouraged to transfer their body weight to avoid venous pooling. Finally, the patient progressively walked within the ward. The treatment was terminated if patients exhibited symptoms of orthostatic intolerance (such as nausea or vomiting, dizziness, blurred vision, visual abnormalities, or syncope) or if there was a fall in systolic blood pressure (SBP) of more than 30 mmHg compared to the supine position. Pulse oxygen saturation (SpO2; %), heart rate (HR; beats per minute), SBP (mmHg), diastolic blood pressure (DBP; mmHg), and respiratory rate (RR; frequency per minute) were continuously measured all over mobilization employing the uMEC6 series continuous patient monitoring system manufactured by Mindray in Shenzhen, China. The Visual Analogue Scale (VAS) was employed to rate the level of pain experienced throughout each mobilization activity for every body position. The scale ranged from 0 to 10 [18].

Measurement

The occurrence of OI on the first day after surgery was assessed using a standardized symptom checklist designed for this research. It was based on the diagnostic criteria of OI [19, 20] (a decrease in SBP ≥ 30 mmHg from supine to stand) and defined symptoms distinguishing OI (i.e., feeling of heat, nausea, vomiting, blurred vision, dizziness, and even syncope) [11, 21]. During the mobility challenge, participants were categorized as having OI if they exhibited symptoms of cerebral inadequate perfusion or a drop in SBP of 30 mmHg or more.

Potential risk factors for OI were also documented: body mass index (BMI), gender, age, comorbidities, presence of preoperative postural hypotension, history of smoking and alcohol, kind of operation, time of surgery, ASA physical status, blood loss during surgery, hemoglobin decline (level of hemoglobin drop (g/L) = postoperative day 1 hemoglobin value - preoperative hemoglobin value), together with postoperative opioid use measured by oral morphine equivalent dose (omeq) [22]. Pain scores during the mobilization and length of stay (LOS) were also documented.

Statistical analysis

The data was submitted in pairs and examined employing the SPSS 22.0 program. Before analysis, all information underwent evaluation for normal distribution using Q-Q plots and histograms. Typically, continuous variables that follow a normal distribution are denoted by the mean (standard deviation [SD]), whereas non-normally distributed variables are presented by the median (interquartile range [IQR]). Categorical variables are often presented as the frequency accompanied by their respective percentages. The t-test or Wilcoxon rank-sum test was employed to identify variations in characteristics between participants who were orthostatic tolerant (OT) and those who were OI. The chi-square or Fisher tests were utilized to compare qualitative variables as deemed suitable. Both bivariable and multivariable binary logistic regression analyses were conducted to evaluate the degree of correlation between the dependent and independent variables. For postoperative OI, variables with a *P*-value less than 0.05 were deemed statistically significant related factors in multivariable regression. P-values less than 0.05 were deemed to be statistically significant.

Results

The investigation included two hundred thirty-eight participants who fulfilled the inclusion criteria. After excluding 5 cases who withdrew midway, 5 patients who changed the type of surgery (3 cases of total lung resection, 1 case of open thoracic exploration, and 1 case combined with mediastinal tumor resection), 6 patients who had postoperative changes in their conditions that prevented them from carrying out early out-of-bed activities, and 7 missing dates, 215 participants were comprised in last analysis.

Among the total participants, 113 (52.56%) were female, and the mean (SD) age was 58.59 (11.28) years. Of the total study participants, 57 (26.51%) had hypertension and 19 (8.84%) had diabetes. Typically, 155 participants (72.09%) had ASA physical status II. Of all cases, 48 (22.33%) had a history of cigarette smoking preoperatively, and 26 (12.09%) of participants drank preoperatively (Table 1).

Incidence of OI

The median (IQR) time from operation to initial evaluation by specialized investigators was 24.10 h (10.87–36.88 h), and there was no significant difference between OI and OT participants ($P = 0.731$). At this point, 29.77% ($n = 64$) of cases experienced OI, and 43.75% ($n = 28$) of these could not ambulate at 24 h after surgery. Symptoms connected with OI were as follows (Fig. 1): Dizziness was reported in 59 cases, accounting for 92.19%. Thirty-nine individuals, accounting for 60.94% of the total, suffered nausea, whereas 8 participants, representing 12.50%, suffered from vomiting. A total of sixteen (25.00%) individuals reported experiencing blurred vision. The feeling of heat and headache was present in 12 (18.75%) and 6 (9.38%), respectively. No syncope appeared.

In the lying position, there was no significant variation in SBP, DBP, and HR between OI and OT groups ($P > 0.05$). HR at the sitting position in the OI group was significantly higher than the OT group (89.48 ± 10.90 vs. 84.74 ± 10.17 beats/min) ($P = 0.002$). In the sitting

Table 1 Patient characteristics and differences in peri-operative factors in the OI and OT groups

Variable	OI (*n* = 64)	OT (*n* = 151)	χ^2/t/Z	*P*-value
Genders [n (%)]			11.520	0.001
Male	19 (29.7%)	83 (55.0%)		
Female	45 (70.3%)	68 (45.0%)		
Age (years)	60.52 ± 11.45	57.89 ± 11.16	1.566	0.119
BMI (kg/m^2)	24.06 ± 3.20	23.84 ± 3.02	0.490	0.625
Comorbidity [n (%)]				
Hypertension	17 (26.6%)	40 (26.5%)	0.000	0.991
Diabetes	6 (9.4%)	13 (8.6%)	0.033	0.856
Coronary artery disease	1(1.56%)	11(7.29%)	1.183	0.082
ASA physical status [n (%)]			0.173	0.944
I	1 (1.6%)	3 (2.0%)		
II	47 (73.4%)	108 (71.5%)		
III	16 (25.0%)	40 (26.5%)		
Smoking [n (%)]	7 (10.9%)	41 (27.2%)	6.815	0.009
Drinking [n (%)]	4 (6.3%)	22 (14.6%)	2.927	0.087
Duration of surgery (min)	100.64 ± 42.05	102.17 ± 45.70	−0.230	0.818
Blood loss (ml)	100 (50,100)	100 (50,100)	−0.159	0.874
Thoracic drainage amount in 24 h after operation (ml)	225.86 ± 119.90	231.69 ± 146.32	−0.281	0.779
Hemoglobin decline (g/L)	17.95 ± 6.46	17.94 ± 9.55	0.010	0.992
Types of resection [n (%)]			0.926	0.629
Lobectomy	30 (46.9%)	81 (53.6%)		
Segmentectomy	21 (32.8%)	41 (27.2%)		
Wedge resection	13 (20.3%)	29 (19.2%)		
Postoperative opioids oMEDD (mg)	66 (64,68)	64 (64,68)	−0.622	0.534
Postoperative antihypertensive medications [n (%)]	6 (9.4%)	9 (6.0%)	0.808	0.369
Pain (VAS 0 to 10)				
Lying	2 (1,2.75)	2 (1,2)	−1.615	0.106
Sitting	3 (2,3)	2 (2,3)	−5.222	0.000
Standing	3 (3,4)	3 (2,4)	−1.683	0.092
Length of stay (d)	5.42 ± 3.37	4.25 ± 2.17	3.036	0.003

Abbreviations: BMI Body mass index; ASA American society of anesthesiologist; oMEDD oral Morphine equivalent daily dose; VAS Visual Analogue Scale; OI orthostatic intolerant; OT orthostatic tolerant

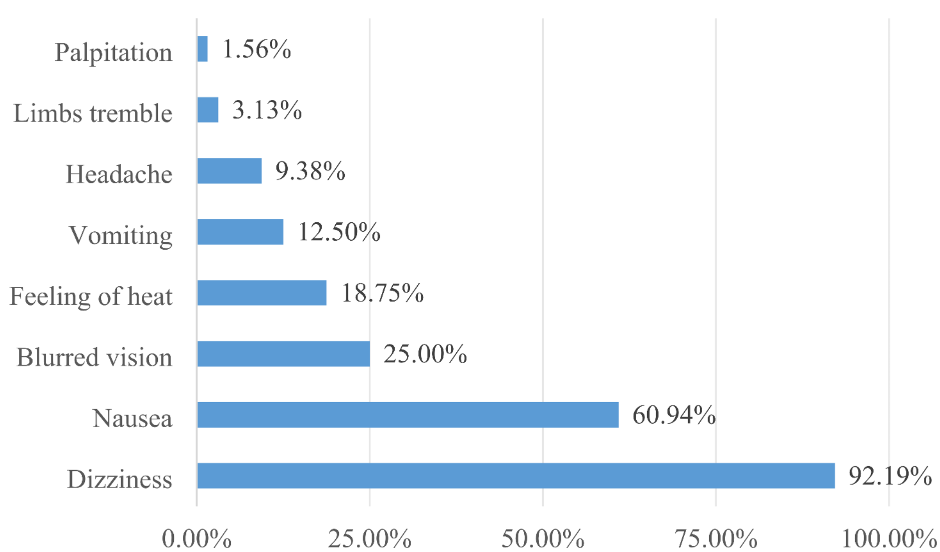

Fig. 1 Occurrence of symptoms in the OI group

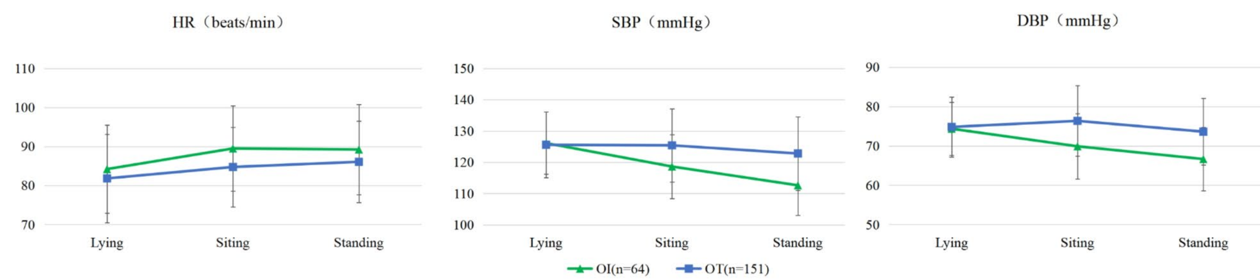

Fig. 2 Changes in HR and BP 24 h after surgery in orthostatic tolerant (OT)and intolerant (OI) patients during a standardized mobilization procedure

Table 2 Multivariate analysis of independent predisposing factors of orthostatic intolerance

Variable	Regression coefficient	Standard error	Wald χ^2	*P*	OR	95% CI
Female	1.092	0.342	10.216	0.001	2.980	1.526–5.821
Siting VAS	0.990	0.208	22.781	0.000	2.692	1.793–4.044

Abbreviations: VAS Visual Analogue Scale

position, patients in the OI group had significantly lower SBP (118.63±10.23 vs. 125.40±11.71 mmHg) and DBP (69.88±8.26 vs. 76.34±8.96 mmHg) than OT group (both $P<0.001$). In the standing position, both SBP (112.62±9.50 vs. 122.79±11.80 mmHg) and DBP (66.64±8.08 vs. 73.60±8.45 mmHg) were lower in the OI group than in the OT group (both $P<0.001$). Changes in HR and BP in different positions during the early ambulation after surgery are shown in Fig. 2.

Risk factors

Patient characteristics and differences in perioperative factors in OI and OT groups are presented in Table 1. There was a significant correlation between the occurrence of OI and being female ($P=0.001$), as well as being a smoker ($p=0.009$) among patients. Participants who had OI exhibited significantly greater peak pain when sitting and being mobilized ($P<0.001$).

All three variables described earlier were included in the logistic regression model. Table 2 shows that the factors independently linked with OI were female (OR=2.98, 1.53–5.82) and pain score during sitting (OR=2.69, 1.79–4.04).

Discussion

The primary outcomes of the current investigation in patients who were subjected to thoracoscopic lung resection were that: (1) 29.77% of the participants developed OI during early mobilization following the operation and 43.75% of these failed to ambulate; (2) the main symptoms experienced in patients who developed OI were dizziness, nausea, and blurred vision; (3) patients in OI group had significantly lower SBP and DBP in both sitting and standing positions than OT group and (4) female and sitting pain score were independent risk factors for OI.

Approximately three in ten patients in our study developed OI during early mobilization, which was lower than reported in previous studies, where 35.2–45.7% of patients undergoing VATS experienced OI [11, 12]. Additionally, 43.75% of patients with OI failed to ambulate because of symptoms associated with OI, including dizziness, nausea, and blurred vision. This was generally consistent with previous studies [11], that which 45.8% of patients following VATS with OI could not ambulate at postoperative day 1. Besides potentially inadequate autonomic cardiovascular control, the loss of blood and fluids during operation [6], surgical stress response [23], pain-induced damage to the vascular vasomotion, and residual effects of anesthesia [11] will all contribute to postoperative OI. Subsequently, when patients get out of bed in the early postoperative period, the sudden change in body position and lack of adaptation process leads to decreased cardiac output and blood pressure, resulting in a series of OI symptoms that hinder early mobilization [24, 25].

The OI not only hinders early mobilization and affects early postoperative recovery but may even lead to serious consequences such as poor wound healing, fractures, and even brain injuries related to falls [7], as well as affecting the length of hospitalization [8]. In our study, the length of stay after surgery in the OI group was significantly prolonged, which is in line with the outcomes of Skarin et al. [8] and Tong et al. [19].

Patients with OI tend to experience a decrease in SBP and DBP from lying to sitting and standing, which is along with the outcomes of Hristovska et al. [9, 26] and may be related to impaired cardiovascular response and postoperative autonomic dysfunction. It is suggested that medical staff should monitor the change in blood pressure in different positions during early mobilization after lung cancer surgery and alert them to the occurrence of OI. Previous studies have shown that patients who develop OI are often accompanied by varying degrees of cerebral hypoperfusion [10, 19]. In this study, all patients in the OI group were accompanied by one or more symptoms of hypoperfusion, with 25% of these having blurred vision, which is a manifestation of severe cerebral hypoperfusion. If not intervened promptly, it could potentially progress to syncope, a manifestation of total cerebral hypoperfusion [19]. Therefore, when guiding and assisting patients to get out of bed early after surgery, we should pay attention to those with hypoperfusion and avoid the precursors of syncope, such as lower limb weakness and generalized wetness and coldness. When patients have syncope precursor symptoms, instruct them to sit, lie, or make limb pressure movements such as legs crossed, hands clasped, and tensed upper limbs [27].

Our investigation found a significant association between being female and experiencing postoperative OI, which was supported by studies conducted in Japan [11], New Zealand [8], Denmark [9], Ethiopia [6], and the United States [28]. The available evidence indicates that this is caused by gender variations in autonomic function and blood pressure control [6]. Males have a rapid and fast-rising sympathetic activity to counterbalance an orthostatic examination, whereas females experience a small and delayed rise in sympathetic activity under the same challenge [29]. Additionally, it is hypothesized that females exhibit elevated venous compliance in their lower limbs, resulting in blood pooling while standing and a decrease in central blood volume when in an upright posture [8], making them more prone to OI.

Female gender was also known as a predisposing factor for postoperative nausea and vomiting (PONV) [30], but the definition of OI includes PONV during early mobilization. The authors differentiated PONV and OI by symptoms not recognized as PONV (dizziness or blurred vision). Actually, in our study, 92.19% of patients who experienced OI suffered dizziness; only 60.94% and 12.50% of them suffered nausea and vomiting separately. Additionally, PONV usually occurs independently of ambulation.

The outcome of the current investigation also showed that pain score during sitting was associated with postoperative OI. Gobezie et al. [6] concluded that pain levels were significantly elevated during rest and the first period of walking, and these scores were correlated with postoperative OI. In contrast, previous studies in lung cancer resection [11, 12] have not found pain scores associated with OI. However, we still consider that pain score was associated with OI. The postoperative retention of closed chest drains in patients after VATS can cause pain by squeezing the intercostal nerves, and as the patient's position changes, the chest drain moves with it, and the stimulation of the thoracic wall nerves by the head of the chest drain will exacerbate pain [31, 32]. Physiologically, intense pain can stimulate the hypothalamus and activate the cardiovascular centers in the medulla, leading to a vasovagal response. This mechanism can cause inadequate constriction of blood vessels during alterations in posture, resulting in a significant drop in systolic blood pressure [8]. Furthermore, intense pain may be linked to feelings of fear and worry, which can further activate the vasovagal response and perhaps lead to postoperative OI [6].

Although it was thought that postoperative opioid use was associated with OI and may hinder ambulation after VATS [11], however, we found no difference in opioid use between OI and OT patients. This was consistent with a prospective cohort study in total hip arthroplasty [8]. Of note, our study did not consider preoperative opioid use. Postoperative opioid dose and its effects on OI may be possibly different between regular opioid users and those who use opioids just at the time of surgery.

The restrictions of this investigation include that it was impossible to schedule the mobilization evaluation at an identical time following an operation for all participants. It has been suggested that postoperative OI after abdominal surgery gradually improves over time [10]. However, our analysis revealed no statistically significant variation in the average time to evaluate early activity appropriateness between the OI and OT groups. We also used a variety of measures, including subjective symptom assessment and objective blood pressure measurement, to ensure credible results. Furthermore, we did not assess the extent of postoperative inflammation, which may be related to the pathogenesis of OI [16]. Ultimately, we did not quantify the perioperative intravenous fluid to mitigate the potential occurrence of hypovolemia. Similarly, all patients received intravenous fluid according to the same regimen. Nevertheless, the use of goal-directed fluid treatment for individuals having open prostatectomy did not have an impact on postoperative OI [33].

Conclusion

The OI was common during early mobilization following thoracoscopic lung cancer resection. Dizziness, nausea, and impaired vision were common hypoperfusion symptoms. OI affected patients' capability to mobilize and prolonged postoperative hospitalization. Two independent predisposing factors for OI (female sex and high pain level during sitting) were identified. This suggests that more emphasis should be given to risky patients, and for these groups, we may optimize pain management to adjust the risk of emerging orthostatic intolerance, facilitating early mobilization and early postoperative rehabilitation.

Abbreviations

VATS	Video-assisted Thoracoscopic Surgery
ERAS	Enhanced Recovery After Surgery
OI	Orthostatic Intolerance
OT	Orthostatic Tolerant
ASA	American Society of Anesthesiologist
SpO2	Pulse Oxygen Saturation
RR	Respiratory Rate
HR	Heart Rate
SBP	Systolic Blood Pressure
DBP	Diastolic Blood Pressure
VAS	The Visual Analogue Scale
BMI	Body Mass Index
LOS	Length of Stay
SD	Standard Deviation
IQR	Interquartile Range
PONV	Postoperative Nausea and Vomiting

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Author contributions
HY, WT performed the investigations and drafted the paper. HY, WT, and YS conducted the statistical analysis and contributed to its design. LT, FZ, and SY participated in collecting data, acquiring, analyzing, and interpreting data. Each contributor thoroughly reviewed and gave their consent to the final version.

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Data availability
The data used to support the findings of this study may be obtained from the corresponding author upon an adequate request.

Declarations

Ethics approval and consent to participate
The investigation has been conducted per the Declaration of Helsinki (2000) established by the World Medical Association. The Clinical Research Ethics Committee of the First Affiliated Hospital of Chongqing Medical University has authorized this research (K2023-197). Informed consent was obtained from each study participant after explaining the study's merits. Participants were informed of their right to refuse to participate in the study at any time. Confidentiality was guaranteed by avoiding questions containing identifiers and keeping completed questionnaires and results in a well-secured area.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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