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Sugammadex or neostigmine for reversal of neuromuscular block on the quality of postoperative recovery in elderly adults undergoing video-assisted thoracoscopic lobectomy: a randomised controlled trial

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Abstract

Background Although neostigmine has been traditionally used for neuromuscular blockade reversal in thoracic surgery, incomplete reversal and potential pulmonary complications remain concerns. However, we did not preclude its clinical use. In contrast, sugammadex offers more predictable recovery of neuromuscular function with a superior safety profile. This study aims to compare the efficacy of sugammadex versus neostigmine in improving postoperative recovery outcomes.

Methods This study is a prospective, randomized, double-blind trial. Patients above 65 years old undergoing video-assisted thoracoscopic lobectomy were randomly assigned to receive either sugammadex (2 mg/kg) or neostigmine (0.04 mg/kg) with atropine for neuromuscular block reversal after T2 appearance on TOF. The primary outcome was the quality of recovery at postoperative day (POD) 1, assessed by the QoR-15 questionnaire. Secondary outcomes included extubation time, PACU stay, incidence of hypoxaemia, PRNB, and postoperative pulmonary complications (PPCs).

Results Data analysis included 77 patients (39 in Group S and 38 in Group N). The QoR-15 scores were significantly higher in the sugammadex group at day 1 (125 vs. 122, $P<0.001$). Sugammadex significantly reduced extubation time (18 vs. 27.5 min, $P=0.001$) and PACU stay (52 vs. 62 min, $P=0.001$). Hypoxaemia (28% vs. 53%, $P=0.029$) and PRNB (5% vs. 24%, $P=0.020$) were less frequent in the sugammadex group. The sugammadex group had fewer PPCs, the difference was not statistically significant (26% vs. 45%, $P=0.079$).

Conclusions For elderly patients receiving VATS lobectomy, sugammadex is beneficial for acute recovery except PONV up to POD1 recovery quality mainly in ease of breath, eating, resting but not in postoperative outcomes over one month.

Trial registration Retrospectively registered, Chinese Clinical Trial Registry, ChiCTR2400089863(Date:18/09/2024).

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Keywords Sugammadex, Neostigmine, Neuromuscular block, Postoperative recovery, Video-assisted thoracoscopic surgery, Elderly adults, QoR-15 score

Introduction

Pulmonary nodules are small, localized growths within the lungs, typically measuring ≤3 cm in diameter. The incidence and detection of these nodules have risen significantly in recent years, largely due to improved health awareness and advancements in diagnostic imaging technologies [1]. Studies indicate that elderly patients are particularly susceptible to pulmonary nodules, with incidence rates increasing with age [2]. For individuals aged 65–75 years, the incidence is approximately 15%, rising to 20% for those aged 75–85 years, and reaching around 25% for those over 85 years. Early and accurate detection is crucial, as some nodules may be malignant and necessitate surgical intervention.

Surgical resection, particularly video-assisted thoracoscopic surgery (VATS), remains the primary treatment for pulmonary nodules. VATS offers significant advantages, including minimal trauma, faster recovery, reduced postoperative pain, and a lower incidence of complications compared to open thoracotomy. The successful implementation of VATS heavily relies on precise anesthetic management. Maintaining an appropriate depth of neuromuscular blockade during surgery is crucial for ensuring both the safety and quality of the procedure. This importance is primarily reflected in three key aspects: optimizing thoracoscopic surgery conditions, ensuring surgical safety, and enhancing the efficacy of one-lung ventilation [3]. However, prolonged use of muscle relaxants can lead to postoperative residual neuromuscular block (PRNB), which is more likely in elderly patients due to age-related physiological changes, such as decreased organ function and slower drug metabolism [4]. PRNB in the elderly is associated with an increased risk of postoperative pulmonary complications (PPCs) and delayed recovery of lung function, significantly impacting postoperative outcomes [5].

Enhanced Recovery After Surgery (ERAS) [6] protocols emphasize optimizing perioperative care to reduce complications and improve recovery, particularly in elderly patients. A key aspect of ERAS is the effective management of neuromuscular blockade during surgery. While neostigmine has traditionally been used as a reversal agent, it has limitations, including a slower onset, the inability to fully reverse deep neuromuscular block, and undesirable side effects such as nausea and vomiting. In contrast, sugammadex offers a rapid and complete reversal of steroidal muscle relaxants like rocuronium, with fewer adverse reactions. Its superior efficacy and safety [7], particularly in elderly patients, make sugammadex an attractive option for enhancing postoperative recovery and minimizing complications.

Despite several comparative studies, research focusing on the use of sugammadex in elderly patients undergoing VATS is limited. This study aims to evaluate the effects of sugammadex on postoperative recovery, pulmonary complications, and the incidence of postoperative nausea and vomiting (PONV) in elderly patients following video-assisted thoracoscopic lobectomy, providing valuable insights into its application in this vulnerable population.

Methods

General information

This study was a single-center, prospective, randomized, double-blind, controlled trial approved by the Research Ethics Committee of the Affiliated Hospital of Xuzhou Medical University (XYFY2024-KL341-01) and registered in the Chinese Clinical Trial Registry (NO. ChiCTR2400089863). This study adheres to CONSORT guidelines (Supplementary 1). All patients provided written informed consent prior to surgery.

Participants

Between July and September 2024, patients aged 65 years and older scheduled for video-assisted thoracoscopic lobectomy were assessed for eligibility. Inclusion criteria included all genders and ASA grades I-III. Exclusion criteria encompassed severe liver or kidney disease; significant heart conditions; history of lung infections; chronic obstructive pulmonary disease (COPD); asthma; bronchiectasis; cognitive dysfunction; mental illnesses; drug allergies; contraindications to neostigmine and atropine; massive intraoperative bleeding; alterations in surgical methods and unplanned ICU transfers.

Anesthesia methods

Upon entering the operating room, oxygen was administered, and standard monitoring (non-invasive blood pressure, ECG, heart rate, SpO_2, temperature, and depth of anesthesia) was performed. An intravenous infusion was established, and radial artery puncture was conducted for arterial blood pressure monitoring. During anesthesia induction, patients inhaled pure oxygen (6 L/min), followed by intravenous administration of etomidate (0.3 mg/kg), sufentanil (0.5 μg/kg), and rocuronium (0.9 mg/kg). A double-lumen endotracheal tube was

inserted and confirmed using a fiberoptic bronchoscope. One-lung ventilation was maintained with end-tidal CO_2 between 30–40 mmHg, and body temperature was kept at approximately 37 °C. Anesthesia maintenance included propofol (1–3 mg/kg/h), remifentanil (0.1–0.3 μg/kg/min), and rocuronium (6–10 μg/kg/min, the infusion rate of rocuronium was adjusted according to the Train-of-Four ratio (TOFr), maintaining a TOFr of 0 during the surgery), with a Bispectral Index (BIS) of 40–60. Upon chest closure, rocuronium infusion was discontinued. Flurbiprofen was administered for pain relief, and tropisetron was given to prevent vomiting. Postoperatively, both groups received analgesic pump analgesia (sufentanil 2 μg/kg and 6 mg tropisetron, diluted to 120 mL with saline, administered at 2 mL/min with a 15-min lock-out interval).

Blinding and randomization

Patients were randomly assigned to either Group N (neostigmine with atropine) or Group S (sugammadex) based on a computer-generated allocation sequence. The randomization process and drug administration were conducted by a research assistant not involved in postoperative data collection. Both patients and data collectors were blinded to the group allocations.

Grouping and treatment

After surgery, patients were transferred to the Post-Anesthesia Care Unit (PACU). Following monitoring setup, four train-of-four (TOF) stimulations were performed, and antagonism was administered upon T2 appearance. Group S received sugammadex (2 mg/kg), while Group N received neostigmine (0.04 mg/kg) and atropine (0.02 mg/kg). The endotracheal tube was removed once the patient was fully awake, with tidal volume and minute ventilation returning to baseline levels. When the patient's modified Aldrete score was ≥ 9, they could be discharged from the PACU.

Study endpoints

The primary endpoint was the quality of recovery at one day post-surgery, assessed using the QoR-15 questionnaire (Supplementary 2). This multidimensional patient-reported outcome evaluates recovery across five domains: pain, psychological state, emotional state, independence, and comfort. It consists of 15 statements rated on a scale of 0–10, with higher scores indicating better recovery [8, 9]. Secondary endpoints included extubation time (defined as the interval from TOF reaching T2 to extubation), duration of PACU stay, incidence of post-extubation hypoxemia ($SpO_2 < 93\%$ or continuous need for supplemental oxygen [10]), PRNB incidence (defined by a TOF ratio < 0.9 [11] at the removal of the endotracheal tube [12]), and PONV incidence. QoR-15 scores on days 2 and 3, incidence of pulmonary complications (defined by the 2015 European Perioperative Clinical Outcomes (EPCO) guidelines [13]), duration of chest tube indwelling, and length of postoperative hospital stay. Rates of pulmonary infection and readmission within one month post-discharge.

Sample size calculation

Based on previous researchs [14, 15], a minimum change of 8 in QoR-15 scores was deemed clinically significant, with a standard deviation of 12. Using $\alpha = 0.05$ and $\beta = 0.2$, each group required 36 participants. To account for a 10% dropout rate, a total of 40 participants per group was determined.

Statistical analysis

Data were analyzed using SPSS 26.0. Normally distributed data were expressed as mean ± standard deviation and analyzed using t-tests. Non-normally distributed data were presented as median (M) and interquartile range (IQR), with the Kruskal–Wallis H test for intergroup comparisons and Mann–Whitney U test for pairwise comparisons. Qualitative data were expressed as rates (%), analyzed using chi-square tests or Fisher's exact probability method. A p-value of < 0.05 was considered statistically significant.

Results

Participant flow

A total of 86 patients were screened. The final analysis included 39 patients in the sugammadex group and 38 in the neostigmine group, with no exclusions from analysis (see Fig. 1).

Baseline data

The baseline demographic and clinical characteristics of the sugammadex and neostigmine groups were well balanced, with no significant differences observed between the groups (Table 1).

Primary endpoints

Preoperatively, overall Quality of Recovery (QoR-15) scores were comparable between groups, with no significant difference. However, at one day postoperatively, the sugammadex group demonstrated relatively higher recovery scores, with a median QoR-15 score of 125 compared to 122 in the neostigmine group ($P < 0.001$). Although the differences were statistically significant, they did not meet the predetermined clinically significant threshold, which was set at 8. Individual parameters showed notable differences, with patients in the sugammadex group reporting better ease of breathing ($P =$

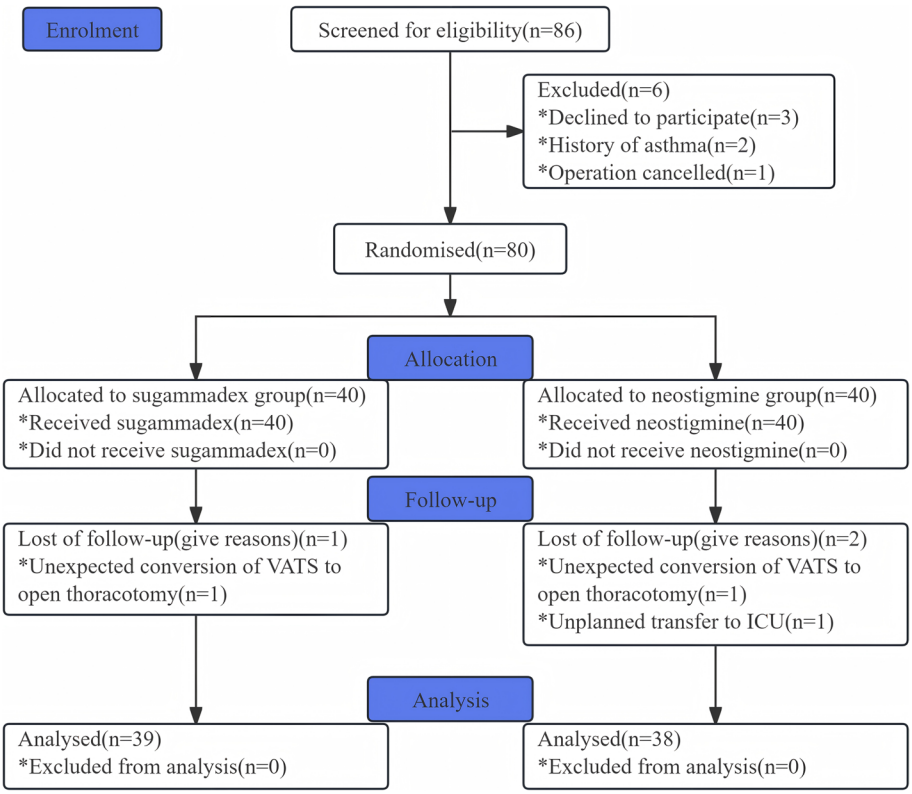

Fig. 1 Consolidated standards of reporting trials flow diagram

0.002), enjoyment of food ($P < 0.001$), feeling rested ($P < 0.001$), and sleep quality ($P = 0.001$). Additionally, they felt more comfortable and in control ($P = 0.012$) compared to the neostigmine group (Table 2).

Data during PACU

Statistically significant differences were observed between the two groups in extubation time, PACU stay duration, incidence of hypoxaemia, and incidence of PRNB. However, the incidence of nausea and vomiting did not differ significantly between groups (Table 3).

Postoperative data and post-discharge data

No significant differences were found between the two groups in postoperative pulmonary complications, duration of chest tube drainage, length of hospital stay, incidence of pulmonary infection after discharge, or readmission rate (Table 4).

Discussion

This randomized controlled trial indicates that the application of sugammadex may enhance early recovery quality in elderly patients undergoing lobectomy compared to the traditional neuromuscular reversal agent, neostigmine. By optimizing the reversal of neuromuscular blockade during anesthesia emergence, patients receiving sugammadex demonstrated a faster recovery process and a reduced incidence of severe complications. The advantages of sugammadex in ensuring postoperative respiratory safety and controlling the occurrence of PRNB underscore the importance of precise neuromuscular function management in the perioperative practice of geriatric thoracic surgery. Although the clinical relevance of early recovery quality scale scores requires further validation, the comprehensive pharmacological benefits of this drug suggest that it could become a significant addition to Enhanced Recovery After Surgery (ERAS) protocols.

This study, using the QoR-15 scale, indicates that patients in the sugammadex group showed improvements in comfort, respiratory ease, appetite, energy, and sleep quality—findings consistent with previous research [16, 17]. These significant improvements may be linked to the enhanced quality of neuromuscular blockade reversal.

However, the QoR-15 is a broad assessment tool that primarily evaluates pain and psychological well-being, with limited sensitivity to neuromuscular recovery [18]. As a result, despite significant differences in specific neuromuscular-related items, the overall score difference

Table 1 Summary of baseline subject characteristics

Variables	Sugammadex ($n = 39$)	Neostigmine ($n = 38$)	*P*-value
Age (yr)	72 (68–75)	69 (67.75–74)	0.256
Sex			0.731
Male	20	18	
Female	19	20	
BMI (kg/m^2)	23.53 (4.29)	23.70(3.24)	0.109
ASA physical status			0.429
I	0	0	
II	14	17	
III	25	21	
Preoperative medical history			
Hypertension	15	12	0.527
Diabetes mellitus	3	0	0.081
Cerebrovascular accident	8	6	0.591
Cerebral infarction	7	2	0.083
Active tobacco	15	18	0.430
Preoperative anxiety scores	3 (2–3)	3(2–3)	0.117
Surgery characteristics			
Surgery duration	118 (110–126)	116 (109.5–125)	0.713
One-lung ventilation duration	100 (93–103)	96.5 (91.5–106)	0.510
Anesthesia duration	137 (128–140)	135 (126.75–138.25)	0.196
Nodule characteristics			0.237
Malignant	33	28	
Benign	6	10	
Lobectomy locations			0.605
Left upper lobe	7	12	0.165
Left lower lobe	4	5	0.692
Right upper lobe	15	11	0.377
Right middle lobe	5	5	0.965
Right lower lobe	8	5	0.389

All values shown are mean (SD) or median (IQR) or n (%) as appropriate

SD standard deviation, *IQR* inter-quartile range, *BMI* Body mass index, *ASA* American Society of Anesthesiologists

between groups was modest, failing to meet the minimal clinically important difference of 8. This suggests that while sugammadex may facilitate the recovery of physiological functions closely tied to neuromuscular recovery, existing general assessment tools may not fully capture the extent of its benefits.

Additionally, variability in self-reported assessments and the relatively small sample size may have influenced the findings, requiring cautious interpretation. These confounding factors could affect recovery outcomes, as suggested by a previous meta-analysis [19]. Consequently, the clinical significance of sugammadex in patient outcomes remains complex and warrants further investigation.

The findings of this study indicate that in elderly adults undergoing video-assisted thoracoscopic lobectomy, the sugammadex group experienced significantly shorter times to spontaneous respiration recovery and extubation compared to the neostigmine group. This aligns with previous research, such as Deng [20], which reported a strong association between sugammadex use and reduced PACU discharge time.

Compared to traditional reversal agents, the earlier discontinuation of mechanical ventilation in the sugammadex group highlights its clinical advantage in facilitating the restoration of independent respiratory function [21]. Notably, the earlier extubation not only reflects the effectiveness of its targeted pharmacological action but may also contribute to an improved postoperative recovery trajectory by reducing the duration of invasive airway management.

This study demonstrates that sugammadex significantly reduces the incidence of PRNB, thereby lowering the risk of hypoxemia—a common complication associated

Table 2 Quality of Recovery (QoR-15) score

Variables	Sugammadex ($n = 39$)	Neostigmine ($n = 38$)	*P*-value
Preoperative total QoR-15 score	147 (147–148)	147 (146–148)	0.949
POD1 QoR-15 score	125 (124–127)	122 (117.75–124)	< 0.001
1.Able to breathe easily	8 (8–8)	7 (7–8)	0.002
2.Enjoy food	8 (7–8)	7 (7–7.25)	< 0.001
3.Feeling rested	8 (8–8)	8 (7–8)	< 0.001
4.Sleep	7 (7–8)	7 (6–7)	0.001
5.Able to look after personal toilet and hygiene	8 (8–9)	8 (7–9)	0.117
6.Support from hospital	10 (10–10)	10 (10–10)	0.543
7.Communicate with family and friends	10 (10–10)	10 (10–10)	0.071
8.Well enough for home or work	7 (7–7)	7 (6–7)	0.219
9.Comfortable and in control	8 (7–8)	7 (7–8)	0.012
10.General well-being	8 (7–8)	8 (7–8)	0.754
11.Moderate pain	7 (6–7)	7 (6–7)	0.705
12.Severe pain	8 (8–9)	8 (8–9)	0.392
13.Nausea or vomiting	10 (8–10)	10 (8–10)	0.239
14.Feeling worried or anxious	10 (9–10)	10 (9–10)	0.845
15.Feeling sad or depressed	10 (9–10)	10 (9–10)	0.261
2 d total QoR-15 score	135 (134–136)	134 (132.75–136)	0.151
3 d total QoR-15 score	139 (138–140)	139 (137.75–140)	0.751

Overall Quality of Recovery (QoR-15) score evaluated within the QoR-15 in the Sugammadex and Neostigmine groups at 1 d, 2 d and 3 d after video-assisted thoracoscopic lobectomy and detailed scores from each of the 15 parameters evaluated at 1 d. All values shown are median (IQR)

Table 3 Data during PACU stratified by randomisation assignment

Variables	Sugammadex ($n = 39$)	Neostigmine ($n = 38$)	*P*-value
Extubation time (min)	18 (15–23)	27.5 (24–36)	0.001
PACU stay duration (min)	52 (49–57)	62 (55.75–68.25)	0.001
Hypoxaemia (n,%)	11 (28%)	20 (53%)	0.029
PONV (n,%)	14 (36%)	18 (47%)	0.307
PRNB (n,%)	2 (5%)	9 (24%)	0.020

All values shown are median (IQR) or n (%) as appropriate

Table 4 Postoperative data and post-discharge data stratified by randomisation assignment

Variables	Sugammadex ($n = 39$)	Neostigmine ($n = 38$)	*P*-value
PPCs (n,%)	10 (26%)	17 (45%)	0.079
Respiratory infection	9	12	0.402
Respiratory failure	0	1	0.308
Pleural effusion	4	8	0.192
Atelectasis	1	0	0.320
Pneumothorax	3	2	0.665
Bronchospasm	0	0	
Aspiration pneumonitis	0	0	
Duration of chest tube drainage (day)	2 (1–2)	2 (1–3)	0.249
Hospitalisation (day)	6 (6–7)	7 (6–8)	0.740
30-day respiratory infection (n,%)	0	3 (8%)	0.073
30-day unplanned readmission (n,%)	0	3 (8%)	0.073

All values shown are median (IQR) or n (%) as appropriate

with neostigmine [22, 23]. This effect may be attributed to residual muscle relaxation impairing respiratory muscle function, such as reduced diaphragm mobility and decreased peak cough flow, which can contribute to early postoperative hypoxemia [24, 25].

The effective management of hypoxemia risk is further reflected in the significant improvement in respiratory function-related QoR-15 scores, particularly in breathing ease and nocturnal oxygen comfort. These factors collectively contribute to an overall enhancement in postoperative recovery quality. These findings indirectly highlight the potential benefits of effective neuromuscular blockade reversal in improving early postoperative recovery.

This study suggests that the numerical trend of reduced postoperative pulmonary complications in the Sugammadex group may be closely related to the compensatory improvement in respiratory function following the reduction of residual neuromuscular blockade [25]. The literature presents mixed findings regarding the impact of sugammadex on pulmonary complications. For instance, Ledowsky's study [12] demonstrated significant reductions in postoperative pneumonia in high-risk patients receiving sugammadex. Additionally, a similar reduction in more recent studies [26–28] while Togioka's research [11] found no significant differences between the two agents. These discrepancies may be attributed to variations in study design, patient populations, and the implementation of Enhanced Recovery After Surgery (ERAS) protocols, which have increasingly focused on minimizing complications through comprehensive perioperative management strategies [29]. Although some confounding factors may obscure statistical differences, the optimization of neuromuscular blockade management might present a more significant clinical benefit inflection point in patients at high risk of postoperative pulmonary complications, a hypothesis that requires further validation through stratified studies.

A common adverse reaction of sugammadex is nausea and vomiting, and the cholinomimetic effect of neostigmine may also cause nausea and vomiting. Controversy still exists regarding whether sugammadex can reduce nausea and vomiting. The results of a prospective randomized controlled trial by Tas Tuna [30] showed that the use of sugammadex can reduce the incidence and severity of nausea and vomiting in patients, while reducing the use of antiemetic drugs. However, a 2016 meta-analysis [31] suggested that sugammadex has no significant effect on PONV. The absence of significant differences in PONV outcomes may be due to the influence of various confounding factors, including anesthesia techniques, patient comorbidities, and the use of prophylactic antiemetics.

We did not find statistically significant differences in postoperative hospitalization duration or chest tube indwelling time between the sugammadex and neostigmine groups. The timing of drain removal is usually determined by the surgeon based on clinical stability and radiographic assessments, which can vary widely among practices [32]. Previous studies [33, 34] have highlighted the negative effects of prolonged chest tube drainage, including increases in pain scores, hospitalization costs, and length of stay. Therefore, in order to improve recovery after thoracic surgery and comply with the ERAS concept, surgeons will remove the drainage tube as early as possible.

Additionally, our analysis revealed no significant differences in the incidence of pulmonary infections or readmission rates within one month post-discharge. While other studies [11, 35] have reported lower readmission rates associated with sugammadex, the limited sample size in our study may have contributed to the lack of statistical significance. It has been reported [36] that there is a dose-dependent relationship between the dose of muscle relaxants during surgery and 30-day readmission. Based on this report, it has been hypothesized [37] that while sugammadex improves the efficacy compared with neostigmine, it avoids negative cardiovascular and upper respiratory tract effects, which may lead to 30% of the sugammadex group in hospital readmission rates. Given that this hypothesis has not yet been tested, future research with larger cohorts will be necessary to clarify the potential impact of sugammadex on long-term outcomes such as readmission and pulmonary infections.

Our study has several limitations. First, it was conducted at a single center with a small sample size, which restricts the generalizability of the findings to the broader population. A larger sample size may yield more definitive clinical results. Secondly, the QoR-15 scale we employed encompasses multiple parameters, and the outcomes of these self-assessments may exhibit variability within the population, thereby hindering a more accurate measurement of the study drug's impact on postoperative recovery.

Conclusion

This study confirmed that sugammadex does improve the acute recovery especially in PACU without increasing the risk of PONV. However, the higher QoR-15 score is significant but limited. Although the reduction in PPCs (particularly postoperative infections) did not reach statistical significance, fewer PPCs may still represent potential clinical benefits for aged patients. The ability to make effort cough as well as swallowing may protect possible aspiration.

Abbreviations

VATS	Video-assisted thoracoscopic surgery
PRNB	Postoperative residual neuromuscular blockade
POD	Postoperative day
QoR-15	Quality of recovery-15
PACU	Post-Anesthesia Care Unit
PPCs	Postoperative pulmonary complications
ERAS	Enhanced Recovery Surgery
PONV	Postoperative nausea and vomiting
ASA	American Society of Anesthesiologists
COPD	Chronic obstructive pulmonary disease
ICU	Intensive care unit
ECG	Electrocardiogram
SpO_2	Pulse oxygen saturation
TOF	Train-of-four
BIS	Bispectral Index
BMI	Body mass index
IQR	Interquartile range
SD	Standard deviation

Supplementary Information

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Supplementary Material 1.

Supplementary Material 2.

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Authors' contributions
Yu Yang, Zeyang Wang and Xueqing He contributed equally to this work. Conception and design: Hao Jiao and Yu Yang Randomization process and drug administration: Xueqing He Acquisition of data: Wensen Jia, Xinfang Sheng, Xiangyu Yao Analysis and interpretation of data: Hao Jiao, Yu Yang, Zeyang Wang Drafting of the article: Hao Jiao, Yu Yang, Zeyang Wang All authors participated in the revision ofthe manuscript, gave final approval of the version to be published and agreed to be accountable for all aspects of the work thereby ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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Data availability
Data and materials are not publicly available, but are available to corresponding or first authors upon reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Research Ethics Committee of the Affiliated Hospital of Xuzhou Medical University (XYFY2024-KL341-01). The study was conducted in accordance with the Declaration of Helsinki. All patients provided written informed consent prior to surgery.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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