Original Article

Minimally invasive surgery, precise anesthesia and effective analgesia are crucial for walking within 1 hour after lung surgery

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Background: The clinical effectiveness of enhanced recovery after surgery (ERAS) strategy, which emphasizes a comprehensive intervention without highlighting key points, seems to have reached a bottleneck. This study focuses on surgery, anesthesia and postoperative analgesia as the three key factors, to observe the related manifestations of ERAS in patients undergoing lung surgery with minimal intervention throughout the perioperative period.

Methods: All patients who underwent lung surgery by micro-invasive video-assisted thoracoscopic surgery (VATS) at Taizhou Municipal Hospital from August 2018 to August 2019 were consecutively enrolled in the study. The clinical data of patients were collected to observe the results of ERAS. The patients were divided into intravenous analgesia group and intercostal nerve block group according to different analgesic methods, and the ERAS results of the two analgesic methods were compared.

Results: A total of 242 patients were included in the study. The time from cessation of anesthesia to extubation was 10 [interquartile range (IQR), 9, 12] minutes (min), the time from extubation to limb activity according to instructions was 18 (IQR, 14, 23) min, time to sit up was 18 (IQR, 14, 23) min, time to stand up was 40 (IQR, 35, 46) min, and time to walk was 48 (IQR, 45, 55) min. No patient had any anesthesia complications. Compared with the intravenous analgesia group, the intercostal nerve block group had shorter time to limb activity according to instructions, time to sit up and time to walk after extubation, and lower postoperative pain scores ($P<0.05$).

Conclusions: For patients undergoing thoracic surgery, focusing on surgery, anesthesia and analgesia the three key factors, using micro-invasive VATS to reduce surgical trauma and shorten operation time, precise individualized anesthesia program and effective postoperative analgesia can achieve early autonomous activity of patients after surgery.

Keywords: Lung resection; micro-invasive video-assisted thoracoscopic surgery (micro-invasive VATS); enhanced recovery after surgery (ERAS); thoracoscopic intercostal nerve block

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Introduction

In 1997, Professor Henrik Kehlet introduced the concept of enhanced recovery after surgery (ERAS) with the aim of minimizing the physiological and psychological trauma and stress experienced by surgical patients. This approach involves the optimization of various perioperative interventions to facilitate rapid recovery (1). ERAS is an evidence-based, multimodal and patient-centered approach aiming at optimizing perioperative patient care and experience (2). In 2005, ERAS perioperative overall management program was proposed by the European Committee on Clinical Nutrition and Metabolism to reduce perioperative complications and speed up postoperative recovery (3), various clinical specialties have carried out clinical practice for fact recovery.

Thoracic surgery has also accomplished a lot of work in this field. In 2018, the European Society of Thoracic Surgeons proposed ERAS guidelines after pulmonary surgery, including preoperative counselling, avoidance of routine administration of sedatives to reduce anxiety preoperatively, venous thromboembolism prophylaxis, preventing intraoperative hypothermia, use of short-acting anesthetics to promote early awakening, administering regional anaesthesia with the aim of reducing postoperative opioid use, control of nausea and vomiting, perioperative fluid management, performing minimally invasive surgery, early chest tube removal, avoidance of urinary catheterization and early postoperative activity (4). These recommendations cover a total of 45 items and continue to expand in content with the refinement of ERAS. Although we have tried our best at each node, clinical practice results over the years have shown that the effect of ERAS program implementation seems to have reached a bottleneck. Thoracic lung surgery involves intra-thoracic operations, which can result in varying degrees of lung function impairment, and thus considered more difficult for fast recovery than other surgeries. It is generally believed that implementing ERAS after thoracic surgery is more challenging than in other medical fields. We believe that surgery, anesthesia and postoperative analgesia are the most crucial factors affecting patient in the ERAS. Effectively addressing these three elements, including minimally invasive surgery to reduce surgical trauma and shorten operation time, implementing individualized anesthesia to maintain stable patient vital signs during surgery, and providing effective postoperative analgesia to enable early patient activity as well as minimizing unnecessary interventions, can significantly enhance the outcomes of ERAS.

Therefore, this study focused on the three key factors: surgery, anesthesia, and postoperative analgesia, with minimal intervention throughout the perioperative period, to observe the manifestations of ERAS after lung surgery in patients. Meanwhile, the effects of intravenous analgesia and intraoperative intercostal nerve block analgesia on ERAS were compared. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-685/rc).

Highlight box

Key findings

- Early ambulation within 1 hour of surgery from the operating room to the ward can be achieved in patients after lung surgery by minimally invasive surgery, precise anesthesia and intercostal nerve block.

What is known and what is new?

- Enhanced recovery after surgery (ERAS) perioperative overall management program has been proposed by the European Committee on Clinical Nutrition and Metabolism to reduce perioperative complications and speed up postoperative recovery.
- Minimally invasive surgery, precise anesthesia and intercostal nerve block for postoperative analgesia are the most critical elements of the ERAS protocol for lung surgery.

What is the implication, and what should change now?

- Minimally invasive surgery, precise anesthesia and intercostal nerve block for postoperative analgesia are the most critical elements of the ERAS protocol for lung surgery. Intercostal nerve block is an effective method of postoperative analgesia, and it may become the primary method of postoperative analgesia for thoracic surgery when combined with long-acting local anesthetics.

Methods

This study retrospectively analyzed the clinical outcomes of ERAS in all patients who underwent a pulmonary segmentectomy or partial lobectomy (wedge resection) by video-assisted thoracoscopic surgery (VATS) performed by our research team from August 2018 to August 2019. Meanwhile, the impact of postoperative intravenous analgesia and intraoperative intercostal nerve block analgesia on ERAS was analyzed. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Taizhou Municipal Hospital (No. 2020-08-20, KS(Y)20258) and individual consent for this retrospective analysis was waived.

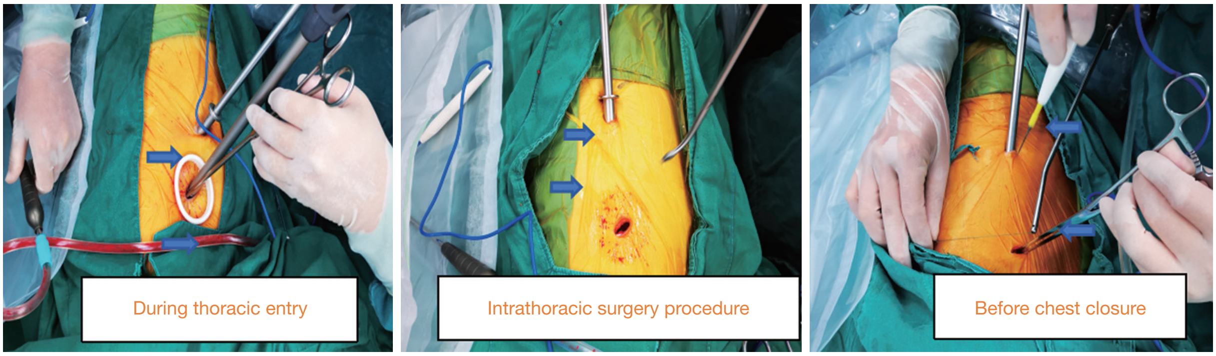


Figure 1 Minimal incision for lung surgery.

Study population

All patients who underwent a pulmonary segmentectomy or partial lobectomy (wedge resection) performed by our research team at Taizhou Municipal Hospital from August 2018 to August 2019 were consecutively enrolled. Inclusion criteria were as follows: (I) all patients undergoing VATS lung surgery and able to perform normal daily activities preoperatively; (II) age ≥18 years; (III) American Society of Anaesthesiologists (ASA) grade I–III. Exclusion criteria were as follows: (I) incomplete clinical or follow-up data; (II) patients who could only undergo open thoracotomy due to intraoperative bleeding, large tumor invasion range or extensive pleural adhesion during surgery; (III) patients undergoing pulmonary whole lobectomy; (IV) patients who could not or refused to implement early postoperative ERAS program for other reasons.

Anesthesia program and early postoperative ERAS program

The preoperative preparation was performed according to routine lung surgery. All surgeries were performed by the same experienced surgical team, using micro-invasive two-port (1–1.5 cm) VATS, as shown in *Figure 1*. The same experienced anesthesia team implemented the standardized anesthesia program and early postoperative ERAS program.

Anesthesia program

All patients received rapid induction double-lumen endotracheal intubation, intravenous composite anesthesia. The size of the double-lumen endotracheal tube was selected according to the size of the trachea and bronchi on the computed tomography (CT) scan, with a tube one size smaller preferred. Non-invasive blood pressure, electrocardiogram (ECG), pulse oximetry and bispectral index (BIS) monitoring were routinely monitored, peripheral veins were opened to ensure smooth fluid infusion during anesthesia.

Anesthetic induction: midazolam 0.025 mg/kg, sufentanil 0.25 μg/kg, observe for 2 minutes (min). Then 1% propofol 1.5–2.5 mg/kg was injected to induce anesthesia, followed by cisatracurium 0.16 mg/kg when BIS reached 40–50. The double-lumen endotracheal tube was inserted after adequate muscle relaxation, and bronchoscopic confirmation was obtained before fixing the tube and controlling bilateral ventilation of the patient's breathing.

Anesthesia maintenance: 1% propofol (4–5 mg/kg/h) and 5% remifentanil (0.01 g/kg/h) were continuously pumped to maintain anesthesia. The infusion rate was adjusted according to the patient's age, response to induction drugs, intraoperative blood pressure, heart rate and BIS to maintain hemodynamic stability. The BIS was usually maintained at 40–60 to prevent intraoperative awareness. In order to achieve the minimum drug dose required for surgery and anesthesia without intraoperative awareness, the BIS was maintained around 55 during surgery. Cisatracurium 0.07 mg/kg/h was continuously pumped for muscle relaxation starting 20 min after induction and stopped 20 min before the end of surgery. 1% Propofol and 5% remifentanil infusion were stopped 5 min before the end of surgery. Muscle relaxation antagonism was performed 10 min after surgery based on the patient's muscle recovery condition. Extubation was performed 3 min after oxygen saturation (SpO_2) >96% when the patient was fully awake and muscle strength recovered.

To minimize patient intervention, no invasive arterial monitoring, central venous catheter or urinary catheter

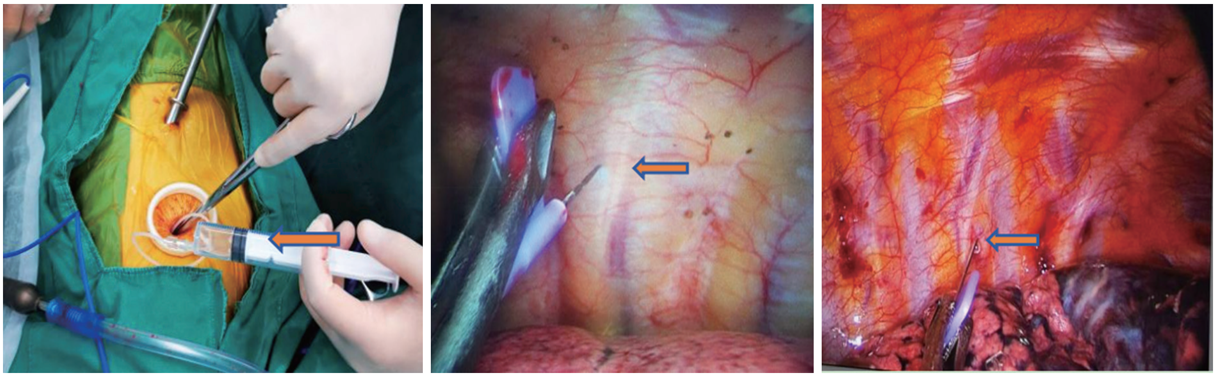


Figure 2 Thoracoscopic intercostal nerve block under direct vision. The arrows indicate the specific operating sites of intercostal nerve block.

were placed during the entire surgical process.

Postoperative analgesia

Two analgesic methods were used, including postoperative intravenous analgesia or intercostal nerve block analgesia.

The intravenous analgesia group: sufentanil 0.1 mg + dexmedetomidine 0.1 mg + butorphanol 4 mg + normal saline, total 150 mL, intravenous analgesia started from half an hour before the end of surgery. The background flow rate of intravenous analgesia pump was adjusted between 1–2 mL/h according to the patient's age, response to sufentanil during anesthesia induction and the patient's response to drugs during surgery.

The intercostal nerve block group: the surgeon performed intercostal nerve block under thoracoscopic direct vision in the chest before closure. Ropivacaine 3.5 mg/mL was used to block the intercostal nerve at the incision and the intercostal nerves above and below the incision, 2–3 mL for each intercostal space. 1% Lidocaine 10 mL was injected into the pleural cavity for pleural block, as shown in *Figure 2*.

Early ERAS protocol after surgery

After being transferred to the recovery room, patients received nasal catheter oxygen inhalation and non-invasive blood pressure, 12-lead ECG and SpO_2. Once the patient was fully awake and peripheral venous access and chest closed drainage were safely established, lower and upper limb activities were gradually carried out with the patient's consent, and the patient described their feelings as good with normal blood pressure and SpO_2. They were slowly transitioned to the sitting position after the patient was able to get out of bed based on their feelings, and bedside activities were started under the premise of ensuring patient safety. During the patient's independent activity, their feelings and SpO_2 were continuously monitored.

Data collection

Clinical data such as general information, diagnosis, surgery name, anesthesia time, type and dosage of anesthetic drugs, intraoperative surgery time, time from cessation of anesthesia to extubation, analgesic method, after extubation time to sit up, time to stand up, time to walk, vital signs and subjective feelings during the entire surgical and ERAS process, pain score (digital analog scale), chest tube removal time and discharge time were collected from the case report form. Some patients' related photos and videos of early postoperative ERAS protocols were also collected.

Statistical analysis

Patients that were unable to complete the ERAS protocol were described, and patients who completed the ERAS protocol were compared between groups based on different analgesic methods. SPSS 26 was used for statistical analysis. Continuous variables with normal distribution were expressed as mean ± standard deviation, and two independent sample *t*-test was used for intergroup comparison; continuous variables with non-normal distribution were expressed as median [interquartile range (IQR)] and Mann-Whitney *U* test was used for intergroup comparison. Categorical variables were expressed as the number (percentage) and intergroup comparison was performed using Chi-squared test or Fisher's exact test. $P<0.05$ was considered statistically significant.

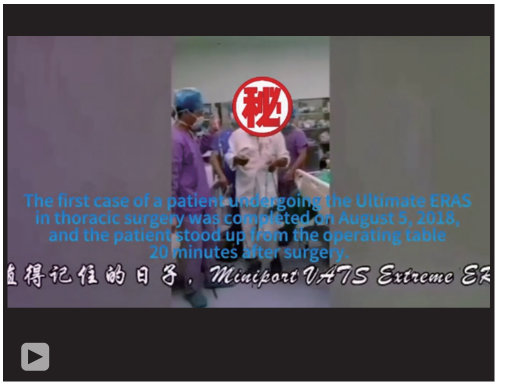
Table 1 Clinical data of patients (n=242)

Item	Parameter
Age (years)	62.5 [53, 68]
Male	107 (44.2)
Weight (kg)	60 [55, 70]
Height (cm)	162 [157, 168]
Operative time (min)	60 [60, 89]
Anesthesia time (min)	90 [90, 120]
Chest tube removal time (days)	3 [3, 4]
Hospital stay (days)	5 [4, 7]
Anesthetic induction	
Midazolam (mg)	1.5 [1.3, 1.5]
Sufentanil (μg)	15 [12, 20]
1% propofol (mL)	15 [12, 15]
Cisatracurium (mg)	10 [10, 10]
Anesthetic maintenance	
1% propofol (mL)	35 [30, 42]
5% remifentanil (mL)	18 [15, 21]
Cisatracurium (mg)	12 [10, 14]
Balance liquid input volume (mL)	600 [500, 765]
Postoperative rehabilitation status	
Time from cessation of anesthesia to extubation (min)	10 [9, 12]
After extubation	
Time to limb activity according to instructions (min)	18 [14, 23]
Time to sit up (min)	30 [25, 35]
Time to stand up (min)	40 [35, 46]
Time to walk (min)	48 [45, 55]
Pain score	0.71±0.71

Data are presented as mean ± standard deviation for continuous variables with normal distribution. Median [interquartile range] is used for continuous variables without normal distribution. Categorical variables are expressed as number (percentage) of subjects. min, minutes.

Results

A total of 249 patients participated in this study, of which 7 patients could not or refused to implement the postoperative early ERAS protocol. Three patients underwent large operations with difficult procedures, extensive intraoperative adhesions or bleeding, changing to large incision surgery, with operation and anesthesia time more than 180 min; 2 patients had low preoperative diffusing capacity of carbon monoxide; 2 patients missed key clinical data. Eventually, 242 patients completed the postoperative ERAS protocol and were included in this study, and the 242 patients were divided into intravenous analgesia group (n=149) and intercostal nerve block group (n=93) for analysis according to postoperative analgesic methods. The specific manifestations of ERAS in some patients who underwent lung surgery were presented in the video (*Video 1*).



Video 1 Patients walked back to ward within an hour after lung surgery.

Clinical data of 242 patients

The average age of the 242 patients was 62.5 (IQR, 53, 68) years, 107 (44.2%) were male, the operative time was 60 (IQR, 60, 89) min, the anesthesia time was 90 (IQR, 90, 120) min, the chest tube removal time was 3 (IQR, 3, 4) days, the hospital stay was 5 (IQR, 4, 7) days. The time from cessation of anesthesia to extubation was 10 (IQR, 9, 12) min, the time from extubation to the patient starting limb activity according to instructions was 18 (IQR, 14, 23) min, the time to sit up was 30 (IQR, 25, 35) min, the time to stand up was 40 (IQR, 35, 46) min, and the time to walk was 48 (IQR, 45, 55) min (*Table 1*). All patients did not experience intraoperative awareness, postoperative nausea and vomiting, or urinary retention.

Comparison of general conditions between the two groups

There were no statistically significant differences in age,

Table 2 Comparison of general conditions between the two groups

Item	Intravenous analgesia group (n=149)	Intercostal nerve block group (n=93)	P
Age (years)	63 [55, 67]	62 [50, 68]	0.37
Male	66 (44.3)	41 (44.1)	0.98
Weight (kg)	60.5 [56, 69]	59.25 [51.25, 70.00]	0.10
Height (cm)	161 [157, 170]	163 [157, 168]	0.95
Operative time (min)	60 [60, 71]	74 [57, 100]	0.002*
Anesthesia time (min)	90 [90, 100]	105 [85, 130]	0.008*
Chest tube removal time (days)	3 [3, 5]	3 [3, 4]	0.01*
Hospital stay (days)	5 [4, 8]	5 [4, 6]	0.02*

Median [interquartile range] is used for continuous variables without normal distribution. Categorical variables are expressed as number (percentage) of subjects. *, P<0.05, the difference is statistically significant. min, minutes.

Table 3 Comparison of intraoperative anesthetic drug dosage between the two groups

Item	Intravenous analgesia group (n=149)	Intercostal nerve block group (n=93)	P
Anesthetic induction			
Midazolam (mg)	1.5 [1.3, 1.5]	1.5 [1.0, 1.5]	0.002*
Sufentanil (μg)	15 [15, 20]	15 [15, 20]	0.02*
1% propofol (mL)	15 [12, 15]	15 [12, 15]	0.61
Cisatracurium (min)	10 [10, 10]	10 [10, 10]	0.98
Anesthetic maintenance			
1% propofol (mL)	35 [30, 42]	36 [28, 45]	0.94
5% remifentanil (mL)	18 [15, 21]	18 [13, 23]	0.68
Cisatracurium (mg)	2 [0, 3]	2 [0, 4]	0.54
Balance liquid input volume (mL)	580 [500, 710]	630 [500, 860]	0.19

Median [interquartile range] is used for continuous variables without normal distribution. *, P<0.05, the difference is statistically significant. min, minutes.

sex, height and weight between the two groups. Compared with the intravenous analgesia group, the operative time and anesthesia time were longer in the intercostal nerve block group, with statistically significant differences (P=0.002 and P=0.008), while the chest tube removal time and hospital stay were shorter, with statistically significant differences (P=0.01 and P=0.02) (*Table 2*).

Comparison of intraoperative anesthetic drug dosage between the two groups

In anesthetic induction drugs, the usage amounts of midazolam and sufentanil detected statistical differences between the two groups (P=0.002 and P=0.02). There were no statistically significant differences in anesthetic drug usage and balanced fluid input volume during anesthetic maintenance between the two groups (*Table 3*).

Comparison of early postoperative recovery between the two groups

There were no statistically significant differences in the time from cessation of anesthesia to extubation and time to stand up between the two groups (P>0.05). Compared

Table 4 Comparison of early postoperative recovery between the two groups

Item	Intravenous analgesia group (n=149)	Intercostal nerve block group (n=93)	P
Time from cessation of anesthesia to extubation (min)	10 [8, 11]	10 [9, 12]	0.08
After extubation			
Time to limb activity according to instructions (min)	19 [15, 25]	16 [12, 20]	0.001*
Time to sit up (min)	31 [26, 36]	28 [25, 35]	0.01*
Time to stand up (min)	41 [36, 48]	38 [35, 46]	0.07
Time to walk (min)	50 [46, 56]	46 [42, 53]	0.03*
Pain score	1.01±0.74	0.33±0.50	<0.001*
Pain while coughing	76 (51.0)	13 (14.0)	<0.001*
Mild dizziness while sitting	33 (22.1)	0 (0.0)	<0.001*
Mild dizziness while standing	15 (10.1)	4 (4.3)	0.11
Mild dizziness while walking	6 (4.0)	1 (1.1)	0.35

Data are presented as mean ± standard deviation for continuous variables with normal distribution. Median [interquartile range] is used for continuous variables without normal distribution. Categorical variables are expressed as number (percentage) of subjects. *, P<0.05, the difference is statistically significant. min, minutes.

with the intravenous analgesia group, the intercostal nerve block group had shorter time to limb activity according to instructions, time to sit up and time to walk after extubation (P=0.001, 0.01 and 0.03, respectively). The pain score of the intercostal nerve block group was lower than that of the intravenous analgesia group (P<0.001). The situation of pain while coughing and mild dizziness while sitting in the intercostal nerve block group were significantly better (P<0.001) (*Table 4*).

Discussion

The ERAS protocol implemented for lung surgery patients in this study mainly optimized the three key elements of surgery, anesthesia and postoperative analgesia. Firstly, the optimization of the surgical plan was to perform lung surgery using an experienced surgical team, using VATS technique for all operations, controlling the incision length within 1–1.5 cm, reducing the patient's surgical trauma and shortening the operation time. Compared with open thoracotomy, VATS surgery causes less trauma, can reduce intraoperative bleeding, reduce chest tube drainage, reduce postoperative pain, and is more conducive to surgical recovery (5). Secondly, the optimization of the anesthesia plan was to reduce unnecessary operations such as deep vein puncture, invasive blood pressure monitoring and catheterization, so as to reduce the patient's own stress response, and to select a slightly smaller double lumen endotracheal tube to avoid damage to the airway during intubation. The types and doses of anesthetic drugs were minimized while meeting the basic requirements of surgery and anesthesia. Finally, in the optimization of the analgesic plan, the postoperative intravenous analgesia pump background flow rate was guided by the patient's response to sufentanil during anesthetic induction, and thoracoscopic intercostal nerve block analgesia was used for postoperative pain management for the first time.

The results of this study showed 242 patients completed the postoperative ERAS protocol. The time for 242 patients to start limb activity according to instructions after extubation was 18 (IQR, 14, 23) min, the time to sit up was 30 (IQR, 25, 35) min, the time to stand up was 40 (IQR, 35, 46) min, and the time to walk was 48 (IQR, 45, 55) min. No anesthesia-related complications occurred in any patients. Compared with the intravenous analgesia group, the intercostal nerve block group had lower time to limb activity, time to sit up, time to walk. Precise intravenous analgesia parameters can also achieve effective postoperative analgesia and early ambulation in patients after thoracic surgery, but thoracoscopic intercostal nerve block has the advantages of accurate localization, definite efficacy and less drug use, and can avoid thoracic sympathetic nerve block caused by paravertebral or epidural block. In addition, the surgery time and anesthesia time of the intercostal nerve block group were longer than those of the intravenous analgesia group, which may be related to the operation time for intercostal nerve block. The use of midazolam and sufentanil for anesthetic induction showed a statistical difference between the two groups, which was due to the actual body weight difference leading to different drug doses.

Studies have shown that applying ERAS protocols for thoracic surgery patients can reduce postoperative complications, shorten patient hospital stays, and reduce hospitalization costs (6). Khandhar *et al.* (7) reported that early postoperative ambulation is a key factor in reducing the incidence of postoperative complications after VATS lung lobectomy. ERAS strengthens preoperative health education and psychological care for patients, which can enhance patients' confidence in recovery, effectively eliminate patients' concerns about diseases and surgeries, and improve patients' psychological status (8). Early ambulation not only promotes the recovery of gastrointestinal function and enables early oral intake to supplement fluids and improve nutrition through diet, which is conducive to patients' recovery, but also effectively prevents the risks of pulmonary infection and deep vein thrombosis in the lower limbs (9), avoiding many unnecessary excessive medical interventions postoperatively. At the same time, early self-care can also reduce postoperative companionship and has significant socioeconomic value. Paci *et al.* (10) evaluated the economic impact of implementing the ERAS protocol and reported that the overall hospitalization costs of ERAS patients were lower. Although we did not directly analyze hospitalization costs in this study, there is a certain correlation between reduced length of hospital stay and hospitalization costs. Lacin *et al.* (11) previously reported that the average hospitalization costs of VATS and open thoracotomy exceeded 20,000 US dollars. These costs were calculated based on the average postoperative hospital stay of 6.15 days for VATS surgery and 7.83 days for open thoracotomy (11). In this study, the average postoperative hospital stay for all patients undergoing VATS surgery was 5 (IQR, 4, 7) days, indicating that implementing the ERAS protocol can shorten patients' hospital stay, reduce waste of medical resources, and lower hospitalization costs for patients. ERAS can also improve patients' postoperative compliance and satisfaction (6). Most patients believe that long-term bed rest is necessary for recovery. Therefore, we also should explain the benefits of early postoperative ambulation and obtain patients' support and cooperation.

Adequate postoperative analgesia is critically important for patients' recovery, as insufficient analgesia may lead to prolong bed rest and impair lung expansion and respiratory function (12). Although VATS has advantages over open thoracotomy in terms of pain, it can cause postoperative pain and temporary lung function impairment (13). Various measures have been adopted to alleviate postoperative pain after VATS, including local analgesia, intravenous analgesia, epidural block and intercostal nerve block (14). In recent years, regional analgesia has been proven to be effective and safe for postoperative analgesia (15). Bolotin *et al.* (16) reported significant advantages of intercostal nerve block in postoperative analgesia after VATS. The advantages of intraoperative intercostal nerve block are the accuracy of block, and local anesthetic injection under direct vision (14). In this study, the thoracoscopic intercostal nerve block was also observed to be more effective for early postoperative self-care in patients.

This study has certain limitations: it was a retrospective study, with inherent biases; secondly, the sample size was small, which may limit statistical power. Future large-scale high-quality multicenter randomized controlled trials are needed to validate the findings of this study.

Conclusions

Early ambulation within 1 hour of surgery from the operating room to the ward can be achieved in patients after lung surgery by optimizing surgical, anesthetic and postoperative analgesic protocols. Minimally invasive surgery, precise anesthesia and intercostal nerve block for postoperative analgesia are the most critical elements of the ERAS protocol for lung surgery. Intercostal nerve block is an effective method of postoperative analgesia, and it may become the primary method of postoperative analgesia for thoracic surgery when combined with long-acting local anesthetics.

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Footnote

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Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-685/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-24-685/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Taizhou Municipal Hospital (No. 2020-08-20, KS(Y)20258) and individual consent for this retrospective analysis was waived.

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