Perioperative Medicine

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Measures to accelerate recovery from stage III tuberculous empyema: tuberculous empyema surgical and recovery methods

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Abstract

Objectives To evaluate the effects of video-assisted thoracoscopic decortication (VATD) and enhanced recovery after surgery (ERAS) in patients with stage III tuberculous empyema.

Methods The 360 participants were divided into four groups according to the treatment received: thoracotomy decortication (TD) + traditional recovery procedures (TRP), TD + ERAS, VATD + TRP, and VATD + ERAS. We evaluated the effects of the treatment modalities on various intraoperative and postoperative outcome measures. Multivariate analysis was then performed to identify risk factors associated with increased postoperative the length of hospital (LOS).

Results There were significant differences between the TD and VATS groups in terms of the duration of surgery, intraoperative blood loss, postoperative drainage, postoperative erythrocyte sedimentation rate (ESR), LOS, and pain levels. The use of ERAS also showed significant effects in certain outcome measures. There were no significant differences in the incidence of postoperative complications among the groups. The use of VATD and ERAS procedures, and preoperative antituberculosis therapy, was inversely associated with the LOS.

Conclusions Implementation of VATD and ERAS procedures in patients with stage III tuberculous empyema can significantly reduce the LOS and improve patient outcomes in a safe and effective manner.

Keywords Enhanced recovery after surgery, Length of stay, Outcome measures, Tuberculous empyema, Video-assisted thoracic surgery

Introduction

Tuberculous empyema is a disease caused by *Mycobacterium tuberculosis*infection of the pleural cavity, resulting in inflammation, exudation, suppuration, and additional manifestations (Sikander 2021). Its diagnosis and treatment methods are subject to frequent revision. The pathophysiological process of tuberculous empyema can be divided into three stages (Pulle 2020). Antituberculous drugs, effusion drainage, and pleural fibrinolytic therapy are effective treatments for stages I and II. However, patients with stage III tuberculous empyema have limited lung function, ranging in severity from simple lung dilatation limitation to rib space narrowing, rib osteoporosis and weakness, restricted respiratory dysfunction, and mixed respiratory dysfunction (Kumar 2017). These pathological changes are difficult to resolve using simple antituberculosis drug therapy, and thoracocentesis and surgery are therefore typically required. Owing to the

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dual influences of tuberculosis infection and the pathophysiological processes of chronic empyema, the surgical procedure is lengthy. Novel strategies to accelerate surgery in patients with stage III tuberculous empyema are urgently needed. The aim of stage III tuberculous empyema surgery is the removal of the thickened pleural fibre plate to relieve lung restriction and restore lung function (Majeed 2020). However, traditional thoracotomy is a traumatic procedure with a long recovery time, which has led to increasing interest in video-assisted thoracoscopic decortication (VATD) (Cai 2023). In addition, enhanced recovery after surgery (ERAS) protocols have improved results in many surgical fields (Olowonyo et al. 1995). Between 2019 and 2023, VATD and ERAS were increasingly used to treat stage III tuberculous empyema at our medical centre. As a surgical technique, VATD has indications for its implementation. However, there are no clear clinical practice guidelines or expert consensus on the indications of its use in stage III empyema.

Therefore, we conducted a prospective study to evaluate the treatment efficacy of the above-mentioned treatment methods for stage III tuberculous empyema, and we also identified factors that shortened the length of hospital stay(LOS).

Patients and methods

Study design and patient characteristics

The Department of Thoracic Surgery at our medical centre treats a large number of patients with tuberculous empyema, and surgery is performed by an experienced team. A total of 360 patients with stage III tuberculous empyema who were eligible for this study were surgically treated in our department between May 2019 and May 2023.

Inclusion criteria were as follows: (1) Preoperative clinical diagnosis of stage III tuberculous empyema; (2) received anti-TB therapy for at least 6 weeks; (3) drainage and other treatment methods were ineffective, and the empyema showed a wrapped shape; and (4) aged 18–75 years. Exclusion criteria were as follows: (1) Nontuberculous empyema confirmed by pathological and bacteriological examinations after surgery, (2) pulmonary unstable tuberculosis, (3) the presence of severe chronic disease, and (4) drug-resistant tuberculosis infection.

A total of 360 patients (187 men and 173 women) with stage III tuberculous empyema were included in the study, with an average age of 56 years, a mean body mass index (BMI) of 23.1 kg/m (Pulle 2020), a mean preoperative ESR of 26.5 mm/h, and an average antituberculosis treatment duration of 11.7 weeks. In terms of comorbidities, 57 patients had diabetes, 47 had hypertension, and 40 had other chronic controllable diseases. There were no significant differences in characteristics among the four groups (Table 1).

We found that VATD was feasible in most patients with stage III empyema without significant narrowing of the intercostal space and without pleural calcification. For patients with significant narrowing of the intercostal space and extensive calcification of the pleura, the thoracotomy decortication(TD) was still used because of the difficulty in accessing the chest cavity. Therefore, based on the indications of VATD and TD, TD surgery was performed in 157 patients and VATD surgery in 203 patients.

Every patient underwent the ERAS process and rehabilitation measures, but not all patients were able to comply with every item in all ERAS measures (Table 2). The implementation of selected components of the ERAS protocol was incorporated into the perioperative care pathway. We defined the ERAS group with compliance rate greater than or equal to 50%, and the TRP group with compliance rate less than 50%. Finally, there were four groups, 71 cases in TD + TRP group, 86 cases in TD

Table 1 Patient characteristics

Characteristic	Total $n = 360$	TD + TRP $n = 71$	TD + ERAS $n = 86$	VATD + TRP $n = 93$	VATD + ERAS $n = 110$	*P*
Age (years)	56.1 ± 13	56.9 ± 12.5	56.8 ± 13.5	56 ± 13.3	55.1 ± 12.8	0.712
Male/female	187/173	38/33	45/41	50/43	54/57	0.381
BMI (kg/m (Pulle 2020))	23.1 ± 3.6	23.7 ± 3.6	22.8 ± 3.1	22.8 ± 3.2	23 ± 3.3	0.176
ESR (mm/h)	26.5 ± 12.1	26.4 ± 12	25.5 ± 11.6	26.5 ± 11.8	26.4 ± 12.7	0.685
Antituberculosis treatment (weeks)	11.7 ± 3.6	11.3 ± 3.4	11.6 ± 3.6	11.8 ± 3.7	11.8 ± 3.6	0.583
Diabetes	54 (15%)	12 (17%)	14 (16%)	13 (14%)	15 (14%)	0.601
Hypertension	47 (13%)	10 (14%)	10 (12%)	11 (12%)	16 (15%)	0.624
Other chronic controllable diseases	40 (11%)	8 (11%)	9 (10%)	11 (12%)	12 (11%)	0.597

Data are presented as the mean ± standard deviation or frequency (percentage). *BMI* Body mass index, *ERAS* Enhanced recovery after surgery, *ESR* Erythrocyte sedimentation rate, *TD* Thoracotomy decortication, *TRP* Traditional rehabilitation procedures, *VATD* Video-assisted thoracoscopic decortication

Table 2 Comparison between TRP and ERAS procedures

	ERAS	TRP
Prehospital management	Request that patients perform simple abdominal breathing exercises at home before admission	None
	Request patients to stop smoking and taking medications that may interfere with surgery	None
Preoperative preparation	Estazolam tablets routinely administered the night before the operation; psychiatrists consulted if necessary	Estazolam administered when necessary
	Pulmonary function tests Abdominal breathing training	Pulmonary function tests
	Nutritionists evaluate nutritional risk status and provide nutritional support	Serum albumin levels tested and high-quality protein diet recommended
	Fast for 6 h before surgery; 500-ml carbohydrate drink 3 h before surgery	Fast for 10 h and no water for 4 h, before surgery
	Isoniazid and rifampicin administered intravenously 2 h before surgery	No antituberculosis treatment administered intravenously 2 h before surgery
Intraoperative management	Body temperature monitored; heated mattress used	Body temperature monitored; operating room temperature recorded
	General anaesthesia combined with thoracic paravertebral nerve block	General anaesthesia
	Avoid volume overload	Maintain haemodynamic stability
Postoperative management	Self-controlled analgesic pumps and nonsteroidal drugs to control pain, and the intercostal nerve tissue was guided by ultrasound	Analgesic pump to control pain; intramuscular injection of tramadol if required
	Antiemetic and antireflux drugs administered regularly within 48 h of surgery	Antiemetics used if vomiting occurs
	Water given after waking up and liquid food 6 h after surgery	Water given 6 h after surgery and food on the first day after surgery
	Transvenous fluids stopped as soon as possible	Intravenous fluids administered for 3 to 7 days after surgery
	Aerosol inhalation of phlegm and bronchiectasis drugs	Aerosol inhalation of phlegm and bronchiectasis drugs
	Concussion expectorator used to assist expectoration	Patient encouraged to expel phlegm by actively coughing
	Respiratory trainers used to aid lung function recovery	Patient encouraged to take deep breaths or practice blowing up balloons
	Catheter removed 6 h (female) and 24 h (male) after surgery	Catheter removed 48–72 h after surgery
	Move limbs in bed after waking up and get out of bed within 24 h of surgery	Move limbs in bed on the 1 st day and get out of bed on the 2nd day after surgery

ERAS Enhanced recovery after surgery, *TRP* Traditional recovery procedures

+ERAS group, 93 cases in VATD + TRP group, and 110 cases in VATD + ERAS group (Fig. 1).

All patients underwent standardised antituberculosis therapy before surgery, and the concomitant chronic disease was effectively controlled, meeting the indications for elective surgery. All perioperative management was subject to informed consent from the patients, and the ethics committee of our medical centre approved the study plan and supervised the research process.

In terms of comorbidities, the study revealed that tuberculous empyema patients primarily presented with diabetes mellitus and hypertension, which constituted the majority of cases. Other comorbidities such as coronary artery disease, cerebral infarction, and autoimmune disorders collectively accounted for a negligible proportion. Therefore, patient characteristics were categorised into three groups: diabetes mellitus, hypertension, and other comorbidities. All patients with these comorbidities, as well as those presenting with malnutrition or hypoproteinemia, underwent preoperative optimization to meet the criteria for surgical safety.

The primary outcome

The primary outcome measure to assess whether different treatment modalities accelerated recovery from stage III tuberculous empyema was the LOS. We set uniform discharge criteria as follows: (1) Body temperature is normal, (2) the patient was well tolerated to postoperative antituberculosis drugs, (3) the patient had no symptoms such as chest tightness and shortness of breath, (4) chest

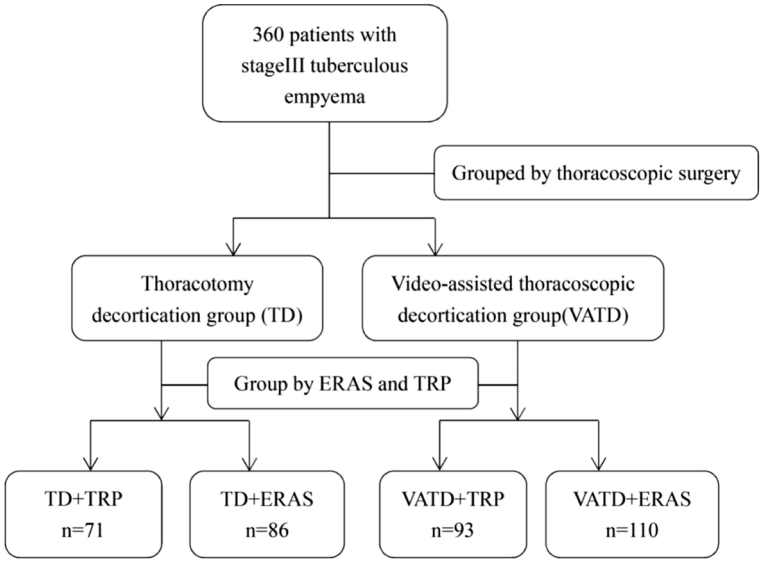

Fig. 1 Flow diagram of the study. ERAS, enhanced recovery after surgery; TRP, traditional rehabilitation procedures

radiography after the drainage was removed showed well-distended lungs with no residual pleural effusion, and (5) the incisions healed well without infection.

The secondary outcomes

The duration of surgery was the time elapsed between the opening of the skin and the closure of the incision. The intraoperative blood loss was estimated according to the volume of thoracic blood drawn and the weight of the oozing gauze. The postoperative drainage volume was defined as the total drainage volume from the time of drainage placement to the time when the drainage tube was removed according to the indications for drainage tube removal. (the indications for extubation were as follows: well-distalised lungs on chest X-ray, no air leak, and a daily drainage volume of less than 100 ml). The postoperative pain level is measured using a numeric rating scale (NRS) which is a numeric rating scale from 0 to 10, where 0 means no pain and 10 means no pain, and the patient chooses a number to describe the pain. These scores were administered at 8, 24, 48, and 72 h after surgery.

Postoperative complication

The postoperative complications we counted included the following: (1) pulmonary infection, (2) wound infection or delayed healing, (3) prolonged tube time due to pulmonary air leak or postoperative bleeding, (4) unplanned reoperation, (5) unplanned readmission within 30 days, (6) postoperative nausea, and vomiting (7) pulmonary embolism.

Statistical analysis

Continuous variables are presented as the mean ± standard deviation and were compared using analyses of variance and *t*-tests. Categorical data are expressed as frequencies and percentages and were compared using chi-squared tests. Based on clinical importance and previous published articles, we collected clinical variables that might be associated with postoperative LOS, including ERAS protocol, surgical approach, and age. Multivariate analysis was then performed to identify risk factors associated with increased postoperative LOS. GraphPad Prism software version 5.0 (GraphPad Software, San Diego, CA, USA) was used to generate a forest diagram to present the results of these analyses.

Results

Length of hospital stay (LOS)

Compared with the other groups, the VATD + ERAS group had the shortest LOS (9.1 ± 1.3 days, $P < 0.001$). The length of stay in other groups from shortest to longest was TD + ERAS (11.3 ± 2.1 days), VATD + TRP (12.3 ± 3.4 days), and TD + TRP (13.7 ± 2.4 days) (Table 3, Fig. 2). Multivariate analysis showed that age less than 56 years old [odds ratio (OR): 0.616, 95% confidence interval (CI): 0.397–0.955, $P = 0.03$] and the application of VATD [*OR*: 0.501, 95% *CI*: 0.322–0.777, $P = 0.002$] and ERAS [*OR*: 0.52, 95% *CI*: 0.335–0.805,

Table 3 Perioperative outcomes of each group

	TD + TRP *n* = 71	TD + ERAS *n* = 86	VATD + TRP *n* = 93	VATD + ERAS *n* = 110
Operative duration (min)	173.7 ± 47.9	176.1 ± 53.5	238.1 ± 65.4	206.2 ± 67.1
Intraoperative blood loss (ml)	356.4 ± 77.6	329.8 ± 89.3	255.4 ± 92	243.7 ± 84.3
Postoperative drainage volume (ml)	2201.4 ± 546.7	2142.4 ± 676.9	1532.4 ± 431.7	1329.4 ± 331.3
Postoperative ESR (mm/h)	38.5 ± 9.3	34.5 ± 8.8	36.8 ± 7.8	28.7 ± 7.3
LOS (days)	13.7 ± 2.4	11.3 ± 2.1	12.3 ± 3.4	9.1 ± 1.3

Data are presented as the mean ± standard deviation. *ERAS* Enhanced recovery after surgery, *ESR* Erythrocyte sedimentation rate, *TD* Thoracotomy decortication, *TRP* Traditional rehabilitation procedures, *VATD* Video-assisted thoracoscopic decortication, *LOS* Length of hospital stay

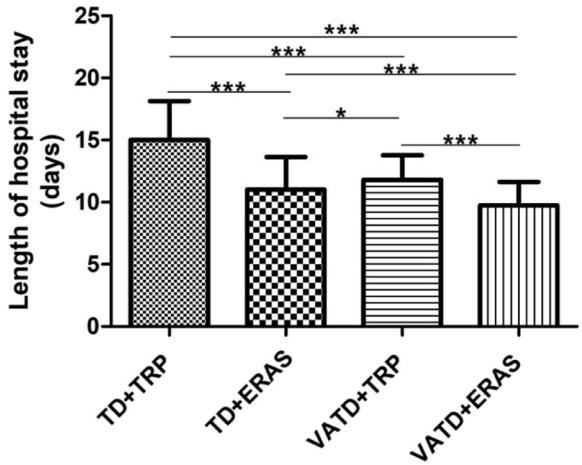

Fig. 2 Comparison of LOS among the groups. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. ERAS, enhanced recovery after surgery; TD, thoracotomy decortication; TRP, traditional rehabilitation procedures; VATD, video-assisted thoracoscopic decortication

$P = 0.003$] were independent influencing factors for shorter length of stay (Fig. 2).

Perioperative outcomes

The operative duration, intraoperative blood loss, postoperative drainage, and postoperative ESR data are presented in Table 3. The operative duration was significantly longer in the VATD groups than the TD groups (Table 3, Fig. 3, Fig. 4a), but the intraoperative blood loss was significantly less (Table 3, Fig. 4b). The groups undergoing VATD had significantly less postoperative drainage than the TD groups, with the least drainage observed in the VATD + ERAS group (Table 3, Fig. 4c). In terms of the postoperative ESR, the lowest ESR was recorded in the VATD + ERAS group (Table 3, Fig. 4d). At 24, 48, and 72 h after surgery, pain levels were highest in patients in the TD + TRP group. Pain levels in the three other groups were significantly lower, with the VATD + ERAS group having the lowest pain levels (Fig. 5). There was no difference in pain levels between TD + TRP and TD + ERAS groups 8 h postoperatively. We recorded the complications in each group, including delayed wound healing, reoperation, spread of tuberculosis, pulmonary

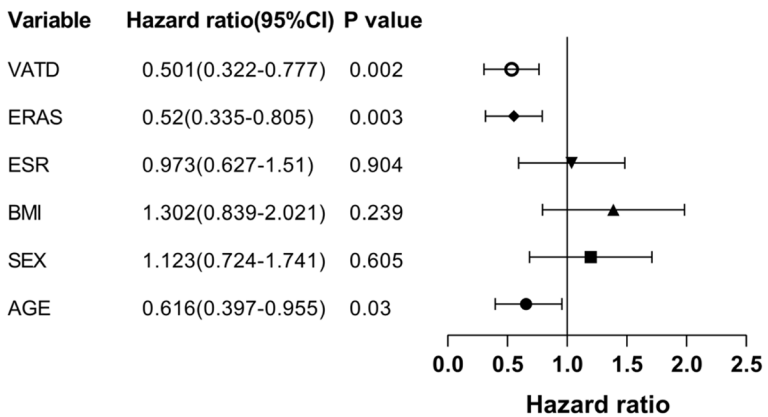

Fig. 3 Forest diagram showing the results of multivariate analyses of factors associated with the LOS. BMI, body mass index; ERAS, enhanced recovery after surgery; ESR, erythrocyte sedimentation rate; VATD, video-assisted thoracoscopic decortication

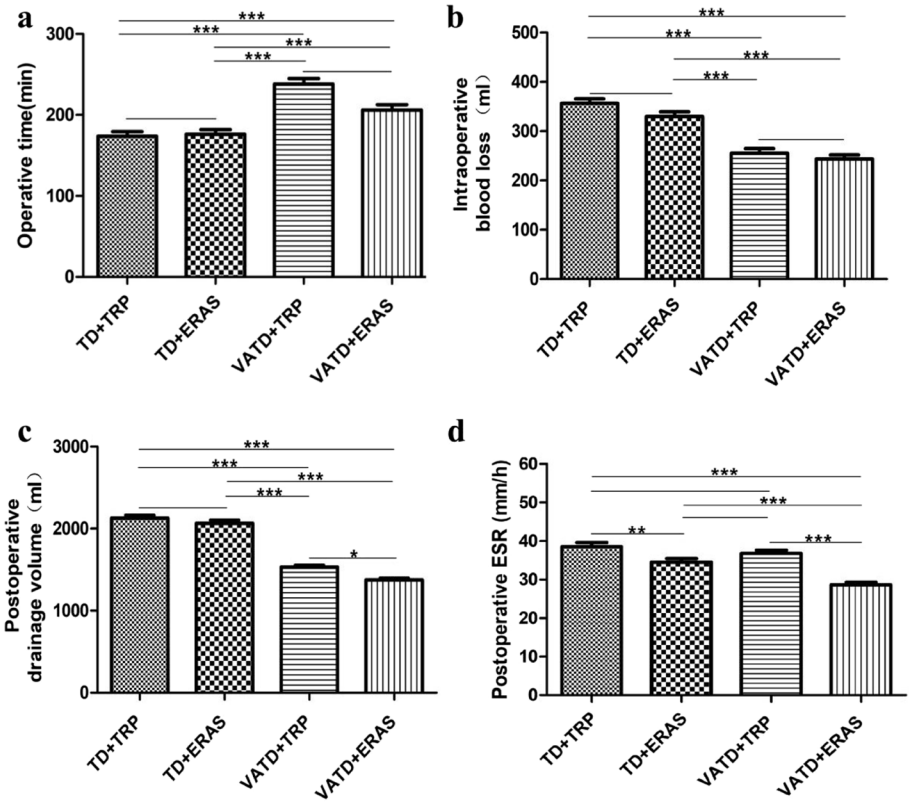

Fig. 4 Comparison of perioperative outcomes among the groups. **a** Operative duration. **b** Intraoperative blood loss. **c** Postoperative drainage volume. **d** Postoperative ESR. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. ERAS, enhanced recovery after surgery; ESR, erythrocyte sedimentation rate; TD, thoracotomy decortication; TRP, traditional rehabilitation procedures; VATD, video-assisted thoracoscopic decortication

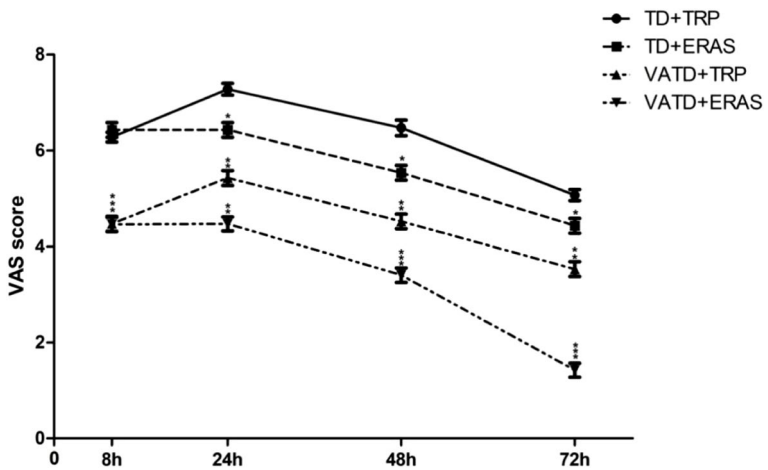

Fig. 5 Comparison of pain levels among the groups. Pain levels were evaluated at 8, 24, 48, and 72 h postoperatively using a VAS. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$. ERAS, enhanced recovery after surgery; TD, thoracotomy decortication; TRP, traditional rehabilitation procedures; VAS, visual analogue scale; VATD, video-assisted thoracoscopic decortication

infection, prolonged drain duration, and readmission within 30 days of surgery. The incidence rates of these

Table 4 Postoperative complications in each group

	TD + TRP *n* = 71	TD + ERAS *n* = 86	VATD + TRP *n* = 93	VATD + ERAS *n* = 110	*P*
Delayed wound healing (I)	0	2 (2.33%)	0	0	N/A
Reoperation (III)	0	1 (1.16%)	1 (1.08%)	0	N/A
Spread of tuberculosis (II)	0	0	1 (1.08%)	0	N/A
Pulmonary infection (II)	1 (1.41%)	0	0	0	N/A
Prolonged drain duration (I)	2 (2.82%)	0	1 (1.08%)	1 (0.91%)	N/A
Readmission within 30 days of surgery (II)	0	0	0	1 (0.91%)	N/A
Total	3 (4.2%)	3 (3.49%)	3 (3.23%)	2 (1.82%)	0.326

Data are presented as the frequency (percentage). *ERAS* Enhanced recovery after surgery, *TD* Thoracotomy decortication, *TRP* Traditional rehabilitation procedures, *VATD* Video-assisted thoracoscopic decortication

The complications were classified according to the Clavien-Dindo classification scale and documented with corresponding grades. However, due to the limited number of cases in each complication category, no statistically significant differences were observed between groups. Consequently, subgroup comparisons based on complication grades were not performed

complications in each group are presented in Table 4. There was no significant difference in the incidence of complications among the groups.

Discussion

In countries with a high tuberculosis burden, the average age of onset is under 40 years; this disease is therefore extremely harmful to the health of young people. *M. tuberculosis*is responsible for approximately 40% of all chest infections in China (Zhai 2016;, Xie 2017). Treatment of tuberculous empyema combines the management of empyema with antituberculosis therapy (Shaw 2019), making the treatment course of tuberculous empyema significantly longer than that of nontuberculous empyema (Subotic 2016;, Im 1995). Patients with stages I and II empyema undergo pleural space drainage followed by prolonged antituberculous therapy; however, a significant number develop stage III tuberculous empyema and require pleural decortication, which further extends treatment times (Fox 2016; Bretscher PA 2023; Skouras 2018). Therefore, ERAS measures have a considerable potential value for patients with stage III tuberculous empyema.

ERAS concepts were initially described in patients undergoing colonic surgery and have been subsequently applied to various surgical fields (Ljungqvist 2017). These measures have been fully adopted in lung and oesophageal surgery (Batchelor 2023), and their application in the surgical treatment of tuberculous empyema has also been explored (Luciani 2022). Video-assisted thoracoscopic surgery has been successful in lobectomy and radical oesophageal resection and is being increasingly used in surgery for tuberculous empyema (Tsai 2016;, Yeung 2019). However, the use of these applications remains to be standardised, and further research is required (Scarci 2015).

Unlike many other studies on ERAS, we did not use postoperative drainage time, first ambulation, and first feeding time (Pettit 2023;, Ljungqvist 2023) as outcomes, because we consider these indicators, which are determined by medical staff, more measures of ERAS than results. For example, the drainage tube can be removed when the daily drainage is 100 or 300 ml, and the patient can be instructed to get out of bed on days 1 or 3. In addition, we do not consider VATD a measure in ERAS because VATD is a surgical approach, whereas ERAS is a series of measures and concepts for rehabilitation optimisation around surgery. TD is necessary for certain patients with stage III tuberculous empyema. Therefore, our study considered the disease itself as the centre and studied the safety and effectiveness of VATD and ERAS as new treatment and rehabilitation methods developed in recent years.

In our medical centre, VATD and ERAS have been increasingly applied to the treatment of stage III tuberculous empyema over recent years. In this study, we analysed the therapeutic effects of four treatment modalities and the factors that influenced the LOS. We found that there were no significant differences between the groups in terms of postoperative complications. This confirmed that the safety of performing VATD surgery was comparable to that of performing TD surgery in patients with stage III tuberculous empyema. However, the operation duration of VATD was slightly longer than TD, which may be caused by the force and speed of the thoracoscopic instruments during the dissection of the pleural fiberboard during the VATD surgery were not as strong and fast as the hand dissection in the TD surgery. Nevertheless, the VATD surgery could enlarge the surgical

field on the screen, which made small bleeding easier to detect and control, so the amount of bleeding in the VATD groups were less. In addition, the total postoperative drainage volume of the VATD groups were significantly less than that of the TD groups, and this should be due to the fact that the treatment of pleural dissection wound during VATD is easier to be refined under the vision of thoracoscopy. At the same time, VATD was also significantly better than TD in reducing postoperative pain due to the smaller incision. However, VATD alone is not enough to shorten the length of stay. We see that VATD + TRP group has longer length of stay than TD + ERAS group, which indicates that ERAS is very helpful in shortening the length of stay. In terms of perioperative outcomes, we can clearly see that the implementation of ERAS measures can further reduce the pain level and ESR in the TD and VATD groups. In addition, in the VATD groups, the implementation of ERAS measures can further reduce postoperative drainage.

This study has the following limitations: First of all, there is no consensus on the surgical indications for VATD, so different enrollment criteria may have an impact on the results. In addition, different researchers and medical centres are limited by their hardware conditions or process cognition, so it is difficult to completely unify the content and quantity of ERAS items, so the connotation of ERAS group must be different, which will also have an impact on the results.

Conclusion

Implementation of VATD and ERAS procedures in patients with stage III tuberculous empyema can significantly reduce the LOS and improve patient outcomes in a safe and effective manner.

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No.

Authors' contributions
AJiakun Liu: Methodology, project administration, investigation, patient management, writing – review & editing. Yanchao Luan: Methodology, visualization, patient management. Qingsong Han: Investigation, data mining and analysis, validation. Wei Zhao: Conceptualization, supervision, project administration, writing – review & editing.

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Data Availability
No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate
The research protocol was established, according to the ethical guidelines of the Helsinki Declaration, and was approved by the Human Ethics Committee of the Ethics Committee of Hebei Chest Hospital. Written informed consent was obtained from individual or guardian participants.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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