

Recent advances in minimally invasive thoracic surgery

Edited by

Yojiro Yutaka and Calvin Sze Hang Ng

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Recent advances in minimally invasive thoracic surgery

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Editorial: Recent advances in minimally invasive thoracic surgery

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KEYWORDS

minimally invasive thoracic surgery, video assisted thoracic surgery (VATS), robot - assisted thoracic surgery, uniportal VATS (U-VATS), radiofrequency identification (RFID)

Editorial on the Research Topic

Recent advances in minimally invasive thoracic surgery

Introduction

Minimally invasive thoracic surgery (MITS) has drastically improved over the past three decades since the first report of video-assisted thoracoscopic surgery (VATS) by Lewis et al. in 1992 (1). Compared with traditional thoracotomy, VATS offers considerable benefits to patients by being less invasive, and it is globally used as a diagnostic and therapeutic tool for a variety of conditions within the chest cavity. The concept of less invasive surgery to greatly reduce the trauma of chest surgery and preserve lung volume led to the development of robotic-assisted thoracic surgery (RATS) or uniportal VATS, and evidence supporting the utility of sublobar resection for early-stage lung cancer has been established (2, 3). Further technological advances have made it possible to perform VATS or RATS *via* a single port. Compared with traditional thoracic procedures through thoracotomy, these MITS techniques are technically feasible, and they will undoubtedly offer considerable benefits to patients in the future. However, the surgeon must control these various techniques or instruments, and caution should be employed when introducing these novel techniques in appropriately selected patients with lung cancer to ensure long-term survival is not compromised. Therefore, further investigations are needed to understand the recent advances in MITS (4). In this section, we shared new insights into the latest techniques currently available in minimally invasive surgery, and the key limitations or aspects requiring improvement for the future were discussed.

Thanks to coworkers who contributed research topics regarding recent advances in MITS, 12 articles were collected in this edition: seven original studies, two review articles, and three case reports.

Ling Wang et al. reported postoperative diaphragmatic hernia following thoracoscopic sympathectomy for primary palmar hyperhidrosis. RATS has allowed surgeons to perform precise procedures with more flexibility during the operation with an enhanced 3D visualization system through smaller incisions compared with conventional open surgery and VATS. However, the visual field is rather limited by the enhanced magnification, and

careful attention should be paid to the possibility of injury to other organs outside the field of vision (5).

Two reviews compared RATS for esophagectomy and thymoma resection with conventional open approaches using meta-analysis, and RATS might be accepted when it is oncologically feasible. There is no established evidence from high-quality randomized controlled trials concerning the clinical difference between conventional approaches and RATS. We should obtain essential information regarding MITS beyond the feasibility of surgical techniques.

In this research topic, more advanced techniques using uniportal RATS were reported. [Edoardo Mercadante et al.](#) reported uniportal RATS lobectomy using three robotic arms of the da Vinci Xi system. The key to the successful introduction of this approach was to avoid potential fighting between the robotic arms. [Bo Yang et al.](#) reported an initial successful experience of single-port RATS for mediastinal tumors using the da Vinci SP system with a flexible double-jointed instrument that ensures that the lens does not conflict with the two Endowrists.

Both authors demonstrated the successful introduction of uniportal RATS through a smaller incision, although careful case selection and preoperative planning should be performed prior to these surgeries. In the near future, these approaches will become advantageous for surgeries requiring wide operative fields including esophagectomy and lung segmentectomy. However, for the standardization and global introduction of uniportal RATS, further technological advancements including the development of new staplers or suturing devices will be required, and additional clinical evidence should be established regarding long-term oncological outcomes from well-designed randomized trials of this technique.

Overall, these valuable contributions provided important information that could be helpful for the introduction of new technology in MITS. Because the methods reported in this topic, including our wireless localization techniques without lung palpation for small faint pulmonary lesions, are relatively new, additional studies in the future will likely improve the efficacy and safety of these techniques (6, 7). Although we should have an open mind regarding these innovative approaches, appropriate evaluation will be required for the introduction of new

techniques or technologies, and treatment should be tailored to each patient to optimize outcomes. The environments surrounding MITS will undergo further development by experienced surgeons. We hope that this supplemental issue of “Recent Advances in Minimally Invasive Thoracic Surgery” will broaden perspectives for thoracic surgeons aiming to improve patient outcomes.

Author contributions

All authors listed have made a substantial, direct, and intellectual contribution to the work and approved it for publication. All authors contributed to the article and approved the submitted version.

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Comparison of perioperative outcomes between robotic-assisted and video-assisted thoracoscopic surgery for mediastinal masses in patients with different body mass index ranges: A population-based study

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Background: The effectiveness of robotic-assisted thoracoscopic surgery (RATS) for mediastinal masses has not been fully evaluated. This study aimed to compare the perioperative outcomes between RATS and video-assisted thoracoscopic surgery (VATS) for mediastinal masses, and then explore which group of people would benefit more from RATS.

Methods: This retrospective study compared the perioperative outcomes of patients with mediastinal masses who underwent RATS and VATS from September 2018 to December 2021. Subgroup analysis were performed according to body mass index (BMI) ranges.

Results: A total of 212 patients with mediastinal masses (106 RATS cases and 106 VATS cases) were included. Compared with the VATS group, the RATS group had a significantly reduced incidence of overall postoperative complications (5.7% vs. 14.2%, $p = 0.039$), complications of grade II or less (3.8% vs. 12.3%, $p = 0.023$), and pneumonia (2.8% vs. 9.4%, $p = 0.045$). Hospitalization costs were significantly higher in the RATS group (¥ 49350.0 vs. ¥ 32551.9, $p < 0.001$). There was no significant difference in operation duration, intraoperative estimated blood loss, postoperative chest tube drainage volume, NRS pain score, day of chest tube removal, complications of grade III or more, or in-hospital mortality rate ($p > 0.05$). Subgroup analysis indicated that the incidence of overall postoperative complications (3.1% vs. 15.2%, $p = 0.017$), complications of grade II or less (1.5% vs. 12.1%, $p = 0.033$) and postoperative length of stay (4 days vs. 4.5 days, $p = 0.046$) were significantly reduced in the RATS group for overweight and obese patients ($BMI \geq 24 \text{ kg/m}^2$), while these differences became insignificant in the $BMI < 24 \text{ kg/m}^2$ subgroup.

Conclusion: RATS could reduce the incidence of postoperative complications, shorten the postoperative length of stay and might be a more cost-effective surgical treatment for overweight and obese patients with mediastinal masses.

KEYWORDS

mediastinal mass, robotic-assisted thoracoscopic surgery, perioperative outcome, body mass index, video-assisted thoracoscopic surgery

Introduction

Mediastinal masses comprise a heterogeneous group of tumors, including thymomas, neurogenic tumors, teratomas, bronchogenic cysts, and thyroid tumors (1). Mediastinal tumors are located in various positions of the mediastinum and account for approximately 3% of thoracic diseases (2). Radical surgical resection remains the gold standard for diagnosis, treatment and staging of the majority of these tumors (3–5). The small space and complex structure of the mediastinum, surrounded by large blood vessels and important organs such as the heart, make this type of surgery a great challenge for thoracic surgeons (6). With the development of minimally invasive techniques, video-assisted thoracoscopic surgery (VATS) has been widely applied for mediastinum masses resection with satisfactory outcomes compared with traditional thoracotomy (7). As an emerging minimally invasive technique, robotic-assisted thoracoscopic surgery (RATS) has gradually become a prevalent surgical method for patients with mediastinal masses.

Since the first robotic-assisted thymectomy was reported by Yoshino et al. in 2001 (8), RATS has become increasingly used for the surgical treatment of mediastinal masses (9, 10). Compared with VATS, robotic-assisted systems can provide surgeons with many advantages, including naked eye three-dimensional (3D) imaging with 10–15 times magnification, 360° rotating mechanical arms with a reduction in hand-related tremors and better maneuverability, improved dexterity, and greater comfort (11). Although there has been a recent increase in the popularity and research on RATS, its effectiveness in mediastinal surgery remains controversial (12, 13). The majority of published studies comparing minimally invasive surgeries for mediastinal mass resection were performed mainly in small cohort and focused only on the treatment of thymoma or anterior mediastinal masses, providing limited evidence to determine which one is a more beneficial surgical approach. In addition, few studies have compared the efficacy of RATS and VATS in the treatment of mediastinal masses in different mediastinal locations. Currently, it is still controversial which minimally invasive approach is superior for the surgical treatment of mediastinal tumors.

The aim of this study was to compare the perioperative outcomes of patients with mediastinal masses who underwent RATS and VATS, and then determine which group of people would benefit more from RATS.

Patients and methods

This retrospective study was approved by the institutional review board of the Qilu Hospital of Shandong University (registration number: KYLL-2020027), and all patients

provided informed consent for the use of their clinical information.

Patient selection

A prospectively maintained departmental database of Qilu Hospital of Shandong University was retrieved for patients who underwent a RATS or VATS for mediastinal mass from September 2018 to December 2021. The inclusion criteria were patients aged ≥ 18 years old who underwent mediastinal mass resection with detailed medical records. The exclusion criteria were: (I) patients aged < 18 years old; (II) pulmonary resection with mediastinal mass resection; (III) thoracotomy; (IV) thymic cancer or thymoma with Masaoka-Koga stage greater than II; (V) patients with a history of myasthenia gravis or thoracic surgery; and (VI) incomplete perioperative data.

Data collection and variable definitions

The following clinical data of enrolled patients were collected from the database of Qilu Hospital: age, sex, smoking history, body mass index (BMI), percentage of predicted value for forced expiratory volume in 1 s (FEV1% predicted), American Society of Anesthesiologists (ASA) score, operative approach (RATS or VATS), tumor location, operation duration, intraoperative estimated blood loss, postoperative drainage volume, day of chest tube removal, postoperative Numerical Rating Scale (NRS) pain score, postoperative complications, postoperative length of stay (POS), total cost of hospitalization, and pathological information. The choice of surgical approach mainly depends on the patients' acceptance of RATS. Based on good preoperative communication with the patients, the patients chose the surgical method independently. Tumor location was determined based on the three-division method of the mediastinum, and tumor size was defined as the maximum tumor diameter. Postoperative complications were classified according to the Clavien–Dindo classification, including pneumonia, chylothorax and arrhythmia. The volume of postoperative drainage was recorded by the nurse at 6:00 am every day after the operation. The NRS pain score was evaluated by the nurse at 24, 48, and 72 h after surgery and was defined as the postoperative day (POD) 1, 2, and 3 NRS score.

Operative procedures

All of the surgeries were performed by 3 qualified surgeons in a single operation group. The patients in both groups

underwent intravenous inhalation combined with anesthesia, and single-lumen tracheal intubation and occluder were used for single-lung ventilation. The patients with anterior mediastinal tumors were placed in a 30-degree semi-supine position with the ipsilateral axilla exposed, while lateral prone position was applied for patients with middle and posterior mediastinal tumors to reduce the interference of lung tissue. Right or left approach was selected according to the location of the tumor body, and right approach was mostly used for tumors located in the middle. VATS was performed using standard thoracoscopic techniques with two conventional incision operations for anterior mediastinal masses: one 3 cm auxiliary operative incision at the 2nd or 3rd intercostal space (ICS) on the anterior axillary line, and one camera port at the 5th ICS mid-axillary line. While uniport VATS was performed for middle and posterior mediastinal masses, and the port was set at the 5th ICS between the mid-axillary line and posterior axillary line. RATS was performed using the fourth-generation Da Vinci surgical system with a three-port approach. For patients whose tumor was located in the front mediastinum, the camera port was selected at the 5th ICS on the anterior axillary line, and two mechanical arm ports were set at the 5th ICS on the midclavicular line and approximately 2 cm posterior to the 6th ICS on the posterior axillary line, respectively. For those with tumors at the middle and posterior mediastinum, the camera port was selected at the 5th ICS on the anterior axillary line, and two mechanical arm ports were set at the 3th ICS on the anterior axillary line and the 7th ICS on the posterior axillary line, respectively. The position of the auxiliary operative incision was located at the

5th ICS between the anterior axillary line and mid-axillary line, and the interval between the three mechanical arms was approximately 6–8 cm. The incisions and ports placement of RATS and VATS are shown in [Figure 1](#). The lesion resection was only performed if thymic cysts, lymphatic cysts, teratoma with intact capsule or other benign tumors were identified during the operation, and thymic tumors resection and total thymectomy were performed for patients whose preoperative clinical diagnosis did not exclude thymoma. One or two chest tubes were placed after the operation depending on surgeon performance.

Postoperative management

All patients received postoperative analgesia with an analgesic pump, and the intravenous use of nonsteroidal anti-inflammatory drugs 3 times a day was applied for pain relief. The chest tube could be removed if there was no pneumonia, subcutaneous emphysema or pneumothorax with daily drainage less than 200 ml. All patients in this study were managed using an enhanced recovery after surgery program.

Statistical analysis

Categorical variables were compared using the Pearson chi-squared test or Fisher's exact test. Normally distributed continuous variables are presented as the mean \pm standard deviation (SD), and Student's *t* test was used for comparisons.

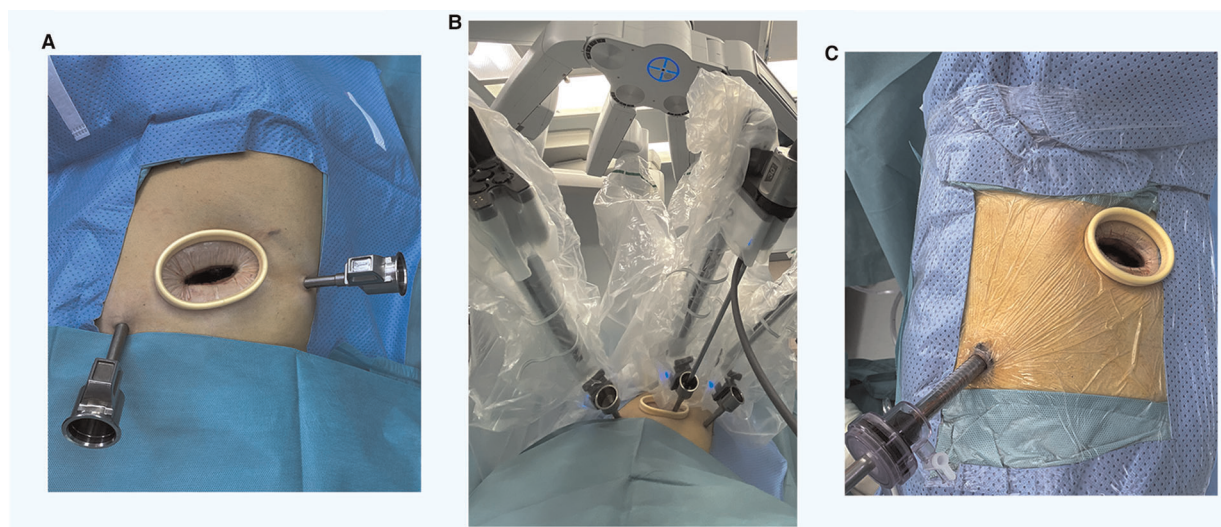


FIGURE 1

The incisions and ports placement of RATS (A,B) and VATS (C). RATS, robotic-assisted thoracoscopic surgery; VATS, video-assisted thoracoscopic surgery.

For continuous variables that were not normally distributed, data are presented as the median (interquartile range [IQR]) and were compared by the Mann-Whitney U test between the groups. The test level between the 2 groups was set at $\alpha = 0.05$ (bilateral), and a two-sided $p < 0.05$ was considered statistically significant. Subgroup analyses were performed for the perioperative outcomes according to BMI ranges. SPSS software v25.0 (SPSS Inc., Chicago, IL, USA) was used for further data analysis.

Results

Patient characteristics

Ultimately, a total of 212 patients with mediastinal masses (106 RATS patients and 106 VATS patients) were included for analysis in this study. The characteristics of the patients are presented in **Table 1**. Benign cyst (43.4%) was the most common histology followed by thymoma (25.9%), neurogenic tumor (12.3%), teratoma (6.1%), and thymic hyperplasia (4.2%). The patients who underwent VATS and RATS were comparable in age, sex, BMI, smoking history, FEV1% predicted, ASA score, mediastinal location, pathological type, and tumor size ($p > 0.05$).

Perioperative outcomes

A comparison of the perioperative outcomes of the patients who underwent RATS or VATS is presented in **Table 2**. The incidence of overall postoperative complications (5.7% vs. 14.2%, $p = 0.039$), complications of grade II or less (3.8% vs. 12.3%, $p = 0.023$), and pneumonia (2.8% vs. 9.4%, $p = 0.045$) were significantly decreased in the RATS group. And hospitalization cost [¥ 49350.0 (IQR, 47938.7–51681.9) vs. ¥ 32551.9 (IQR, 29971.5–35555.3), $p < 0.001$] were significantly increased in the RATS group. However, there were no significant differences in operation duration operation duration [75 min (IQR, 60–95) vs. 75 min (IQR, 60–90), $p = 0.329$], intraoperative estimated blood loss [55 ml (IQR, 45–70) vs. 60 ml (IQR, 50–70), $p = 0.113$], the drainage volume on POD 1 [120 ml (IQR, 70–200) vs. 100 ml (IQR, 60–200), $p = 0.117$] and POD 2 [152.5 ml (IQR, 100–232.5) vs. 120 ml (IQR, 80–200), $p = 0.086$], NRS pain score on POD 1 [3 (IQR, 3–3) vs. 3 (IQR, 3–3), $p = 0.088$] and POD 2 [3 (IQR, 3–3) vs. 3 (IQR, 3–3), $p = 0.690$], day of chest tube removal [3 days (IQR, 3–4) vs. 3 days (IQR, 3–4), $p = 0.533$], POS [4 days (IQR, 3–5) vs. 4.5 days (IQR, 3–6), $p = 0.062$], complications of grade III or more (1.9% vs. 1.9%, $p = 1.000$), incidence of chylothorax (1.9% vs. 3.8%, $p = 0.683$) and arrhythmia (0.9% vs. 1.9%, $p = 1.000$), or in-hospital mortality rate (0.9% vs. 0, $p =$

TABLE 1 Clinicopathological characteristics of patients with mediastinal masses.

Characteristics	VATS (<i>n</i> = 106)	RATS (<i>n</i> = 106)	<i>p</i>
Age (years), median (IQR)	48 (39.75–56)	46 (33.75–57)	0.127
Sex, <i>n</i> (%)			1.000
Female	45 (42.5)	45 (42.5)	
Male	61 (57.5)	61 (57.5)	
BMI (kg/m ²), median (IQR)	25.0 (22.5–27.4)	24.8 (22.9–26.9)	0.969
Smoking history, <i>n</i> (%)			0.730
Non-smoker	86 (81.1)	84 (79.2)	
Smoker	20 (18.9)	22 (20.8)	
FEV1% predicted, median (IQR)	99.9 (92.8–107.9)	100.4 (91.7–107.0)	0.909
ASA score, <i>n</i> (%)			0.571
I	26 (24.5)	28 (26.4)	
II	78 (73.6)	78 (73.6)	
III	2 (1.9)	0	
Mediastinal location, <i>n</i> (%)			0.388
Anterior	80 (75.5)	88 (83.0)	
Middle	4 (3.8)	3 (2.8)	
Posterior	22 (20.8)	15 (14.2)	
Pathological type, <i>n</i> (%)			0.479
Thymoma	23 (21.7)	32 (30.2)	
Thymic hyperplasia	5 (4.7)	4 (3.8)	
Benign cyst	53 (50.0)	39 (36.8)	
Neurogenic tumor	12 (11.3)	14 (13.2)	
Teratoma	6 (5.7)	7 (6.6)	
Other	7 (6.6)	10 (9.4)	
Tumor size (cm), median (IQR)	5.0 (3.5–7.0)	4.9 (3.5–6.3)	0.225

IQR, interquartile range; *RATS*, robotic-assisted thoracoscopic surgery; *VATS*, video-assisted thoracoscopic surgery; *BMI*, body mass index; *FEV1% predicted*, percentage of predicted value for forced expiratory volume in 1 s; *ASA*, American Society of Anesthesiologists.

1.000). There was no readmission and conversion to thoracotomy in either group.

Subgroup analysis

To explore which group of people would benefit more from RATS, a subgroup analysis was performed for the perioperative outcomes according to BMI ranges. The patients were divided into 2 groups based on their BMI: BMI < 24 kg/m² and BMI ≥ 24 kg/m², and the subgroup comparisons of perioperative outcomes between the RATS and VATS groups are presented in **Table 3**. Interestingly, we found that the incidence of overall postoperative complications (3.1% vs. 15.2%, $p = 0.017$), complications of grade II or less (1.5% vs. 12.1%, $p = 0.033$) and POS [4 days (IQR, 3–5) vs. 4.5 days (IQR, 4–6), $p = 0.046$] were significantly reduced in the RATS

TABLE 2 Perioperative outcomes of VATS and RATS for mediastinal masses.

Perioperative outcomes	RATS (<i>n</i> = 106)	VATS (<i>n</i> = 106)	<i>p</i>
Operation duration (min), median (IQR)	75 (60–95)	75 (60–90)	0.329
Estimated blood loss (ml), median (IQR)	55 (45–70)	60 (50–70)	0.113
Conversion to thoracotomy, <i>n</i> (%)	0	0	
Chest tube drainage (ml), median (IQR)			
POD 1	120 (70–200)	100 (60–200)	0.117
POD 2	152.5 (100–232.5)	120 (80–200)	0.086
Chest tube removal (d), median (IQR)	3 (3–4)	3 (3–4)	0.533
NRS score, median (IQR)			
POD 1	3 (3–3)	3 (3–3)	0.088
POD 2	3 (3–3)	3 (3–3)	0.690
Postoperative complications, <i>n</i> (%)	6 (5.7)	15 (14.2)	0.039
Severity grade of complications, <i>n</i> (%)			
Clavien-Dindo ≤ II	4 (3.8)	13 (12.3)	0.023
Clavien-Dindo ≥ III	2 (1.9)	2 (1.9)	1.000
Frequent complications, <i>n</i> (%)			
Pneumonia	3 (2.8)	10 (9.4)	0.045
Chylothorax	2 (1.9)	4 (3.8)	0.683
Arrhythmia	1 (0.9)	2 (1.9)	1.000
In-hospital mortality, <i>n</i> (%)	1 (0.9)	0	1.000
Readmission, <i>n</i> (%)	0	0	
POS (d), median (IQR)	4 (3–5)	4.5 (3–6)	0.062
Hospitalization cost (¥), median (IQR)	49350.0 (47938.7–51681.9)	32551.9 (29971.5–35555.3)	<0.001

NRS, numerical rating scale; *POD*, postoperative day; *POS*, postoperative length of stay; *IQR*, interquartile range; *RATS*, robotic-assisted thoracoscopic surgery; *VATS*, video-assisted thoracoscopic surgery.
P values less than 0.05 are bolded.

group for overweight and obese patients ($\text{BMI} \geq 24 \text{ kg/m}^2$), while these differences became insignificant in the $\text{BMI} < 24 \text{ kg/m}^2$ subgroup. There was no significant difference in operation duration, intraoperative estimated blood loss, postoperative chest tube drainage volume, NRS pain score, day of chest tube removal, complications of grade III or more, or in-hospital mortality rate ($p > 0.05$).

Discussion

In recent years, there has been a remarkable increase in the popularity of RATS, but its role and potential advantages as a surgical treatment for mediastinal masses have not been well illustrated. This retrospective study compared the

perioperative outcomes between RATS and VATS for mediastinal masses, and aimed to explore which group of people would benefit more from RATS. We have performed subgroup analyses according to age, BMI and tumor location, and found that the advantages of RATS might be more obvious in overweight and obese people. The results of our study indicated that RATS might have potential advantages compared with VATS in terms of reducing the incidence of postoperative complications and shortening POS for overweight and obese patients with mediastinal masses, while RATS and VATS have comparable perioperative outcomes in patients with a BMI less than 24 kg/m^2 . It is the first study to explore the advantages and disadvantages of RATS for patients with mediastinal masses in different BMI ranges.

Mediastinal masses are mainly treated by surgical resection in clinical practice, and some patients require adjuvant postoperative radiotherapy and chemotherapy (14). At present, VATS is the mainstream surgical method for mediastinal tumors. The incision of VATS is small and located in the intercostal space, which well protects the bony thorax and reduces the damage to the body to a certain extent (4, 7). RATS, as an emerging minimally invasive surgical approach, has become increasingly used for the surgical treatment of mediastinal masses with good clinical efficacy and safety since the first application reported by Yoshino et al. in 2001 (8, 9). The naked 3D visualization and better maneuverability provided by the surgical robotic system allow the surgeons to dissect the tissues, vessels and nerves surrounding the tumor more clearly. In addition, RATS has revealed unique superiority over VATS while dealing with locally invasive diseases and tumors in narrow space (15).

Several studies have been conducted to compare the safety and efficacy of RATS and VATS as surgical treatments for mediastinal masses. Zeng et al. conducted a retrospective study to identify the feasibility of RATS compared with VATS in the resection of mediastinal lesions (16). The results showed that RATS had non-inferior postoperative outcomes and better intraoperative safety with a lower incidence rate of unplanned thoracotomy than the VATS approach. Christine et al. retrospectively compared the outcomes of mediastinal tumor resection with RATS and VATS, and found that RATS resection was associated with fewer conversion, fewer positive margins, shorter length of stay and less composite adverse events (17). In this study, we found that RATS might provide better safety due to a significantly reduced incidence of postoperative complications. However, total hospitalization costs with RATS were significantly higher than those with VATS. Therefore, it is necessary to consider cost performance when choosing RATS as an alternative surgical treatment for mediastinal masses.

A highlight of this study is the comparison of perioperative outcomes between RATS and VATS in patients with different BMI ranges, aiming at exploring which group of people would benefit more from RATS. The results of subgroup analysis

TABLE 3 Perioperative outcomes of VATS and RATS for mediastinal masses in patients with different BMI ranges.

Characteristics	BMI < 24 kg/m ²			BMI ≥ 24 kg/m ²		
	RATS (n = 41)	VATS (n = 40)	p	RATS (n = 65)	VATS (n = 66)	p
Operation duration (min), median (IQR)	65 (60–90)	75 (60–90)	0.490	85 (65–100)	75 (60–90)	0.068
Estimated blood loss (ml), median (IQR)	50 (40–67.5)	57.5 (50–75)	0.144	55 (45–70)	60 (50–70)	0.395
Chest tube drainage (ml), median (IQR)						
POD 1	120 (80–215)	100 (42.5–200)	0.244	120 (65–200)	120 (60–195)	0.273
POD 2	160 (80–260)	115 (62.5–175)	0.060	150 (100–220)	160 (100–200)	0.542
Chest tube removal (d), median (IQR)	3 (3–4)	3 (2–4)	0.455	3 (3–4)	3.5 (3–4)	0.153
NRS score, median (IQR)						
POD 1	3 (3–3)	3 (3–3)	0.060	3 (3–3)	3 (3–3)	0.446
POD 2	3 (3–3)	3 (3–3)	0.750	3 (3–3)	3 (3–3)	0.441
Postoperative complications, n (%)	4 (9.8)	5 (12.5)	0.737	2 (3.1)	10 (15.2)	0.017
Severity grade of complications, n (%)						
Clavien-Dindo ≤ II	3 (7.3)	5 (12.5)	0.482	1 (1.5)	8 (12.1)	0.033
Clavien-Dindo ≥ III	1 (2.4)	0	1.000	1 (1.5)	2 (3.0)	1.000
Frequent complications, n (%)						
Pneumonia	2 (4.9)	5 (12.5)	0.264	1 (1.5)	5 (7.6)	0.208
Chylothorax	2 (4.9)	0	0.494	0	4 (6.1)	0.119
Arrhythmia	0	0		1 (1.5)	2 (3.0)	1.000
In-hospital mortality, n (%)	0	0		1 (1.0)	0	0.496
POS (d), median (IQR)	4 (3.5–5)	4.5 (3–6)	0.641	4 (3–5)	4.5 (4–6)	0.046
Hospitalization cost (¥), median (IQR)	49938.1 (47979.6–52752.0)	32501.0 (30019.8–35653.0)	<0.001	49191.1 (47841.9–50685.5)	32594.6 (29806.6–35458.8)	<0.001

BMI, body mass index; NRS, numerical rating scale; POD, postoperative day; POS, postoperative length of stay; IQR, interquartile range; RATS, robotic-assisted thoracoscopic surgery; VATS, video-assisted thoracoscopic surgery.
P values less than 0.05 are bolded.

demonstrated that the incidence of postoperative complications and POS was significantly reduced in the RATS group for overweight and obese patients (BMI ≥ 24 kg/m²). However, for patients with BMI < 24 kg/m², RATS did not achieve better perioperative outcomes than VATS but had a significantly increased expense, indicating it might be not cost-effective to select RATS for these patients with mediastinal masses. In recent years, there was a significant increase in the number of obese and overweight patients with mediastinal tumors. Thoracic surgeons would encounter great challenges when operating on overweight and obese patients due to increased internal fat, limited movements of instruments, deeper thoracic cavity and their well-known poor outcomes (18). In this study, we found that RAL might achieve better perioperative outcomes for overweight and obese patients, and RATS might be a more beneficial surgical treatment for overweight and obese patients with mediastinal masses.

This study has several limitations that should be considered. First, the single-center retrospective nature of this study makes it less persuasive than a multicenter prospective randomized controlled trial. Second, some outcomes, such as intraoperative estimated blood loss, and operative duration, are closely related not only to the surgical approaches but also

to the performance of the surgeon. It is difficult to untangle the effects of the two on the outcomes. Third, the fourth-generation DaVinci robot surgical system is typically applied for RATS, thus further investigation is needed to determine whether our results can be generalized to other centers where other robotic systems may be more common. Finally, the long-term prognostic outcomes were not compared because the follow-up period has not been reached, which need to be further investigated in future studies.

Conclusion

RATS could reduce the incidence of postoperative complications, shorten the postoperative length of stay and might be a more cost-effective surgical treatment for overweight and obese patients with mediastinal masses.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

Ethics statement

The studies involving human participants were reviewed and approved by The Ethical Committee of the Qilu Hospital of Shandong University. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Study design: HT, RL and ZM. Data collection: RL and JQ. Data analysis: RL, ZM and CQ. Drafting the manuscript: RL and KW. Project supervision: HT and WY. All authors contributed to the article and approved the submitted version.

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A universal incision for robot-assisted thoracic surgery

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Objective: This paper aimed to design and explore the versatility of the incision for the robot-assisted thoracic surgery.

Methods: The concept of universal incision was designed and put forward. The clinical data of 342 cases of robot-assisted thoracic surgery were summarized, including sex, age, clinical diagnosis, operative method, operative time, conversion to thoracotomy, intraoperative blood loss, number of lymph node dissections, postoperative hospital stays, postoperative pathology, and postoperative complications of the patients.

Results: The 342 cases of robot-assisted surgery included 178 pulmonary surgery cases (94 lobectomy cases, 75 segmentectomy cases, 6 wedge resection cases, and 3 sleeve lobectomy cases), 112 esophageal surgery cases (107 McKeown approach cases and 5 esophageal leiomyoma resection cases), and 52 mediastinal tumor cases (42 anterior mediastinum cases and 10 posterior mediastinum cases). Among these, two cases were converted to thoracotomy (both esophageal cases), and the rest were successful with no massive intraoperative bleeding and no perioperative death.

Conclusion: The universal incision of robot-assisted thoracic surgery is safe and feasible and is suitable for most cases of thoracic surgery.

KEYWORDS

robot-assisted, minimally invasive thoracic surgery, lobectomy, segmentectomy, esophagectomy, mediastinal mass

Introduction

At the end of the last century, the extensive development of thoracoscopic surgery brought thoracic surgery into the era of minimally invasive surgery. In the last 10 years, robot-assisted thoracic surgery (RATS) has developed rapidly. The Da Vinci Surgical System, which specializes in fine operations such as a high-definition, three-dimensional view, and articulating EndoWrist instruments, has made up for the deficiency of thoracoscopic surgery (1, 2). However, the selection of the incisions for RATS is diverse and has not been unified. Since the Da Vinci Si Robot Surgical System was installed in our hospital in 2016, more than 300 robot-assisted thoracic surgeries have been completed, and some preliminary experience has been accumulated. Currently, a retrospective analysis and summary are made on the case data of robot-assisted surgery in the thoracic surgery department of our hospital to explore the universal incision of RATS.

Research methods

General clinical data

The clinical data of 342 patients undergoing RATS in the Thoracic Surgery Department of the First Affiliated Hospital of Chongqing Medical University and the First Affiliated Hospital of Zhengzhou University from April 2016 to September 2021 were analyzed, including sex, age, clinical diagnosis, operation method, operation time, transfer to thoracotomy, intraoperative blood loss, number of lymph node dissections, and postoperative complications.

Postoperative complications mainly included active thoracic bleeding, pulmonary infection, atelectasis, chylothorax, thoracic infection, wound healing, esophagogastric anastomotic fistula, diaphragmatic hernia, and recurrent laryngeal nerve palsy.

Surgical methods

Surgical position and anesthesia intubation

The patient was placed in the lateral decubitus position, and single-lung anesthesia was administered *via* double-lumen endotracheal intubation (for pulmonary surgery) or single-lumen endotracheal intubation and artificial pneumothorax with a CO₂ pressure of 8 mmHg (for esophagus and mediastinal tumor surgery). Abdominal and neck operations for patients with esophageal cancer were performed through the McKeown approach, with the patients' head tilted to the right side with high shoulder pads.

Incision selection

Four-port incisions were made at the positions indicated in [Figure 1](#). A 10 mm port in the sixth intercostal space (ICS) in the midaxillary line was placed as the camera port. The other two incisions were placed at the midaxillary axillary line in the third ICS for the first robotic arm and at the subscapular line in the ninth ICS for the second robotic arm. The assistant port (12 mm trocar for esophagus and mediastinum tumor surgery or extended to a 3-cm incision for pulmonary surgery) was placed at the anterior axillary line in the fourth ICS. These incisions were standard and suitable for all thoracic surgeries, except for the tumor in the anterior mediastinum. When the tumor was located in the anterior mediastinum, the incisions for the second robotic arm were placed at the anterior axillary line in the sixth ICS, and the assistant port was placed at the posterior axillary line in the eighth ICS.

Abdominal incisions for the patients with esophageal cancer undergoing the McKeown approach: the first, second, and third arms were selected for abdominal operation. The incisions were as follows: the camera port was placed above the level of the umbilicus (12 mm trocar); the incisions for the first/third



FIGURE 1

Port placement for the Da Vinci Si System using three robotic arms (thoracic cavity). C, camera port; A, assistant port; F, first robotic arm; S, second robotic arm.

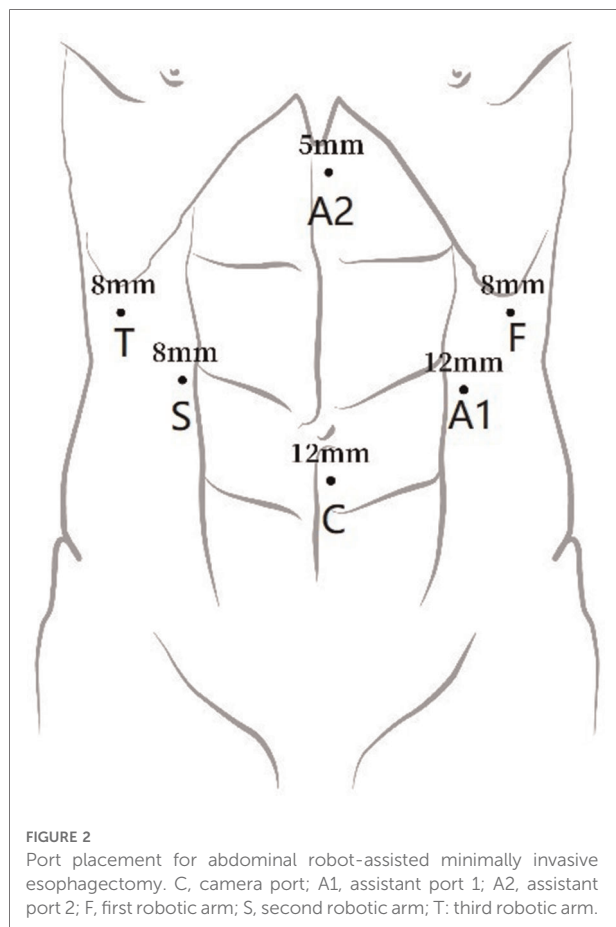
robotic arm were selected at the left/right middle clavicular line and at the left/right costal margins; and the incisions for the second robotic arm were placed at the right midclavicular line and at the umbilical level. Two other 8-mm assistant incisions were then placed as follows: each at the left middle clavicular line and at the midclavicular umbilical level and another below the xiphoid process, as shown in [Figure 2](#).

Device selection

The Da Vinci Si Robot Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) was brought into the field, coming over the patient's head. In the thoracic operation, we used robotic instruments as follows: the first robotic arm was used for the permanent cautery hook and the second robotic arm was used for the fenestrated bipolar forceps. When the left and right recurrent laryngeal nerve chain lymph nodes were dissected in esophageal surgery, the first robotic arm could be temporarily replaced by Maryland bipolar forceps. For the abdominal part of esophageal surgery, we used robotic instruments as follows: the first robotic arm Harmonic ACE was used for the curved shears, the second robotic arm was used for the fenestrated bipolar forceps, and the third robotic arm was used for the Cadiere forceps (mainly used to expose the liver).

Surgical methods

Lobectomy and segmentectomy: All patients underwent single-direction thoracoscopic anatomic pulmonary surgery as reported ([3](#), [4](#)). Systemic mediastinal lymph node dissection was performed for patients with invasive lung cancer (Station



5, 6, 7, 8, and 9 lymph nodes for left lung cancer and Station 2, 4, 7, 8, and 9 lymph nodes for right lung cancer).

Esophagectomy: All patients underwent the traditional McKeown approach, which includes thoracic esophageal dissection, abdominal mobilization of the gastric conduit, and cervical anastomosis (5). Lymph nodes of the left and right recurrent laryngeal nerve chains were dissected during the operation.

Mediastinal tumor resection: The tumor was removed completely along its outer membrane.

Statistical methods

The SPSS 22.0 statistical software package was used for statistical analysis. Clinical and pathological characteristics were described as the mean \pm standard deviation for continuous variables and frequencies (%) for categorical variables.

Results

General Information

The 342 robot-assisted surgeries included 178 pulmonary surgery cases (94 lobectomy cases, 75 segmentectomy cases, 6

wedge resection cases, and 3 sleeve lobectomy cases), 112 esophageal surgery cases (107 McKeown approach cases and 5 esophageal leiomyoma resection cases), and 52 mediastinal tumor cases (42 anterior mediastinum cases and 10 posterior mediastinum cases). The general information is detailed in [Table 1](#).

Perioperative data

The average docking time of the 342 patients experiencing robot-assisted surgeries was 7.7 ± 3.3 min, with 2 patients transferred to thoracotomy (both esophageal cases) and the rest successfully completed with no intraoperative massive bleeding. The mean numbers of harvested lymph nodes in the pulmonary group and esophageal group were 15.5 ± 4.9 and 25.3 ± 6.5 , respectively. The mean days of postoperative hospital stay in the pulmonary group, esophagus group, and mediastinum group were 6 ± 3 , 16 ± 9 , and 5 ± 2 , respectively. Pneumonia occurred in nine patients (three pulmonary cases and six esophagus cases), who were treated with antibiotics. Rib fracture occurred in three patients (three pulmonary cases). Six patients experienced an anastomotic leak, and vocal cord palsy was found in ten patients in the esophageal group, who recovered after conservative treatment. There was no perioperative death. This is detailed in [Table 2](#).

Discussion

Since the 1990s, thoracoscopic technology has been widely used and developed in thoracic surgery. Thoracoscopic

TABLE 1 The general characteristics of 342 patients.

	Pulmonary	Esophagus	Mediastinum
Cases	178	112	52
Gender (male/female)	85/93	72/40	29/23
Age	59	62	49
Lesion location			
Right upper lung	68	Esophageal cancer 107	Anterior mediastinum 42
Right middle lung	16		Posterior mediastinum 10
Right lower lung	32	Esophageal leiomyoma 5	
Left upper lung	27		
Left lower lung	35		
Surgery types		McKeown approach 107	
Lobectomy	94		
Segmentectomy	75	Leiomyoma resection 5	
Wedge resection	6		
Sleeve lobectomy	3		

TABLE 2 Perioperative outcome.

	Pulmonary	Esophagus	Mediastinum
Docking time (min)	6.8 ± 4.9	7.7 ± 3.3	7.9 ± 4.3
Operation time (min)	Lobectomy 162 ± 59 Segmentectomy 194 ± 53 Wedge resection 69 ± 14 Sleeve lobectomy 212 ± 31	Esophageal cancer 391 ± 108 Robot console time 213 ± 98 Esophageal leiomyoma 142 ± 32	Anterior mediastinum 112 ± 78 Posterior mediastinum 82 ± 47
LN stations dissected	5.76 ± 2.23	12.2 ± 3.2	
Number of LNs			
Total LNs	15.5 ± 4.9	25.3 ± 6.5	
RRLN LNs	—	3.1 ± 1.9	
LRLN LNs	—	3.9 ± 2.3	
Thoracotomy conversions	0	2	0
Lung infection	3	6	
Vocal cord palsy	0	10	
Respiratory failure	0	3	0
Anastomotic fistula	/	6	—
Postoperative hospital stays (days)	6 ± 3	16 ± 9	5 ± 2
Tumor type	139 (78.1%)	3 (2.8%)	0
Adenocarcinoma	12 (6.7%)	103 (92.0%)	25 (59.5%)
Squamous cell carcinoma	27 (15.2%)	6 (5.2%)	
Other	Lung cancer (163)	Esophageal cancer (107)	17 (40.5%) /
Pathology T stage			
Tis	62 (38.0%)	3 (2.8%)	
T1	68 (41.7%)	36 (33.6%)	
T2	19 (11.7%)	43 (40.2%)	
T3	12 (7.4%)	22 (20.6%)	
T4	2 (1.2%)	3 (2.8%)	

LN, lymph nodes; LRLN, left recurrent laryngeal nerve; RRLN, right recurrent laryngeal nerve; Tis, tumor *in situ*.

surgery inevitably has its own limitations, such as limited visual information with two dimensions, restricted maneuverability of instruments, and an unsteady camera platform. The Da Vinci Surgical System (Intuitive Surgical, Sunnyvale, CA, USA) has revolutionized minimally invasive surgery by offering a more minimally invasive and precise approach to surgery (6). The Da Vinci Surgical System is composed of three parts: a surgeon control platform, a patient cart, and a three-dimensional view high-definition video cart. RATS approaches can be performed with a complete portal [described as robotic portal (RP) operation] or with the assistance of an access or utility incision [described as robotic-assisted (RA) operation] (7). There were different operative approaches between the RA and the RP operations. RA operations are usually a continuum from video-assisted thoracic surgery (VATS) to RATS for most surgeons. Additionally, either three or four robotic arms were used to perform RATS. Although a few surgeons used a completely port-based approach (RP operation: four robotic arms and no assistant port/incision)

with the closed chest insufflated with CO₂, RA operations with three robotic arms were more popularly used in RATS. In this article, all thoracic surgeries were performed through RA operations with three robotic arms, and a universal incision was also designed under this background, which may not be suitable for RP operations.

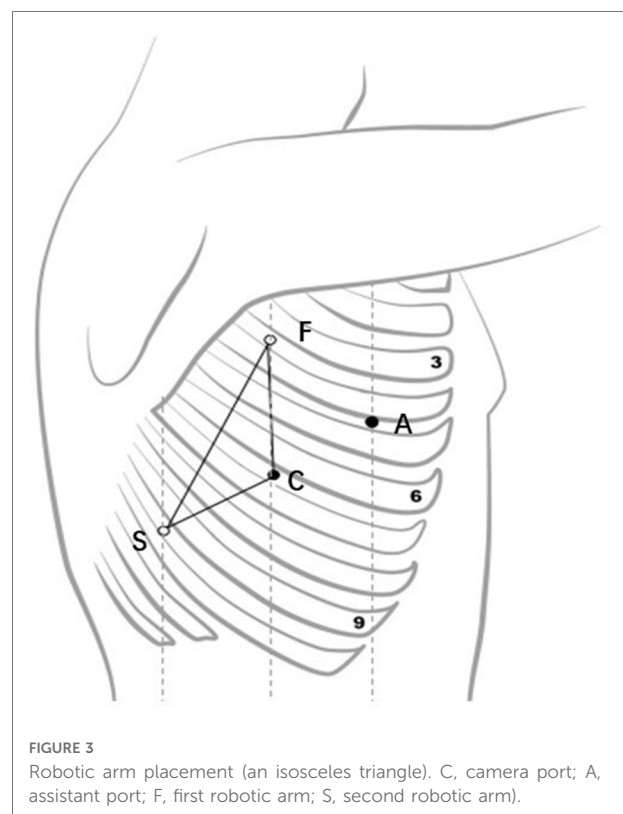
The selection of robot-assisted surgical incision should follow certain principles, which could ensure that the instruments are flexible in the thoracic cavity during the surgery and do not interfere with one another. The general principle of surgical incision selection is that the distance between the camera port and the incisions for the first robotic arm and the second robotic arm should be more than 8 cm. The triangle target principle for the placement of trocars during VATS was first named by Sasaki et al. (7), and these principles should be followed during RATS. According to our experience, the incision for the camera port, which serves as the vertex of the isosceles triangle, and its connection with the incisions for the first and

TABLE 3 A brief summary of the incisions for robot-assisted thoracic surgery.

	Camera port	The first robotic arm	The second robotic arm	The assistant port	The third robotic arm
Pulmonary					
Veronesi et al. (6)	7th ICS, MAL	4th ICS, AAL	8th ICS, PAL	—	7th ICS, ISL
Pardolesi et al. (16)	7th/8th ICS, MAL	8th ICS, PAL	Posteriorly in the AT	4th/5th ICS, AAL	—
Zhao et al. (22)	8th ICS, MAL	7th ICS, PAL	5th ICS, AAL	9th/10th ICS, PAL	—
Li et al. (14)	8th ICS, PAL	7th ICS, MAL	9th ICS, ISL	4th ICS, AAL	—
Esophageal surgery					
Kim et al. (13)	8th ICS, ISL	10th ICS, ISL	6th ICS, PAL	7th ICS, MAL	—
Kingma et al. (10)	6th ICS between PAL and SL	10th ICS	8th ICS between PAL and ISL	5th ICS, PAL	4th ICS between PAL and ISL
Anterior mediastinum Surgery					
Augustin et al. (8)	5th ICS, AAL	3rd ICS, AAL	5th ICS, MCL	5th ICS, MAL	—
Kamel et al. (12)	6th ICS, PAL	3rd ICS, AAL	5th ICS, AAL	—	—

ICS, intercostal space; AAL, anterior axillary line; MAL, midaxillary line; PAL, posterior axillary line; MCL, midclavicular line; ISL, infrascapular line; AT, auscultatory triangle.

second robotic arms form an isosceles triangle. The selection for the assistant port should not be placed in the isosceles triangle to the greatest extent, as shown in [Figure 3](#). There are many types of thoracic surgery, including pulmonary, esophageal, and mediastinum tumor surgery. While the thoracic cavity is large and requires extensive coverage, different operations have different emphases and different exposures of the surgical area. For example, esophageal surgery is mainly located in the posterior mediastinum, and pulmonary surgery mainly requires wide exposure from the lung hilum to the tracheal carina and superior mediastinum, while mediastinal tumor surgery requires different exposure parts according to different lesion locations. Therefore, while selecting the robot-assisted surgical incision, different surgeons usually have different choices (6, 8–22), as given in [Table 3](#). Even for pulmonary surgery, at present, there are still a variety of robot-assisted surgical incision selections (6, 9, 14–17, 19, 20, 22). Oh et al. (23) summarized robotic port placement, which was used by high-volume thoracic surgeons in the United States who performed robot-assisted lobectomy, and they found that the precise locations of the robotic ports were heterogeneous for each lobectomy. The most common locations for camera and instrument trocars were the seventh and eighth interspaces for all types of lobectomies. The placement of trocars for robot-assisted lobectomy was flexible and based on the clinician's experience or the unique anatomic issues of a specific patient. These incisions are suitable only for pulmonary or esophageal surgery and mediastinal tumor surgery, and they do not constitute a universal incision for RATS.



As there are many types of thoracic surgery, the variety of incision selection presents some difficulties to the chief surgeon, especially for a beginner in carrying out RATS. Robot-assisted surgeons are skilled in thoracoscopic surgery, and the learning curve of robot-assisted surgery is much

shorter than that of thoracoscopic surgery (24–26). Based on the practice, exploration, and summary of more than 300 cases of robot-assisted surgery, the concept of universal thoracic incision in robot-assisted surgery was proposed. The incision for the camera port was placed at the midaxillary line in the sixth ICS. The incisions for the first robotic arm were placed at the midaxillary line in the third ICS, the incision for the second robotic arm was placed at the subscapular line in the ninth ICS, and the assistant port was placed at the anterior axillary line in the fourth ICS. This incision is applicable to all lung, esophageal, and posterior mediastinal tumor surgeries. For anterosuperior mediastinal tumors, the incision for the second robotic arm was adjusted at the anterior axillary line in the sixth ICS. If necessary, the assistant port could be adjusted at the posterior axillary line in the eighth ICS. The distance between the incisions for the first robotic arm and the second robotic arm from the camera port should be kept a palm wide (approximately 8 cm). The incision for the camera port should be made first in practice, and the remaining incisions are placed under direct visualization to guarantee the incision within the thoracic cavity. Blind operations are strictly forbidden to avoid injury to the diaphragm or entry into the abdominal cavity.

Among the 342 cases of clinical surgery, there were 107 cases of esophageal cancer surgery (McKeown approach), 5 cases of esophageal leiomyoma, 178 cases of pulmonary surgery, and 52 cases of mediastinal tumor surgery. Two cases of early surgery were transferred to VATS with a small incision for serious chest adhesion, and the remaining cases were not transferred to VATS or thoracotomy. All the surgeries were successfully completed, with no deaths during the perioperative period or one month after surgery. In our previous study (27, 28), the safety and feasibility of robot-assisted minimally invasive esophagectomy (RAMIE) compared with video-assisted minimally invasive esophagectomy (VAMIE) and RATS lobectomy compared uniportal VATS lobectomy were evaluated individually. There was no significant difference in the rate of overall complications between RATS and VATS. Compared with VATS, a greater number of lymph nodes harvested were found in RAMIE and RATS lobectomy. There have been several reports on the advantages of robots in lymph node dissection (14, 18). RAMIE could retrieve more thoracic lymph nodes along the recurrent laryngeal nerve areas. Park et al. (18) reported a mean total of 43.5 ± 1.4 retrieved lymph nodes. Although the number of lymph nodes harvested in the present study was smaller, there was also statistical significance between the RAMIE and the VAMIE groups in our previous study (28).

The initial design of this robot-assisted thoracic incision gave priority consideration to esophageal surgery, and nearly all 40 robot-assisted surgery cases during the early period

were patients with esophageal tumor. Based on robot-assisted surgery experience, it was found in subsequent lung surgical explorations that the universal incision for pulmonary surgery also had very good exposure and operation effects. Thus, lobectomy and segmentectomy were carried out afterward. The assistant port was placed at the anterior axillary line in the fourth ICS, which fits the operation habits of VATS, especially with regard to the exposure in uniportal VATS and the placement of a linear cut stapler. The assistant with uniportal VATS experience can conveniently operate on the table and shorten the operating time, thus ensuring skilled coordination between the assistant and the chief surgeon. The location of the assistant port in the anterior chest wall is also conducive to rapid thoracotomy in cases of emergency massive bleeding during surgery (although we have not encountered such situations). Two cases of esophageal cancer complicated with nodules in the upper lobe of the right lung successfully underwent RATS through this surgical incision. After the separation of the esophagus and lymph node dissection, resection of the right upper lobe was completed, which further reflected the superiority of the universal surgical incision. The EndoWrist® in the da Vinci system is superior to the human wrist, as it is flexible in all directions. There are a few reports about the cases of RATS sleeve or double-sleeve lobectomy for central-type lung cancer (29–32). Due to the small number of surgical cases, only three cases of bronchial sleeve resection of the pulmonary lobe (one case for the right upper pulmonary lobe and two cases for the left upper pulmonary lobe) were completed. The 3-0 prolene sutures (ETHICON 24 mm 1/2c, USA) in a continuous way were used to perform the bronchial sleeve resection. It was found to be more successful for intraoperative sutures than for thoracoscopic sutures, which showed a great advantage over the former.

For the anterior mediastinal tumor, the lesion is located in the substernal part with a narrow space. When the lesion is too large, its exposure under the thoracoscope is poorer. The advantages of robot-assisted surgery are obvious for fine operations within such a narrow space. For the anterior mediastinal tumor, the incision for the second robotic arm is moved to the anterior chest wall, and the anterior superior mediastinal tumors with lesions below 3 cm can be completed independently without an assistant port, while solid tumors with lesions above 3 cm often require an additional assistant port to enhance the exposure of the operative field. The assistant port can be placed at the posterior axillary line in the eighth ICS. The largest anterior superior mediastinal tumor (solid thymoma) was completely excised through this incision, which was nearly 8 cm in diameter, avoiding thoracotomy or sternum splitting and minimizing trauma to the patient.

Good robotic surgical incision design is the premise of a successful operation and can display robot platform

advantages. A relatively simple and fixed general surgical incision, good intraoperative exposure, and quick and skilled cooperation of the assistant can reduce the difficulty in RATS for the surgeon and shorten the learning curve of robot-assisted surgery. Our preliminary experience suggests that universal robot incisions are feasible for esophageal, lung, and most mediastinal tumors. The proposal of a universal robot incision provides a simple and easy incision design for an increasing number of thoracic surgeons to ensure the smooth and successful development of RATS.

This study also has some limitations. Due to the small number of surgical cases, there is no relevant experience in the Ivor Lewis approach for esophageal cancer and pulmonary artery plasty, and as a result, only three cases of bronchial sleeve resection have been completed. In addition, this paper included data from only two surgical centers. More surgical centers need to try and verify the safety and convenience of this universal incision. However, this universal incision for RATS has great value as it may guide standardized port placement, which would be important for the learner and the instructor.

Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors without undue reservation.

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Author contributions

JJ is the experimental designer and executor of this study, and completed the data analysis and wrote the first draft of the paper; JG and JZ participated in the experimental design and analysis of the experimental results; XL and MD came up with the idea for the project. The author and person in charge guided the experimental design, data analysis, and thesis writing and revision. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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A modified survival model for patients with esophageal squamous cell carcinoma based on lymph nodes: A study based on SEER database and external validation

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Background: The counts of examined lymph nodes (ELNs) in predicting the prognosis of patients with esophageal squamous cell carcinoma (ESCC) is a controversial issue. We conducted a retrospective study to develop an ELNs-based model to individualize ESCC prognosis.

Methods: Patients with ESCC from the SEER database and our center were strictly screened. The optimal threshold value was determined by the X-tile software. A prognostic model for ESCC patients was developed and validated with R. The model's efficacy was evaluated by C-index, ROC curve, and decision curve analysis (DCA).

Results: 3,629 cases and 286 cases were screened from the SEER database and our center, respectively. The optimal cut-off value of ELNs was 10. Based on this, we constructed a model with a favorable C-index (training group: 0.708; external group 1: 0.687; external group 2: 0.652). The model performance evaluated with ROC curve is still reliable among the groups. 1-year AUC for nomogram in three groups (i.e., 0.753, 0.761, and 0.686) were superior to that of the TNM stage ($P < 0.05$). Similarly, the 3-year AUC and the 5-year AUC results for the model were also higher than that of the 8th TNM stage. By contrast, DCA showed the benefit of this model was better in the same follow-up period.

Conclusion: More than 10 ELNs are helpful to evaluate the survival of ESCC patients. Based on this, an improved model for predicting the prognosis of ESCC patients was proposed.

KEYWORDS

nomogram, esophageal squamous cell carcinoma, examined lymph nodes, prognosis, decision curve analysis

Introduction

Esophageal squamous cell carcinoma (ESCC) is the most common histological form of esophageal cancer, which has made a major contribution to cancer-related mortality worldwide (1, 2). Remarkably, ESCC is mainly characterized by lymph node metastasis (LNM). Less than one-third of ESCC patients are able to cross the 5-year survival period

(3–5). Due to the complex lymphatic network in and around the esophagus, the possible LNM of ESCC involves multiple fields, including the neck, chest, or/and abdomen (6–8). Therefore, radical lymphadenectomy for ESCC is regarded as an important method to improve the survival rate.

The lymph node resection during cancer surgery is generally performed for 2 main reasons, (a) staging and (b) dissemination prevention. Thus, the counts of resected nodes

TABLE 1 Patients' demographics, clinical characteristics at diagnosis.

Variables	Total (%)	2004–2009	2010–2015	P value
<i>n</i>	3,629	1,732	1,897	
Age				
<60	1,077 (29.68%)	516 (29.79%)	561 (29.57%)	0.415
≥60	2,552 (70.32%)	1,216 (70.21%)	1,336 (70.43%)	
Race				
White	731 (67.13%)	1,085 (62.64%)	1,192 (62.83%)	0.993
Black	220 (20.2%)	441 (25.46%)	481 (25.36%)	
Other	138 (12.67%)	206 (11.9%)	224 (11.8%)	
Sex				
Male	2,349 (64.73%)	1,130 (64.57%)	1,219 (64.26%)	0.536
Female	1,280 (35.27%)	602 (35.43%)	678 (35.74%)	
Pathology grade				
Well	207 (5.7%)	83 (4.79%)	124 (6.54%)	0.052
Moderately	1,875 (51.67%)	880 (50.81%)	995 (52.45%)	
Poorly	1,517 (41.8%)	754 (43.53%)	763 (40.22%)	
Undifferentiated	30 (0.83%)	15 (0.87%)	15 (0.79%)	
Lymph node metastasis				
No	1,654 (45.58%)	848 (48.96%)	806 (42.49%)	0.000
Yes	1,975 (54.42%)	884 (51.04%)	1,091 (57.51%)	
Metastasis				
No	2,748 (75.72%)	1,309 (75.58%)	1,439 (75.86%)	0.845
Yes	881 (24.28%)	423 (24.42%)	458 (24.14%)	
Tumor size				
≤3 cm	895 (24.66%)	424 (24.48%)	471 (24.83%)	0.172
>3 cm	2,734 (75.34%)	1,308 (75.52%)	1,426 (75.17%)	
Examined LNs				
≤10	3,052 (84.1%)	1,441 (83.2%)	1,611 (84.92%)	0.156
>10	577 (15.9%)	291 (16.8%)	286 (15.08%)	
T stage				
T1	422 (11.63%)	187 (5.15%)	235 (12.39%)	0.00
T2	1,428 (39.35%)	623 (35.97%)	805 (43.49%)	
T3	1,024 (28.21%)	526 (30.37%)	498 (26.25%)	
T4	755 (20.8%)	396 (22.86%)	359 (18.92%)	
8th TNM stage				
I	520 (14.33%)	276 (13.91%)	244 (12.86%)	0.051
II	1,033 (28.47%)	486 (41.89%)	547 (28.83%)	
III	1,200 (33.07%)	552 (35.43%)	648 (34.16%)	
IV	881 (24.28%)	423 (8.77%)	458 (24.14%)	
Median survival (M)	9 (4–23)	9 (4–23)	9 (4–22)	

increases with the counts of suspicious nodes (up to a certain limit) and with the striving for dissemination prevention. In the first case, more nodes might indicate a bad prognosis, while in the latter, better dissemination prevention might be achieved by excising more nodes. However, the counts of examined lymph nodes (ELNs) in predicting prognosis remains controversial (9–11). In addition, the American Joint Committee on Cancer indicated the number of ELNs was beneficial as many as possible (12–16).

Although ELNs were an independent factor for survival, there remained to be no associated study that reported the precision of the survival model for patients with ESCC based on the optimal threshold of ELNs. Factors such as age, grade, and tumor size may also significantly affect the prognosis of ESCC patients. Regarding these divergences and lack of relevant research, this study aimed to identify the optimal number of ELNs and build a nomogram model based on the grouping of ELNs by SEER database and data from our hospital. The optimal threshold value of ELNs was made out by X-tile software which was extensively used and credible for figuring out optimal cut-off values (17, 18). Through the SEER database and data collected from our hospital, we built and validated a nomogram model according to the results of multivariate cox analysis to predict the survival of ESCC patients. Combined with Cox analysis results of the data collected from SEER database and our hospital, a prediction model for patients with ESCC based on lymph nodes was established and verified.

Material and methods

Research material

The SEER database and the cases from our hospital were used to enroll patients. The SEER database the information was collected by SEER*Stat software (version 8.3.6), tumors with codes 8,070, 8,071, 8,072, 8,073, 8,074, 8,075, 8,076, and 8,078 were set as ESCC according to the ICD-O-3 criteria (19, 20).

We made the inclusion criteria for the SEER database: (1) patients aged over 20 years old and diagnosed as ESCC by histology; (2) patients who had detailed records of living status; (3) patients with valid information such as race, grading of tumors, ELNs, pathologic findings, and tumor size; (4) chemotherapy free before surgery. The following cases were excluded: the required information is missing or incomplete.

Cases were also selected from our center. Patients diagnosed from January 2016 to December 2019 were selected to analysis their information of diagnosis and treatment for ESCC. The criteria for including patients were: (1) Patients over 20 years of age with ESCC; (2) without preoperative adjuvant therapy. The exclusion criteria were: (1) no information on tumor progression or stage was available; (2) with chronic disease or

organ dysfunction. Patients who did not participate in the follow-up were excluded. **Tables 1, 2** show the data feature of SEER database and our center adoptive in this study respectively.

TABLE 2 Patients' demographics, clinical characteristics at diagnosis in our centre.

Variables	Patients from the our centre
<i>n</i>	268 (100%)
Age	
<60	89 (33.21%)
≥60	179 (66.79%)
Sex	
Male	222 (82.84%)
Female	46 (17.16%)
Pathology grade	
Well	17 (6.34%)
Moderately	16 (5.97%)
Poorly	44 (16.42%)
Unknown	191 (71.27%)
Lymph node metastasis	
No	160 (59.7%)
Yes	108 (42.3%)
Metastasis	
No	259 (96.64%)
Yes	9 (3.36%)
Tumor size	
≤3 cm	117 (43.66%)
>3 cm	151 (56.34%)
Examined LNs	
≤10	92 (34.33%)
>10	176 (65.67%)
T stage	
T1	36 (13.43%)
T2	32 (11.94%)
T3	155 (57.84%)
T4	45 (16.79%)
8th TNM stage	
I	36 (13.43%)
II	32 (11.94%)
III	191 (71.27%)
IV	9 (3.36%)
Chemotherapy	
No	244 (91.04%)
Yes	24 (8.96%)
Smoking	
No	95 (35.45%)
Yes	173 (64.55%)
Drinking	
No	123 (45.90%)
Yes	145 (54.10%)
Median survival (M)	28.5 (9–43)

Variable definition

The clinicopathological variables included demographics, pathology, clinical stage, treatment, ELNs, and 8th TNM stage. In the latest version, some of the data were marked the status of TNM stage according to the 8th AJCC TNM system, while some data remained to be old edition. Therefore, after we abstracted the data, we transformed the old TNM staging system into the 8th AJCC TNM system because the number of positive examined lymph nodes and T stage were provided in the original data. Gender includes male and female. Age was converted to a dichotomous variable: <60 years and ≥ 60 years. Race mainly includes white, black and other races. The pathology was graded according to the degree of differentiation. LNM was recorded as positive (Y) and negative (N). Also, M1 indicated distant metastasis. The tumors were grouped according to their size as follows: ≤ 3 cm and >3 cm. While for ELNs, based on the result of X-tile software, the cut-off value was 10(18). Hence, ELNs were categorized into two groups: ≤ 10 and >10 . Chemotherapy was described as Yes or No, as well as smoking. Overall survival (OS) and cancer-specific survival (CSS) were the main indicators.

Statistical analysis

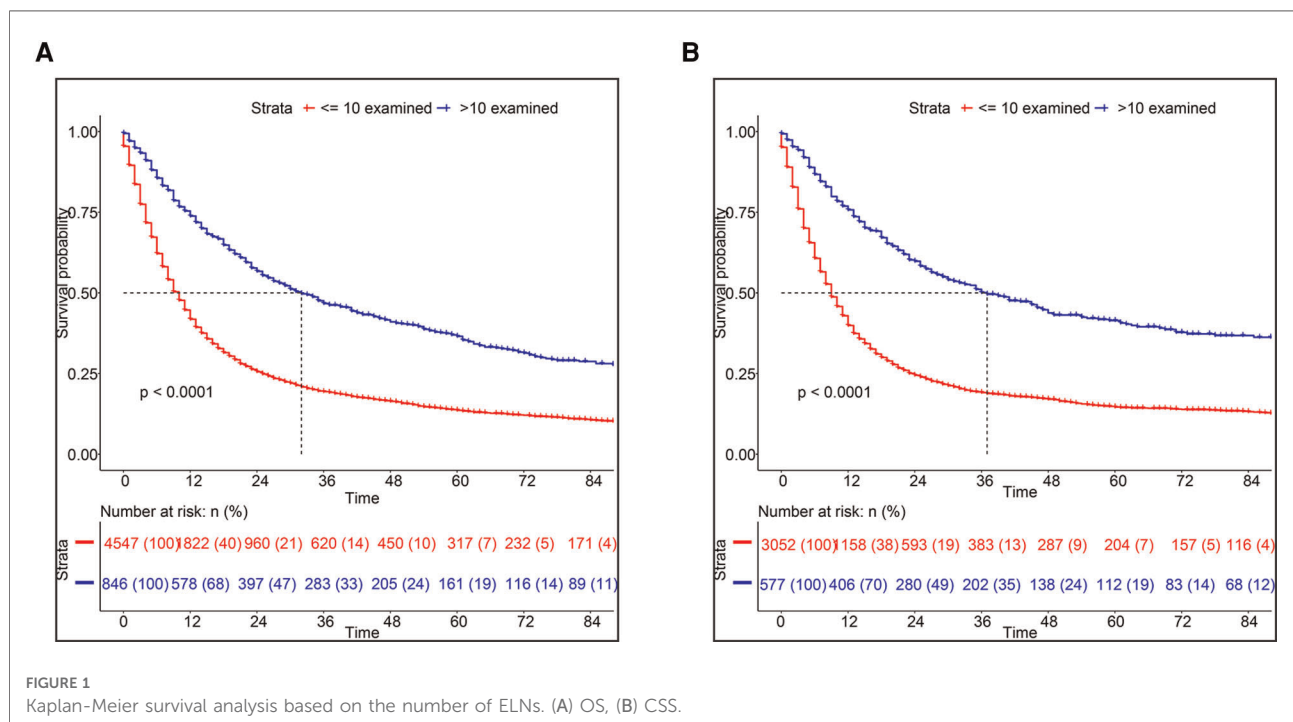
For data from the SEER database was investigated by the association among the categorical variables utilizing Pearson's

Chi-square test. a K-M survival curve was applied to analyze the OS and CSS according to the previous study (21). In addition, Univariate and multivariate Cox regression were used to determine the prognostic risk factors. After that, we build a nomogram model according to the results and validated it internally and externally. The cases from 2004 to 2009 were used as the training group, while the cases from 2010 to 2015 and the cases from our hospital were used as the validation group. C-index value, ROC curves, and decision curve analysis (DCA) were chosen to identify the value of model (22–24). All statistical analyses were performed using R version 4.1.3 and related packages. The difference was considered statistically significant when P -value < 0.05 .

Results

Basic characteristics

According to the flow chart (Supplementary Figures S1, S2), 3,629 patients diagnosed as ESCC from the SEER database were enrolled. We determined the diagnosis of ESCC based on pathological diagnosis, and then excluded patients with no information about TNM stage and survival status. As shown in Table 1, we included 3,629 patients from the SEER database including 1,732 patients from 2004 to 2009 and 1,897 patients from 2010 through 2015. According to



Pearson's Chi-square analysis, we found patients aged more than 50 years old accounted for a larger ratio than younger patients in ESCC patients, and male patients were more than female patients ($P < 0.05$). Furthermore, the total LNM rate was 54.42% and the distant metastasis rate was 24.28%. Accordingly, the median survival time was 9 months (range: ranged from 4 to 23 months). Also, we included 268 patients

from our centre. The median survival time was 28.9 months (range: ranged from 9 to 43 months). In line with the SEER database, we also found patients with ESCC were inclined to be older people (66.79% vs. 33.21%) and male gender (82.84% vs. 17.16%). However, we found the rate of LNM and metastasis in our patients was lower than that in patients from the SEER database, which could be because our patients

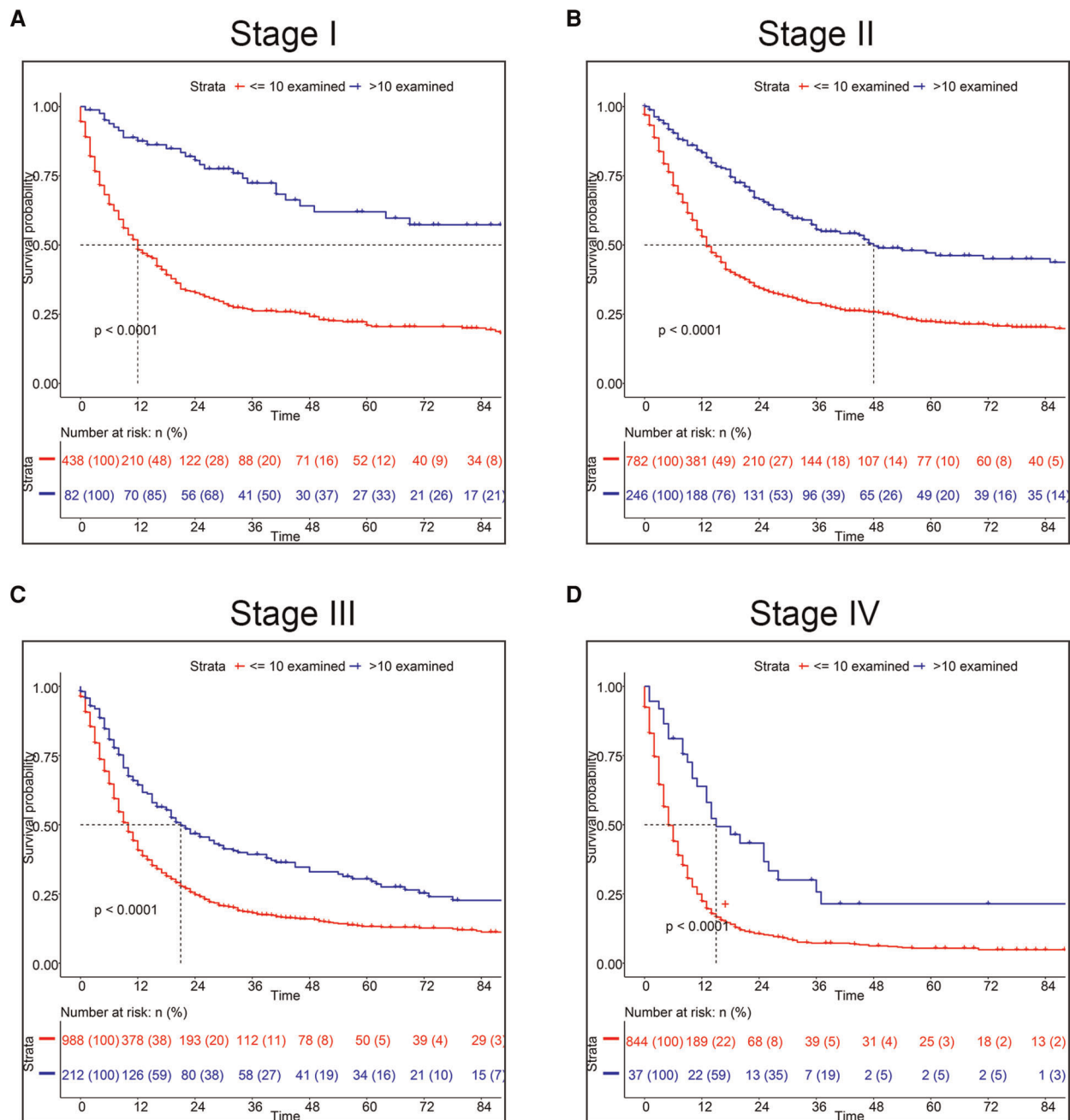


FIGURE 2

Kaplan-Meier survival analysis for CSS based on the number of ELNs. (A) Stage I, (B) Stage II, (C) Stage III, (D) Stage IV.

were diagnosed from 2016 to 2019 when endoscopy was extensively used.

Grouping of ELNs in ESCC patients

Using X-tile software, we found the optimal cut-off of ELNs was 10 and divided into two groups (<10 vs. ≥ 10) (Supplementary Figure S3). As shown in Figure 1A, the OS rate between the two groups could be considered significantly different. Consequently, the CSS of patients with less than 10 ELNs was worse than patients with more than 10 ELNs (Figure 1B). Additionally, K-M survival analysis showed patients with >10 examined LNs who were in the different clinical TNM stages had better survival, of which the difference was statistically significant according to the grouping of ELNs ($P < 0.0001$) (Figure 2). Furthermore, to verify previous results, we analyzed whether the grouping of examined LNs was suitable for our clinical data. As shown in Figure 3, we found that patients with >10 examined LNs in our center had a higher survival rate ($P = 0.037$).

Prediction model of ESCC survival

To determine the most suitable features to build a nomogram, we performed a multivariate cox analysis, and the independent prognostic factors included age, tumor size, TNM stage and ELN (Figure 4). Patients who were aged ≥ 60 , with tumor size >3 cm, or with lymph node metastasis had a worse prognosis, while patients with ELNs >10 have a better prognosis. After multivariate cox analysis, compared to the white race, the black race was a risk factor for survival, however, the other races were not associated with survival. Therefore, the race was excluded. The record of marital status contained much uncertain information, hence it is hard to accurately identify marital status as an independent factor. Then a nomogram predicting prognosis was constructed based on the results above (Figure 5). As shown in the survival model, T stage had the greatest impact on prognosis, followed by ELNs, distant metastasis, tumor size, and age, while LNM did the least effect on prognosis.

Nomogram validation

Firstly, in our training cohort, the C-index of the nomogram model has a value of 0.708 which ranged from 0.678 to 0.753, which were better than that of the 8th TNM staging system (Table 3). The external validation cohort also showed our model had a good C-index value (0.687, ranging from 0.601

to 0.734). In line with the training cohort and external validation, the result of analyzing data from our center also demonstrated nomogram model with a C-index value of 0.652 was better than that of the traditional 8th TNM stage of which the C-index was 0.604 (Table 3). For specificity and sensitivity of diagnosis, the model also outperformed TNM stage in both cohorts ($P < 0.001$, Table 3 and Figures 6A–C) and external cohort ($P < 0.001$, Table 3 and Figures 6D–F). Finally, we performed DCA to compare the clinical usability, finding nomogram showed a greater benefit compared to the TNM staging system for predicting the CSS with different survival time (Figure 7). Furthermore, the above results were additionally testified by data from our center. As shown in Table 3 and Figures 8A–C, the nomogram model was better than the TNM stage for predicting survival ($P < 0.05$). However, the difference in predicting 5-year survival had no significance ($P = 0.149$). The results of DCA also showed nomogram was more favorable for clinical decision and assessment (Figures 8D–F).

Discussion

ESCC is the predominant histologic subtype of EC over the world, while adenocarcinoma is mainly distributed in North America and Europe. ESCC was derived from an epithelial cell of the mucosa, which was often stimulated due to alcohol and smoke (5). Radical surgery is considered the

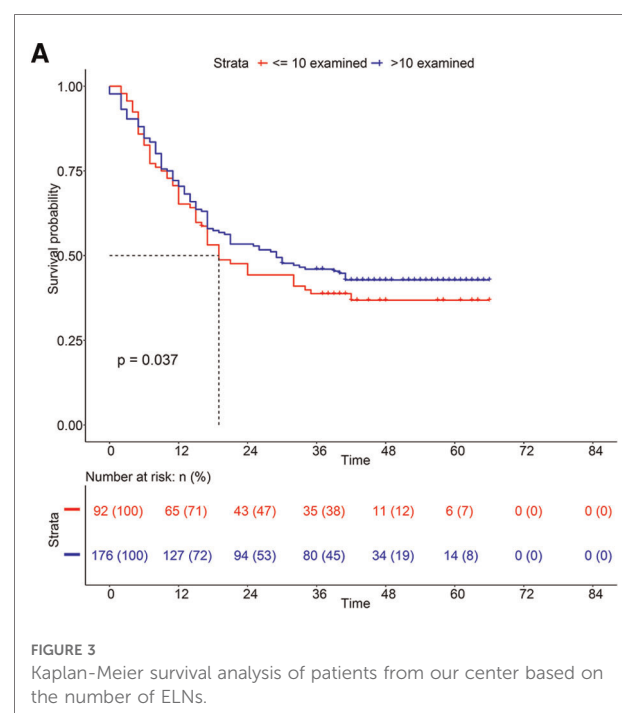
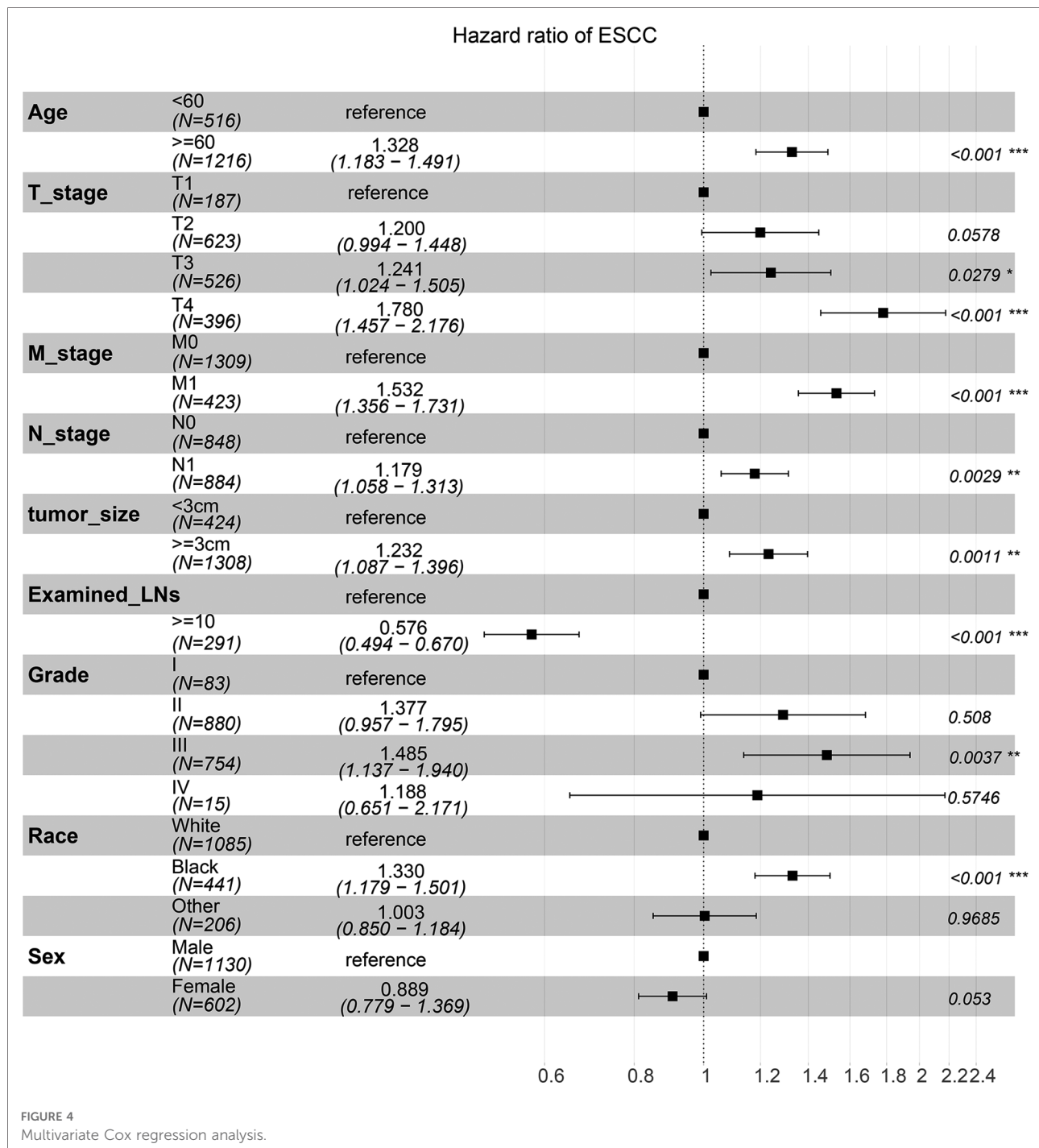


FIGURE 3
Kaplan-Meier survival analysis of patients from our center based on the number of ELNs.



preferable therapeutic method, especially for some minimally invasive surgery such as endoscopic surgery (25). However, the long-term survival was still low because of high recurrence or distant metastasis. Therefore, radical resection and adequate lymph node dissection were critical. This study shows that the number of ELNs has a significant impact on the prognosis of ESCC patients. Moreover, we determined

the optimal demarcation of ELNs was 10 using X-tile software and divided patients into two groups: ≤10 ELNs and >10 ELNs. At the same time, we performed multivariate regression analysis and built a nomogram model, of which the process was credible and accurate (26). Furthermore, the nomogram was validated by the training cohort and two external cohorts, suggesting it was superior to the traditional

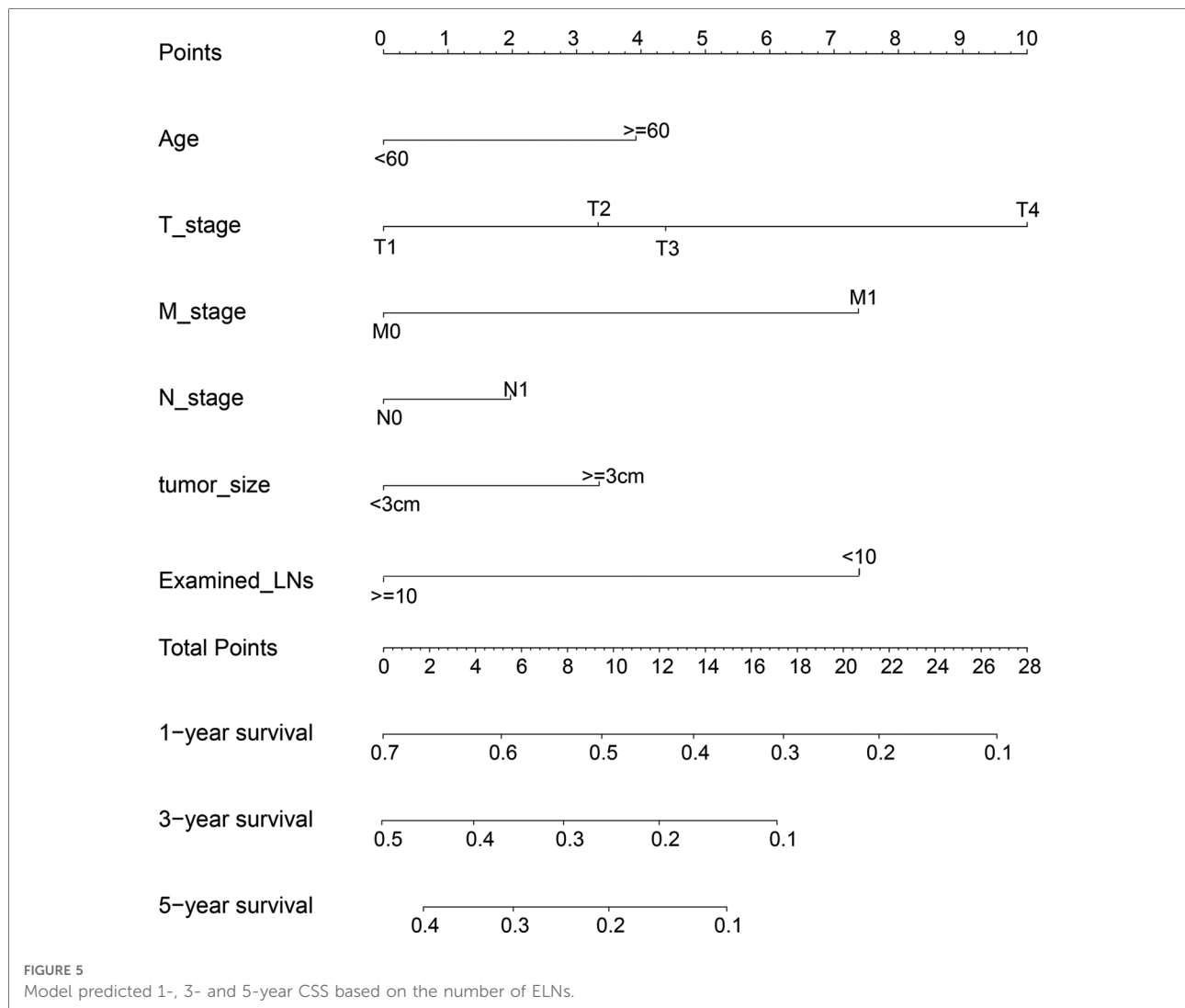


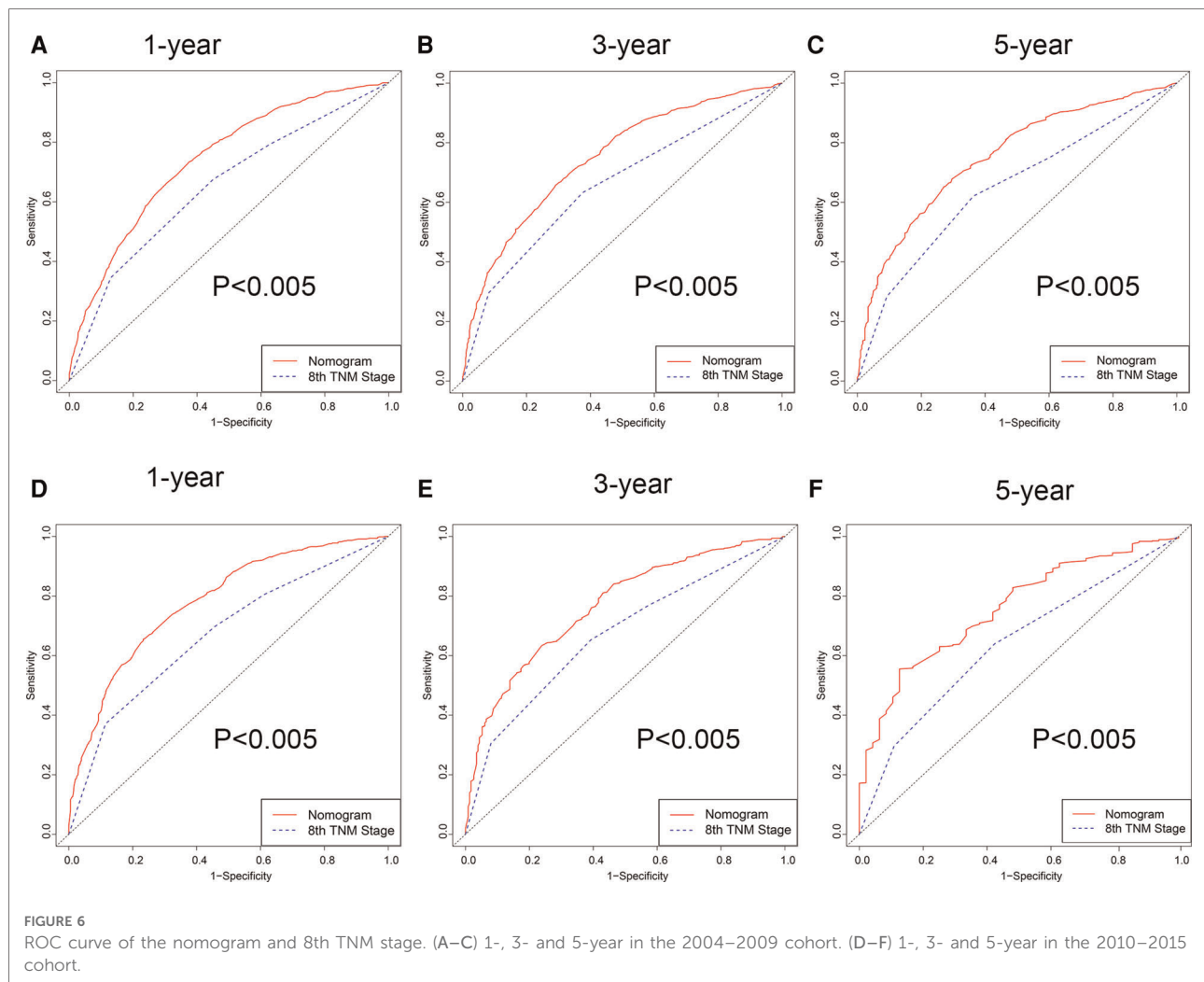
TABLE 3 Prediction accuracy of modified model vs. TNM stage in survival of ESCC patients.

Variable	Value (95%CI)		
	Internal validation	External validation	Validation in our center
C index for nomogram	0.708 (0.678–0.753)	0.687 (0.601–0.734)	0.652 (0.589–0.703)
C index for TNM stage	0.601 (0.573–0.656)	0.605 (0.563–0.659)	0.604 (0.561–0.673)
1-year AUC for nomogram	0.753 (0.711–0.821)	0.761 (0.715–0.831)	0.686 (0.621–0.752)
3-year AUC for nomogram	0.761 (0.712–0.813)	0.753 (0.659–0.818)	0.73 (0.67–0.788)
5-year AUC for nomogram	0.783 (0.753–0.848)	0.75 (0.753–0.847)	0.679 (0.548–0.798)
1-year AUC for TNM stage	0.653 (0.611–0.701)	0.641 (0.605–0.715)	0.625 (0.574–0.675)
3-year AUC for TNM stage	0.701 (0.675–0.784)	0.687 (0.655–0.738)	0.662 (0.609–0.715)
5-year AUC for TNM stage	0.733 (0.613–0.781)	0.685 (0.643–0.727)	0.655 (0.545–0.765)

8th TNM staging system as far as clinical usefulness was concerned.

It is well-known that ELNs are one of the important factors associated with patients' prognosis, which was also

demonstrated by many previous studies (27, 28). Several studies found the number of ELNs (>15) affects the prognosis of ESCC patient (29). In our study, we found that the best cut-off value of ELNs was 10, which was in line with other

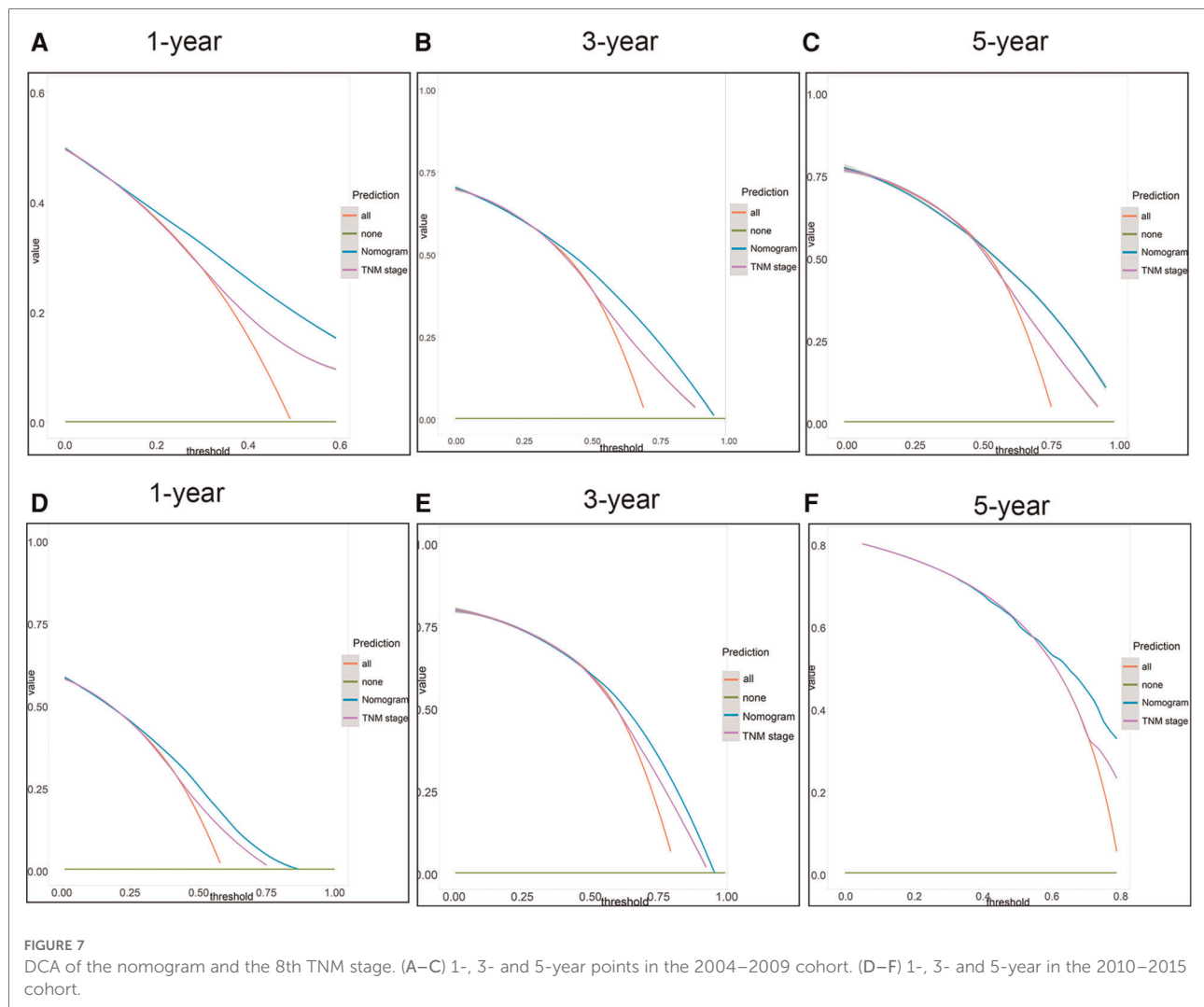


studies (15, 30, 31). Considering the AUC value of ROC, the nomogram performed well with a value of 0.7 and was better compared to the 8th TNM staging (32, 33). In addition, some researchers put forward other different views on TNM stage (15, 34, 35). By figuring out the C-index value and performing tdROC and DCA, we demonstrated nomogram was more effective on clinical usability compared to the TNM staging system, which was also tested by many previous studies (32, 33).

In our model, we totally included age, TNM stage, tumor size, and ELNs to build the model. Usually, the pathological grade was considered as an independent factor for patients' survival. However, we excluded it according to multivariate analysis (36). We thought the main reason was the limited sample of different pathological subtypes. Regarding the cut-off value in our study, of course, different studies reported diversely. As for stage IV of ESCC, a study thought 18 ELNs were necessary for determining accurate staging and

improving survival (37), while another study indicated that 15 ELNs at least were favorable for patients' survival (38). However, removing lymph nodes and assessing LNM depended on the surgeon and pathological clinicians to some extent (14). Therefore, the differences in studies may be due to the heterogeneity of the study population. Although there were similar studies focused on the cut-off value of ELN (29), our study further constructed a predicting model of survival based on the number of ELN, which made the study more clinically meaningful. To some extent, we could assess the survival of patients after surgery according to the nomogram.

Our study also has some limitations that cannot be ignored. First, we excluded patients with missing data such as the TNM staging and pathological grade, leading to the increased selection bias. Next, our manuscript has not included other characteristics both in the SEER database and in our own data, such as hematological biomarkers and molecular

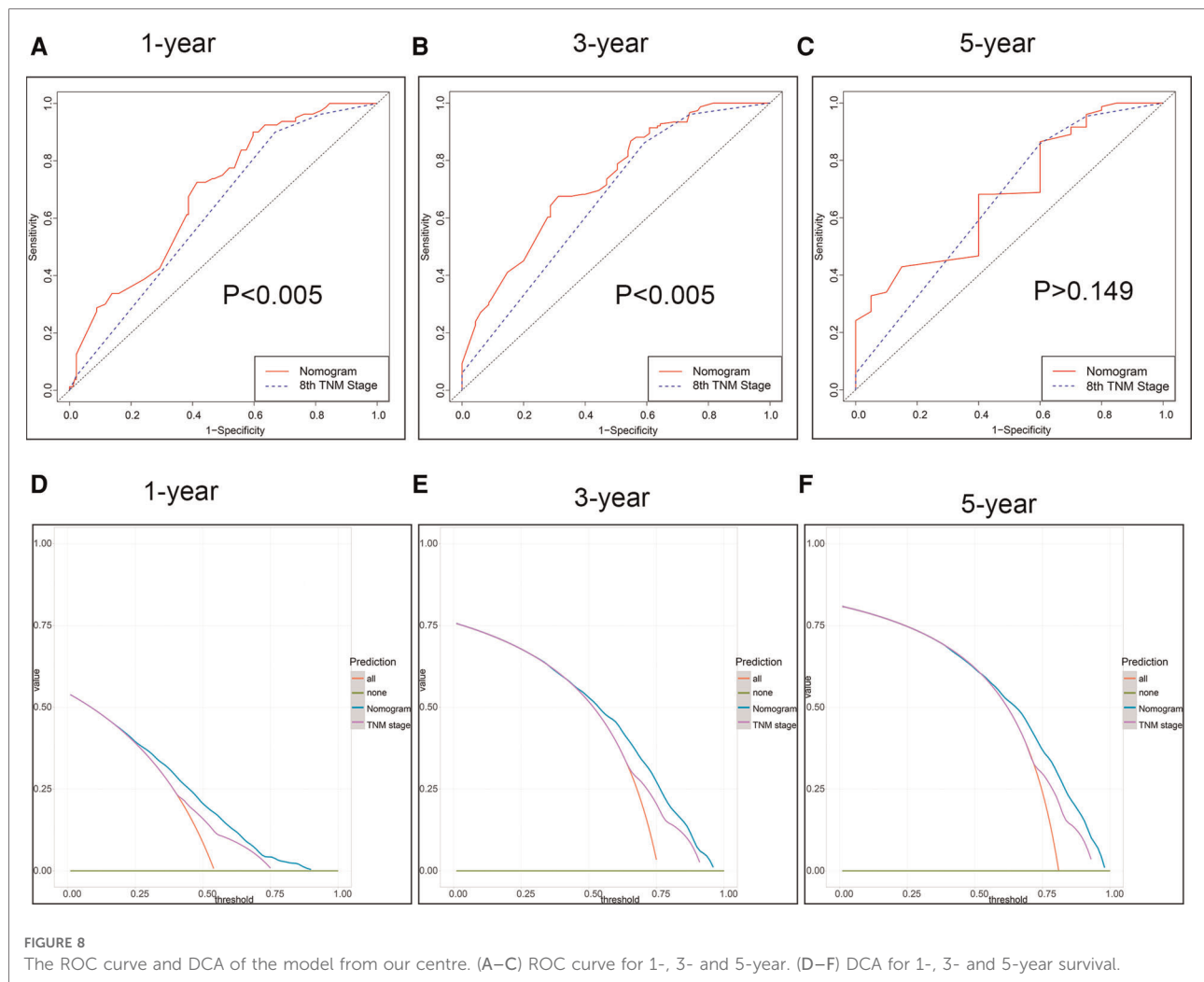


parameters, which made our model limited. Next, in fact, we found the SEER data showed of 85% patients with less than 10 ELN, which was inconsistent with our data, affecting our analysis of survival in general. But we checked other studies about SEER data, we found there was a similar rate of less than 10 ELNs (9). Moreover, the low rate of ELN would underestimate the stage of the tumor, decreasing the reliability of our study. Finally, whether patients from the SEER database received chemotherapy after surgery or radiotherapy was not known to us, which did make a great difference for our analysis. However, in our data, we included the information about chemotherapy, making an explanation to problems to some extent. Also, as for the result of own data, we found the nomogram model was similar to the TNM stage for predicting 5-year survival ($P = 0.149$). We thought the limited samples of patients with 5-year survival were the main reason because the nomogram model performed well in the internal and external validation group which had sufficient

patients with 5-year survival. Of course, this hypothesis needs to be proven by enrolling a larger sample of patients in the future.

Conclusions

In addition to ELNs was an independent protective factor, variables including age, tumor size, and TNM stage were the independent risk factor for CSS according to the results of multiple statistical analyses. The number of ELNs was more favorable when it was more than 10. More than 10 ELNs are helpful to evaluate the survival of ESCC patients. Based on this, an improved model for predicting the prognosis of ESCC patients was constructed and could serve as an assistive tool for survival evaluation compared to the 8th TNM staging system.



Data availability statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Ethics statement

The studies involving human participants were reviewed and approved by the Ethics Committee of the Affiliated Hospital (Group) of Putian University [approval no. PY-KY-2020(2)-0032]. The patients/participants provided their written informed consent to participate in this study.

Author contributions

Study concept and design: WL and YC. Acquisition of data: TY, SH, and BC. Analysis and interpretation of data: TY.

Drafting of the manuscript: TY. Critical revision of the manuscript for important: WL and YC. Statistical analysis: TY. Obtained funding: WL and YC. The authors had full access to the data and take full responsibility for the results. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fsurg.2022.989408/full#supplementary-material>.

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Early experience with uniportal robotic thoracic surgery lobectomy

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Background: Invasiveness is considered one of the cornerstones of every field of surgery, and video-assisted thoracoscopic (VATS) approaches are now routinely used worldwide to perform pulmonary resections. Recently, robotic-assisted thoracic surgery (RATS) has become the preferred technique in many centers; it is routinely performed using three or four ports with at least one service incision, contrasting with the real concept of invasiveness, especially when compared to uniportal VATS (U-VATS). Hereby, we present our early experience with uniportal RATS (U-RATS) pulmonary resections for early-stage lung cancer. Technical details of surgical steps are accurately described and commented on.

Results: Twenty-four consecutive patients with lung cancer underwent U-RATS anatomical pulmonary resections at our institute. All procedures were completed with the uniportal approach. The mean operative time was 210 min (range 120–350); in the last 10 cases, the operative time was significantly reduced (180 min) compared to the first 10 cases (232 min) ($p < 0.02$), showing a very fast learning curve. The postoperative pain score was comparable to that for U-VATS and was constantly low.

Conclusions: U-RATS is a safe and feasible technique, combining the advantages of U-VATS with the well-known advantages of robotic surgery.

KEYWORDS

robotic thoracic surgery, rats, uniportal RATS, thoracoscopic surgery, VATS, uniportal VATS, robotic thoracic surgery (RATS)

Introduction

Invasiveness is considered one of the cornerstones of every field of surgery due to less morbidity and faster postoperative recovery compare to open surgery. Video-assisted thoracoscopic (VATS) approaches are now routinely used worldwide to perform pulmonary resections and are not only limited to standard procedures or early-stage lung cancer but also in the case of advanced stages requiring complex reconstructions (1–4). In particular, since 2004, uniportal VATS (U-VATS) has progressively gained relevance in the thoracic surgery units, including our center, due to its invasiveness compared to multiportal approaches, without differences in feasibility and oncological outcomes (5, 6). Recently, robotic-assisted thoracic surgery (RATS) is increasingly becoming the preferred technique in many centers worldwide. The main advantages are the 3D vision in the operative field, the intuitive management, and the easy maneuverability, allowing safer and more accurate surgical acts due to the wristed arms

and the use of bipolar energy and grasping in both hands (7, 8). However, RATS is routinely performed using three or four ports with at least one service incision (9) in contrast to the real concept of less invasiveness. The possibility of blending the uniportal approach with robotic technology would be an enormous improvement in terms of feasibility, safety, oncological outcomes, and enhanced postoperative recovery. An update of the literature during the revision process of our paper showed a very recent description of the technique (10, 11) and a previous case report (12). Thus, considering our personal experience with U-VATS and standard robotic techniques, we recently started our U-RATS program. Herein, we present our early series of U-RATS pulmonary resections for early-stage lung cancer, focusing on feasibility, safety, surgical technique, and early postoperative outcomes.

Patients and methods

Based on our experience with U-VATS and four-port robotic surgery, in January 2022 at the IRCCS “G. Pascale Foundation” National Cancer Institute of Naples, we started the U-RATS program. Twenty-four consecutive patients (9 males and 15 females, mean age 64 ± 11 years) with lung cancer underwent anatomical pulmonary resections. All patients signed a standard informed consent form as this approach does not have an experimental purpose. Patient characteristics are reported in Table 1. Standard preoperative workup was performed including routine blood examinations, pulmonary function tests, arterial blood gas analysis, cardiological assessment, total body computed tomography (CT), and total body positron emission tomography (PET). In most patients, whenever possible, a preoperative diagnosis of lung cancer was achieved by CT fine needle biopsy or fiberoptic bronchoscopy; in other cases, the diagnosis was intraoperatively confirmed after wedge resection. Our standard pain control for minimally invasive surgery includes intraoperative nerve blocking of 3–4 intercostal spaces with 100 mg of local anesthesia (Ropivacain) performed at the beginning of surgery, followed by intravenous postoperative Ketorolac 90 mg/24 h for 2 days, plus 1 g of paracetamol if needed in selected cases. No opioids are routinely used. All surgical procedures have been performed at the console by the same surgeon. In this report, we focus on surgical technical steps, feasibility, and early postoperative outcomes, including pain evaluation using the Numeric Pain Rating Scale (NRS), complications, and functional recovery, evaluated during the outpatient visit through specific questions about life activities.

Surgical technique

All procedures were performed under general anesthesia with single-lung ventilation using the *da Vinci Xi* robotic surgical system. The patient is placed in lateral decubitus like

a posterolateral incision and flexed to expose the intercostal space better. A 4-cm skin incision is made at the V or VI intercostal space in the middle axillary line. The correct location of the incision is of paramount importance, and it can vary based on the target of surgery and the chest shape. The incision must be as close as possible to the vascular

TABLE 1 Patients' characteristics.

Pts	Sex	Age	Tumor size (cm)	Lesion location	Smoking	Comorbidities
1	M	78	3.2	Right lower lobe	Ex	Ischemic heart disease, hypertension
2	F	68	0.9	Left lower lobe	No	Hypertension
3	M	67	2.3	Left lower lobe	Yes	Hypertension, COPD
4	F	57	1.2	Left upper lobe	Yes	Hypertension
5	F	66	2.0	Right upper lobe	Yes	Hypertension, COPD,
6	M	68	2.0	Left upper lobe	Yes	COPD
7	F	47	1.6	Right upper lobe	Yes	Hyperthyroidism
8	M	77	1.3	Left upper lobe	Yes	Hypertension
9	F	78	2.5	Right upper lobe	No	Vasculopathy
10	F	58	2.0	Right middle lobe	Ex	Hypertension
11	F	60	1.2	Left lower lobe	Yes	
12	M	79	1.7	Right lower lobe	Yes	Ischemic heart disease, hypertension, COPD
13	F	43	0.8	Right lower lobe	Ex	
14	M	66	2.2	Right upper lobe	Yes	Hypertension, COPD
15	F	62	1.8	Left lower lobe	Yes	COPD
16	F	56	1.6	Left upper lobe	No	
17	M	60	2.8	Right upper lobe	Ex	Diabetes
18	M	79	2.4	Left lower lobe	Ex	Hypertension
19	F	47	1.5	Right middle lobe	Ex	
20	F	80	3.0	Left upper lobe	Yes	Hypertension, COPD
21	F	70	1.3	Right upper lobe	Ex	Hypertension, diabetes
22	M	53	1.8	Left lower lobe	Yes	Hypertension
23	F	62	2.4	Right lower lobe	Ex	Hypertension
24	F	53	1.5	Left lower lobe	Ex	

structures that must be resected. This allows the robotic arms to be perpendicular to the target, limiting their conflict and optimizing the available space (Figure 1A). A soft wall protector is used to avoid excessive trauma to the chest wall.

Three robotic arms are always used, and the trocars are directly anchored to the arms without any pressure valve. A 30-degree 10-mm camera is placed on the posterior edge of the incision as in U-VATS surgery, and the other two arms are placed in the remaining space anteriorly. The operative robotic arms work by crossing each other inside the chest; thus, the right robotic arm will be the left surgeon's hand and the left robotic arm will be the right surgeon's hand, as shown in Figure 2. With this setting, to avoid the mirroring effect, it is necessary to apply a reverse mode to the console touchpad, allowing the right hand to control the left robotic arm and vice versa. Gauze peanuts are freely inserted in the chest to be used to mobilize the lung, reducing parenchymal trauma and optimizing movements. A robotic Maryland bipolar forceps dissector is controlled by the right surgeon's hand, and a monopolar fenestrated forceps is controlled by the left surgeon's hand. As usual, the assistant surgeon stands anterior to the patient handling the suction catheter in the space between the three trocars. A suction catheter is not used only to suck fluids but mainly for retraction and exposure of structures. Vascular structures and pulmonary parenchyma are sutured with Sureform 45 Robotic Staplers or with Hem-o-lok robotic clips. Lobectomy or segmentectomy is performed respecting the standard anterior approach (13) to the hilar structures and the fissureless technique (14), whenever possible. At the end of

the surgery, a single chest drain toward the apex is placed by the assistant surgeon.

Results

No intraoperative or perioperative mortality was observed. All procedures were completed with the uniportal approach. We performed 22 lobectomies and 2 segmentectomies; systematic hilar and mediastinal lymph node dissection was accomplished in all patients but 3—the patients with secondary lesions (laryngeal and cervical cancer metastasis). Mean operative time at console including docking was 210 ± 63 min (range 120–350) (Table 2); in the last 10 cases, the operative time was significantly reduced (180 ± 30 min) compared to the first 14 cases (232 ± 72 min) ($p = 0.02$). No patient required blood transfusion, and the mean blood loss was 110 ± 35 ml. No patient required adjunctive administration of drugs to control postoperative pain and no opioid drugs were administered. Furthermore, the mean score of NRS measured on the first postoperative day was $2.6 (\pm 0.6)$, on the third day was $1.6 (\pm 0.7)$, and at discharge was $1.3 (\pm 0.4)$, showing a constant decrease. In four patients (16.7%) minor complications occurred: one prolonged fluid leak (>350 cc/day) was solved spontaneously on day 6, one prolonged air leak was solved spontaneously on day 8, and two atrial fibrillation was treated with pharmacological cardioversion. The mean length of hospital stay was 5.2 ± 1 days (range 3–9). All patients performed an outpatient visit after 30 days from discharge, and in all cases, the functional

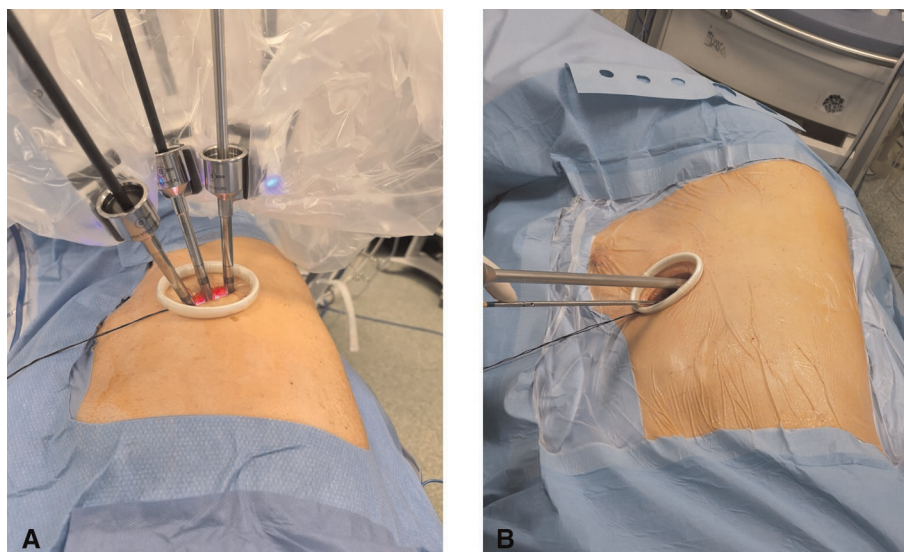


FIGURE 1

(A) U-RATS: incision in the middle axillary line with trocars perpendicular to the target. (B) U-VATS: incision by the anterior approach with trocars tangential to the target.

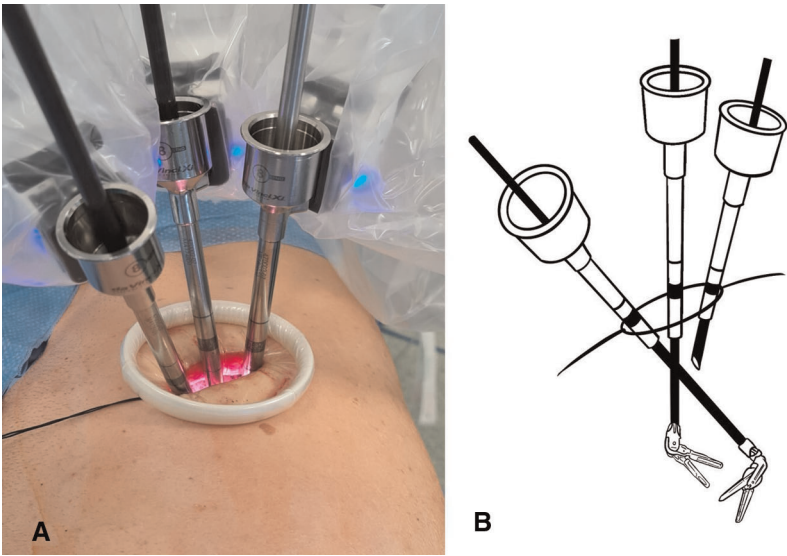


FIGURE 2
(A) External trocars vision. (B) Vision of instruments crossing inside the chest.

TABLE 2 Surgical procedures and postoperative results.

Pts	Procedure	Histology	Complications	Hospital stay (days)	Operative time (min)
1	Lower lobectomy	Adenosquamous	0	6	245
2	S6 segmentectomy	Cervix Mtx	Fluid leak	7	240
3	Lower lobectomy	ADC	0	6	315
4	Upper lobectomy	ADC	0	5	290
5	Upper lobectomy	ADC	0	4	350
6	Upper lobectomy	ADC	0	5	330
7	Upper lobectomy	ADC	AF	6	240
8	Upper lobectomy	Squamous cell	AF	6	270
9	Upper lobectomy	ADC	0	4	200
10	Middle lobectomy	Squamous cell	0	4	165
11	S6 segmentectomy	Laryngeal Mtx	0	5	120
12	Lower lobectomy	ADC	0	5	170
13	Lower lobectomy	ADC	0	3	135
14	Upper lobectomy	Squamous cell	0	4	185
15	Lower lobectomy	ADC	0	4	165
16	Upper lobectomy	ADC	Air leak	9	190
17	Upper lobectomy	Laryngeal Mtx	0	6	210
18	Lower lobectomy	Adenosquamous	0	5	180
19	Middle lobectomy	ADC	0	5	190
20	Upper lobectomy	ADC	0	6	185
21	Upper lobectomy	ADC	0	5	210
22	Lower lobectomy	ADC	0	6	135
23	Lower lobectomy	Carcinoid	0	5	215
24	Lower lobectomy	ADC	0	4	125

recovery ranged from satisfactory to good; only two patients were referred to mild local paresthesia.

Discussion

Typical weaknesses of lung cancer patients have led the surgical community to look for less invasive techniques. Nowadays, U-VATS is the less invasive approach available in thoracic surgery and can be applied to the majority of thoracic surgery procedures, including bronchovascular resection and reconstruction (3, 4). Nevertheless, RATS experience is increasing in many Thoracic Surgery Centers due to well-known advantages such as the 3D vision, lack of physiological tremors, stability of the camera, and a shorter learning curve compared to VATS. However, the RATS technique is always described with three or four incisions plus a utility incision of 4 cm. This is certainly more invasive than the uniportal incision used in U-VATS (15), and uniportal RATS is exclusively a newborn technique that is growing nowadays (10–12).

According to our experience with U-VATS and borrowing from the experience described in the literature (10–12), we started a Uniportal RATS program at the IRCCS “Pascale Foundation” National Cancer Institute of Naples.

The great maneuverability and adaptability of the *da Vinci* Xi robotic system allow many tailored configurations that are of paramount importance using the system through uniportal access. Docking the system in U-RATS is certainly faster than in standard RATS because of the single incision, but it should be performed very carefully to avoid potential fighting between the robotic arms. This can be obtained by keeping a distance of 10 cm between the robotic elbows and a working angle with the chest wall greater than the ones in U-VATS. As the operative arms must cross each other inside the chest (Figure 2), to avoid damage to the ribs, it is mandatory to work as perpendicular to the target as possible. For this reason, differently from U-VATS, in which the instruments enter the chest wall anteriorly with a 45° angle, the surgical incision of U-RATS should be more posterior to allow the arms to work with a mean 70° angle with the chest wall (Figures 1A,B). Due to the intracavity crossing of the instruments, at the touchpad console, the control setting should be modified, changing the arm control, allowing the right master to control the left robotic arm and vice versa. Large movements of masters during surgery should be limited to avoid arms conflict.

Respecting these rules, vessel isolation is easy and always possible without any vessel tension or damage. However, the most time-consuming step of the procedure, in our experience, is represented by vascular stapling due to the dimensional mismatch between robotic staplers and thoracic

anatomy. Most of all left upper lobe artery branches or minor right upper lobe branches can be safely managed with the robotic Hem-o-lock clips applier, being smaller and easier to be introduced in the chest. Although using the 45 Sureform Robotic stapler is feasible, it is not easy to approach the vessels and avoid external conflicts between arms and, of course, avoid tension to the vessels. In this scenario, the best equilibrium can be found by balancing the correct stapler angle with a countertraction of the underlining lung parenchyma. The use of the 30 Endowrist curved tip stapler could certainly be helpful but unfortunately it was unavailable in our institute during the study period.

In our opinion, the learning curve of this technique in U-VATS experienced surgeons is quite fast, and we found a significant shortening of the surgical time in the last 10 cases ($p=0.02$), thus confirming the well-known rapid learning curve of robotic surgery. We did not record any intraoperative complication that needed conversion, but in this case, the switch from U-RATS to U-VATS or thoracotomy is certainly quicker than in standard RATS because removing three arms from a single incision is very fast, without jeopardizing the safety of the patient.

The advantages of RATS have been extensively described in the literature (16–18) and were not the focus of our paper. Still, our experience with both techniques, U-VATS and RATS, showed better postoperative pain control in U-VATS than in RATS patients. Starting from this statement and according to the frailty of our patient population, we decided to evaluate the feasibility and the efficacy of the U-RATS technique, combining the advantages of U-VATS with the well-known advantages of RATS.

The evaluation of the NRS scale was satisfactory in our series and comparable to U-VATS patients in the early postoperative time and 1 month later, confirming that the number of chest incisions is directly related to the postoperative pain, supporting the early recovery.

This technique needs to be tested on a bigger patient population, but in our early experience, we can conclude that U-RATS is certainly safe, feasible, and comparable to U-VATS in terms of postoperative pain results. It remains a time-consuming technique, but the learning curve for skilled U-VATS surgeons is quite fast; furthermore, new suturing devices could simplify the surgical steps through standardization and worldwide spreading of U-RATS.

Data availability statement

The original contributions presented in the study are included in the article/supplementary material; further inquiries can be directed to the corresponding author/s.

Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study.

Written informed consent was obtained from the individual (s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

EM contributed to the conception and design of the study and wrote the main part of the manuscript. NM contributed to the conception and design of the study and drew the figures. GL and AR organized the database. CM performed the statistical analysis. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Single-port robotic surgery for mediastinal tumors using the da Vinci SP system: Initial experience

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Purpose: Studies of single-port robot-assisted thoracic surgery (RATS) using the da Vinci SP system, which uses a smaller surgical incision than the conventional multiport robot, have yet to be reported because of its smaller operating range. We report our initial experience using the da Vinci SP system in thoracic surgery for the resection of mediastinal tumors that requires a smaller workspace.

Description: Two patients diagnosed with superior mediastinal tumors underwent RATS performed with the da Vinci SP surgical system in January 2022. We used three-dimensional reconstruction to preoperatively determine the surgical incision. This is the first report of single-port RATS using the SP system in China.

Evaluation: R0 resection was achieved in both operations without complications. Operation times and bleeding volumes were similar to the use of multiport RATS. No perioperative complications occurred.

Conclusions: The da Vinci SP system can be used for the resection of superior mediastinal tumors. Case selection and preoperative planning should be performed prior to these surgeries.

KEYWORDS

single-port robotic surgery, mediastinal tumors, da Vinci SP system, minimally invasive thoracic surgery, superior mediastinal tumors

Technology

Single-port robot-assisted thoracic surgery (RATS) using the da Vinci SP system has yet to be reported. Robot-assisted surgery has demonstrated superiority in the resection of mediastinal tumors, particularly tumors in the superior mediastinum (1). In the past 5 years, our group has performed more than 40 consecutive robot-assisted surgeries for superior mediastinal tumors and accumulated valuable technical experience. In January 2022, two cases of single-port robot-assisted surgery for superior mediastinal masses were performed in our institute using the da Vinci SP system. To our knowledge, this was the first use of the da Vinci SP for single-port thoracic surgery in China.

Technique

First, we performed a three-dimensional (3D) reconstruction to choose the incision in case all workspace was covered in the SP system operating range. Then, SP RATS was

performed according to preoperative planning. Patients' characteristics and perioperative data were recorded to evaluate technical feasibility.

Clinical experience

Material and methods

Patients

Two consecutive patients diagnosed with superior mediastinal tumors underwent RATS performed with the da Vinci SP surgical system in January 2022. Case 1 was a 48-year-old female with an incidental finding of a mediastinal mass during a medical checkup without clinical symptoms. Case 2 was a 45-year-old male presenting with right ptosis and blurred vision who was diagnosed with Horner's syndrome. A mediastinal mass was found on subsequent CT examination (Figure 1A). Both surgeries were performed by the same surgeon who had performed more than 40 surgeries

for mediastinal tumors using the conventional da Vinci Si or S robot over the last 5 years and had completed da Vinci SP system training and certification.

Preoperative procedure

Both patients underwent an MRI examination to exclude mass extension through the intervertebral foramen and vascular or nerve invasion (Figure 1B). Preoperative cardiopulmonary function and other basic assessments were favorable, with no contraindications to general anesthesia observed. As the instrument arm position was limited, the surgical procedure relied entirely on the activity of the "elbow" and multijoint "endowrist" (Figure 2). 3D reconstruction was performed preoperatively to determine the incision location using OsiriX software (Fondation OsiriX, Geneva, Switzerland), which can be downloaded free from the Internet. The choice of incision was based on two principles. According to the SP system instructions, the location for the SP cannula should be greater than 10 cm from the nearest

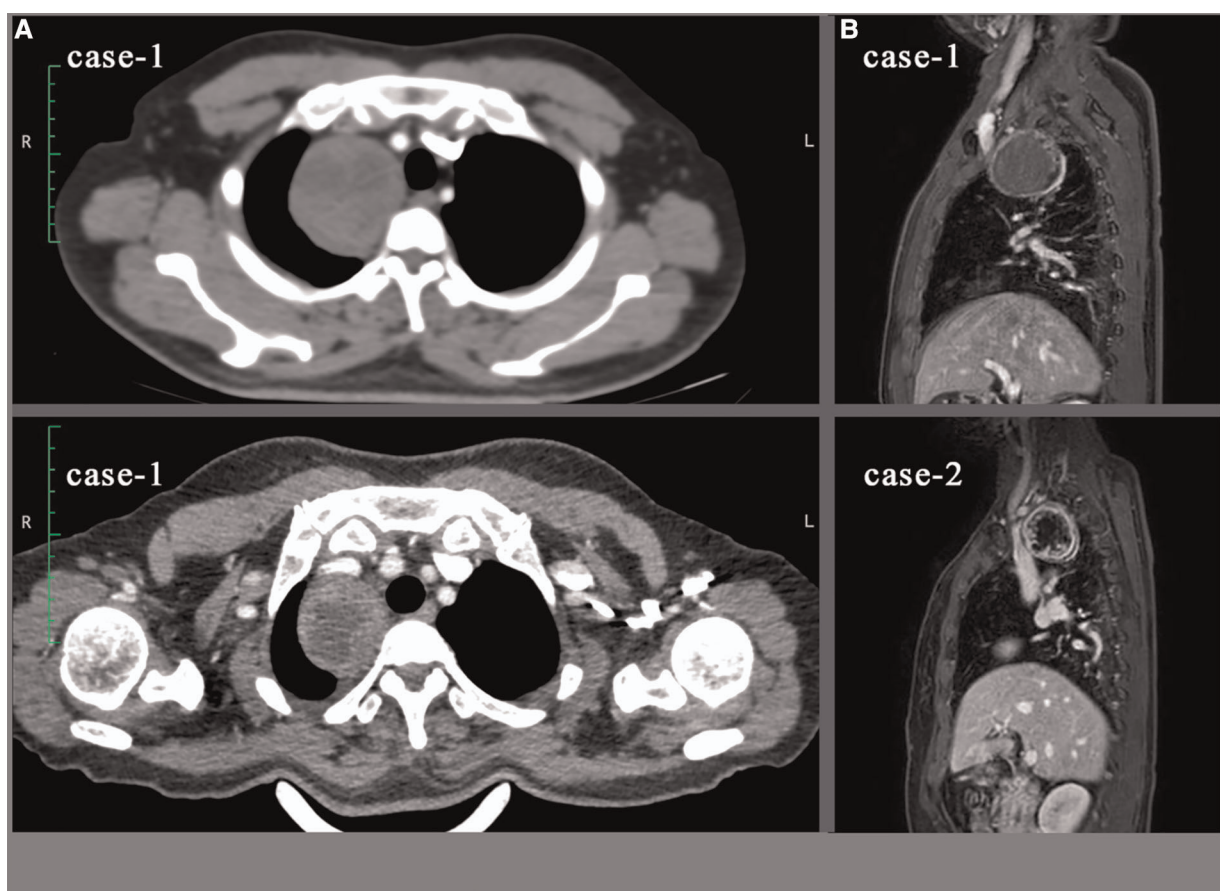


FIGURE 1
Ct and MRI images of both tumors. (A): Cross-sectional view of the tumor on CT examination; (B): Sagittal view of MRI. In case-2, the tumor has cystic component.

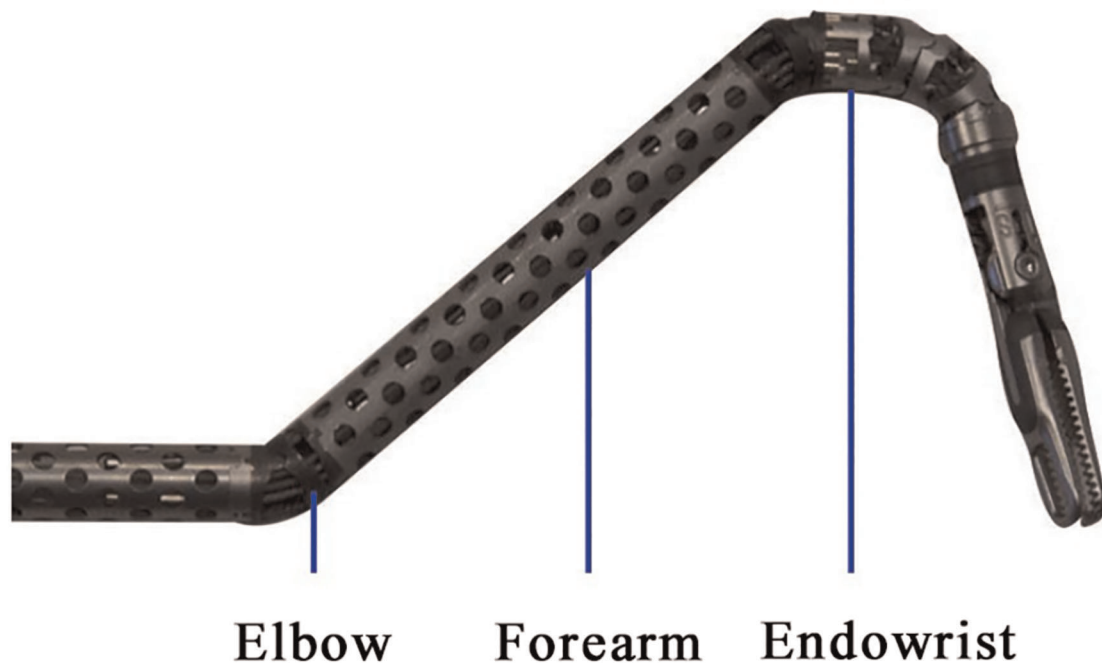


FIGURE 2

Demonstration of the flexible double-jointed instrument. The movement of the “elbow” joint ensures that the lens does not conflict with the two Endowrists.

border of the surgical workspace and less than 25 cm from the farthest border of the surgical workspace. Then, the cannula and the center of the tumor should be maintained in a straight line. We made measurements based on the above criteria (Figure 3). Incisions were selected to allow full instrument articulation and reach.

Surgical procedure

Both patients were positioned in the lateral decubitus position after general anesthesia with the use of a double-lumen endotracheal tube (Covidien IIc, Athlone, Ireland). According to preoperative 3D reconstructions, a 4 cm incision was made in the third (case 1) and fourth (case 2) intercostal space around the anterior axillary line. An incision retractor (HK-60/70-60/100) was used to enlarge the intercostal space. The robot was then docked over the head (Figure 4). The diameter of the cannula used with the SP system was 25 mm. Because of the limited intercostal width, the cannula was unable to be directly inserted into the intercostal space. Therefore, we mounted the cannula outside the body to ensure alignment between the incision and the tumor. A 3D camera lens and operating instruments were passed through the cannula and the intercostal space into the thoracic cavity. We favored using the camera at the 12 o'clock position with a permanent cautery hook (Surgical Intuitive, Mountain View,

CA, USA) at 3 o'clock (arm 2) and fenestrated bipolar forceps (Surgical Intuitive, Mountain View, CA, USA) at 9 o'clock (arm 1). The instruments of arms 1 and 2 were interchanged when required. The bedside assistant used suction apparatus to assist the operation through the same incision site (Figure 5).

First, the relationship between the tumors and the sympathetic nerve chain was explored. Both tumors were found to be outside the pleura. The tumor in case 2 was found to originate from the pleura. Consistent with preoperative imaging, both tumors had intact envelopes and no clear trophoblastic vessels. Tumors were separated along their borders. Extreme care was taken to prevent damage to subclavian vessels. The use of electrical energy devices was avoided near sympathetic nerves. Based on MRI findings, the tumor capsule in case 2 was incised to internally decompress the cyst to increase the operative field. Both tumors were removed through the incision with a sample bag after complete resection. A 16-Fr drainage tube was placed through the same incision site as per routine practice (Figure 6).

Results

A 3D view of the surgical field allowing full exposure and separation was provided using the fully wristed camera and

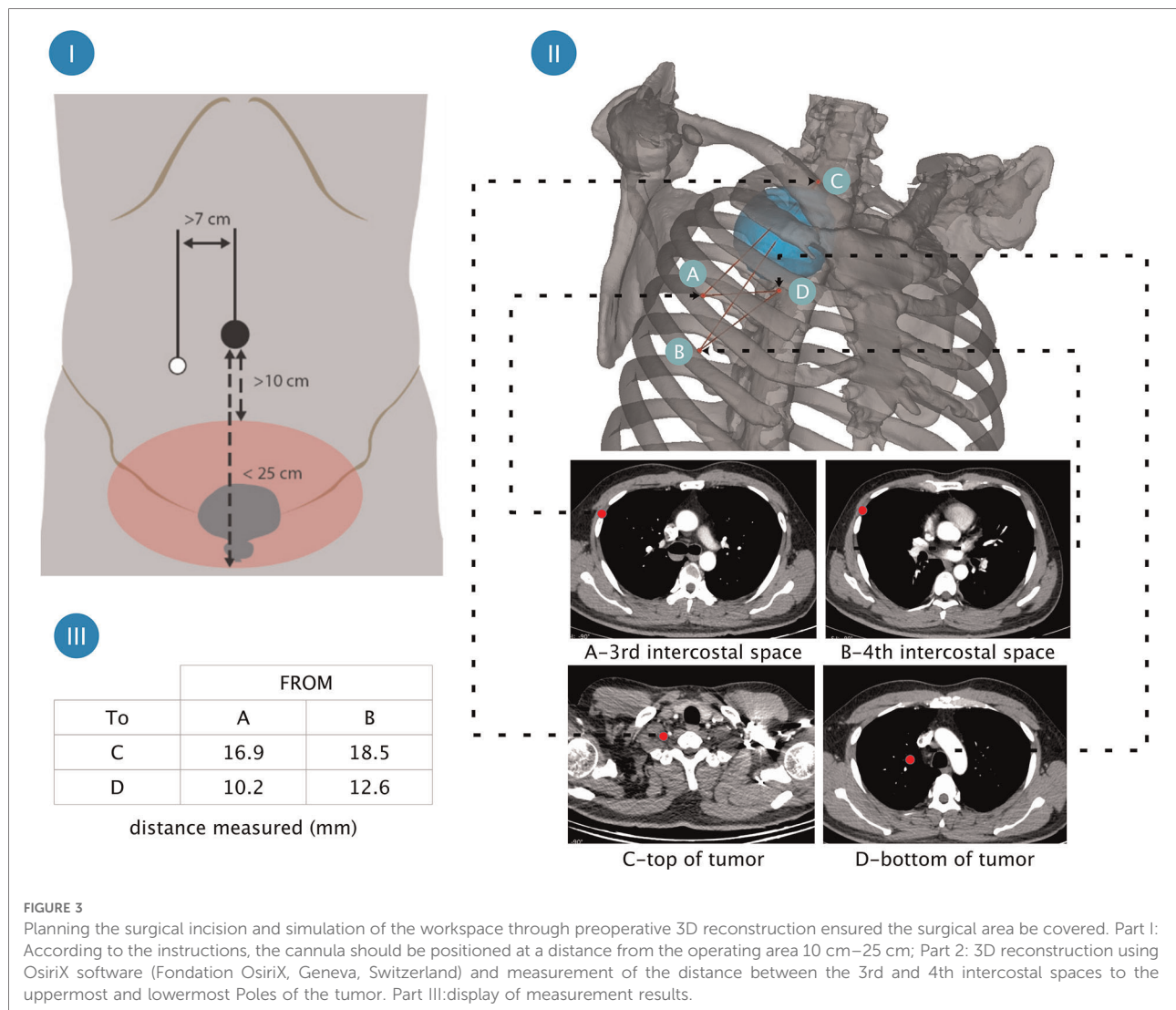


FIGURE 3

Planning the surgical incision and simulation of the workspace through preoperative 3D reconstruction ensured the surgical area be covered. Part I: According to the instructions, the cannula should be positioned at a distance from the operating area 10 cm–25 cm; Part 2: 3D reconstruction using OsiriX software (Foundation OsiriX, Geneva, Switzerland) and measurement of the distance between the 3rd and 4th intercostal spaces to the uppermost and lowermost Poles of the tumor. Part III: display of measurement results.

double-jointed instruments. Pathological examination demonstrated schwannoma in both cases. R0 resection was achieved in both cases. Conversion to video-assisted or open surgery was not required in either case. **Table 1** shows the patients' demographics and perioperative data. The total operative time was 113 and 103 min, respectively. No intraoperative complications occurred, with intraoperative blood loss volumes of 50 and 100 ml, respectively. These results are comparable with the use of conventional multiport RATS. No complications greater than Clavien–Dindo (2) grade I occurred postoperatively. Drainage tubes were removed in both patients on the first postoperative day when the following criteria were met: plain chest radiography demonstrating no pneumothorax, pleural effusion, or focal consolidation; drainage volume less than 100 ml per day; and no obvious abnormality in laboratory measures, including routine blood tests, inflammatory markers, and indicators of

coagulation function. Both patients were discharged on the second postoperative day.

Outpatient follow-up was conducted 1 month postoperatively. Both patients recovered well. There was no obvious amelioration of Horner's syndrome (right ptosis and blurred vision) in case 2. Satisfactory cosmetic results were achieved in both patients.

Comment

The da Vinci SP robot, which represents a more minimally invasive surgical approach, has been successfully used in urology (3–5) and gynecology (6) surgeries. Although conventional multiport robot-assisted surgery has long been used for the treatment of various thoracic diseases, da Vinci SP RATS has not previously been reported because of its



FIGURE 4
Robot docked over the head.

limited workspace and the large operating range required for thoracic surgery. First, the operating depth range was only 15 cm. As the diameter of the cannula was much larger than

the intercostal space, we referred to previous reports of single-port transoral robot-assisted surgery (7) and left the cannula outside the thoracic cavity while inserting the

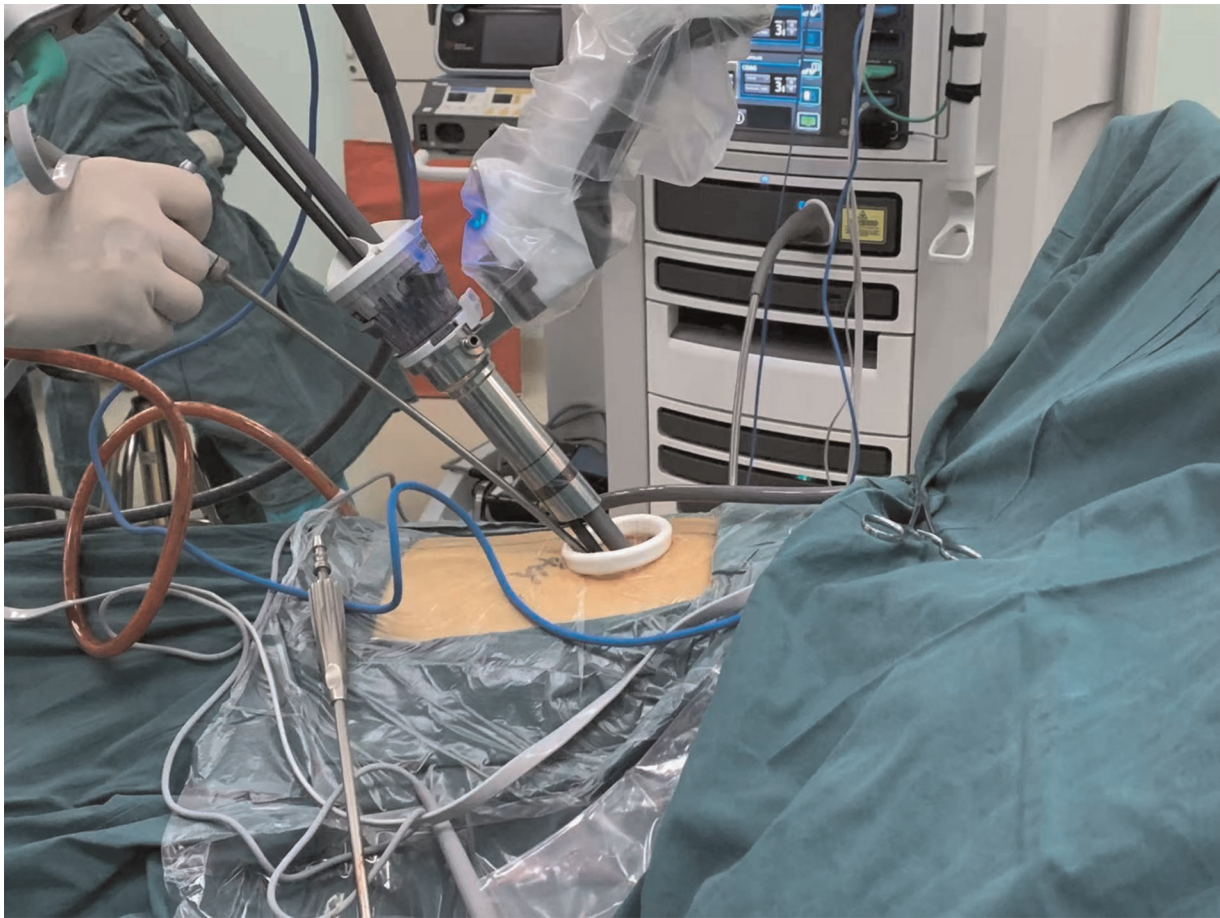


FIGURE 5
Placement of the instruments and suction apparatus used by bedside assistant.

camera and instruments into the cavity. This approach solved the docking problem but further shortened the operating range. Second, movements in both up/down and left/right directions rely on the rotation of the instrument arm, which could not be performed because of the limitations of the thoracic bony structure, particularly when the required movement was in the direction vertical to the incision. Neurogenic tumors in the mediastinum required only a limited surgical range, which can be met by the SP robot despite the above limitations. Previous experience with multiport RATS for mediastinal tumors has shown that the location of the incision should be individualized (8). This is particularly important in SP RATS. Based on our experience in planning pulmonary segmentectomy using 3D reconstruction (9), we believe that 3D reconstruction can accurately measure the operational limits that may be encountered intraoperatively. Planning the surgical incision and simulation of the workspace through preoperative 3D reconstruction (10) ensured that the surgical area could be covered. As a next step, we aim to explore

the use of 3D printed models to simulate surgical incisions. The surgical procedure was performed without the use of artificial pneumothorax, and the bedside assistant was able to use the incision for additional retraction and suction as well as specimen retrieval, which represents an advantage of the SP robot.

We believe that these two successful surgeries demonstrate that SP robot-assisted surgery can be successfully used to perform resection of small- to medium-sized mediastinal tumors. The SP robot is advantageous for surgery with limited surgical space, such as the resection of esophageal smooth muscle tumors and neurogenic tumors. However, this approach is not feasible for surgeries requiring wide operative fields such as the resection of esophageal and lung cancers. Accordingly, further studies of surgical methods are required before the SP robot can be applied to these surgeries. Additionally, we were unable to compare the advantages and disadvantages of the SP robot compared with the previous generation of multiport robots because of the small sample of the present study.



FIGURE 6
Placement of drainage tube, incision length and cosmetic result after suture.

To our knowledge, this is the first report of single-port RATS using the da Vinci SP robot system in China. We plan to extend the findings of the present study to evaluate the utility of this system in lung and esophageal surgeries.

Disclosures and freedom of investigation

The da Vinci SP system used in this study was purchased by our institute. The authors are fully

TABLE 1 Patients' characteristics and perioperative data.

Characteristic	Patient NO. 1	Patient NO. 2
Age (year)	48	45
Sex	Female	Male
Body mass index (kg/m ²)	23.83	27.46
Operative time (min)	113	103
Docking time (min)	15	10
Console time (min)	86	90
Suture time (min)	12	13
Intraoperative complications	No	No
Conversion to other surgery	No	No
Estimated blood loss (ml)	20	100
Tumor size (cm)	5 × 5 × 3	7 × 5 × 2.5
Histological type	Schwannoma	Schwannoma
Duration of the chest tube	1	1
Total chest tube drainage	100	40
Discharge	POD 2*	POD 2*
Pain at discharge, VAS score	3	5
Postoperative complications	No	No

*POD: postoperative day.

responsible for the design of the study, methods used, outcome measurements, analysis of data, and production of the written report.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

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Ethics statement

Ethical review and approval was not required for the study on human participants in accordance with the local legislation and institutional requirements. The patients/participants provided their written informed consent to participate in this study.

Author contributions

BY, surgery assistant and paper revision; RC, paper writing and picture editing; YiL, paper writing; YaL, surgeon and the project leadership. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Robot-assisted Ivor Lewis Esophagectomy (RAILE): A review of surgical techniques and clinical outcomes

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In the past 20 years, robotic system has gradually found a place in esophagectomy which is a demanding procedure in the deep and narrow thoracic cavity containing crucial functional structures. Ivor Lewis esophagectomy (ILE) is a mainstream surgery type for esophagectomy and is widely accepted for its capability in lymphadenectomy and relatively mitigated trauma. As a minimally invasive technique, robot-assisted Ivor Lewis esophagectomy (RAILE) has been frequently compared with the video-assisted procedure and the traditional open procedure. However, high-quality evidence elucidating the advantages and drawbacks of RAILE is still lacking. In this article, we will review the surgical techniques, both short and long-term outcomes, the learning curve, and explicate the current progress and clinical efficacy of RAILE.

KEYWORDS

robotic surgery, Ivor Lewis esophagectomy, minimally invasive esophagectomy, esophageal cancer, clinical outcomes

Introduction

Esophageal cancer is one of the most life-threatening cancers with 544,076 patients dead in 2020 (1). The establishment of multimodal therapy effectively enhances surgical outcomes and long-term survival (2, 3). Currently, surgery remains the crucial and primary measure for the eradication of early and locally advanced esophageal cancer. The introduction of the da Vinci robotic system to esophagectomy, as a promising minimally invasive technique, aimed at reducing morbidity and mortality, improving long-term survival, and raising patients' quality of life. It has been nearly 20 years since the first reported case of robot-assisted minimally invasive esophagectomy (RAMIE) case, and RAMIE is now frequently applied in high-volume esophageal surgery centers around the world (4–6). The robotic platform's ergonomic design, tremor filtration, flexible articulation and three-dimensional vision, make it particularly suitable for a demanding esophagectomy which combines dissection and reconstruction in a deep dark cavity with important anatomical structures. Ivor Lewis procedure and McKeown procedure are both considered to be the mainstream surgery types nowadays, while transhiatal esophagectomy is less utilized for its skeptical ability

in lymph node (LN) dissection (7). The theoretical advantages of robot-assisted Ivor Lewis esophagectomy (RAILE) have so far not been statistically defined. In this review, we summarize the existing publications to overview surgical techniques, short-term outcomes, long-term outcomes and the learning curve of RAILE, and offer our perspective on RAILE.

Surgical techniques

In most high-volume centers, RAILE is performed with a da Vinci Surgical System (Intuitive Surgical, Inc., Sunnyvale, CA) and a four-arm technique. As many publications reported experience and details of different parts of RAILE (8–13), we generally summarize the well-accepted procedure. We propose several possible ways for the same step and the literature in which they are described in detail if they are currently performed with no significant increase in adverse events.

Patient setup

For the abdominal portion, the patient is positioned supine and in a 15°–25° reverse Trendelenburg position (with or without a ~10° rotation to the right). Five trocars are most commonly placed (three for robotic arms, one for observation, and one as an assistant port). We normally do not apply a liver retractor but an additional subxiphoid incision may be formed to place a Nathanson liver retractor in certain institutions (9, 10). For the thoracic portion, the patient is placed in the left-lateral decubitus position in the thoracic phase with single-lung ventilation. Similarly, five trocars are usually placed. An example of trocar placement is demonstrated in [Figure 1](#).

Abdominal portion

The abdominal portion starts by retracting the liver, using either the purse-string suture and clips or a Nathanson retractor (10, 14). After the aberrant left gastric artery is evaluated, the hepatogastric ligament is dissected along the lesser curvature up to the right crus of the diaphragm. A D2 lymphadenectomy is then performed, covering LNs around the common hepatic artery, the left gastric artery, and the splenic artery. The left gastric vessels are ligated using Hem-o-lok Clip and the da Vinci Endowrist Vessel Sealer or Harmonic scalpel ([Figure 2](#)). As the lesser sac is now visualized by gently lifting the fundus, all colonic mesentery adhesions, residual ligaments, and short gastric arteries should be carefully dissected or ligated. The right crus of the diaphragm can be severed, which facilitates the opening of the gastrocolic ligament. The gastrocolic ligament is dissected along the greater curvature

towards the spleen, from approximately 2 cm away from the gastroepiploic arcade. The left gastroepiploic vessels are divided, while the right ones are preserved. Kocherization of the duodenum is not routinely performed. At this point, the stomach has been completely mobilized (10). The abdominal portion can also begin with the greater curvature of the stomach and mobilize the stomach towards the crus of the diaphragm if preferred (12).

Thereafter, a gastric conduit measuring 4–5 cm is required to be formed. The conduit is developed from the pyloric antrum to the fundus along the greater curvature with several fires of an Endostapler with 45 mm/60 mm staplers. The apex of the conduit is connected to the inferior portion of the specimen by two interrupted silk sutures and marked with a stitch, allowing it to be lifted into the thoracic cavity without any torsion (14). Another possible option is to partially form the gastric tube in the abdominal cavity and then insert the circular stapler from the remnant stomach to alleviate microvascular damage and serve for end-to-end anastomosis (10).

Most institutions prefer to inject indocyanine green (ICG) intravenously to assess the perfusion of the conduit, which is reported to potentially decrease the risk of anastomotic leakage (15). Some institutions perform intramuscular Botox injections to the pylorus to improve early gastric emptying and prevent postoperative reflux (9, 16). However, these measures are not obligatory and must be further validated for effectiveness. Jejunostomy is regularly performed (usually 20–30 cm distally away from the ligament of Treitz), as the last step of the abdominal portion (9), to implant a feeding probe to ensure postoperative enteral feeding. However, the role of jejunostomy has not been concluded yet (17, 18).

Thoracic portion

To begin the thoracic esophageal dissection, LNs are dissected around the right recurrent laryngeal nerve (RLN) and the arch of the azygos vein is divided. The esophagus is then mobilized *en bloc* down to the gastroesophageal junction, with all surrounding LNs in the periesophageal, periaortic, and subcarinal areas dissected. To avoid heat injury, periesophageal tissue should be meticulously cleared with special attention (11), using cutting devices such as Monopolar Cautery Hook, Harmonic Scalpel, and Bipolar Forceps. The thoracic duct is selectively clipped in some centers. After pulling up the conduit through the hiatus, the specimen and conduit are disconnected. The proximal esophagus is divided with robotic scissors 2–3 cm above the level of the azygos vein and sometimes to the thoracic inlet depending on tumor location. The specimen is removed through the wound protector and frozen section analysis is performed (This step is after anastomosis in case of the aforementioned partially formed gastric tube).

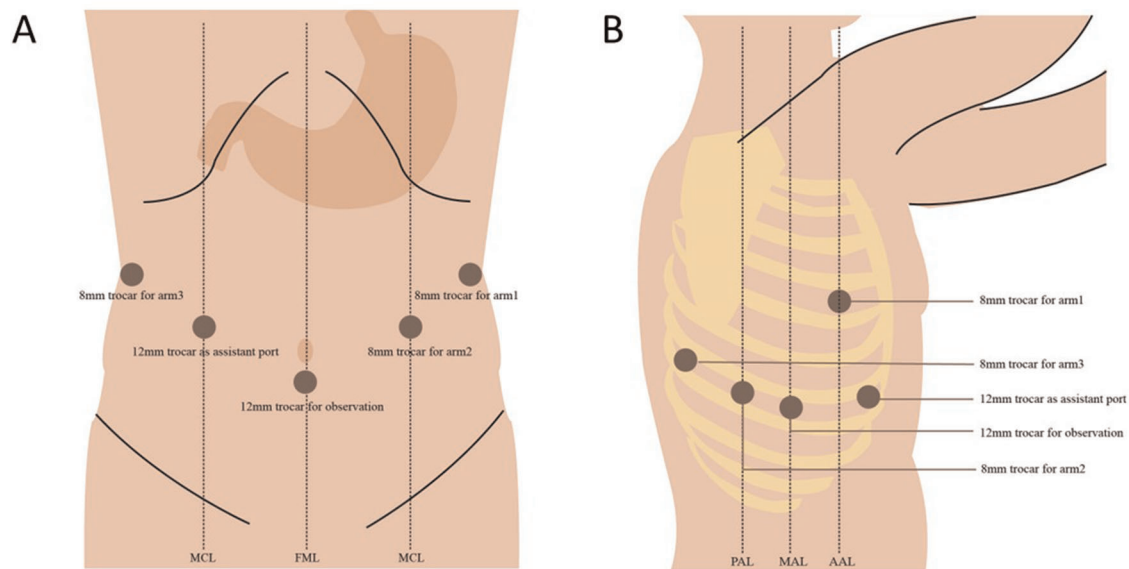


FIGURE 1

An example of patient positioning and trocar placement in our hospital. (A) Abdominal phase and (B) thoracic phase.

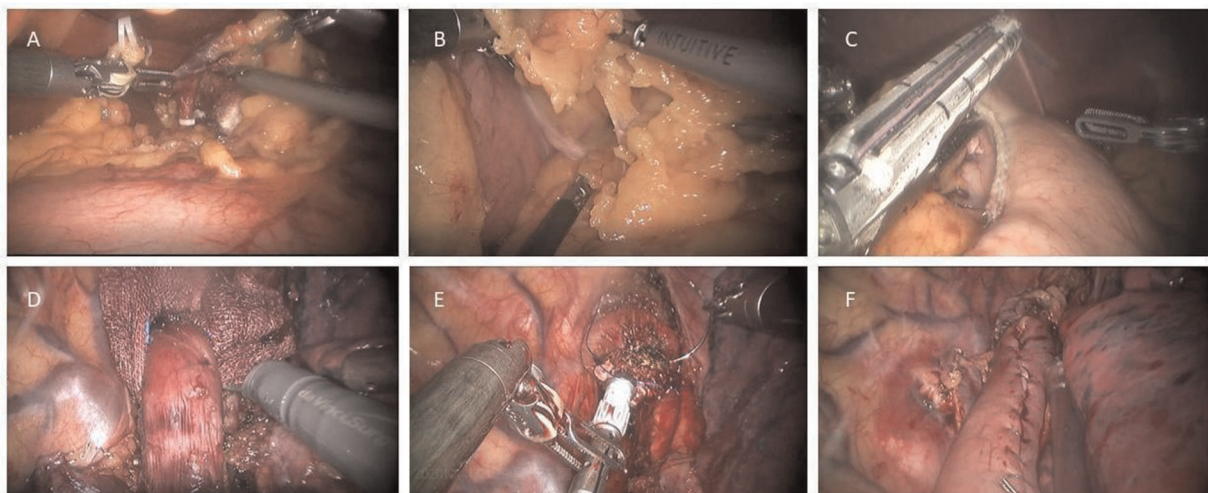
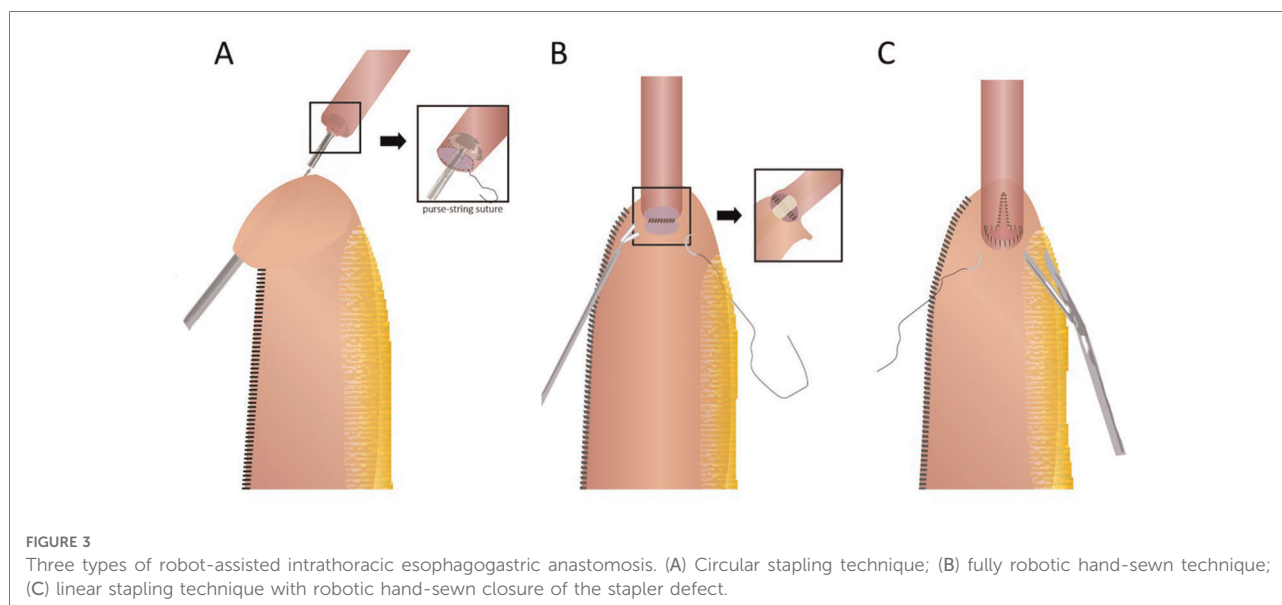


FIGURE 2

Key steps in robot-assisted Ivor Lewis esophagectomy. (A) After the lesser omentum was divided, the left gastric pedicle was exposed and divided with Hem-o-lock clips and a vessel sealer. (B) The gastrocolic ligament was divided toward the left gastroepiploic pedicle. (C) A 4–5 cm wide gastric conduit was formed toward the fundus with several fires of an Endostapler. (D) The esophagus was mobilized *en bloc* down to the gastroesophageal junction with dissection of all surrounding lymph node tissues. (E) The anvil of a 25-mm Premium Plus CEEA circular stapler was carefully inserted into the distal esophageal stump and fixated with two separate concentric purse-string sutures. (F) The form of a completed esophagogastric anastomosis.

After the frozen section analysis, the esophagogastric reconstruction follows. There are three major methods used for reconstruction as described in the following paragraphs and Figure 3. The anastomosis can be finally reinforced with an omental wrap to prevent leakage (9, 12).

Circular stapled anastomosis: This is the most commonly used anastomosis technique in RAILE because of its relative reliability and simplicity. A 25/28/29 mm circular stapler anvil is inserted into the esophageal stump either transorally or transthoracically and fixated with two separate concentric



purse-string sutures. The handle is then inserted into the conduit *via* an incision on the tip and pierced through the stomach wall on the greater curve side. After appropriately marrying the spike and anvil, the anastomosis is formed by firing. Finally, the proximal redundant conduit and gastrotomy are closed with an endostapler (12, 19).

Robotic hand-sewn anastomosis: Using a double-layer technique, the surgeon generally constructs the posterior and anterior walls of the anastomosis in order. The posterior seromuscular layer of the esophageal remnant is interruptedly sutured to the serosa on top or side of the gastric tube, followed by gastrotomy along the suture line and a running suture of the posterior mucosal layer. Then, the inner and outer layers of the anterior wall can be closed respectively with a single running suture and interrupted sutures or with interrupted sutures for both layers (11, 20).

Linear stapled anastomosis: The conduit and the esophageal remnant are partly overlapped. A small gastrotomy is performed about 4–5 cm below the tip of the conduit. The anvil parts are then placed separately in the conduit and the esophageal lumen, and an approximately 3 cm anastomosis is formed. The stapler defect is finally completed with a robotic hand-sewn technique, including the inner layer by running barbed sutures and the outer layer by interrupted sutures (13, 21, 22).

Short-term outcomes

Several studies have demonstrated the feasibility and safety of robot-assisted esophagectomy *via* the Ivor Lewis procedure. As a promising technique of minimally invasive esophagectomy, thoracic surgeons are encouraged to compare it with the conventional laparoscopic-thoracoscopic one to

discover latent benefits or defects. Angeramo et al. recently published the first meta-analysis of 5,275 video-assisted Ivor Lewis esophagectomy (VAILE) patients and 974 RAILE patients to statistically clarify the difference in surgical outcomes between these two minimally invasive approaches (23). An evidence-based comparison between RAILE and VAILE was also carried out as a subgroup analysis in the study conducted by Manigrasso et al. (24). However, heterogeneity existed between the included studies in terms of certain indicators, which impaired the credibility to some extent. The relevant studies on RAILE are illustrated in Table 1, categorized by their objectives.

An overview of short-term outcomes of RAILE

Short-term outcomes of RAILE, as shown in Table 1, are generally satisfactory when compared with a modern global benchmark for outcomes associated with esophagectomy (25). The operation time ranges from 304 to 445 min and the median blood loss ranges from 28 to 331 ml. The average LN yield is between 19 and 29, which was theoretically adequate to retain precise *N* staging and guarantee long-term survival (26). Common complications related to esophagectomy include anastomotic leakage, pulmonary complications (such as pneumonia, respiratory failure, pleural effusion, and pneumothorax), vocal cord paralysis, severe cardiac complications (mainly arrhythmia), chylothorax, and wound infection. The anastomotic leak rate ranges from 1.9 to 19.6% (4, 8, 11, 22, 27–36). Despite using different anastomotic methods, some centers had leak incidences of less than 5%, suggesting the underlying importance of personal proficiency.

TABLE 1 Patient characteristics and short-term outcomes of studies on robot-assisted Ivor Lewis esophagectomy (more than 50 patients).

Author	Objective	N	Patient characteristics			Intraoperative outcomes		Morbidity and mortality						Hospitalization					
			Median age	Sex, Male (%)	Histology, EAC (%)	Neoadjuvant therapy (%)	Anastomotic method	Op Time (min)	EBL (ml)	LNH	Anastomotic leaks (%)	Pneumonia (%)	Vocal cord paralysis (%)	Chylothorax (%)	Atrial fibrillation (%)	Overall morbidity (%)	In-hospital/30-day mortality (%)	ICU stay (day)	LOS (day)
Zhang Y (2019) (36)	RAMIE vs. VAMIE	76	62	78	0	0	CS/HS	304	200	19	9.2	6.6	6.6	1.3	6.6 ^a	31.6	0.0 (90 d = 1.3)	NA	9.0
Tagkalos (2020) (35)	RAMIE vs. VAMIE	50	62	NA	NA	86	CS	383	331	27	12.0	12.0	NA	NA	NA	24.0	0.0 (90 d = 5.0)	1.0	12.0
Meredith (2020) (33)	RAMIE vs. VAMIE	144	66	79	NA	78	CS/HS	409	155	20	2.8	6.9	NA	NA	11.8 [*]	23.6	NA (90 d = 1.4)	NA	9.0
Pointer (2020) (34)	RAILE vs. Open	350	66	83	87	81	CS	425	232	21	14.9	15.7	NA	1.7	23.7	74.3	2.6	NA	9.0
Kingma (2020) (32)	RAILE: multicenter experience	331	NA	NA	NA	NA	CS/HS/LS	400	100	28	19.6	23.3	1.0	4.8	15.0 ^a	52.6	3.0	2.0	12.0
Griminger (2021) (4)	RAILE: multicenter experience	175	61	85	81	82	CS/HS	385	28	28	10.3	16.0	NA	2.9	NA	32.0	1.1	NA	13.0
Egberts (2022) (29)	RAILE: multicenter experience	220	64	86	80	81	CS	425	200	25	13.2	19.5	NA	NA	NA	NA	NA (90 d = 3.6)	2.0	15.0
de la Fuente (2013) (28)	RAILE: single center experience	50	66	78	30	70	CS	445	146	20	2.0	10.0	NA	4.0	10.0	28.0	0.0	3.4	10.9
Hernandez (2013) (30)	RAILE: single center experience	52	65	79	88	67	CS	442	NA	19	1.9	9.6	NA	3.8	9.6	26.9	0.0	NA	NA
Cerfolio (2016) (27)	RAILE: single center experience	85	63	87	NA	75	LS	360	35	22	4.3	7.1	NA	5.9	7.1	36.5	3.5 (90 d = 10.6)	NA	8.0
Egberts (2017) (11)	RAILE: single center experience	75	66	68	96	79	CS/HS/LS	392	180	29	16.0	NA	NA	NA	NA	69.3	NA (90 d = 3.9)	NA	16.0
Zhang H (2019) (22)	RAILE: single center experience	77	62	88	18	21	CS/LS	350	111	21	6.5	9.0	6.5	1.3	1.3	39.0	0.0	1.0	12.3
Berth (2020) (8)	RAILE: single center experience	100	66	84	NA	84	NA	NA	NA	NA	5.0	7.0	NA	NA	NA	NA	1.0	1.0	11.0
Kandagala (2022) (31)	RAILE: single center experience	112	64	84	87	76	LS	357	65	19	8.5	10.4	1.9	NA	28.3 [*]	NA	0.9 (90 d = 3.8)	NA	NA

RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy; RAILE, robot-assisted Ivor Lewis esophagectomy; EBL, estimated blood loss; LNH, lymph node harvested; ICU, intensive care unit; LOS, length of hospital stay; 90 d, 90-day mortality; NA, not available.
#Rate of total cardiac complication.
*Rate of arrhythmia.

The evidence to compare the surgical outcomes of these three methods is still limited (37). The prevalence of pneumonia ranges from 6.6% to 23.3% (benchmark: 13.4%). The frequency of chyle leaks ranges from 1.3% to 5.9% (benchmark: 4.7%). The records of cardiac complications were particularly inconsistent and showed an evident discrepancy in the incidence of atrial fibrillation ranging from 1.3% to 23.7% (benchmark: 14.5%). Vocal cord paralysis was barely recorded in the listed studies. As the documentation of complications and morbidity varied among the studies, results are recommended to be recorded in line with the Esophagectomy Complications Consensus Group (ECCG) agreements (38). Mortality is a more fundamental indicator to assess the quality of surgery. Most studies in Table 1 show uplifting results of 30-day mortality (0% in five studies, 0%–3% in four studies, 3%–5% in one study). However, it is worth mentioning that 90-day mortality can be observed as evidently higher than 30-day mortality, which is still concerned to be caused by tumor- and management-related factors (39). The 90-day mortality may be an appropriate and valuable indicator of quality after the complex RAILE surgery.

Comparison between RAILE and VAILE

The mean operative time of RAILE was longer in all three studies comparing RAILE and VAILE (33, 35, 36). This was considered a disadvantage of RAILE because excessive prolongation of the operation (defined as over 422 min) raises the risk of pulmonary and infectious complications (40). However, we believe a factor that ought not to be neglected is the robotic repositioning time from the thoracic to the abdominal phase. Yang et al. applied a more scientific method of operation time calculation, i.e., excluding the period between the uninstallation of devices and the abdomen incision. In this scenario, they obtained an unexpected result that a significantly shorter operation time was taken in RAMIE ($p < 0.001$) (41). Angeramo's meta-analysis showed lower intraoperative estimated

blood loss (EBL) in RAILE (144.3 ml vs. 213.6 ml, $p = 0.006$) (23). Of the three studies independently comparing RAILE and VAILE, one reported significantly higher LN yield conducted by RAILE (33), one showed a trend in favor of RAILE (35), and one reported no significant difference (36), suggesting better or similar LN yield in RAILE.

Comparison between RAILE and Open ILE

Comparison between RAILE and Open ILE has been relatively scarce, mainly because of its minimally invasive nature. As certain benefits of VAILE over Open ILE have been explicit (42–44), once we understand that RAILE and VAILE have similar or even better postoperative outcomes, we can assume that RAILE would possess benefits over Open ILE. Na et al. found that RAILE led to comparable complication incidence, lower rate of major complications and decreased LOS (13 vs. 15 days, $p = 0.03$) than Open ILE (45). Meanwhile, RAILE showed stronger capability in LN retrieval (42.8 vs. 35.3, $p < 0.01$). In another existing study in which 222 RAMIE were matched 1:1 to the Open ILE control, RAILE demonstrated shortened LOS (9 vs. 10 days, $p = 0.01$), lower reoperation rates (2.3 vs. 12.2%, $p = 0.001$), and extended operative time (427 vs. 311 min, $p = 0.001$) (34). An RCT has already demonstrated fewer surgery-related complications and better postoperative quality of life brought by RAMIE instead of open esophagectomy in the McKeown procedure (46). A similar trial in the Ivor Lewis procedure is still pending.

Long-term outcomes

Overall survival and recurrence-free survival of RAILE

Both 5-year overall survival (OS) and 5-year recurrence-free survival (RFS) are still fundamental metrics to evaluate the effect of RAILE (Table 2). Na et al. reported in their

TABLE 2 Patient characteristics and long-term outcomes of studies on robot-assisted Ivor Lewis esophagectomy.

Author	N	Patient characteristics					Survival outcomes				
		Median age	Sex, Male (%)	Histology, EAC (%)	Neoadjuvant therapy (%)	Median positive LN	Median retrieved LN	Median follow-up period (m)	Median OS (m)	5-year OS (%)	5-year RFS (%)
Pointer (2020) (34)	350	66	83	87	81	0.7	22.4	NA	63.3	NA	NA
Na (2021) (45)	136	65	90	0	26	1.4	42.8	31.8	NA	75.1	68.8
Kandagatla (2022) (31)	112	64	84	87	76	0	19	NA	NA	49.4	44.0

5-year OS, 5-year overall survival; 5-year RFS, 5-year recurrence-free survival.

propensity score-matching (PSM) analysis that 5-year OS was significantly higher in the RAILE group (75.1% vs. 57.9%, $p = 0.02$), while 5-year RFS was comparable (68.8% vs. 54.7%, $p = 0.15$) (45). They additionally noted that the 5-year rate of RFS regarding regional LN recurrence was higher in the RAILE group, with local and distal recurrence being detected with no positive finding. Another two relevant studies were carried out under hybrid RAILE, in both of which the transthoracic part was performed by a robotic platform (31, 34). Kandagatla found a 5-year OS of 49.4% and a 5-year RFS of 44.0% in patients undergoing the RAILE procedure (31). Although the results seem to be inferior to those by Na et al., it is explicable because of the more advanced pathologic staging in the patient population. Meanwhile, 343 RAILE patients being matched to the Open ILE cohort in the PSM analysis by Pointer showed a tendency of superior median overall survival (63 vs. 53 months, $p = 0.13$) (34). Such superiority in long-term survival can be possibly explained by the elevated capacity of LN dissection of RAILE over Open ILE (47). A recent population-based study analyzing the long-term effects of RAMIE revealed that RAMIE brought us significantly better overall survival over OE [hazard ratio (HR) 0.81, 95% CI: 0.68–0.96, $p = 0.017$], and no difference was detected between RAMIE and VAMIE (HR 0.99, 95% CI: 0.90–1.09, $p = 0.8$) (5).

An elevated quality of life brought by RAILE

Patients who underwent RAILE procedures also tend to have a better quality of life than those who underwent Open ILE. This is utterly important in our view because creating a maximum quality of life for patients with esophageal cancer within their expected limited lifespan aligns with the humanitarian imperative. Mahdorn et al. investigated self-perception and quality of life of postoperative RAILE patients with the European Organization for Research and Treatment of Cancer (EORTC) Quality of Life Questionnaire Core-30 (QLQ-C30) questionnaire at 4 and 18 months after surgery, respectively (48). RAILE patients reported better global health status after 4 months than Open ILE patients, with less fatigue, nausea, vomiting, pain, dyspnea, appetite loss, and diarrhea, as well as better function in all dimensions. After a longer period of 18 months, RAILE patients were reported to have significantly better recovery, with the symptoms further alleviated, functions further reestablished and some even returned to the level of the general population (48).

Learning curve of RAILE for thoracic surgeons

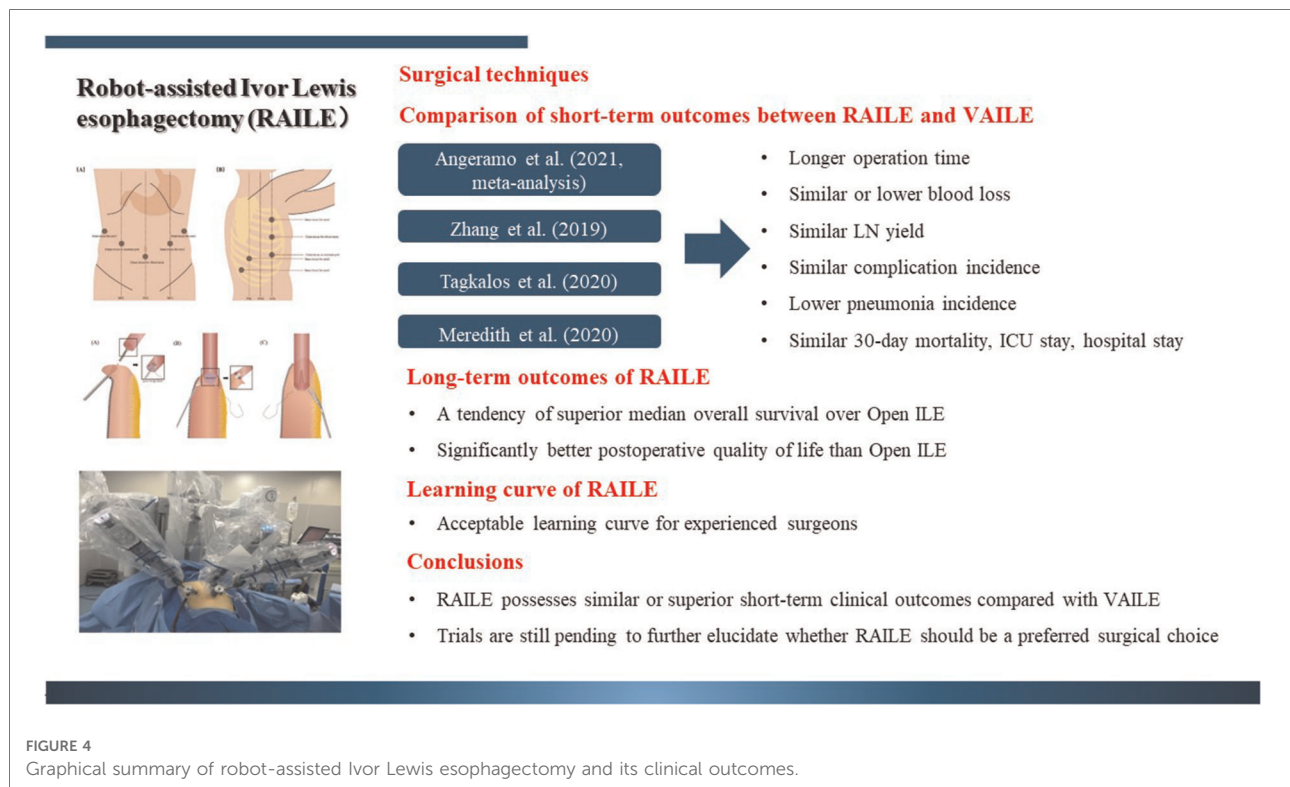
To optimize the surgical outcomes of RAILE, thoracic surgeons will have to experience a learning curve. Our group lately presented our results of the learning curve of RAILE within 124 consecutive

patients by risk-adjusted-cumulative sum analysis (49). We found that 51 cases were the baseline to achieve acceptable surgical outcomes and proficiency and 73 cases were needed to further make a difference in blood loss and LN yield (49). In comparison, the 22nd case represented the inflection point, resulting in less blood loss, shorter operative time, and a lower rate of postoperative pneumonia in German multicenter research (29). We thus speculate the Upper GI International Robotic Association (URIGA) structured training pathway implemented in Germany may be a crucial factor. Several earlier studies agreed with the reduction of operation time after approximately 20 cases without reporting perioperative outcomes (19, 30). Most of the RAILE articles in the past 20 years, as shown in Table 1, are inevitably influenced by the effect of the learning curve. Future publications may better illustrate the strength of RAILE, with more senior surgeons successfully surpassing the learning curve and obtaining proficiency.

Perspective

Since its introduction into esophagectomy, the robotic platform has developed and thrived in the field of esophageal surgery (50, 51). With more advantages of RAILE being confirmed, it may develop into a popular surgical option for patients in the future. First, as a robotic platform provides us with high-quality images and makes stable and flexible movements in the thoracic cavity (51), it has noninferior clinical results to VAILE. Second, RAILE patients have similar survival and elevated quality of life after the operation. Meanwhile, the learning curve of RAILE is acceptable. Demerits of RAILE mainly point toward the cost issue and the relatively inferior outcomes in low-volume centers (52). Soon, the ROBOT-2 Trial (NCT04306458) will be the first study to directly compare RAILE with VAILE in middle/distal esophageal or GEJ adenocarcinoma, with LN dissection as the primary endpoint (53). RAILE Trial (NCT03140189) conducted by our center, as a prospective, single-arm trial (phase II) collecting major complication rates and OS, recently finished patient follow-ups and the results will soon be posted. The trials above may further elucidate whether RAILE should be a preferred surgical option.

Besides, the theoretical survival benefit of three-field lymphadenectomy turned out to be limited and may add postoperative complication risks in esophageal cancer patients with lower tumor locations in recent studies. Koterazawa found that three-field lymphadenectomy resulted in a higher incidence of RLN palsy (14% vs. 26%, $p = 0.046$) without elevating 5-year OS (54). The research article published by Li et al. in 2020 strongly indicated that in middle and lower esophageal cancer, there was no significant difference in OS and disease-free survival (DFS), as well as in postoperative complications, between patients receiving three-field lymphadenectomy and two-field lymphadenectomy (55, 56).



These clues suggest that RAILE could be more widely accepted in the future when it is oncologically feasible.

In conclusion, RAILE is an effective minimally invasive technique to ensure the feasibility and safety of esophagectomy, with similar or superior clinical outcomes compared with VAILE (Figure 4). With more studies aiming at uncovering the latent advantages, RAILE is likely to have a broader and more mature application.

Author contributions

TS and YJZ were responsible for reviewing relevant publications, drafting the manuscript, and creating tables and figures for the manuscript. YQC and CL were responsible for the critical revision of the manuscript. HL was responsible for the conception, critical revision, and supervision of the manuscript. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Two-rope method for dissecting esophagus in McKeown MIE

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Objective: Minimally invasive McKeown esophagectomy (McKeown MIE) is performed at many hospitals in esophageal cancer (EC) treatment. However, secure and quick methods for dissecting the esophagus and dissecting lymph nodes in this surgery are lacking. This study introduces a simple, secure and feasible esophagus dissecting technique named two-rope method. Two mobile traction ropes are placed around the esophagus and we tow these ropes to free the esophagus, dissect the lymph nodes, and decrease the operative trauma.

Materials and Methods: Retrospective analysis was performed on 112 patients who underwent McKeown MIE in our center from January 2019 to September 2021. They were assigned into two groups based on the method of dissecting the esophagus: Group A (two-rope method, 45 cases) and Group B (regular method, 67 cases). Operation time, thoracic operation time, the number of dissected thoracic lymph nodes, and postoperative complications were compared between the two groups after propensity score matching.

Results: Using 1:1 nearest neighbor matching, we successfully matched 41 pairs of patients. Operation time, thoracic operation time, and the duration (ac to as) was significantly shorter and the size of the abdominal incision was significantly smaller in the Group A than Group B ($p < 0.05$). There was no statistically significant difference in the number of dissected thoracic lymph nodes, pulmonary infection, anastomotic leak, recurrent laryngeal (RLN) injury, and chylothorax between the two groups ($p > 0.05$).

Conclusions: Two-rope method to free the esophagus and dissect thoracic lymph nodes in McKeown MIE has significant advantages compared with the regular method. The technique is, therefore suitable for widespread adoption by surgeons.

KEYWORDS

minimally invasive esophagectomy, esophagectomy, esophagus suspension method, thoracoscope, esophageal carcinoma

Introduction

Esophageal cancer (EC) is the sixth most common cause of cancer-related death worldwide (1). The incidence and mortality of esophageal cancer in China are higher than the global average (2). Esophagectomy, including complete primary tumor removal and radical lymphadenectomy with or without cervical lymphadenectomy,

has been accepted as a radical esophagectomy that remains a standard treatment choice for esophageal squamous cell carcinoma (ESCC) (3). Earlier studies have reported low incidences rate of pulmonary infection and mortality, and better long-term survival in minimally invasive esophagectomy (MIE), compared with open esophagectomy (OE) (4–6). Since most esophageal cancers are squamous cell carcinoma (SCC) and located in the middle of the esophagus in China, minimally invasive McKeown esophagectomy (McKeown MIE) is preferred in our center (7).

Location and size of esophageal tumors are variable and meanwhile, freeing of esophagus as well as lymphadenectomy along the esophagus and recurrent laryngeals (RLNs), which have a high incidence of lymphatic metastasis in these regions, are fundamental steps of McKeown MIE (8, 9). Thus, surgeons should be able to expertly free the entire thoracic esophagus, and perform the dissection of lymph nodes along esophagus, left and right RLNs lymph nodes, and subtrochanteric lymph nodes in the thoracic procedure of the operation (10). However, McKeown MIE keeps a challenge. First, since freeing the esophagus and dissecting lymph nodes around the esophagus under the thoracoscope were difficult, surgeons often need to spend much time and energy to complete the standard surgical steps, which means a long anesthesia time and an enormous cardiorespiratory burden on the patient. Moreover, the anatomy of the aorta, thoracic duct, and trachea in the region of the left RLN is complex and variable, and it isn't easy to dissecting in the narrow space, which was indispensable in McKeown MIE. The exact dissection under the thoracoscope frequently takes more time than OE (5, 6), and may irritate RLNs.

In the past, some experts proposed a method to suspend and free esophagus (11). With the application of the suspension line, the upper esophagus could be suspended. And the surgeon could easily reveal the surgical field of the esophagus-trachea groove and the aortic arch and then free the upper thoracic esophagus, inferior lymph nodes of the aortic arch, the lymph nodes, and soft tissues surrounding the left RLN. This method is particularly advantageous for isolating the left RLN lymph nodes and upper esophagus.

Inspired by it, we strived to improve the esophageal suspension method during McKeown MIE. While performing the operating, two ropes were placed around the esophagus to suspend and free the entire thoracic esophagus and thoracic lymph nodes. The upper rope was used to release the upper thoracic esophagus, dissect the lymph nodes around the left RLN, and accurately locate the cervical esophagus. The lower rope was used to free the lower thoracic esophagus, accurately tow the free-esophagus from the thoracic cavity into the abdominal cavity through the esophageal hiatus and then quickly tow to the abdominal surface together with the free-stomach.

The purpose of this study was to propose a two-rope method for freeing the esophagus and dissecting thoracic lymph nodes in McKeown MIE. And then evaluate the feasibility of this method.

Materials and methods

Patients

We retrospectively analyzed the clinical data of 112 patients who underwent McKeown MIE from January 2019 to September 2021. Forty-five cases underwent McKeown MIE with the help of the two-rope method (Group A), while 67 cases were operated with the help of the regular method (Group B). All patients were diagnosed with ESCC by a gastroscopy biopsy before the operation and the clinical stage of the patients was determined by comprehensive physical and imaging examination, including contrast-enhanced CT of chest and upper abdomen and PET-CT. All operations were performed by an experienced thoracic surgeon. Data of intraoperative, demographics, and postoperative complications were analyzed retrospectively.

The inclusion criteria were: tumor stage I–III [International Union Against Cancer (UICC) Version 3, 2020]; the cardiopulmonary function was sufficient to allow for single-lung ventilation during the operation; complete clinical data.

The exclusion criteria for the patients were as follows: chemotherapy, radiotherapy and neoadjuvant therapy before surgery; upper esophageal tumor; inability to tolerate surgery; concomitant multiple operations; not willing to provide informed consent; anamnesis of thoracic diseases; cancer other than esophageal cancer; tuberculosis; silicosis.

This study was approved by the Clinical Ethics Committee of Jining No.1 hospital, Shandong province, China. All patients provided written informed consent.

Data collection

Demographic and intraoperative data were collected retrospectively. Demographic data constituted age, sex, body mass index (BMI), tumor node metastasis (TNM) stage, tumor location (upper middle, or lower third), pathologic stage, and histology. Intraoperative data constituted operation time, thoracic operation time, the duration of the free-esophagus and free-stomach from the abdominal cavity to surface [Duration (ac to as)], the number of dissected lymph nodes in the thoracic cavity, and the length of the abdominal center incision. Operation time was defined as the time (min) from the first incision to final closure. The thoracic operation time was defined as the start of thoracic incision to the closure of the thoracic incision. The duration (ac to as) was

defined as the time (s) required to pull out the severed free-esophagus and free-stomach completely to the abdomen surface after the abdominal center incision was made.

Postoperative complications included chylothorax, anastomotic leakage, pulmonary infection, and recurrent laryngeal nerve injury. We diagnose these complications by expert consensus (12).

Surgical technique

Thoracic operation: After successful general anesthesia and double-lumen endotracheal intubation into the left lung for single lung ventilation. The patient was placed in the left lateral decubitus position, and operation holes were made on the 3 or 4th intercostal space of the anterior axillary line, 5th intercostal space of the posterior axillary line, and 8th intercostal space of the anterior axillary line. The thoracoscope was inserted into the 6th intercostal space of the mid-axillary line. The lungs were pushed forward, dissected the lymph nodes of the right RLN and the azygos arch was freed and cut. The posterior mediastinal pleura was opened with an electric hook. The esophagus was explored to determine the location of the tumor. The esophagus was freed 1–2 cm medially or above and below the esophageal tumor. And two mobile

traction ropes were placed around the esophagus in these locations (**Figure 1A**). The esophagus was kept under traction ropes to provide more operating space in the posterior mediastinum. The surgeon towed the two mobile ropes to suspend the esophagus and dissect the adhesions of the esophagus and trachea, bronchus, hilum, and pericardium and remove mediastinal, para-esophageal, paratracheal, subcarinal, and lower pulmonary ligament lymph nodes. Meanwhile, towing ropes to control the esophagus helped to dissociate the tissue between the posterior esophagus and left pleura (**Figure 1C**). Finally, the surgeon hauled the upper rope to suspend and free the upper esophagus making it easier to hollow out the lymph nodes and connective tissue around the left RLN (**Figure 1B**). As the operation went on, the upper rope was pulled from the tumor or midpoint area to the pleural roof (**Figure 1D**) and the lower rope was removed to the esophageal hiatus for subsequent use. Thicker blood vessels or lymphatic vessels were cut with an ultrasonic knife. After ascertaining that there is no damage to the thoracic duct and RLNs, the chest was closed with an in-dwelling drain.

Neck operation: The patient was placed in a supine position. An oblique incision (4 cm) was made on the cephalic side at the medial edge of the left sternocleidomastoid muscle. The cervical esophagus was located and freed by the blue upper rope in the neck operation (**Figure 2B**).

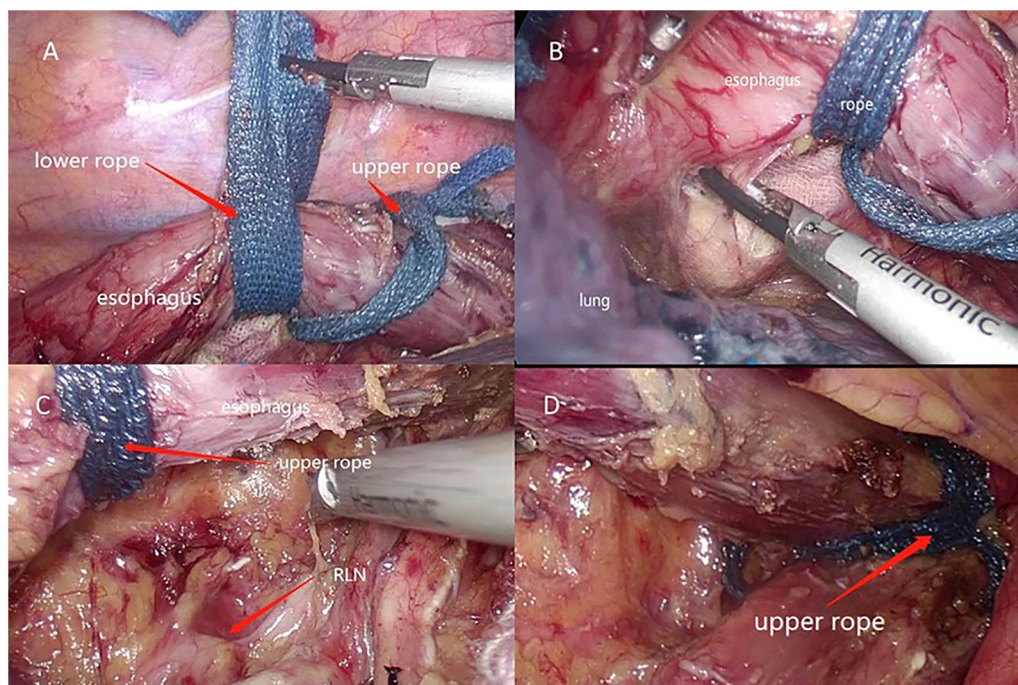


FIGURE 1

(A) Two ropes to free esophagus. (B) Suspend the esophagus to reveal the area of posterior esophagus and left pleura. (C) Tow the upper rope to enlarge the operation space. (D) Upper rope was placed in pleural roof.

Abdominal operation: The patient was placed in a supine position. Artificial pneumoperitoneum was established. Dissect the stomach and the lymph nodes around the stomach. Once the cervical esophagus was transected, the lower rope was pulled from the thoracic cavity to the abdominal cavity through the esophageal hiatus together with the free-esophagus (**Figure 2A**). Once the abdominal center incision was made, the lower rope was towed together with the free-esophagus and free-stomach directly from the abdominal cavity to the surface (**Figure 2C,D**). And then the tubular stomach was created. The cutting stump was wrapped with a continuous suture. The tubular stomach was then drawn to the neck incision through the esophageal bed and a circular stapler was used to perform end-to-side anastomosis.

After all steps were completed, the abdominal incisions were sutured and the size of the incision on the center of abdomen was recorded.

Statistical analysis

To address potential bias in the patients' characteristics between the two groups, we used propensity score matching

(PSM). Variables such as age, sex, BMI, comorbidities, tumor location and TNM stage were covariates. We created propensity score matching pairs with no replacement (1:1 matching) and set the caliper definition at 0.05. χ^2 test and Fisher's exact test were used for categorical data. Student's *t*-test was used for groups of data that were normally distributed, and the Mann-Whitney *U* test was used for non-normally distributed data. All statistical analyses were performed using SPSS 26 software (IBM Corp Armonk, NY). Values of $p < 0.05$ were considered statistically significant.

Results

Demographics

Forty-five patients underwent McKeown MIE with the help of the two-ropes method defined as Group A and 67 with the use of the regular method defined as Group B. Using 1:1 nearest neighbor matching, we successfully matched 41 pairs of patients. There was no significant difference in the demographics and clinical background between the two groups ($p > 0.05$) (**Table 1**).

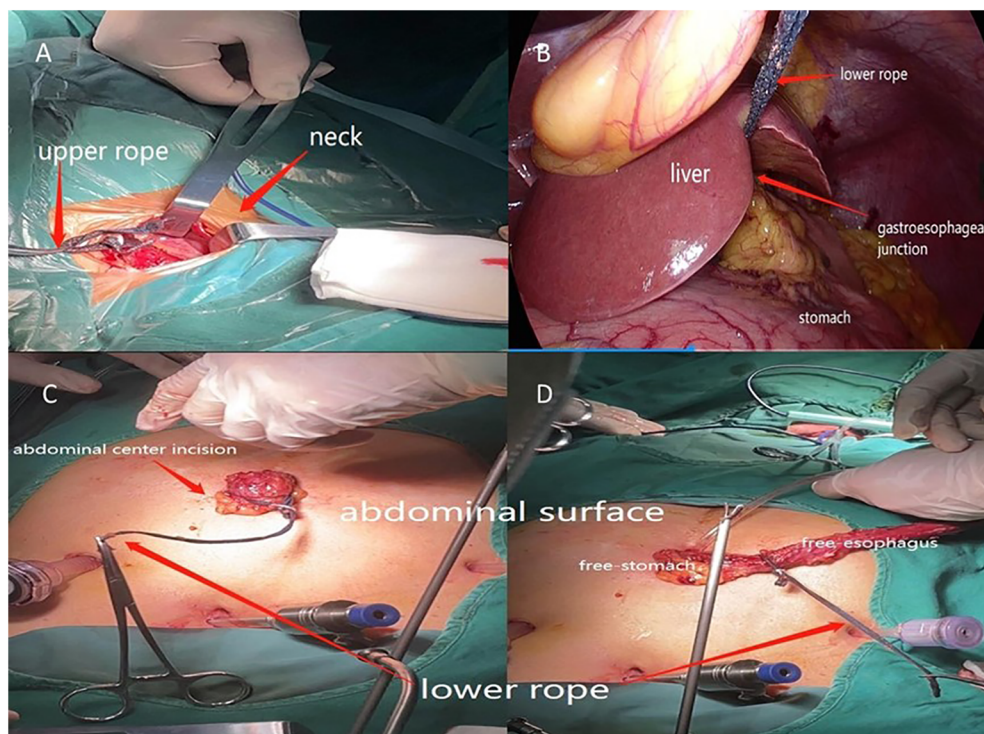


FIGURE 2

(A) Upper rope was used to locate and dissect the cervical esophagus. (B) Free-esophagus was towed by the lower rope to abdominal cavity. (C, D) Lower rope was used to tow the free-stomach and free-esophageal out of abdominal cavity.

Intraoperative data

The intraoperative data for the two groups are presented in **Table 2**. All operations were R0 resection and no patient in the two groups were required to undergo OE. The total operation time of Group A was significantly lower than that of Group B (237.66 ± 30.34 min vs. 270.68 ± 43.10 min; $p < 0.01$). The thoracic operation time of Group A was also significantly lower than that of Group B (70.93 ± 8.88 min vs. 87.98 ± 14.28 min; $p < 0.01$). Similarly, the duration (ac to as) of Group A was significantly lower than that of the Group B (15.24 ± 3.81 s vs. 166.1 ± 28.19 s; $p < 0.01$). The length of the abdominal center incision was significantly smaller in Group A than that in Group B (4.01 ± 0.54 cm vs. 6.26 ± 1.09 cm; $p < 0.01$). There was no significant difference between the two group in the number of thoracic lymph nodes dissected and perioperative bleeding ($p > 0.05$).

Postoperative complications

Table 3 details the postoperative complications for the two groups. There was no statistically significant difference in anastomotic leakage (4 vs. 6, $p > 0.05$), pulmonary

complications (5 vs. 9; $p > 0.05$), recurrent laryngeal nerve injury (1 vs. 1; $p > 0.05$) and chylothorax (1 vs. 1; $p > 0.05$) between two groups.

Discussion

McKeown MIE is an essential surgical procedure in EC treatment. As a safe and wide used surgical method, it enables the complete removal of the entire thoracic esophagus and radical lymph node dissection (5, 13). Compared with OE, MIE has been shown to shorten the risk of morbidity and mortality and be good in postoperative complications, lymph node dissection, blood loss and hospital stay (14, 15). However, there are still some problems troubling us. First, since freeing the esophagus and dissecting lymph nodes around the esophagus in thoracoscope, which were indispensable in McKeown MIE, were difficult, surgeons often need to spend more time and energy to complete the standard surgical steps. Moreover, the anatomy of the aorta, thoracic duct, and trachea in the region of the left RLN is variable. It is difficult to dissect in a narrow space (16). Finally, compared with the prone position, lung tissue is frequent to obscure the operative field in the left lateral

TABLE 1 Characteristics of patients in two groups.

Characteristic	Before PSM		<i>p</i>	After PSM		<i>p</i>
	Group B, <i>n</i> = 67	Group A, <i>n</i> = 45		Group B, <i>n</i> = 41	Group A, <i>n</i> = 41	
Age, years	65.57 ± 7.43	64.46 ± 7.27	0.332	64.66 ± 7.45	65.12 ± 6.77	0.769
Sex, male/female	50/17	30/15	0.361	32/9	28/13	0.319
BMI	23.12 ± 3.22	23.45 ± 6.26	0.597	23.34 ± 3.26	23.61 ± 3.36	0.712
Comorbidities						
CVD	5	5	0.519	2	3	1
PD	4	2	1	3	2	1
T2DM	6	4	1	5	4	1
Tumor location			0.528			0.756
Upper segment	4	3		1	3	
Middle segment	37	20		21	20	
Lower segment	26	22		19	18	
Pathologic stage			0.626			0.628
0	2	0		2	0	
I	13	7		6	7	
II	26	16		16	14	
III	26	22		17	20	

CVD, cardiovascular disease; PD, pulmonary disease; T2DM: type 2 diabetes mellitus; BMI, body mass index; Group B, regular method to free esophagus; Group A, two-rope method to free esophagus.

TABLE 2 Intraoperative data in two-ropes group Bnd regular group.

Variable	Group B, <i>n</i> = 41	Group A, <i>n</i> = 41	<i>p</i>
the length of abdominal center incision, cm	6.26 ± 1.09	4.01 ± 0.54	0
Total operation time, min	270.68 ± 43.10	237.66 ± 30.34	0
Thoracoscopy time, min	87.98 ± 14.28	70.93 ± 8.88	0
Duration (ac to as), second	166.1 ± 28.19	15.24 ± 3.81	0
No. of thoracic lymph nodes removed	14.83 ± 3.89	14.44 ± 4.01	0.656
To open	0	0	1
R0	0	0	1

Duration (ac to as) was defined as the time (s) required to pull out the severed free-esophagus and free-stomach completely to the abdomen surface after the abdominal incision was made; Group B, regular method to free esophagus; Group A, two-rope method to free esophagus.

TABLE 3 Postoperative complications in two-ropes group Bnd regular group.

Variable	Group B, <i>n</i> = 41	Group A, <i>n</i> = 41	<i>p</i>
Pulmonary infection	9	5	0.24
Anastomotic leak	6	4	0.5
Recurrent laryngeal injury	1	1	1
Chylothorax	1	1	1

Group B, regular method to free esophagus; Group A, two-rope method to free esophagus.

decubitus position that we always choose. To solve the difficulty, some scholars have reported their valuable experience of freeing the esophagus and dissecting lymph nodes in McKeown MIE. Zheng et al. (11), described an esophageal suspension method. The surgeons could use one silk that was punctured out in the fifth intercostal space of the scapular inner edge to suspend the esophagus and then dissect the left RLN lymph nodes and the thoracic esophagus easily. This method not only reduces the probability of injury to the left RLN, but also increases the number of left RLN lymph nodes removed, which is corrected closely with the patient's health, pathological staging and prognosis (17). Zhang (18) et al. proposed the application of esophageal wire traction in McKeown MIE to dissect lymph nodes. Because of the use of a wire to generate traction, the esophagus was suspended. The wire could be towed to keep the esophagus under traction and to move the right lung forward, thereby increasing the working space in the posterior mediastinum and improving the stability of the video-assisted-thoracoscopy.

The two-rope method to suspend the esophagus proposed herewith is an improvement on the esophageal suspension method described by Zheng (11). First, application of the

upper rope could assist in freeing and suspending the upper esophagus to dissect the lymph nodes and connective tissue around the left RLN during the thoracic operation (Figure 1B). Also, the upper rope could locate and free the cervical esophagus during the neck operation (Figure 2B). Finally, the lower rope could be used to free the lower esophagus and tow the free-esophagus and free-stomach from the thoracic cavity *via* abdominal cavity to surface through the abdominal center small incision (Figure 2C,D).

Compared with the Group B, the Group A had a significant advantage in operation time, including thoracic operation time, total operation time and the duration (ac to as). Why does Group A take less time? First, we think the two-rope method was significantly faster in freeing the thoracic esophagus and dissecting left RLN lymph nodes compared with the regular method. The surgeon could fully expose the esophageal bed by pulling the two ropes severally, making the anatomy of the thoracic esophagus clearer, speeding up the detachment of the esophagus and lymph nodes, and avoiding damage to the blood vessels and nerves. Pulling the upper ropes could expose the area of esophagus-trachea groove by suspending the esophagus to the right space, which could reduce the difficulty of dissection and increase the thoroughness of left RLN lymph nodes dissection, therefore the thoracic operation time was shorter in Group A than Group B. Then, since the lower rope was a long sterile rope, the surgeon could quickly and accurately drag the long rope out of the internal cavity (from thoracic cavity *via* abdominal cavity to surface) (Figure 2C,D) through abdominal center incision together with the free-stomach and free-esophagus after the abdominal incision was made. This method saves the process of probing the free-stomach by hand or oval forceps. Therefore, the duration (ac to as) was very short. Finally, by avoiding hand exploration, the surgeon could drag out the free-stomach with a smaller size abdominal center incision, requiring a shorter suture time. Thus, the total operation time was shorter than Group B. In a word, with this method, the surgeon could expose the operation field, speed up the detachment of the esophagus and lymph nodes, avoid directly touching the esophagus and stomach wall and tow the free-esophagus and free-stomach out of the abdominal cavity easily.

In regular McKeown MIE, it is primary for the assistant to repeatedly clamp the esophagus to help exposing the operation field. This may not only damage the esophageal muscular layer, increase intraoperative bleeding, and obstruct the visual field, but may also increase the surgeon's fatigue, increase the difficulty of the dissection, and waste time. And the surgeon always clamps the free-stomach and free-esophagus out of abdominal cavity through the abdominal center small incision by oval forceps or by hand directly for creating the tubular stomach outside during surgery. This is time-consuming, and increases the chances of accidental injury to the surrounding tissue and the stomach wall, and may cause complications

such as intrathoracic hemorrhage, intraabdominal hemorrhage and tumor spread.

In esophagectomy, the number of lymph nodes dissected is closely related to prognosis and an essential index for evaluation of the quality of thoracoscopic esophagectomy (19, 20). We found that the accuracy of dissection and the number of thoracic lymph dissected by the two-ropes method was comparable with the regular method. It showed both methods were safe and reliable.

Pulmonary infection, anastomotic leakage, RLNs injury, and chylothorax are common complications after esophagectomy (21). Once happen, the patients can be challenging to solve and can ultimately be life-threatening in some situations. There was no statistically significant difference in these postoperative complications between the two groups. It indicated that there was no difference in the prognosis and postoperative recovery between the two groups. This further illustrated the effectiveness, safety, and feasibility of the two-rope method for freeing the esophagus in McKeown MIE.

Conclusion

Two-rope method to free the esophagus and dissect lymph nodes in McKeown MIE has significant advantages compared with the regular method. The technique is therefore suitable for wide-spread adoption by the surgeons.

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Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

Author contributions

Qian Wang is the first author. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Postoperative diaphragmatic hernia following endoscopic thoracic sympathectomy for primary palmar hyperhidrosis: A case report

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Postoperative diaphragmatic hernia (DH) following endoscopic thoracic sympathectomy for primary palmar hyperhidrosis is extremely rare. We present a 21-year-old female patient who developed a left DH with herniation of the stomach and gastric perforation on the first postoperative day after undergoing bilateral video-assisted thoracoscopic sympathectomy R4 ablation. She complained of severe dyspnea and chest pain, and an emergency chest x-ray and computed tomography revealed left pleural effusion, collapsed lung, and left DH, which allowed the stomach to herniate into the chest. Emergency thoracoscopic surgery was performed. We repaired the diaphragmatic defect intraoperatively and replaced the stomach with the peritoneal cavity from the thoracic field. The patient was discharged without complications. She did not present with recurrent symptoms at the 3-month follow-up. Postoperative DH should be considered when patients complain of gastrointestinal or respiratory symptoms after sympathectomy, although it is very rare.

KEYWORDS

primary palmar hyperhidrosis, sympathectomy, diaphragmatic hernia, case report, video-assisted thoracoscopic sympathectomy

Introduction

Primary palmar hyperhidrosis (PPH) is defined as a pathologic condition of excessive sweating over 6 months in duration that impairs daily activities without occurring secondary to other specific diseases or medications (1). Currently, endoscopic thoracic sympathectomy (ETS) is an effective therapeutic method for the treatment of PPH (2), but there are also some common complications, including Horner's syndrome, pneumothorax, and hemorrhage, which have been reported worldwide (3). A few cases of diaphragmatic hernia (DH) or tension gastrothorax as a complication of thoracic and abdominal surgery occur (4, 5). DH after ETS has not been reported before, which leads to misdiagnosis or late diagnosis, resulting in high morbidity and mortality rates.

Here we report an extremely rare case of left DH with herniation of the gastric fundus and body following bilateral video-assisted thoracoscopic sympathectomy (VATS) R4 ablation for PPH, and the patient's primary clinical manifestation was respiratory distress. We successfully repaired the DH and the stomach defect by thoracoscopy with mesh placement.

Case presentation

A 21-year-old female patient without any specific medical history presented at our hospital with excessive palmar sweating for 10 years. She had previously received conservative treatments from a local hospital, including topical antiperspirants containing aluminum chloride hexahydrate; however, the symptoms were not relieved. We evaluated the severity of the disease based on the Hyperhidrosis Disease Severity Scale (HDSS) (6), and the preoperative diagnosis was severe PPH. A bilateral video-assisted thoracoscopic sympathectomy R4 ablation was recommended for the patient. The patient was administered general anesthesia and double-lumen endotracheal intubation. The patient was positioned supine in a semi-sitting position with the arms abducted 90°. A 1-cm access port was inserted in the midaxillary lines over the third intercostal space with a 30°, 10-mm video camera placed in the anterior and a 5-mm endoscopic hook placed in the posterior. No CO₂ insufflation was used for exposure. The chest was visualized, and the sympathetic chain was identified. Sympathectomy was performed with an electrocautery section of the sympathetic chain over the head of the rib, extending the burn along the rib for a length of 2–3 cm to cauterize potential bypassing branches of the chain (nerve of Kuntz). The level of sympathectomy (R4) was performed according to Chinese expert consensus (7). After lung expansion, no chest tube was routinely left in the thoracic cavity. The procedure was performed successfully, and sweating from the hands stopped immediately.

On the day of surgery, she began to complain of epigastric discomfort and vomiting, and fasting therapy was given. Chest radiography revealed a pneumothorax in the left lung with an elevated left hemidiaphragm (Figure 1A). The following day, the patient complained of severe dyspnea and chest pain. On chest auscultation, low breath sounds were heard on the left side, and the systemic examination was normal. Chest x-ray revealed a left pleural effusion and a mediastinal shift toward the right with an elevated left hemidiaphragm (Figure 1B). Thoracentesis was performed, both for diagnostic testing and drainage of the pleural fluid; and 60 ml of brown fluid, clinically suggestive of gastric juices, was drained by a needle. Emergency chest computed tomography (CT) demonstrated left pleural effusion, collapsed lung, and left DH, which

allowed the stomach to herniate into the chest (Figures 2A,B). We diagnosed left DH incarceration and performed an emergency thoracoscopic repair of the hernia.

Emergency surgery was performed, and the patient was administered general anesthesia with double-lumen endotracheal intubation and placed in the right hemilateral position for surgery. The operation was performed thoracoscopically and conducted through the eighth intercostal space to expose the pleural cavity. Intraoperatively, a contaminated thoracic cavity with stomach contents was observed, without pleural adhesions (Figure 3A). There was an approximately 6-cm diaphragmatic defect in the left posteromedial diaphragm, and the stomach had a 1-cm rupture and was herniated into the thorax through the defect (Figure 3B). There were no obvious ischemic findings. Abundant irrigation and direct repair of the damaged stomach and replacement of it into the peritoneal cavity from the thoracic field were performed by the general surgery team. We repaired the diaphragmatic defect with nonabsorbable sutures and reinforced it with polypropylene hernia repair mesh all around the defect. The operation was completed after the placement of drains in the thoracic cavities. The postoperative chest x-rays were normal, and the patient was discharged in good condition 10 days after the second operation without complications (Figure 1C). The patient did not receive any other medical treatment, and there were no other concomitant medical conditions requiring attention. The 3-month follow-up confirmed the absence of symptoms. At the time of this writing, her sweating had stopped for approximately 8 months, and there were no adverse effects during that period. Written informed consent was obtained from the patient.

Discussion

Thoracoscopic bilateral dorsal sympathectomy is the standard therapeutic method for PPH. To our knowledge, DH is a rare complication of sympathectomy and leads to life-threatening cases of strangulation or perforation as well as cardiovascular and respiratory insufficiencies (8). In this case, the patient complained of severe dyspnea and chest pain after ETS and was diagnosed with left DH with herniation of the gastric fundus and body. We repaired the damaged stomach and replaced it in the peritoneal cavity with VATS alone. In this case, we believe that the thoracic approach is more advantageous for the following reasons: (1) the thoracotomy wound that was used for the endoscopic orifice in the endoscopic thoracic sympathectomy can be used again; and (2) the patient complained of severe dyspnea and chest pain on the second day after the first operation. Considering the complexity of intrathoracic surgery and potentially serious complications, we chose the thoracoscopic approach in this

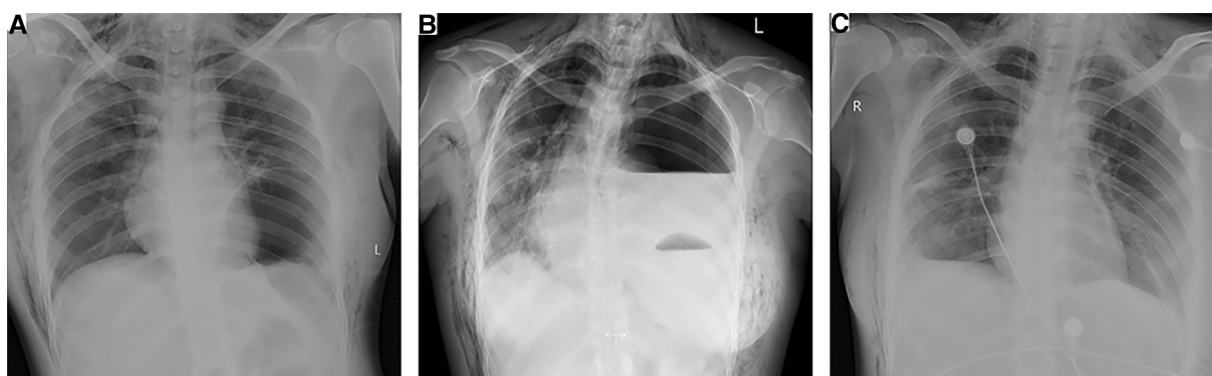


FIGURE 1

Chest radiographs. (A) Initial chest radiograph revealing an elevated left hemidiaphragm and pneumothorax in the left lung. (B) Chest radiograph showed left pleural effusion and a mediastinal shift toward the right with an elevated left hemidiaphragm. (C) Postoperative chest radiograph revealed normal positions of the stomach bubble and diaphragmatic contour.

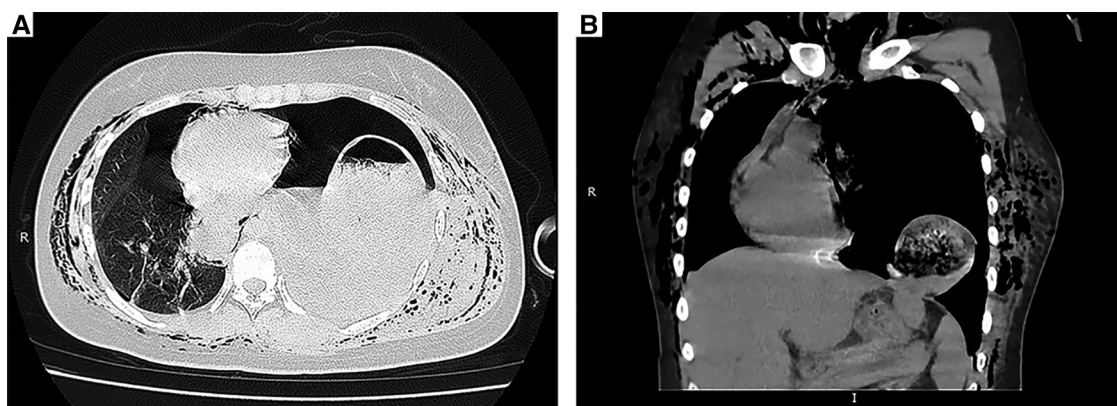


FIGURE 2

CT scans. (A) Preoperative chest CT image showed left pleural effusion, collapsed lung and intragastric gas with an air-fluid level in the left thoracic cavity. (B) Coronal CT image demonstrating that the stomach had migrated into the thorax.

case; (3) the preoperative images showed no obvious free gas under the diaphragm and additional intra-abdominal organ injuries.

The majority of the patients with diaphragmatic defects have defects that remain small, and they only complain of gastrointestinal symptoms (such as vomiting, postprandial discomfort, nausea) and respiratory symptoms (such as chest pain, cough, dyspnea). Patients can be asymptomatic for a long time and be diagnosed with delayed iatrogenic DH after surgery (5). Patients with DH incarceration and rupture of hernia contents can be critically symptomatic immediately after surgery, such as in our case, complaining of dyspnea on the first postoperative day.

Considering the pathogenesis of DH in our case, it could be related to congenital weakness of the diaphragm. Moreover, prolonged anesthesia induction led to gastric pouch dilatation

and continuous high airway pressure, which might amplify the transabdominal-pleural cavity pressure. The dilated gastric wall compressed the left diaphragm, and prolonged intense compression caused severe ischemia, which decreased the elasticity and strength of the diaphragm and eventually led to rupture of the left diaphragm and the formation of an incarcerated diaphragmatic hiatal hernia. During the surgery, the patient is intubated with positive pressure ventilation in the chest, and small perforations in the diaphragm remain collapsed and prevent the migration of abdominal structures. However, in the postoperative period, the respiration and the pressure gradient between the pleural cavity and abdomen consistently pull the small, defective diaphragm radially, gradually extending the small orifice over time until it allows abdominal organ herniation, especially on the left side, because of the cushioning effect of the liver protecting the right hemi diaphragm.

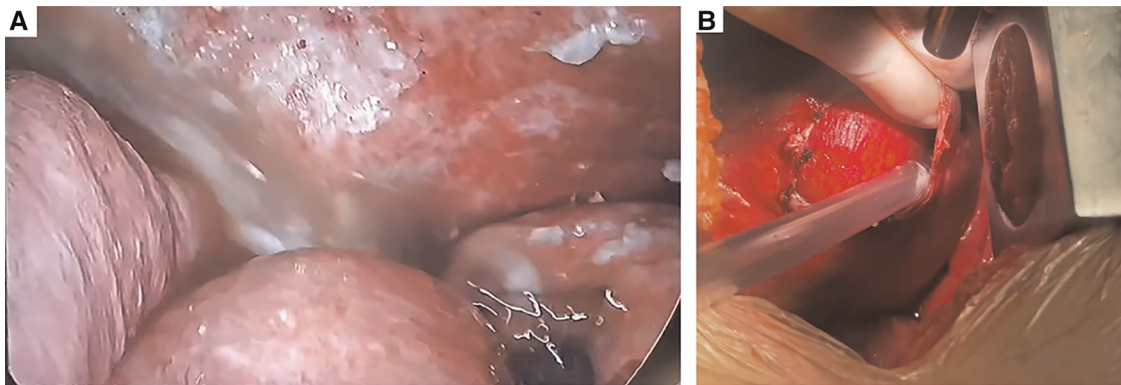


FIGURE 3

Intraoperative findings of the second operation. (A) Contamination of the thoracic cavity with stomach contents. (B) Intraoperatively, a 6-cm-diameter diaphragmatic defect was found.

Several reports have shown that initially, the chest x-ray is normal or can mimic pleural effusion, pneumonia, or pneumothorax, which can lead to a misdiagnosis. CT is the imaging modality of choice; whenever we see a chest x-ray or CT suggesting obscured diaphragmatic shadow, irregularity of the diaphragmatic contour, pleural effusion, and mediastinal shift, we should suspect the possibility of DH (9).

There are several limitations in our approach to this case. First, on the day of the first surgery, the patient began to complain of nausea and vomiting, and we were not aware of the risk and clinical presentation of diaphragmatic hernia. Second, we should use emergent gastric decompression with a nasogastric tube that may control the situation and let us buy some time to save the patients with fluids and acid–base balance adjustment. Third, the deficiency of thoracentesis is the lack of ultrasound guidance, which is dangerous in such situations. Fourth, a total follow-up period of 3 months by a surgeon may be too short to evaluate the prognosis of the patient.

In conclusion, it is important that thoracic surgeons inspect the integrity of the diaphragm at the end of surgery and consider the possibility of this rare complication in patients presenting with gastrointestinal or respiratory symptoms, especially after a left-sided thoracic procedure. After confirmation of DH, a feasible and reliable thoracoabdominal approach could be immediately used for treatment, including reduction of herniated organs and progression to more serious complications (10).

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author.

Ethics Statement

Written informed consent was obtained from the individual for the publication of any potentially identifiable images or data included in this article.

Author contributions

LW prepared and wrote this article. YT, XW, and ZF were involved in managing the patient. XW prepared the intraoperative pictures. ZF revised the manuscript and acted as the corresponding author. YT and XW were the main surgeons. All authors contributed to the article and approved the submitted version.

Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Robot-assisted thoracoscopic surgery vs. sternotomy for thymectomy: A systematic review and meta-analysis

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Introduction: Surgeons have widely regarded sternotomy (ST) as the standard surgical method for thymectomy. Minimally invasive methods for thymectomy, including video-assisted and robot-assisted thoracoscopic surgery (RATS), have been explored. There are some studies have researched and compared the outcomes of patients after robotic and sternotomy procedure.

Methods: We searched the databases of Pubmed, the Cochrane Library, Embase and selected the studies on the efficacy and safety of RATS or ST for thymectomy. Meta-analysis was performed for operation time, operation blood loss, postoperative drainage time, operative complications and hospitalization time.

Results: A total of 16 cohort studies with 1,089 patients were included. Compared to ST, RATS is an appropriate alternative for thymectomy which reduced operation blood loss [standardized mean difference (SMD) = -1.82, 95% confidence interval (95% CI): (-2.64, -0.99), $p = 0.000$], postoperative drainage time [SMD = -2.47, 95% CI: (-3.45, -1.48), $p = 0.000$], operative complications [odds ratio (OR) = 0.31, 95% CI: (0.18, 0.51), $p = 0.000$] and hospitalization time [SMD = -1.62, 95% CI: (-2.16, -1.07), $p = 0.000$].

Conclusions: This meta-analysis based on cohort studies shows that RATS has more advantages over ST. Therefore, RATS is a more advanced and suitable surgical method for thymectomy.

KEYWORDS

robot-assisted thoracoscopic surgery, sternotomy, thymectomy, systematic review, meta-analysis

Introduction

Thymus is an important immune and endocrine organ in human body. Thymoma is an unusual thymic tumor. Its annual incidence rate in the population is about 0.15/100,000 (1). Surgical intervention is the only effective method for its treatment. In the past, median sternotomy was regarded as the first surgical approach for all types of thymomas, which ensured the safety of tumor resection. Sternotomy has been widely considered and applied to the standard surgical method of thymectomy. Because sternotomy is an invasive operation, the operation involves the incision of long bone,

which may lead to complications such as intraoperative bleeding, postoperative pain and infection (2). Surgeons have explored many minimally invasive surgery approaches, including video-assisted and robot-assisted thoracoscopic surgery. In minimally invasive surgery, video-assisted thoracoscopic surgery (VATS) is the most popular and commonly used approach. Thoracoscopic surgery is considered to be the first choice for thymectomy because it can reduce intraoperative bleeding, postoperative pain and the incidence of postoperative complications (3–5). However, video-assisted thoracoscopy has some limitations. Thymectomy sometimes requires fine anatomy or complex surgery in the narrow upper mediastinum, which is technically challenging.

As an advanced minimally invasive surgery platform, robot-assisted surgery overcomes the limitations of traditional thoracoscopic surgery. The introduction and development of the da Vinci Robotic System has brought many obvious conveniences to surgeons, such as providing clear three-dimensional images, greater freedom of movement of surgical instruments in limited space, and reducing hand-related tremors. The da Vinci Robotic System also can help surgeons achieve more accurate anatomy, resulting in better clinical and tumor results, especially when thymectomy is performed in a narrow space (6). At present, it is not clear whether robot-assisted minimally invasive surgery can bring more benefits to doctors and patients. Many researchers have explored robotic treatment of thymic diseases, and some comparative studies on the surgical effects of robotic and sternotomy surgery have been published. The original purpose of this meta-analysis is to confirm the feasibility and safety advantages of robot-assisted thymectomy compared with sternotomy.

Methods

Search strategies

We searched and identified relevant studies from the databases of Pubmed, the Cochrane Library, Embase (from the establishment time of database to August 2022). The search terms that related to thymectomy, sternotomy and robot assisted are as follows: “thymectomy”, “thymoma”, “thymus”, “sternotomy”, “transsternal”, “thoracotomy”, “robot assisted”, “robotic”, “robot”, “da Vinci” and “daVinci”. **Figure 1** shows the search strategy. In addition, if we find other studies closely related to robot-assisted thoracoscopic thymectomy in other literatures, we will further search and evaluate them.

Inclusion and exclusion criteria of studies

Inclusion criteria

(1) The English language journal study; (2) the study described robot-assisted surgery and sternotomy for thymectomy; (3) the study provided original data.

Exclusion criteria

(1) Article was not in English; (2) review, conference abstracts, or case report; (3) unable to extract data.

Identification of literature

Three independent researchers reviewed titles or abstracts of the studies. The studies that meet the inclusion

```
#1 thymectomy
#2 thymoma
#3 thymus
#4 #1 OR #2 OR #3
#5 robot assisted
#6 robotic
#7 robot
#8 da Vinci
#9 daVinci
#10 #5 OR #6 OR #7 OR #8 OR #9
#11 sternotomy
#12 transsternal
#13 thoracotomy
#14 #11 OR #12 OR #13
#15 #4 AND #10 AND #14
```

FIGURE 1
The search strategy.

criteria were searched for full-text evaluation. The trials selected for detailed analysis were analyzed by three researchers, and disagreements were resolved by the fourth researcher.

Collection of study indicators

The data that we collected included: (1) publication date and country of literature; (2) the number of subjects of each research; (3) the mean age of patients; (4) outcomes include: operation time, operation blood loss, postoperative drainage time, operative complications and hospitalization time.

Quality assessment of included studies

We assessed the quality of all included studies from the perspectives of selection, comparability and exposure by the Newcastle–Ottawa Scale (NOS). The star system was used to score all studies, with a maximum of 9 stars. The specific evaluation criteria are that 8–9 stars represent high quality and 6–7 stars represent reasonable.

Statistical methods and analysis

We used Stata/SE 17.0 software to estimate statistical significance. The odds ratio (OR) was used to assess binary variables and the standardized mean difference (SMD) was used to assess continuous variables. The identification of heterogeneity of studies was calculated by the I^2 statistics. When the heterogeneity test result is significant ($I^2 > 50\%$ or $p < 0.05$), a random-effect model was used to evaluate. Otherwise, a fixed-effect model was used. At the same time, publication bias was assessed by Egger's test and Begg's test.

Results

Study selection process

We identified 186 studies, of which 16 (2, 6–20) were included in our analysis. All studies involved a total of 1,089 patients. [Figure 2](#) shows the study selection process.

Characteristics and quality of study

[Table 1](#) shows the characteristics and quality of the studies.

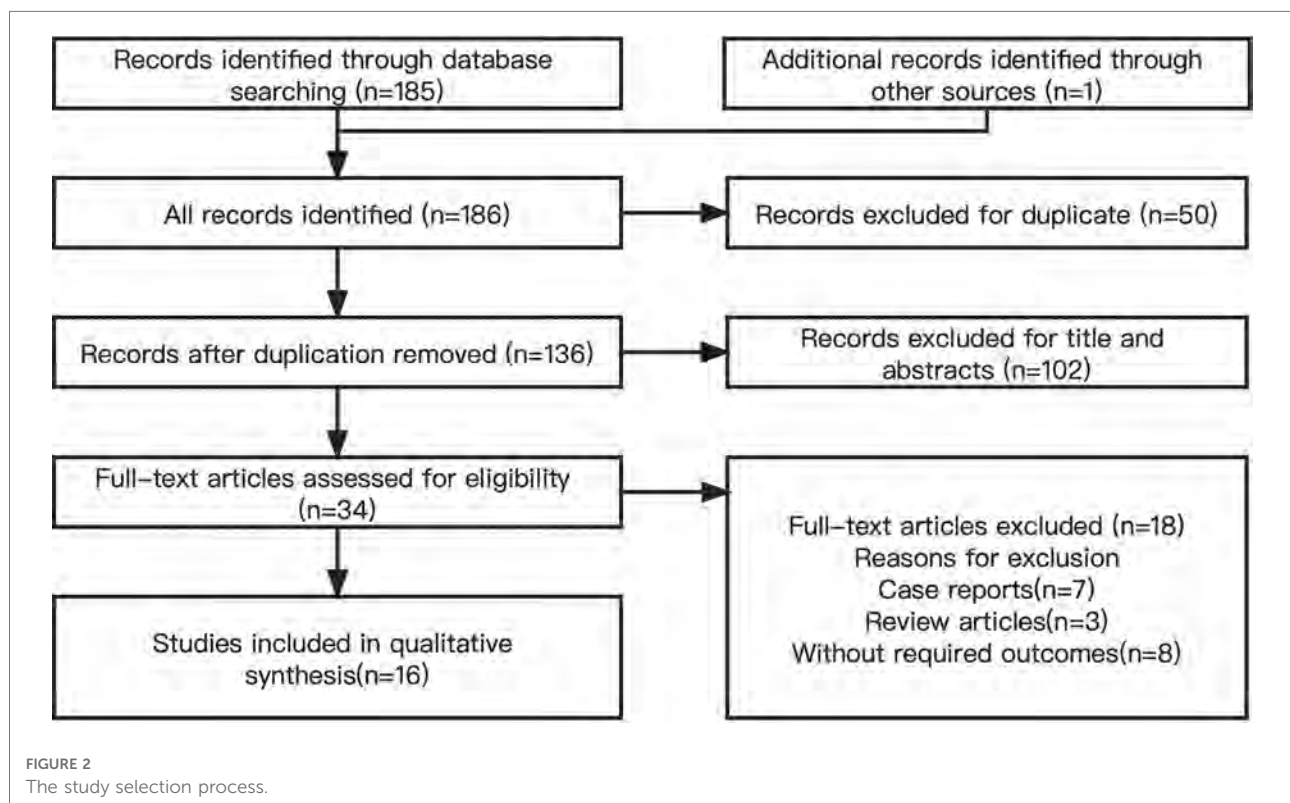


TABLE 1 Included studies characteristics.

Study	Country	Study design	Number of patients		Mean age		Outcome	NOS
			RATS (M/F)	ST (M/F)	RATS	ST		
Cakar 2007 (7)	Austria	CS	9	10	–	–	①④	7
Balduyck 2011 (8)	Belgium	CS	14 (4/10)	22 (12/10)	49.0 (18.0–63.0)	56.0 (23–84)	①⑤	7
Weksler 2012 (9)	United States	CS	15 (7/8)	35 (18/17)	56.8 ± 16.3	50.7 ± 17.7	②④⑤	7
Renaud 2013 (10)	France	CS	6 (1/5)	15 (6/9)	40 (27–57)	27.9 (6–46)	①③⑤	7
Seong 2014 (11)	Korea	CS	34 (15/19)	34 (18/16)	53.7 ± 2.2	52.4 ± 1.8	①③④⑤	7
Ye 2014 (12)	China	CS	23 (11/12)	51 (31/20)	52.5 ± 7.4	50.1 ± 12.7	①②③④⑤	8
Kang 2016 (2)	Korea	CS	100 (48/52)	100 (51/49)	52.1 ± 13.6	52.3 ± 13.4	①②④	7
Wilshire 2016 (13)	United States	CS	23 (11/12)	17 (12/5)	58 (50–67)	59 (52–69)	①②③⑤	7
Kamel 2017 (14)	United States	CS	22 (8/14)	22 (9/13)	58 (50–67)	59 (51–72)	①②③④⑤	8
Kneuert 2017 (15)	United States	CS	20 (5/15)	34 (14/20)	59 (47–65)	61 (47–73)	①②③④⑤	8
Qian 2017 (16)	China	CS	51 (21/30)	37 (15/22)	48.8 ± 13.3	46.8 ± 13.7	①②③④⑤	7
Casiraghi 2018 (6)	Italy	CS	24 (10/14)	24 (7/17)	61.6 ± 11.1	59.3 ± 11.5	①④⑤	7
Marulli 2018 (17)	Italy	CS	41 (18/23)	41 (19/22)	58.24 ± 10.97	57.66 ± 10.30	①③④⑤	7
Ancin 2019 (18)	Turkey	CS	12	16	31.5 (28.25–40.00)	41.50 (37.35–45.75)	①③⑤	7
Imielski 2020 (19)	United States	CS	54 (29/25)	69 (38/31)	44.9 ± 15.8	53.2 ± 16.8	①④⑤	7
Luzzi 2021 (20)	Italy	CS	57 (22/35)	57 (27/30)	50.8 (18–81)	54 (11–82)	①⑤	7

M, male; F, female; CS, cohort study; ① operation time, ② operation blood loss, ③ postoperative drainage time, ④ operative complications, ⑤ hospitalization time.

Analysis results

Operation time

Fifteen studies reported operation time. According to the heterogeneity test results, it can be concluded that statistical heterogeneity was significant between the fifteen studies ($p = 0.000$, $I^2 = 92.3\%$), we used random-effect model for calculation. The data revealed that significant difference did not exist between the RATS and the ST [SMD = 0.24, 95% CI: (−0.25, 0.74), $p = 0.328$] (Figure 3).

Operation blood loss

Operation blood loss was compared in seven studies. According to the heterogeneity test, it can be concluded that statistical heterogeneity was significant between the seven studies ($p = 0.000$, $I^2 = 93.4\%$), we calculated by random-effect model. The result revealed that operation blood loss was less in the RATS group [SMD = −1.82, 95% CI: (−2.64, −0.99), $p = 0.000$] (Figure 4).

Postoperative drainage time

Nine studies reported complete data of postoperative drainage time. The statistical heterogeneity was significant in the nine studies. We used the random-effect model for calculation ($p = 0.000$, $I^2 = 94.2\%$). The result indicated that postoperative drainage time were less in the RATS group [SMD = −2.47, 95% CI: (−3.45, −1.48), $p = 0.000$] (Figure 5).

Operative complications

According to the heterogeneity test results, it can be concluded that statistical heterogeneity was not significant between the eleven studies ($p = 0.307$, $I^2 = 14.4\%$), we adopted fixed-effect model for calculation. The data revealed that operative complications was less in RATS group. [OR = 0.31, 95% CI: (0.18, 0.51), $p = 0.000$] (Figure 6).

Hospitalization time

Fourteen studies with complete data compared hospitalization time. Statistical heterogeneity was significant ($p = 0.000$, $I^2 = 91.3\%$). We used the random-effect model for calculation. The result indicated that hospitalization time was less in the RATS group [SMD = −1.62, 95% CI: (−2.16, −1.07), $p = 0.000$]. There were twelve studies reported total hospitalization time and two studies reported postoperative hospitalization time. We performed subgroup analysis and found that total hospitalization time was less in the RATS group [SMD = −1.37, 95% CI: (−1.85, −0.88), $p = 0.000$], but postoperative hospitalization time was similar in two groups [SMD = −3.07, 95% CI: (−7.36, 1.21), $p = 0.160$] (Figure 7).

Assessment of publication bias

The Begg's test ($z = 1.29$, $\text{Pr} > |z| = 0.198$) and the Egger's test ($t = 1.15$, $p > |t| = 0.273$) revealed that publication bias did not exist in these included studies, and the results of this meta analysis are stable (Figure 8).

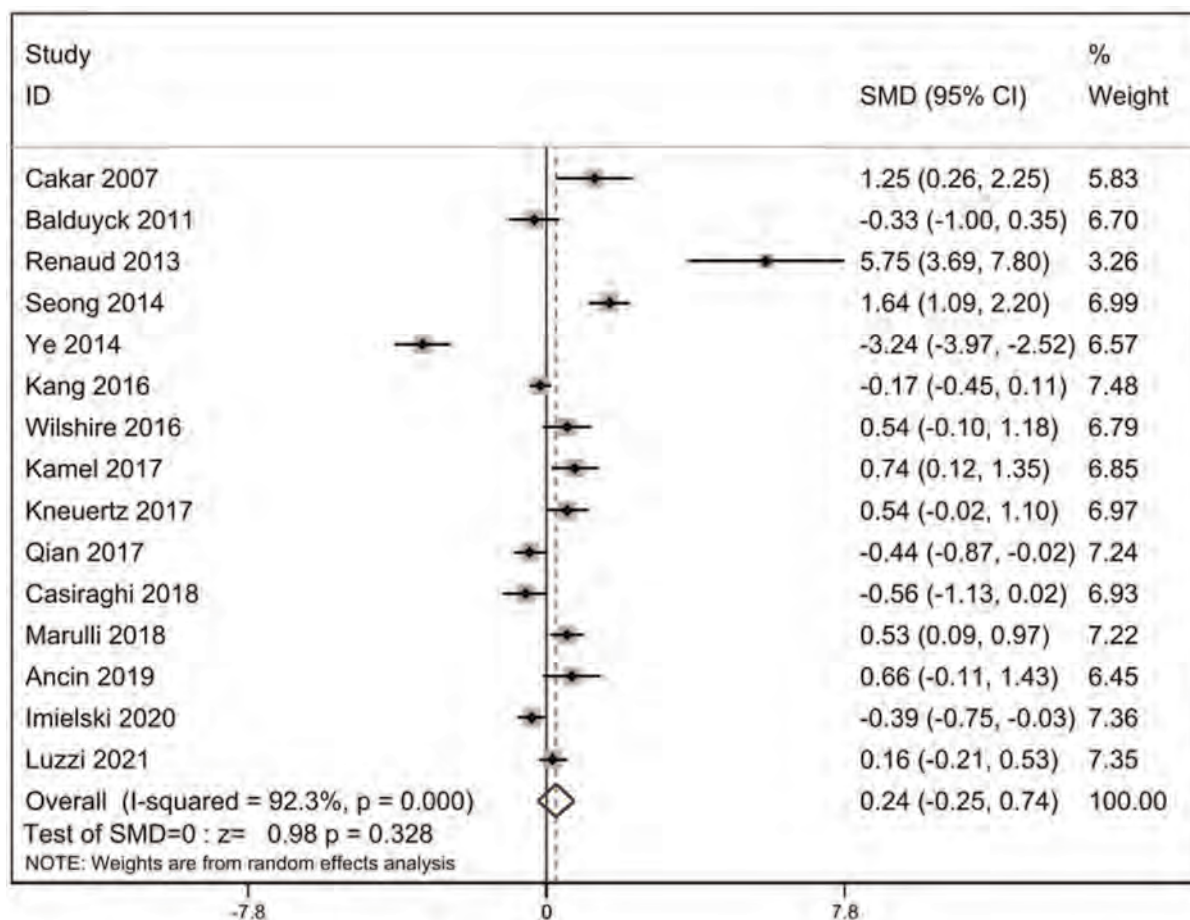


FIGURE 3

Comparison of operation time between RATS and ST. SMD, standardized mean difference; CI, confidence interval; RATS, robot-assisted thoracoscopic surgery; ST, sternotomy.

Discussion

The best surgical method of thymectomy has always been a controversial issue. So far, sternotomy has been regarded as the first choice for thymectomy, especially for thymoma. Surgeons can expose the entire mediastinum in this way to get the best surgical field of vision. In the era of rapid development of artificial intelligence, the introduction of robotic surgery system has brought a valuable choice to doctors. The daVinci robot has all the advantages of minimally invasive surgery. It provides a clearer, three-dimensional 3D field of vision than video-assisted thoracoscopy, reduces the impact of surgeons' hand tremors, and makes the movement of instruments more accurate (21, 23). Many original studies have explored robot-assisted thymectomy for the treatment of thymic diseases, some scholars have studied the surgical results of patients after robotic surgery and sternotomy. Therefore, a meta-analysis was performed to confirm the advantages of robot-assisted thoracoscopic surgery for thymectomy.

From our meta-analysis, it can be concluded that compared with ST, RATS thymectomy has obvious advantages, including less operative blood loss, less drainage time, less postoperative complications and less hospitalization time. The comparison of operation time was not significant.

Our meta-analysis revealed that the significant difference did not exist in operation time between RATS and ST. For surgeons, robotic-assisted surgery has a learning curve, so the operation time may be affected by the surgeons' technology. With the improvement of the surgeons' surgical technology, the operation time will be reduced (11, 24). The comparison results of operation time had significant heterogeneity ($I^2 = 92.3\%$). Based on the sensitivity analysis, we conducted that the studies of Ye (12), Renaud (10) and Seong (11) caused the heterogeneity. After reviewing the full texts carefully, there was no significant difference between these three studies and the other fifteen studies. We eliminated the three studies, the heterogeneity decreased slightly ($I^2 = 73.6\%$). We speculate that although the general surgical procedures are roughly the

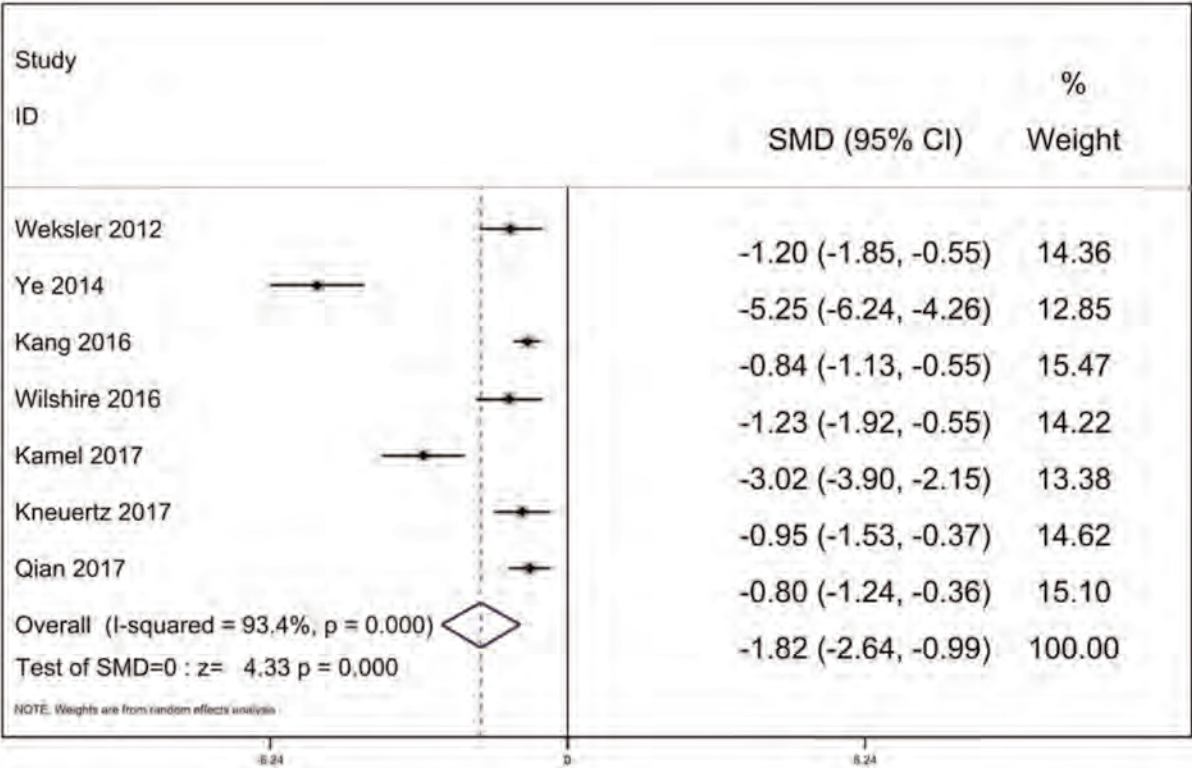


FIGURE 4
Comparison of operation blood loss between RATS and ST. SMD, standardized mean difference; CI, confidence interval; RATS, robot-assisted thoracoscopic surgery; ST, sternotomy.

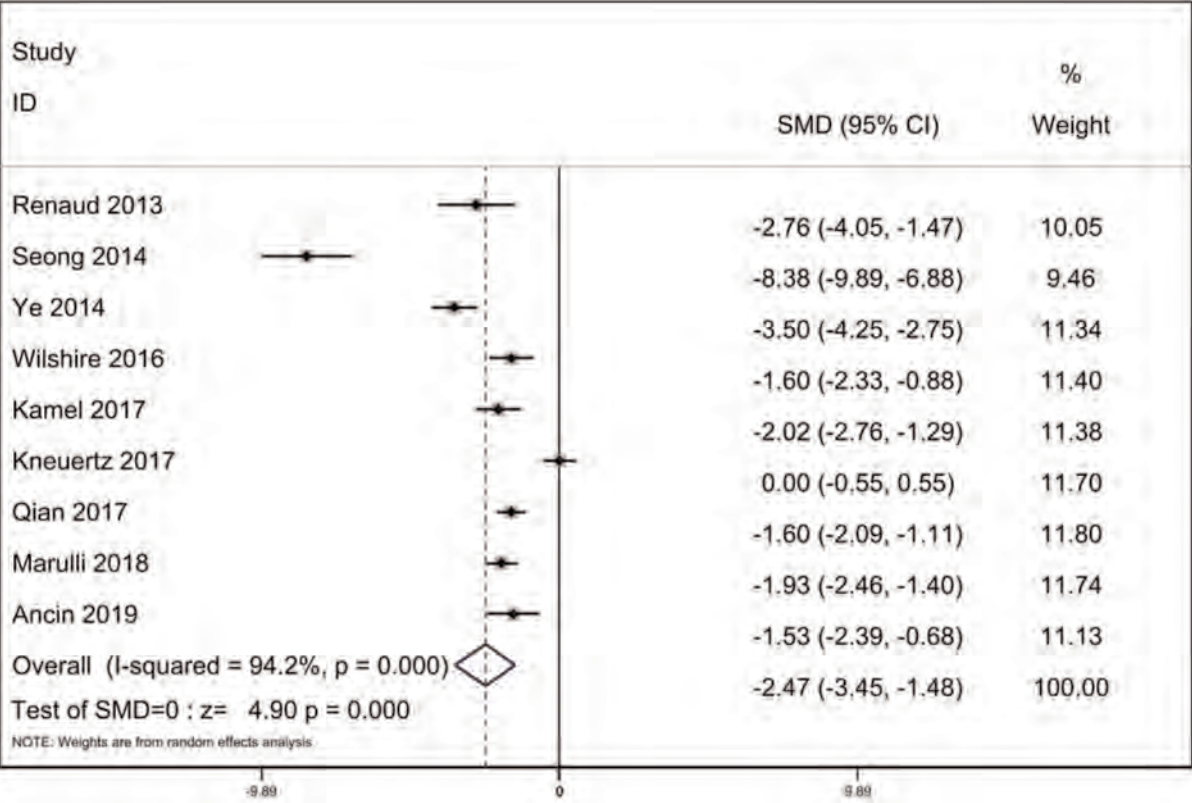


FIGURE 5
Comparison of postoperative drainage time between RATS and ST. SMD, standardized mean difference; CI, confidence interval; RATS, robot-assisted thoracoscopic surgery; ST, sternotomy.

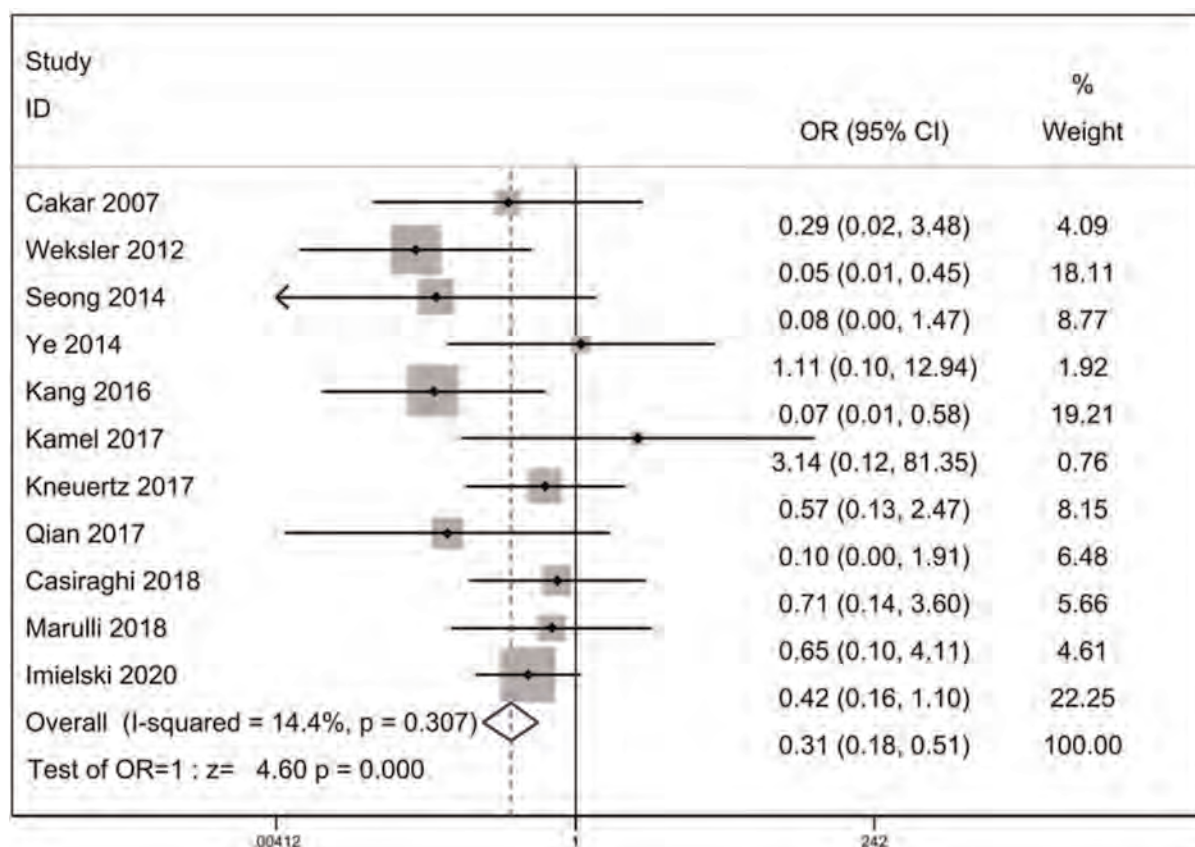


FIGURE 6

Comparison of operative complications between RATS and ST. OR, odds ratio; CI, confidence interval; RATS, robot-assisted thoracoscopic surgery; ST, sternotomy.

same, there are great differences in surgical skills among different institutions, resulting in temporal heterogeneity. Of course, it is also possible that the definition of operation time is different in different studies. Some studies define the startup of the robot system as the start time, some count the operation time according to the anesthesia time, and some choose the skin-to-skin time. These may help us to understand the heterogeneity of this result.

From the results of our meta-analysis, operation blood loss of RATS group was less compared with ST group ($p = 0.000$). We speculate that during the operation, the robot can provide surgeons with clearer three-dimensional images, and its flexible operating arm can avoid hand tremors, help doctors more effectively separate the complex anatomical structures of the chest and accurately expose the thymus, and help surgeons perform accurate operations (25). We observed significant heterogeneity of intraoperative blood loss ($I^2 = 93.4\%$), and our sensitivity analysis showed that the study of Ye (12) was most likely to

lead to heterogeneity. After excluding the study, the heterogeneity decreased ($I^2 = 78.5\%$).

With regard to the postoperative drainage time, the result of heterogeneity test is significant ($I^2 = 94.2\%$). The sensitivity analysis was performed and suggested that the heterogeneity was caused by three studies by Seong (11), Ye (12) and Kneuert (15). We eliminated the studies, the heterogeneity disappeared ($I^2 = 0\%$). After reviewing the full texts carefully, we found no significant difference between these three studies and the other six studies. Therefore, we speculated that there are differences in the indicators of removing drainage tube in different institutions, which may explain the heterogeneity of postoperative drainage time. Our analysis suggested that the postoperative drainage time of RATS was less compared with ST ($p = 0.000$).

Operative complications are related to the recovery of patients. Our meta-analysis indicated that for thymectomy, robotic surgery had a lower incidence of operative complications than sternotomy. This result is due to

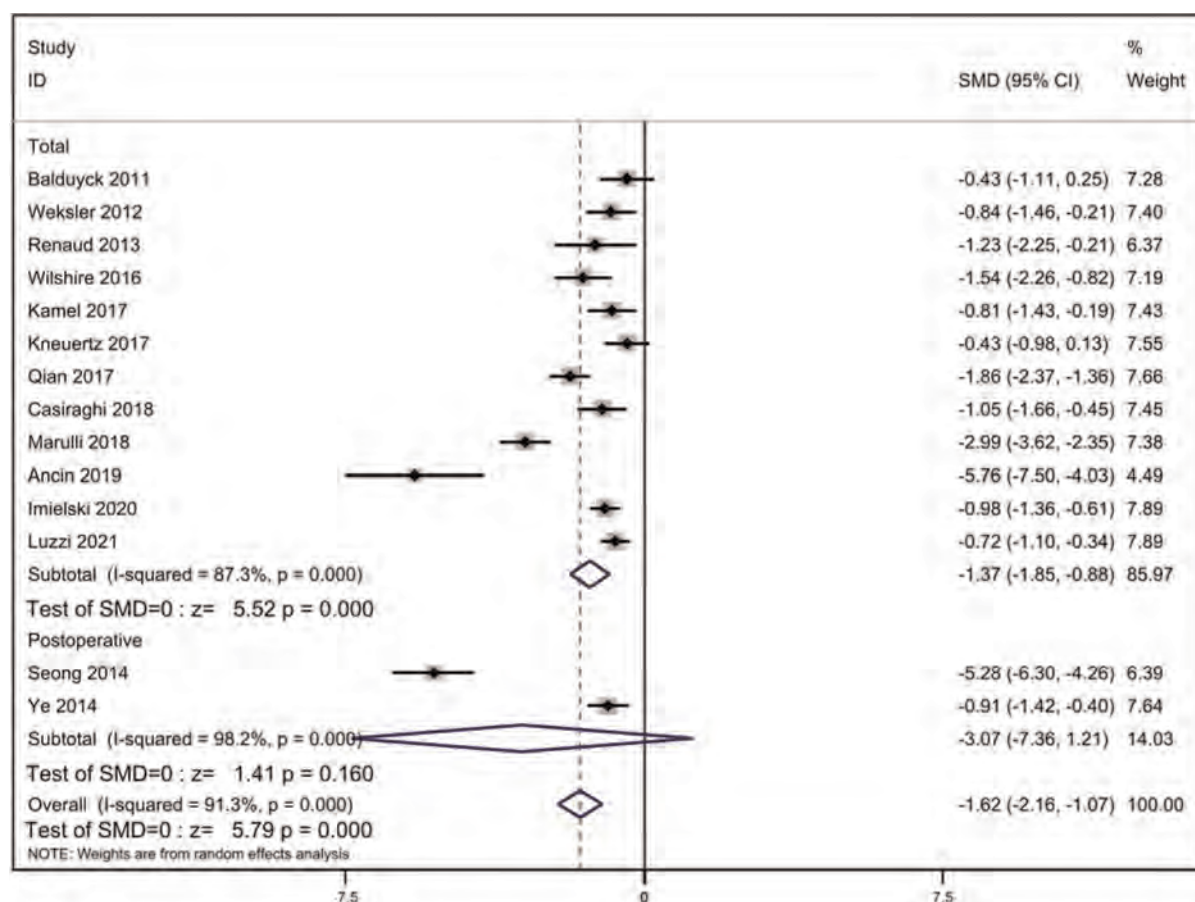


FIGURE 7

Comparison of hospitalization time between RATS and ST. SMD, standardized mean difference; CI, confidence interval; RATS, robot-assisted thoracoscopic surgery; ST, sternotomy.

the fact that robotic surgery provides a clear field of vision and precise manipulation, which can reduce tissue damage and reduce complications including postoperative pain and infection.

As for hospitalization time, the analysis suggested that hospitalization time of patients in RATS group was shorter. The result is observably attributed to the minimally invasive characteristics of robot-assisted surgery, which can avoid tissue injury, reduce intraoperative blood loss, shorten the time of pleural drainage days and accelerate the postoperative recovery of patients. The heterogeneity of hospitalization time was significant ($I^2 = 91.3\%$). Through the sensitivity analysis, we can conclude that the heterogeneity was mainly caused by the studies of Seong (11), Marulli (17) and Ancin (18). Heterogeneity decreased after the elimination of the two studies ($I^2 = 56.2\%$).

Shen et al. (26) and Wu et al. (27) compared the effects of RATS and VATS thymectomy by meta-analysis. They all came to a similar conclusion: RATS has more advantages over VATS,

including reducing operation blood loss, postoperative drainage time, postoperative drainage volume, hospitalization time, and postoperative complications. It can be concluded that compared with ST and VATS, RATS is a more suitable surgical method for thymectomy.

The operation field of traditional video-assisted thoracoscopy is two-dimensional, and the field is not clear enough. The robot surgery operating system adds a new dimension, and its camera system can achieve a 10-fold magnification of the surgical field of vision, which helps surgeons to observe complex and small structures in more detail. The flexibility of the robot system is significantly higher than that of traditional surgical instruments, and its surgical arm can flexibly perform complex three-dimensional operations, overcoming some technical and methodological limitations. During thymectomy, the clear, flexible and stable characteristics of the robot system can ensure the structural integrity of blood vessels and nerves which are often damaged (28, 29).

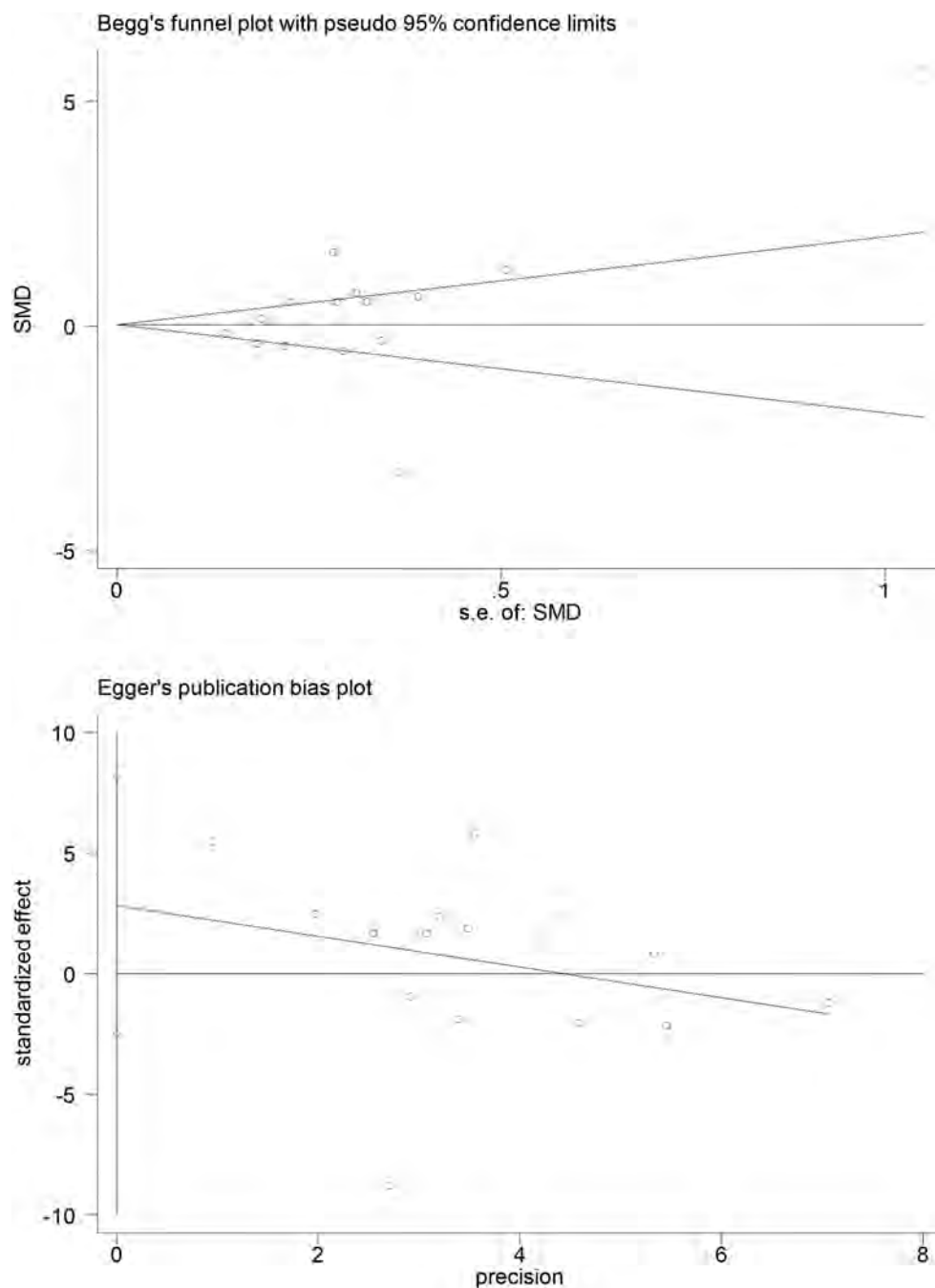


FIGURE 8

Assessment of publication bias. Begg's test and Egger's test did not imply a publication bias.

What we need to admit is that our meta-analysis has some limitations. First of all, the studies we searched and included are cohort studies. There is no randomized controlled trial concerning the clinical difference between RATS and ST in databases at present. We will focus on randomized controlled trials in the future so that we can update this meta-analysis.

Conclusion

According to this meta-analysis of cohort studies, it can be concluded that RATS has more advantages over ST, including reducing operation blood loss, postoperative drainage time, incidence of operative complications and hospitalization time.

Therefore, robot-assisted thoracoscopic surgery is a more appropriate surgical option for thymectomy.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

Author contributions

Conception: WW and C-qW. Collection of data: C-qW, JW, F-yL. Data analysis and interpretation: C-qW, JW, F-yL. Manuscript writing and revising: C-qW, F-yL, WW. Final approval of manuscript: C-qW, JW, F-yL, WW. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Large mediastinal mass diagnosed as Nocardia infection by endobronchial ultrasound-guided transbronchial needle aspiration in a ceramic worker: A case report

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Background: Nocardia is a ubiquitous soil saprophyte transmitted through airborne or direct cutaneous inoculation routes. Although Nocardia is more common in immunocompromised patients, Nocardia may also arise in apparently immunocompetent patients.

Case presentation: We report a rare case of Nocardia infection presenting as a large mediastinal mass in an immunocompetent ceramic worker. A 54-year-old man with no previous history of immune dysfunction, a ceramic worker by profession, was referred and admitted to our hospital because of a persistent fever for 19 days. Chest CT showed a large middle mediastinal mass. However, conventional anti-infective treatment was ineffective. Under the guidance of the Virtual bronchoscopic navigation (VBN) system, he underwent Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). The purulent exudate obtained by EBUS-TBNA was further identified as Nocardia by weak acid-fast and metagenomic next-generation sequencing (mNGS). He was subsequently treated with intravenous imipenem/amikacin, switched to intravenous imipenem and oral trimethoprim/sulfamethoxazole, and the clinical symptoms were significantly improved.

Conclusions: Even in immunocompetent patients, Nocardiosis cannot be excluded. For the public, especially soil contact workers, precautions should be taken to avoid Nocardia infection from occupational exposure. This rare case may provide a diagnosis and treatment reference for clinicians.

KEYWORDS

nocardia, mediastinal mass, EBUS-TBNA, weakly acid-fast stain, MNGs

Background

The *Nocardia* genus is a Gram-positive, branching, filamentous bacterium that is ubiquitous in soil and is transmitted by airborne or direct skin inoculation routes. Nocardiosis is an opportunistic infection that often occurs in immunocompromised patients, such as those with acquired immune deficiency syndrome (AIDS), and rarely in patients with normal immune function. The specific site of *Nocardia* infection is the respiratory tract, with subsequent spread to distant organs. *Nocardia* infection could commonly manifest in the pulmonary, central nervous, and cutaneous systems (1, 2). Diagnosis of pulmonary *Nocardia* is challenging due to Pulmonary *Nocardia* being a rare condition with variable and non-specific clinical presentation. *Nocardia* can have high morbidity and mortality, especially in patients with immunocompromised or comorbidities (3, 4). A timely and accurate diagnosis of pulmonary *Nocardia* is a challenging and critical task for further effective treatment. Here, we report a rare case of a large mediastinal mass caused by *Nocardia* in an immunocompetent patient and describe the clinical and epidemiological findings and timely diagnosis and management.

Case presentation

A 54-year-old male, a ceramic worker with no previous history of immune dysfunction, was admitted to the hospital

with persistent fever for 19 days. The patient had a cough occasionally and joint soreness but denied any other symptoms. On initial clinical evaluation, the patient's body temperature was 38.4 °C, and other signs were within normal limits. Pulmonary, abdominal, cardiac, and neurologic examinations showed unremarkable findings. Laboratory tests revealed that the patient had leukocytosis ($20.72 \times 10^9/\text{ml}$) with 87.4% neutrophils. His C-reactive protein level was high (90.61 mg/L), and a procalcitonin level was slightly increased (0.173 ng/ml). Contrast-enhanced chest CT revealed a large mediastinal mass measuring approximately $7.76 \times 4.55 \text{ cm}$ (Figure 1A). The rest of the examination was regular.

At initial admission, the patient was treated with empiric antibiotic therapy, including piperacillin and sulbactam. However, he still had a recurrent fever, and there was no significant improvement in inflammatory indicators and blood routine examination. To determine the etiology, the patient underwent Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) on the fifth day of admission. The Virtual bronchoscopic navigation (VBN) system is a method to guide the bronchoscope to the lesion by making a bronchial path on a virtual image. The digitized information from the patient's CT scan was imported into the Archimedes VBN system, in which multislice views of the chest and virtual bronchoscopy images were reconstructed. The VBN system shows the bronchial tree, the anatomical structure of the mediastinal mass and visualizes the best path to reach the mediastinal mass (Figures 2A–E). With the guidance of the VBN system, the bronchoscope was navigated

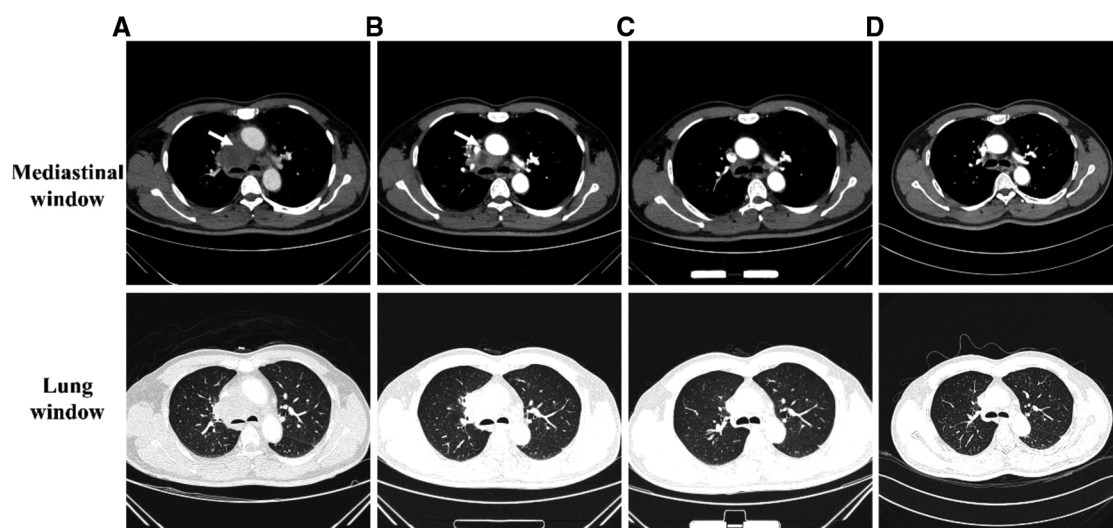


FIGURE 1

The dynamic changes in enhanced chest CT images at different time points. Mediastinal (top) and lung window (bottom). (A) At admission, Chest CT showed a mediastinal mass measuring $7.76 \times 4.55 \text{ cm}$ (arrow). (B) During discharge, Chest CT showed a decrease in the size of mediastinal mass to $5.53 \times 4.51 \text{ cm}$ (arrow). (C) After six months of treatment, Chest CT showed obvious absorptance of the mediastinal lesions. (D) One and a half years follow-up Chest CT showed obvious absorptance of the mediastinal lesions.

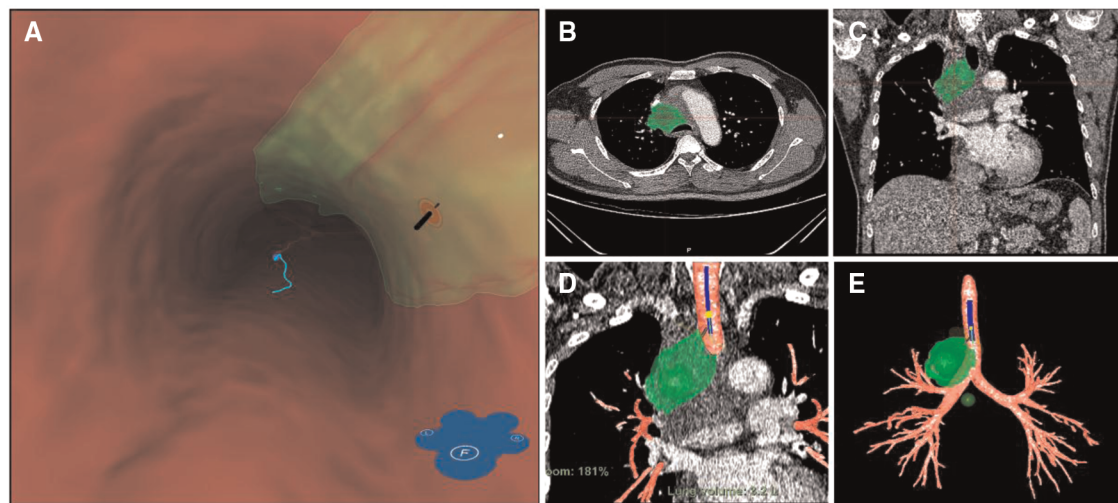


FIGURE 2

Three-dimensional anatomical structures were reconstructed using a VBN system (archimedes virtual bronchoscopy navigation system). (A) Intraluminal view and puncture sight (green). (B) Axial view of the location of the mediastinal lesion (green dot). (C) Coronal view of the location of the mediastinal lesion (green dot). (D) VBN image showed the target lesion (green dot) and the route for TBNA (light blue line). (E) the anatomical structure of the mediastinal mass and bronchial tree.

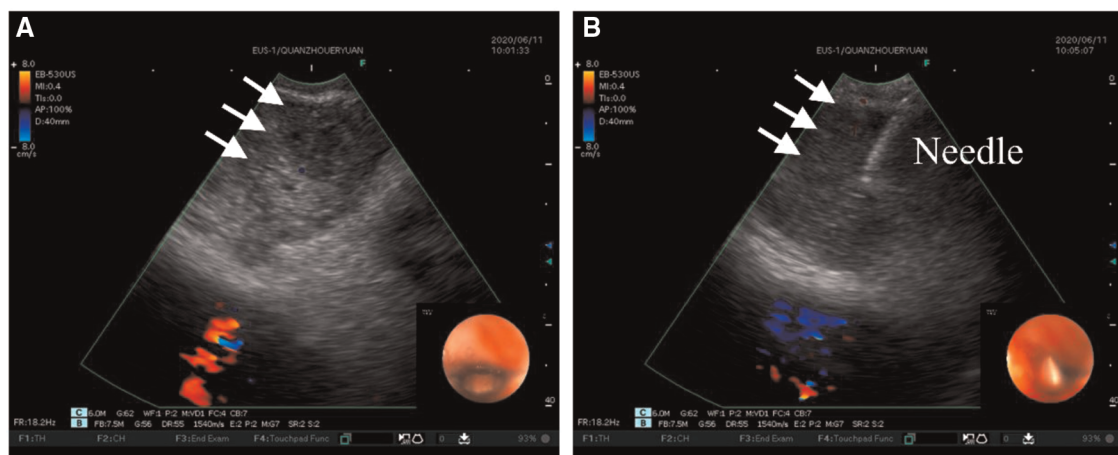


FIGURE 3

Ultrasound images of EBUS-TBNA. (A) Convex-probe ultrasound demonstrates the hypoechoic lesion (arrows), while the endoscopic Doppler image reflects the blood flow within the right atrium. (B) EBUS-TBNA was performed using a 22-gauge needle.

to the target bronchus and advanced to the lesion, and then EBUS-TBNA was performed to obtain purulent exudate (Figures 3A–D). Biopsy showed more purulent secretions and a few lymphocytes and macrophages (Figure 4A). Microscopic analysis revealed numerous weakly acid-fast and branching filamentous rod bacteria were identified from the samples on the aspirate smear, and a presumptive microbiological diagnosis (*Nocardia*) was made (Figure 4B). Metagenomic next-generation sequencing (mNGS) subsequently identified the pathogens as *Nocardia* species

(*Nocardia arizonensis* and *Nocardia cyriacigeorgica*). And after seven days of culture, the cultures of purulent exudates ultimately grew the *Nocardia* species (Figure 4C).

After microscopic examination and mNGS confirmed *Nocardia*, intravenous imipenem/amikacin was given. The clinical symptoms of the patient were significantly improved after 6 days of treatment. Then he was switched to intravenous imipenem with oral trimethoprim/sulfamethoxazole (TMP/SMX, 80 mg of TMP, and 400 mg of SMZ/tablet) 3 tablets q6h. One month after treatment, the

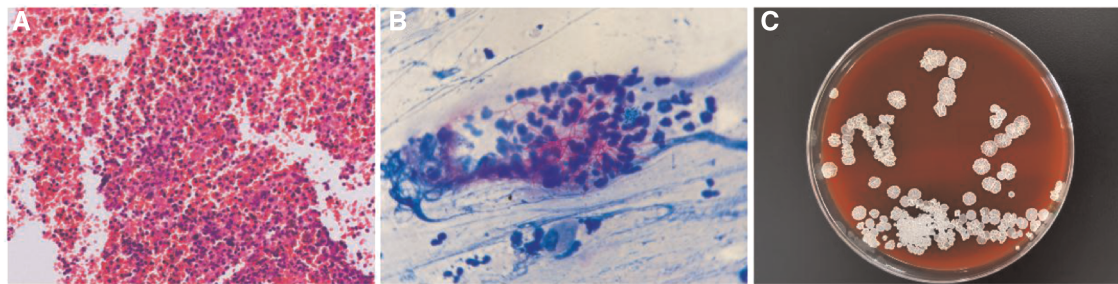


FIGURE 4

(A) H&E stain for the biopsy showed more purulent secretions and a few lymphocytes and macrophages (X40). (B) Kinyoun stain for the samples on the aspirate smear showed numerous weakly acid-fast and branching filamentous rod bacteria (X100). (C) The biopsy samples were incubated at 35 °C for 7 days and formed milky colonies floating on the medium liquid surface. The medium liquid was clarified.

patient improved, and their Chest CT showed a decrease in the size of the mediastinal mass (**Figure 1B**). He was discharged and continued to be treated with oral TMP/SMX 3 tablets q8h and sodium bicarbonate for 3 months. Over the next 3 months, he continued on oral TMP/SMX 2 tablets q8h and sodium bicarbonate. After six months of treatment, the patient was asymptomatic. His CT showed significant improvement in the mediastinal mass size (**Figure 1C**). At one and a half years of follow-up, the patient recovered well, and no complications were noted (**Figure 1D**).

Discussion and conclusions

Nocardia is ubiquitous soil saprophytes transmitted by either airborne or direct cutaneous inoculation routes. Although *Nocardia* more frequently causes invasive infections in immunocompromised patients, it can also occur in immunocompetent patients. Pulmonary *Nocardia* could manifest pulmonary airspace consolidation, pulmonary nodules, pulmonary infiltrates, cavitation, and pleural effusion (5). Herein, we report an immunocompetent patient who had a large mediastinal mass and presented with a fever. The patient was a ceramic worker who had frequent exposure to soil and may have acquired *Nocardia* infection from the soil. For the public, especially soil contact workers, precautions should be taken to avoid *Nocardia* infection from occupational exposure. In our case, occupation-related *Nocardia* infection may have been reported for the first time.

Nocardia infection presenting as a mediastinal mass is a rare type, and only 9 cases of this disease have been previously reported (6–12). The clinical, diagnostics and treatment features of 9 cases were summarized in **Table 1**. Invasive methods may be required to obtain a tissue diagnosis to guide treatment when evaluating mediastinal masses. Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-

TBNA) is an invaluable technique in assessing patients with mediastinal and hilar lesions (13). EBUS-TBNA is mainly used for staging non-small cell lung cancer, for diagnosing lung cancer without endobronchial lesions, and for diagnosing benign (especially tuberculosis and sarcoidosis) and malignant mediastinal lesions (14). Virtual bronchoscopic navigation (VBN) is generally used to guide the diagnosis of peripheral pulmonary lesions (especially peripheral nodules <2 cm). VBN facilitates safe and effective sampling of peripulmonary lesions, independent of bronchial sign location, lesion size, and presence or absence of a bronchus sign (15). Moreover, VBN improved the diagnostic accuracy of mediastinal lesions by visualizing mediastinal lesions and accurately identifying puncture sites (16). The VBN system provides an accurate and virtual map for intra- and extra- bronchial landmarks of hilar and mediastinal lymph nodes, thereby increasing the chances of proper collection and minimizing the risk of major bleeding. This may improve the diagnostic accuracy of mediastinal masses and/or lymphadenopathy and assist bronchoscopists in practicing EBUS-TBNA (16). In this case, we successfully diagnosed a >7 cm mediastinal mass using VBN-guided EBUS-TBNA.

Diagnosis of *Nocardia* is challenging because *Nocardia* species grow very slowly and are difficult to culture. This could lead to delays in diagnosis and treatment. Acid-fast staining and mNGS can be a fast and definite diagnostic method for *Nocardia* species. In this case, we successfully treated this rare infection through this rapid diagnosis and aimed to raise *Nocardia* diagnosis awareness among clinicians.

Subacute to chronic respiratory symptoms, elevated inflammatory markers, a mediastinal mass, a history of soil-related occupational exposure, and the absence of common respiratory pathogens on assessment was high indicators of suspected *Nocardia* infection. Once *Nocardia* infection is confirmed, prompt antibiotic therapy should be administered immediately. Sulphonamides are the first-line

TABLE 1 Case summary of *Nocardia* infection presenting as a mediastinal mass.

References	Age	Clinical presentation	Lesion location	Lesion size (cm)	Surgical operation	Diagnostic Modality	Treatment	Immunocompromised
Kim 2016 (6)	64	Dyspnea and chest wall pain	Right anterior cardiophrenic angle	4	Video-assisted thoracic surgery	16S rRNA sequencing	TMP-SMX	Immunocompetent
Salazar2013 (7)	30	Cough, hoarseness, and shortness of breath	Mediastinal mass	7 × 5 × 9	Cervical mediastinoscopy and biopsies of mediastinal mass	DNA sequencing and sputum cultures	Imipenem and linezolid	A renal transplant recipient
Jastrzebski2002 (8)	32	Dyspnea, cough, and fever	Large right mediastinal mass	NA	Transverse parasternal thoracotomy	mediastinal fluid cultures	TMP-SMX	Patient with sarcoidosis
Maya 2014 (9)	29	Fever and productive cough	Mid-Mediastinum	NA	A biopsy from the mediastinal mass	Culture and polymerase chain reaction	Imipenem and cotrimoxazole	Immunocompetent
Chaya2006 (10)	60	Productive cough	Mediastinal mass	3.5	EUS–FNA	Romanowsky stain and Gomori methenamine silver –stained	NA	NA
Chaya2006 (10)	26	Nonproductive cough	Mediastinal lymphadenopathy	NA	EUS–FNA	Papanicolaou stain and Kinyoun acid –fast stain	NA	HIV–positive
Chaya2006 (10)	35	Cough	Mediastinal Mass	NA	EUS–FNA	Kinyoun acid–fast stain	NA	HIV–positive
El-Herte2012 (11)	49	Chest pain, fever, chills, sweating, cough, and greenish sputum production	Anterior mediastinal mas	NA	Median sternotomy and biopsy of suspicious tissue	NA	Imipenem, amikacin, and TMP-SMX	Patient with myasthenia gravis
Dawood 2020 (12)	59	Chronic dyspnea, fatigue, and myalgias	Lymphadenopathy in NA the subcarinal area	NA	Transbronchial needle aspiration	Cytopathologic examination	TMP-SMX and linezolid	Refractory and relapsed acute myeloblastic leukemia

EUS–FNA, Endoscopic ultrasound–guided fine–needle aspiration; TMP-SMX, Trimethoprim/sulfamethoxazole; HIV, human immunodeficiency virus.

drugs for treating *Nocardia* infections, and trimethoprim-sulfamethoxazole (TMP-SMX) is considered the first choice for the treatment of susceptible strains. These appropriate medications can lead to significant radiological improvement.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

Ethics statement

Written consent was exempted by the ethics committee of the Second Affiliated Hospital of Fujian Medical University since no identifying images or other personal information was included. The patients/participants provided their written informed consent to participate in this study.

Author contributions

XSS, LC, and ZSZ conducted the literature review and wrote the draft. WJW, YXZ, and XPL collected clinical data. ZZZ and HPZ investigated the case. JH was involved in laboratory work. All authors contributed to the article and approved the submitted version.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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Initial experience with robotic-assisted thoracic surgery for superior mediastinal masses

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Objective: Minimally invasive surgery is challenging for masses located in the superior mediastinum, especially for those close to the chest outlet. This study aimed to evaluate the feasibility and safety of robotic-assisted thoracic surgery (RATS) for these masses.

Methods: From June 2015 to January 2020, 35 patients (19 males, 16 females), with a mean age of 41.6 (range, 13–66) years, underwent RATS for the treatment of superior mediastinal masses. Data regarding the operation time, blood loss, pathology, conversion rate, morbidity, mortality, and cost were collected and analyzed.

Results: The mean (\pm standard deviation) operation time, blood loss, chest tube use duration, and postoperative hospital day were 117 ± 45.2 (range, 60–270) min, 59.7 ± 94.4 (range, 10–500) ml, 4.1 ± 2.1 (range, 1–10) days, and 5.1 ± 2.1 (range, 2–11) days, respectively. The pathological diagnoses included schwannoma (26 cases), ganglioneuroma (4 cases), bronchogenic cysts (3 cases), ectopic nodular goiter (1 case), and cavernous hemangioma (1 case). The mean diameter of the resected tumor was 4.6 ± 2.0 (range, 2.5–10) cm. No conversion or mortality occurred. Postoperative complications included Horner's syndrome (18 cases: 6 patients with preoperative Horner's syndrome), weakened muscular power (2 cases), and chylothorax (2 cases). The mean cost was \$ 8,868.7 (range, \$ 4,951–15,883).

Conclusions: Our experience demonstrated that RATS is safe and feasible for superior mediastinal mass resection. However, the high incidence of postoperative Horner's syndrome requires further research.

KEYWORDS

robotic-assisted thoracic surgery, mediastinal mass, superior mediastinum, horner's syndrome, minimally invasive surgery

Introduction

Minimally invasive surgery for mediastinal masses has been widely reportedly comparable to conventional thoracotomy in terms of symptom improvement, recurrence, and survival rate (1, 2). However, surgeons are having difficulty performing video-assisted thoracic surgery (VATS) for masses located at the superior mediastinum, especially for those close to the chest tube outlet due to the narrow complex anatomy, difficulty with hand-eye coordination, and limited movement of VATS instruments.

Abbreviations

RATS, robotic-assisted thoracic surgery; VATS, video-assisted thoracic surgery; MRI, magnetic resonance imaging; dVS, Da Vinci system; cm, centimeter; min, minutes; ml, milliliter.

Robotic surgery provides advantages of instrumentation with 6 degrees of freedom, stable operating arms, and improved visualization with a three-dimensional high-definition camera and has been successfully used to perform mediastinal tumor resection (3, 4). However, studies on RATS for masses in the superior mediastinum are rarely reported.

To our best knowledge, this study included the largest number of masses at this location. Therefore, we aimed to determine the feasibility and safety of robotic-assisted surgery for performing superior mediastinal tumor dissection.

Materials and methods

Patients

From June 2015 to January 2020, 35 patients with superior mediastinal masses underwent RATS using the da Vinci

S Surgical System (Intuitive Surgical, Inc, Sunnyvale, CA, USA). All of these masses were centrally located above the horizontal plane formed by the sternum angle and the T4–T5 intervertebral discs in a sagittal image. The mass was defined as a cervical-mediastinal mass if its center was further above the horizontal plane formed at the uppermost of the sternal manubrium and T1 vertebra. A contrast-enhanced thoracic magnetic resonance imaging (MRI) sagittal image was routinely obtained preoperatively to confirm (a) the absence of neurovascular, chest wall, or vertebral body involvement and (b) intraspinal extension (Figure 1). Patients aged younger than 16 or over 70 years, those with a mass diameter >10 cm, those with imaging findings that were suspicious of malignancy, and those with MRI signs of invasiveness or intraspinal extension were excluded. A biopsy specimen was not obtained, except for two patients who underwent biopsy in another hospital and were diagnosed with schwannoma. This retrospective review was conducted after obtaining

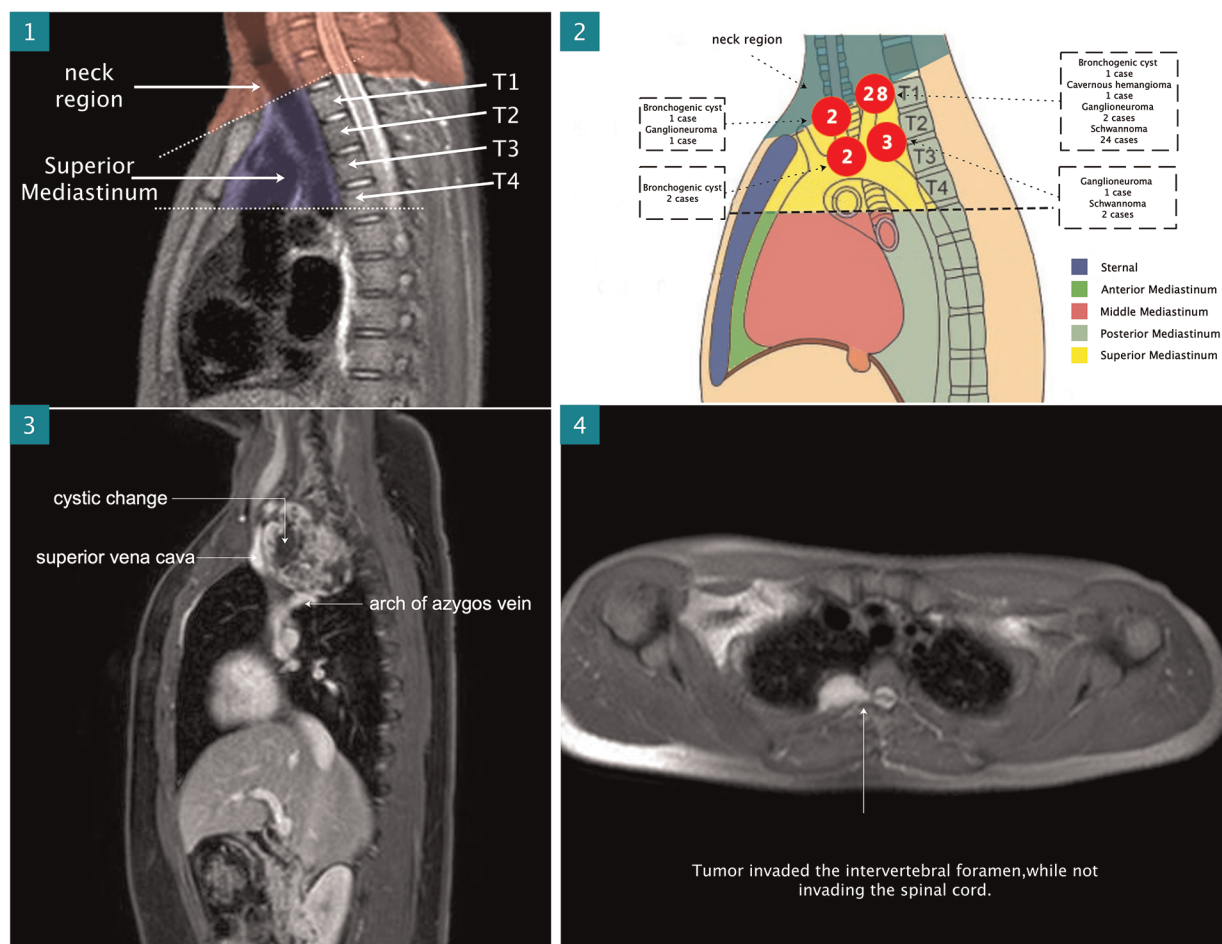


FIGURE 1

(1) Sagittal MR was used to assess the location of the lesion, which was very helpful in assessing resectability. (2) The schematic diagram shows the location and pathological diagnosis of lesions. (3) Contrast-enhanced thoracic MR was performed preoperatively to exclude neurovascular, chest wall, and vertebral body involvement and intraspinal extension. MR: magnetic resonance.

approval from the Institutional Review Board of the Chinese People's Liberation Army, General Hospital. Informed patient consent was not required because of its retrospective nature.

Surgical procedure

Positioning and anesthesia

The patient was placed in a lateral decubitus position with the lower limbs flexed downward to avoid the hips from interfering with the instrument's arm movement. Surgery was performed under general anesthesia with one-lung ventilation using a double-lumen endotracheal tube (Covidien IIC, Athlone, Ireland) or bronchial blockers (WELL LEAD MEDICAL CO, LTD, Guangzhou, China).

Robot positioning and ports' layout

The Da Vinci system with three arms was universally used. The robot was docked from the patient's head. The incision and instrument arm placement depended on the location of masses. The trocar was placed at least 5 cm apart from each other to avoid instrument arm clashing. In 31 patients with masses located posteriorly, the procedure was started with a 12-mm trocar in the 7th intercostal space on the anterior axillary line. A 30° camera was then placed through this port to assess the surgical anatomy and guide the optimal placement of the 8-mm metallic trocar usually at 1 arm in the 6th intercostal space on the posterior axillary line and 2 arms in the 3rd intercostal space on the anterior axillary line. A 12-mm trocar was placed as an assistant port in the 6th intercostal space on the anterior axillary line as needed. In another four patients with masses located anteriorly, the camera port was placed in the 7th intercostal space on the posterior axillary line. The remaining three holes also moved backward as a whole (Figure 2). The general principle is that the center of the mass, operation ports, and camera port together form a diamond shape.

Surgeons and surgical technique

Low-flow (8 L/min) carbon dioxide insufflation (8 mmHg) was routinely used. Fenestrated bipolar forceps, a permanent cautery hook, and monopolar curved scissors (Surgical Intuitive, Mountain View, CA, USA) were used to grasp and resect the mass. First, the relationship between the tumor and the sympathetic nerve chain was explored. The tumor was separated along its borders. Extreme care was taken to prevent damage to the subclavian vessels. The use of electrical energy devices near sympathetic nerves was avoided. In the study institution, monopolar instruments were used for tissue dissection, bipolar instruments were used for vascular transection and hemostasis, and scissors were used for sharp dissection (Figure 3).

All specimens were removed with an endoscopic bag after expanding the port in the front (1-arm port), and a 24-Fr chest tube was placed through the camera port for drainage.

All operations were performed by two thoracic surgery specialists (Yang Liu and Bo Yang) who were certified to use the da Vinci Surgical System by the manufacturer.

Postoperative management and follow-up

Chest x-ray was performed on postoperative day 1. Our criteria for chest tube discontinuation are (1) drainage of <100 ml per day, (2) no air leakage in the chest cavity, and (3) no active clinical complications. The postoperative follow-up period was 6 months. Symptoms and imaging (CT or MR) are evaluated at 1- and 6-month postoperatively.

Data collection and analysis methods

Age, sex, comorbidities, length of surgery, estimated blood loss, length of hospital stay, early and late postoperative complications, conversion to open surgery, pathological diagnosis, and follow-up were reviewed. Operative mortality was defined as death from any cause within 30 days postoperatively or before discharge. The reported mass size was the largest tumor diameter as reported by the pathologist. Data were stored in Excel (Microsoft Corp, Seattle, Wash), and descriptive statistics were shown using the frequency, mean, and standard deviation. Statistical analysis was performed using SPSS 26.0 (IBM, Armonk, NY, USA).

Results

Patient characteristics

A total of 35 patients (19 males and 16 females) who underwent robotic-assisted surgery for the treatment of a superior mediastinal mass were included. Their mean age was 41.6 ± 13.5 (range, 13–66) years. The common comorbidities included hypertension (nine patients, 25.7%), diabetes (one patient, 2.9%), and hypothyroidism (one patient, 2.9%). Five patients had a smoking history. Preoperative mass-related symptoms included chest pain (four patients, 11.4%), chest tightness (two patients, 5.7%), Horner's syndrome (six patients, 17.1%), and brachial plexus compression (four patients, 11.4%, three with upper limb numbness, and one with upper limb weakness). The patient characteristics are shown in Table 1.

Preoperative imaging

All 35 patients underwent enhanced CT examination preoperatively, and 22 of them additionally underwent enhanced MR examination. A total of 30 tumors were diagnosed as cervical-mediastinal tumors. Pathological diagnosis was issued in 10 CT and 17 MR reports. One patient underwent angiography and embolization due to a large mass and abundant blood supply. The imaging report of four

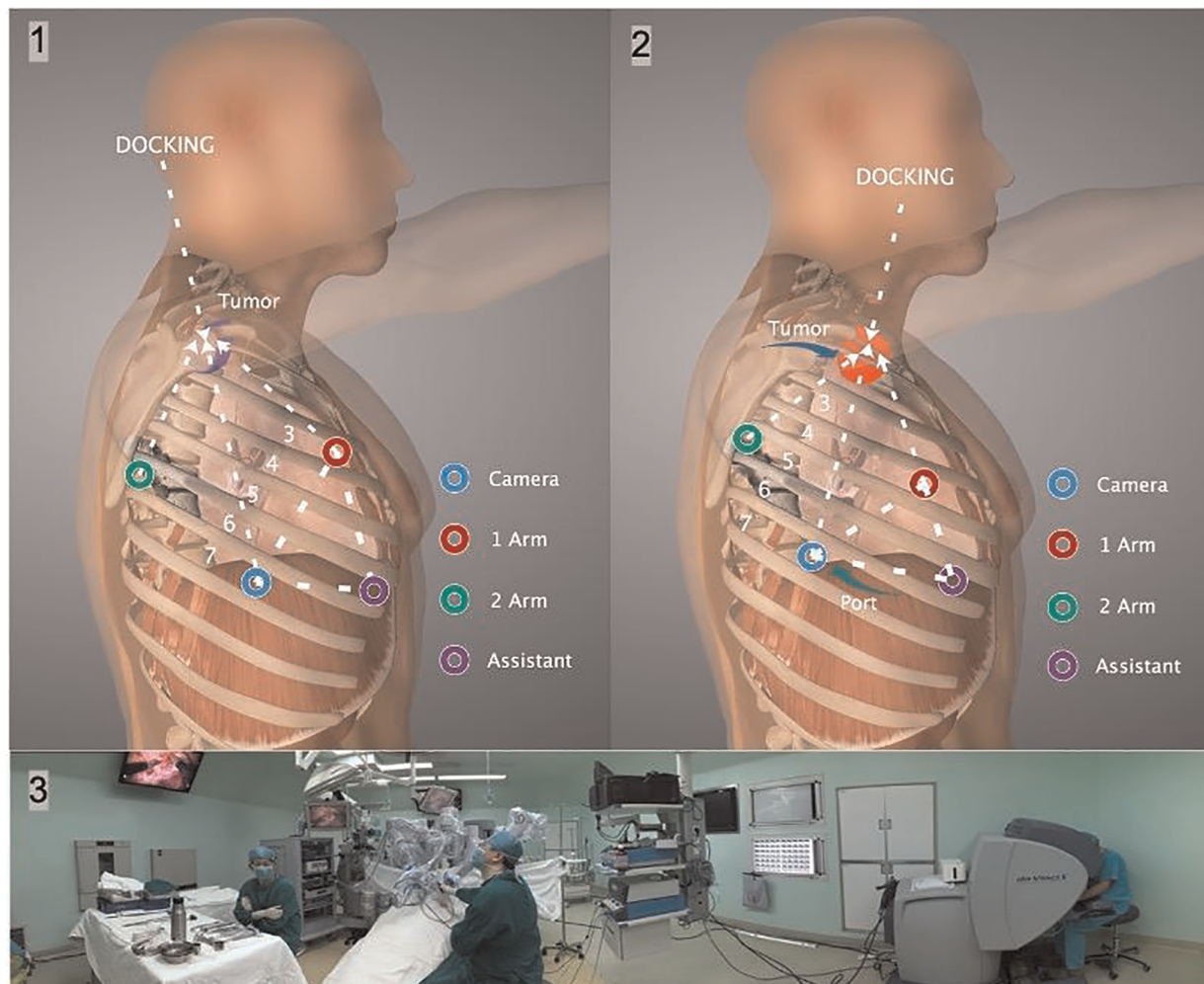


FIGURE 2

(1), (2) The incision and instrument arm placement depended on the tumor location. Each port was placed at least 5 cm apart from the other ports to prevent instrument arm clashing. The dVSR was docked from the head. (3) The panoramic photo shows the intraoperative situation. dVSR: Da Vinci system.

patients (four MR and two CT) showed an enlarged intervertebral foramen. CT reports of seven patients suggested that the masses were closely related to blood vessels; however, none of them were mentioned in MR reports. Preoperative imaging characteristics are shown in [Table 2](#).

Surgical procedure

All 35 operations were performed by a robot without conversion to thoracotomy: 20 through the right and 15 through the left thoracic cavity. The mean docking time (the duration from the assistant making the first incision to the surgeon getting to manipulating the robotic arms) was 11.2 ± 3.2 min. The mean operative time (defined as the duration from skin incision until skin closure) was 117 ± 45.2 min, and blood loss was 59.7 ± 94.4 ml. One patient experienced 500 ml of bleeding due to vascular injury to an

intercostal artery and received 200 ml blood transfusion during the surgery. Hemostasis was successfully completed using bipolar forceps. The intraoperative characteristics are shown in [Table 3](#).

Postoperative outcome, pathology, and follow-up

A total of 18 patients presented with Horner's syndrome (six with preoperative Horner's syndrome) and 12 newly occurred (12/29, 41.4%). All three patients with preoperative symptoms of brachial plexus compression were relieved postoperatively. However, two (2/32, 6.25%) new patients developed symptoms of brachial plexus injury (postoperative weakened muscular power). The final diagnosis and postoperative outcomes are shown in [Table 2](#). Complete (R0) resection was accomplished in all patients. No mortality

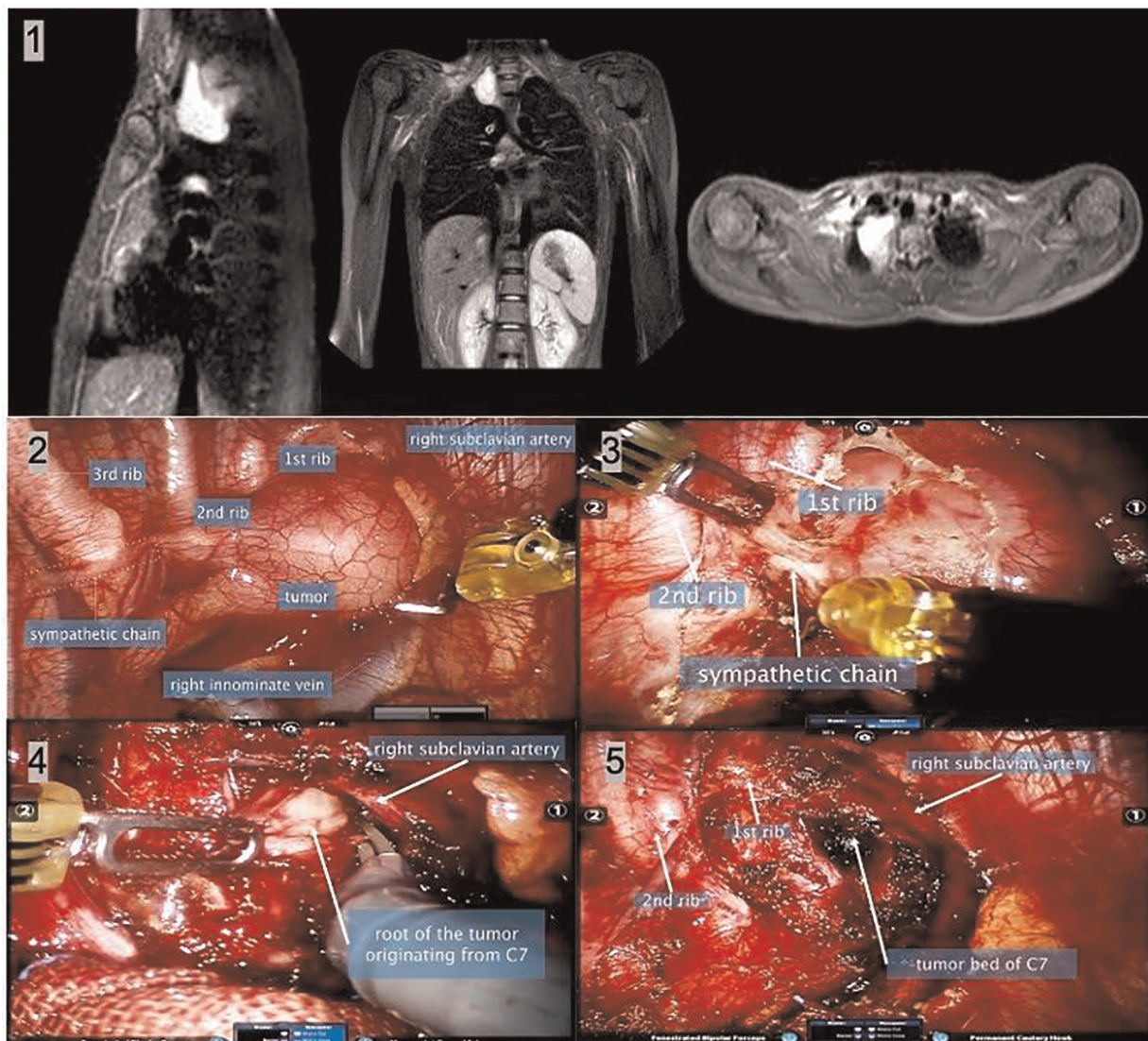


FIGURE 3

A 13-year-old girl with cervical-mediastinal ganglioneuroma. (1) The thoracic MR shows a lesion located at the right outlet of the chest with a wide base. (2) Intraoperative image shows the lesion and adjacent structures. (3) After separating the mediastinal pleura, the sympathetic nerve chain was found to enter the tumor, which was disconnected, resulting in postoperative Horner's syndrome. (4) Intraoperative frozen diagnosis was a benign tumor. To fully reveal the root of the tumor, most of the tumors were removed first, and the tumor was found to originate from the C7 nerve root. The root of the tumor was sharply separated with monopolar curved scissors. (5) The image shows the surgical field after complete tumor resection. Postoperatively, the patient developed right upper limb weakness, and symptoms were relieved 2 months postoperatively. MR, magnetic resonance.

occurred. Chylothorax occurred in two patients, which were both eventually resolved with conservative care.

The mean mass size was 4.6 ± 2.0 (range, 2.5–10) cm. The diagnoses included schwannoma (26 patients), ganglioneuroma (four), bronchogenic cysts (three), ectopic nodular goiter (one), and cavernous hemangioma (one).

The mean chest tube use was 4.1 ± 2.1 (range, 1–10) days, and the postoperative hospital length of stay was 5.1 ± 2.1 (range, 2–11) days. Our hospital uses RMB for settlement, which is equivalent to 8868.8 ± 2207.1 (range, 4,951–15,883) USD based on the 1:6.5 exchange rate.

Follow-up was completed in all patients, and none of them developed local recurrence or distant metastasis. The postoperative characteristics and pathological outcomes are shown in Table 4.

Discussion

Why RATS

In the era of conventional thoracotomy, resection of superior mediastinal tumors often requires supraclavicular incision or

TABLE 1 Patient characteristics.

Variables	Value
Sex, male/female	19/16
Age, years	41.6 ± 13.5 (range, 13–66)
Smoking/non-smoking	5/30
Comorbidities	
Hypertension	9 [25.7]
Diabetes	1 [2.9]
Hypothyroidism	1 [2.9]
Symptom	
Horner's syndrome	6 [17.1]
Chest pain	4 [11.4]
Chest tightness	2 [5.7]
Upper extremity numbness	3 [8.6]
Upper extremity weakness	1 [2.9]

Data are number, number (percentage), or mean ± SD (standard deviation).

TABLE 2 Preoperative imaging characteristics.

Variables	Value
Imaging method	
CT	35
MR	22
CT&MR	22
Mass location	
Superior mediastinum	35
Cervical-mediastinal	30 [85.7]
Pathologic diagnosis and accuracy with postoperative pathology	
CT-Neurogenic tumor	9 [100%]
CT-Bronchial cyst	0
CT-Ectopic thyroid gland	1 [100%]
CT-Cavernous hemangioma	0
MR-Neurogenic tumor	
MR-Bronchial cyst	1 [100%]
MR-Neurogenic tumor	16 [100%]
MR-Cavernous hemangioma	0
Enlarged intervertebral foramen	
CT	4
MR	2
CT and MR	2
Closely related to blood vessels	
CT	7
MR	0
CT and MR	0

Data are numbers or numbers (percentage).

CT, computed tomography; MR, magnetic resonance.

sternotomy, which are excessively invasive procedures. With the advent of the minimally invasive era, several approaches have been attempted, some of which still require combined incision

TABLE 3 Intraoperative characteristics.

Variables	Value
Surgical approach	
Left	15 [42.9]
Right	20 [57.1]
Time	
Docking	11.2 ± 3.2 min
Operation	117 ± 45.2 min
Blood loss	59.7 ± 94.4 ml
Heavy bleeding	1 case [2.9], 500 ml
Blood transfusion	1 case [2.9], 200 ml
Conversion	0

Data are number, number (percentage), or mean ± SD (standard deviation).

TABLE 4 Postoperative characteristics and pathological outcomes.

Variables	Value
Chest tube use	4.1 ± 2.1 days
Postoperative hospital stay	5.1 ± 2.1 days
Cost	8868.8 ± 2207.1 USD
Postoperative complications	
Horner's syndrome	12 [41.4] ^{1a}
Upper limb weakness (paralysis)	2 [6.5] ^{2b}
Chylothorax	2 [5.7]
Pathological outcomes	
Mass diameter	4.6 ± 2.0 cm
R0 resection	35 [100]
Schwannoma	26 [74.3]
Ganglioneuroma	4 [11.4]
Bronchogenic cyst	3 [8.6]
Ectopic nodular goiter	1 [2.9]
Cavernous hemangioma	1 [2.9]

Data are number, number (percentage), or mean ± SD (standard deviation).

^{1a}1:6 patients with preoperative Horner's syndrome were excluded.

^{2b}2:4 patients with preoperative symptoms of brachial plexus compression were excluded.

(5, 6). In 2010, Tanaka et al. (7) introduced two cases of total thoroscopic resection of superior mediastinal tumors extending above the thoracic inlet. In the next few years, we used the same procedure in several cases but found that the approach was challenging to perform during the delicate handling required in the thoracic inlet area, the narrowest and farthest, during VATS. Compared to VATS, RATS provides a stable three-dimensional high-resolution view of the surgical field controlled by the surgeon. The EndoWrist operative arm of the dVS can replicate minute human wrist-like movements within the narrow space of the superior mediastinum, the most crucial limitation of the long, rigid instruments of VATS. Moreover, the dVS provides instruments with different

functions. Although the instrument arm is also hindered by the intercostal space during surgical procedures such as VATS, the elbow and wrist joints in the thoracic cavity enable a stable and fine operation. However, compared to VATS, the instrument arms require wider trocars, usually 8 mm in diameter. To maintain stability, it also poses greater force on the ribs. These two factors can potentially increase the postoperative incision pain. Besides, the instrument arms occupy more space outside the body and the patient's arm is stretched to prevent interference, which may also cause postoperative discomfort. Finally, increased cost compared to VATS is another disadvantage. Patients with inferior mediastinal masses were excluded from the present study because these tumors could be conventionally resected *via* VATS. The present study specifically included masses located in the superior mediastinum, which present challenges in VATS. Despite the disadvantages of painful incisions, arm discomfort, and increased costs, we believe that RATS is a safe, smooth, and feasible approach for superior mediastinal masses.

Key points of RATS

An accurate setup of the dVS was crucial for successful operations (8, 9). The tumor, camera, two robotic arms, and assistant port formed three isosceles triangles at least 5 cm apart from each other to prevent clashing of instrument arms. All operations were performed successfully. A rolled gauze was prepared in case of uncontrolled bleeding. Pressure applied with a rolled gauze helped control the bleeding until an emergency open thoracotomy incision could be performed. For RATS beginners, the operation and docking times progressively decreased. We conducted >100 RATS and passed the learning curve. Therefore, the docking time was constant. In our experience, the fine operation near the intervertebral foramen and the mass isolation with a wide base required the longest time. Decompression of cystic lesions facilitated exposure and shortened the operative time.

The crucial role of MR in patient selection

The anatomy of the superior mediastinum is complex due to the presence of important neurovascular structures that traverse this area. This has traditionally posed a challenge for surgical access. Due to the difficulty of performing surgery, various surgical methods have been used to achieve adequate exposure (10, 11). To ensure operation safety, preoperative MR examination helps select suitable patients: (1) Assess for vascular/nerve/vertebral involvement (12, 13); (2) The cystic lesions suggested that the tumor could be simplified by decompression; (3) For patients with intraspinal extension, combined thoracoscopic surgery should be considered (14).

Enlarged intervertebral foramen on MR should not be considered a contraindication. In this study, four patients with enlarged intervertebral foramen underwent R0 resection. (4) Evaluation of mass blood supply (for masses with abundant blood supply, preoperative embolization can reduce the possibility of intraoperative bleeding). In this study, one patient with an ectopic thyroid gland significantly reduced the blood supply using this method. For patients with intraspinal extension, combined scopic surgery (RATS with tubular retraction system) should be considered. The intraoperative examination of all patients was consistent with the preoperative MR examination, and no vascular/nerve invasion was detected. Based on accurate preoperative imaging evaluation, all surgeries were completed successfully, without conversion to thoracotomy.

Postoperative outcomes

Hospital stay

All patients recovered rapidly and successfully. Compared to other relevant reports, our postoperative hospital stay is significantly longer due to the following reasons: (1) In our hospital, a patient cannot be discharged until the tube was removed. Our criteria for tube removal is drainage of <100 ml/day instead of 200 or 300 ml as required in some hospitals. (2) In this study, the masses were larger, leading to more postoperative exudation. (3) Two patients with postoperative chylothorax were treated and then discharged after conservative management, leading to longer mean postoperative hospital stay (11 and 10 days, respectively).

Complications

Nerve injury complications were mainly related to the location of the lesion. Three patients with preoperative brachial plexus compression symptoms were relieved; however, ≥ 2 patients developed symptoms of brachial plexus injury. All these five masses were cervical-mediastinal tumors. As brachial plexus was invisible in conventional MR and RATS, preoperative FSE-cube sequence MRI examination and intraoperative neural probes may be required to predict and reduce the risk of nerve injury (15).

To prevent Horner's syndrome, sympathetic nerve chains should be identified and protected first. Although the sympathetic nerve chain was visible in RATS in all patients intraoperatively, the incidence of Horner's syndrome was higher than in other studies (16, 17). Horner's syndrome was diagnosed in six patients preoperatively (six with facial hypohidrosis and two with ptosis). The symptoms of these patients were not relieved postoperatively. Twelve patients developed Horner's syndrome postoperatively (eight with facial and upper limb hypohidrosis, three with upper limb hypohidrosis, and one with ptosis only). Among these, six

patients had ptosis. All 18 patients were pathologically diagnosed with neurogenic tumors close to the paravertebral sulcus. Our analyses indicated that, after the exclusion of six patients preoperatively diagnosed with Horner's syndrome, the mean mass diameter was even smaller in patients with postoperative Horner's syndrome than in those without it, among the remaining 29 patients. This finding might indicate that the mass location is more significant than the mass diameter in predicting the occurrence of postoperative Horner's syndrome.

By reviewing the surgical video, we classified 18 patients with sympathetic chain injury into three types based on the relationship between tumor and sympathetic chain. First, no boundary was observed between tumor and sympathetic chain in 11 patients (including all six patients with Horner's syndrome preoperatively). During these operations, the sympathetic chain could be observed traversing the tumor, suggesting that the tumor may originate from the sympathetic chain. Such patients may be unable to avoid Horner's syndrome. Second, the sympathetic chain was adjacent to the tumor in five patients. Although the sympathetic chain was preserved intraoperatively, Horner's syndrome still occurred postoperatively. This may be related to the use of intraoperative electrical energy devices. Third, the tumor was far from the sympathetic chain in two patients, which may be related to the stimulation of the sympathetic chain intraoperatively. Indeed, the sympathetic chain is easily damaged and stimulation of the thoracic drainage tube can cause Horner's syndrome.

The increased incidence of Horner's syndrome may be caused by surgical approach changes. In open surgery, the tumor is first isolated from the surrounding tissue, and the deepest root is finally treated. Unless the tumor originates from the sympathetic chain, most can be separated bluntly, and the risk of nerve injury is low. Conversely, in RATS surgery, the tumor base is first exposed and can only be pulled near aside by breaking off the tumor base. When the tumor base is closely related to the sympathetic chain, the dissociation process may increase the risk of sympathetic nerve injury. Therefore, careful identification and protection of the sympathetic nerve chain intraoperatively and avoidance of clamping and using electrical energy devices around the sympathetic nerve chain are keys to preventing the occurrence of Horner's syndrome.

Cost

The mean cost was \$ 8,868.8 ± 2,207.1 (range, \$ 4,951–15,883), which was comparable with another study (4). The cost-effectiveness of this technique was not within the scope of this study, and thus, further studies regarding this issue are needed.

Lack of research

There was a single-center retrospective study and was not feasible to conduct a randomized controlled study due to the low incidence of the disease. However, to our knowledge, this is the largest series report on RATS for superior mediastinal masses.

Conclusions

In preoperative MR, appropriate patients can be selected for safe robotic surgery. More attention should be paid to protecting nerves intraoperatively to prevent complications.

Due to surgical approach changes, robotic surgery may increase the risk of sympathetic nerve chain injury, leading to an increased incidence of Horner's syndrome, which should be closely considered intraoperatively.

Data availability statement

The original contributions presented in the study are included in the article/Supplementary Material, further inquiries can be directed to the corresponding author/s.

Author contributions

BY: Surgery assistant paper writing and paper revision. RC: data collecting, paper writing and picture editing. CL: Surgery assistant and data collecting. KF: Surgery assistant and data collecting. YL: data collecting. YL: Surgeon paper revision and project director. BY and RC contributed equally to this article. All authors contributed to the article and approved the submitted version.

Conflict of interest

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Tracheal or bronchial wedge resection: Case report

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Background: Primary tracheal or bronchial tumors are relatively uncommon, whether benign or malignant. Sleeve resection is an excellent surgical technique for most primary tracheal or bronchial tumors. However, depending on the size and location of the tumor, thoracoscopic wedge resection of trachea or bronchus can be performed with the assistance of a fiberoptic bronchoscope for some malignant and benign tumors.

Case Description: We performed a single incision video-assisted bronchial wedge resection in a patient with a left main bronchial hamartoma with a size of 7 × 5 × 5 mm. The patient was discharged from the hospital six days after the surgery with no postoperative complications. There was no obvious discomfort during the 6-month postoperative follow-up, and the reexamination of fiberoptic bronchoscopy revealed no evident stenosis of the incision.

Conclusions: Through the detailed case study and literature review, we believe that tracheal or bronchial wedge resection is a significantly superior technique under the appropriate conditions. Video-assisted thoracoscopic wedge resection of trachea or bronchus should be a new and excellent development direction of minimally invasive bronchial surgery.

KEYWORDS

tracheal or bronchial tumor, tracheal or bronchial wedge resection, videoassisted thoracoscopic surgery, parenchymal sparing procedure, case report

Introduction

Primary tracheal or bronchial tumors are relatively uncommon, whether benign or malignant. Tracheal or bronchial tumors are classified into three types: malignant, low-grade, and benign on their degree of differentiation. Tracheal or bronchial segmental resection with end-to-end anastomosis is currently the standard surgical treatment for tracheal or bronchial tumors. Sleeve resection is an excellent surgical technique for most primary tracheal or bronchial tumors. However, depending on the size and location of the tumor, thoracoscopic wedge resection of trachea or bronchus can be performed with the assistance of a fiberoptic bronchoscope for some malignant and benign tumors (1, 2). It significantly reduces the difficulty and trauma of surgery while preserving the lung tissue and ensuring surgical results. It also reduces the incidence of postoperative complications (3–8). This article comprehensively demonstrates the advantages, disadvantages and indications of this technique through a detailed case study and previous literature.

Case description

A 46-year-old man was admitted with a left main bronchus tumor. He was in good health in the past. Physical examination, routine blood examination, biochemistry and tumor markers revealed no abnormalities. After admission, fiberoptic bronchoscopy

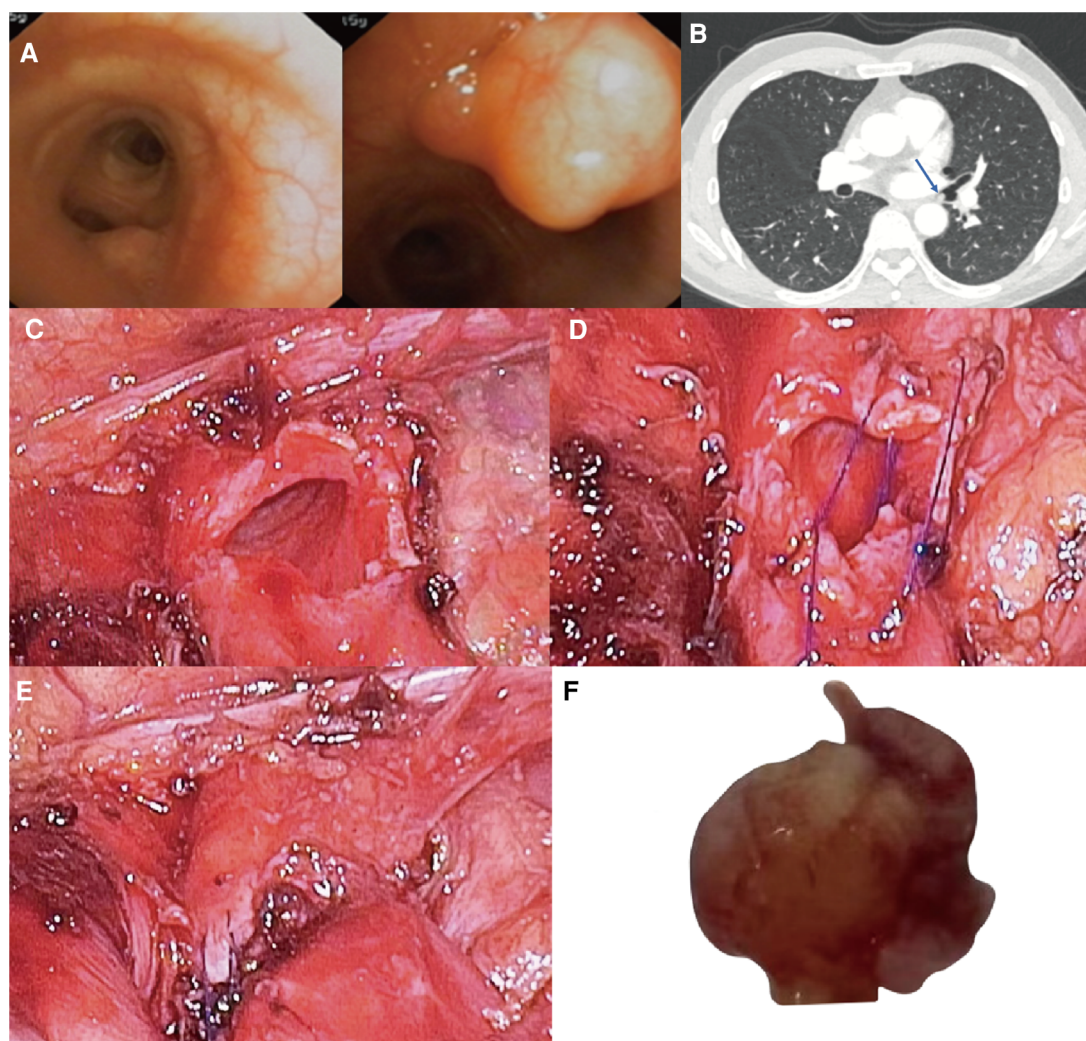


FIGURE 1

(A) neoplastic bulge was seen on the medial wall of left main bronchus terminal, 1 cm away from the opening of left lower lobe bronchus. (B) Bronchial tumor at the end of left main bronchus (arrow), the diameter of tumor base is 5 mm, and the diameter of bronchus is 8 mm. Surgical Technique: (C) The left main bronchus wall after wedge-shaped resection of the tumor with endoscopic scissors. (D) Continuous suture of the incision using 4-0 Prolene. (E) Left main bronchus wall after suture. (F) Left main bronchus tumor with a size of 7 × 5 × 5 mm.

(Figure 1) and chest computed tomography (CT) (Figure 1) were performed. At the bronchoscopy, a certain amount of tissue was taken for biopsy, although we found that the tumor was tough and difficult to clamp.

Bronchoscopy results revealed a neoplastic bulge on the medial wall of left main bronchus terminal, 1 cm away from the left lower lobe bronchus opening. The surface mucosa was still smooth, and the surface blood vessels were visible. The histopathological results of the biopsy showed that there were very small pieces of proliferated spindle cells with background myxoid changes under microscope, and the cell heterogeneity was not obvious. Although there was no definite diagnosis, it also helped us to preliminarily rule out the diagnosis of malignant tumor. In this case, we first communicated with a respiratory endoscopist and were told that the tumor could not be safely removed by intraluminal bronchoscopic treatment due to the large basal area of the tumor, so we decided to perform a single incision video-assisted bronchial wedge resection first.

Surgical technique

We drilled a 3 cm left thoracic and axillary midline fifth intercostal hole into the patient's chest. After loosening some adhesions and dividing the inferior pulmonary ligament, the lung tissue was pulled to expose the left main bronchus from the back. The left main bronchus was separated after the mediastinal pleura was opened. At this time, the visual fiberoptic bronchoscope was used to determine tumor location and margin by two methods: (1) We asked the anesthesiologist to place the bronchoscope lens under the tumor and turn the lens direction so that the light source of the lens was directed directly at the bronchial wall. And then we could clearly see the position of the lens under the thoracoscopy. (2) We pressed the bronchus gently with the instrument under the thoracoscopy, and the part we pressed could be clearly seen under the fiberoptic bronchoscope. By comparing these two noninvasive methods, we could determine the location of the tumor.

After the bronchial tumor was leaked, the left main bronchus was cut along the distal end of tumor with endoscopic scissors, and the tumor was wedge-shaped along the edge of tumor. When the left main bronchial hamartoma was confirmed from the frozen section of the removed tumor, the incision was sutured by 4 - 0 Prolene with a continuous suture, needle distance 5 mm, and margin 5 mm (Figures 1, 2). There was no apparent stenosis or distortion of the bronchi observed by thoracoscopy and fiberoptic bronchoscopy after suturing. The operation lasted 1.5 h, and there was no visible bleeding during surgery.

The chest drain was removed five days after the surgery, and the patient was discharged from the hospital six days after the surgery with no postoperative complications. Thoracoscopic wedge resection is significantly superior to sleeve resection in terms of recovery. There was no obvious discomfort during the 6-month postoperative follow-up, and the reexamination of fiberoptic bronchoscopy revealed no evident stenosis of the incision.

Discussion

Through the detailed case study and literature review, we believe that tracheal or bronchial wedge resection is feasible and excellent in treating some benign and malignant tumors of the trachea or bronchus. The indications for wedge resection include (1) Tumors with a base diameter smaller than the diameter of trachea or bronchus. (2) Tumors that are confined to the carina or bronchial corner. (3) Local tumor infiltration in the cranial and the caudal parts of adjoining main bronchus.

Indication 1

In the 6 cases in the [Supplementary Table \(9–13\)](#), the authors performed wedge resection of the trachea or bronchus to treat

benign or low-grade bronchial tumors. Wedge resection significantly reduces the difficulty and risk of surgery while preserving the lung tissue and ensuring surgical results. Based on their experience with 83 cases of bronchial carcinoid tumors, Ismail Cüneyt Kurul et al. concluded that wedge resection could be considered if the diameter of the trachea or bronchial tumor base to be resected is smaller than the diameter of bronchus (2). In addition, Florian Augustin believe that the maximum distance between the upper and lower edge of the bronchus in wedge resection is preferably no longer than the transverse diameter of the bronchus (14), which can effectively avoid postoperative anastomotic stenosis. For benign and low-grade malignant tumors of the trachea or bronchus, the preferred surgical approach should be minimally invasive thoracoscopic wedge resection.

Indication 2

Dong Xie et al. performed wedge resection on a patient with a 1 cm squamous cell carcinoma confined to the tracheal carina, and a clear margin was confirmed during the surgery. The wedge-shaped excision and reconstruction of the carina under the original carina ensured no separation between the trachea and the main bronchus (Figure 3). The trachea and the bronchus remained continuous without creating longitudinal tension. The problem of longitudinal tension encountered by sleeve resection was skillfully circumvented with wedge resection, and the patient recovered well after surgery (15). Hiromasa Yamamoto et al. performed a bronchial wedge resection for a carcinoid tumor of the left upper bronchus near the upper and lower lobar bronchi bifurcation. The upper and healthy lower lobar bronchial corner was resected longitudinally, and the bronchial corner was reconstructed at a distance. At the five-month postoperative follow-up, there was no stenosis at the suture, indicating that this technique avoided anastomotic stenosis and longitudinal tension (16).

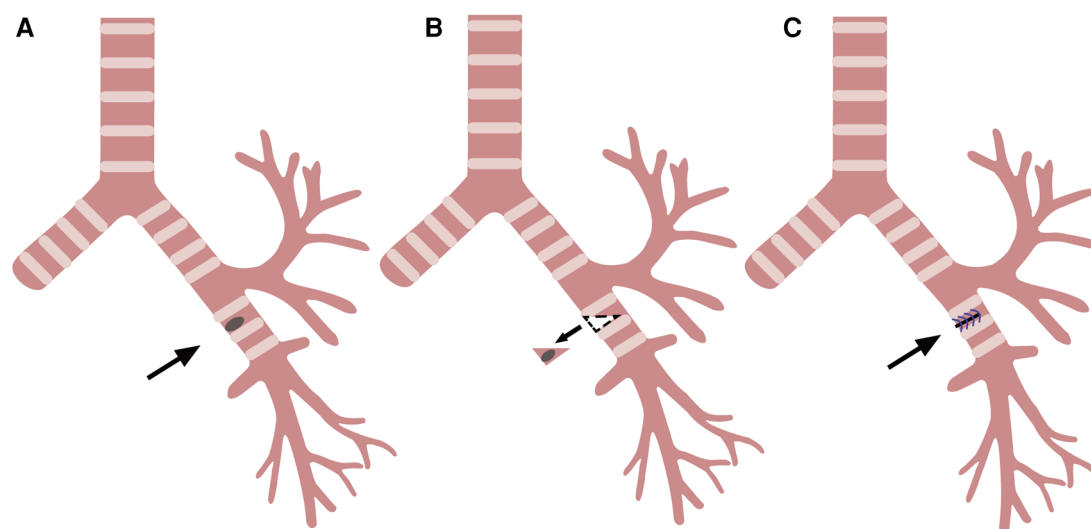


FIGURE 2

Wedge resection and reconstruction of the bronchi. (A) Left main bronchus tumor (arrow). (B) Resection of the tumor along the dotted line (arrow). (C) Left main bronchus wall after suture (arrow).

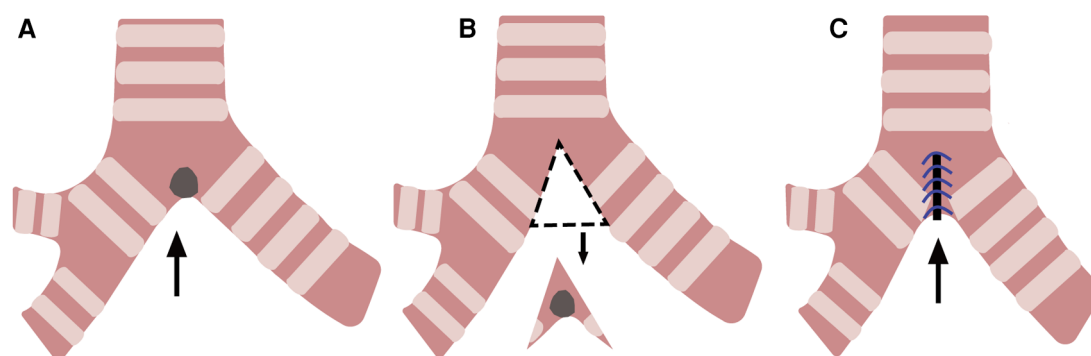


FIGURE 3

Wedge resection and reconstruction of the carina. (A) A tumor at the carina (arrow). (B) Resection of the tumor along the dotted line (arrow). (C) Reconstruction of the carina (arrow).

Daisuke Yuki et al. performed a deeper wedge resection and the reconstruction of right secondary carina for a 13 mm recurrent mucoepidermoid carcinoma located at the orifice of upper lobar bronchus with main bronchus involvement. The lung tissue was successfully preserved, and no recurrence occurred 18 months after surgery (17). Dong Xie, Hiromasa Yamamoto, and Daisuke Yuki performed wedge resection and reconstruction of the carina, bronchial corner, and the secondary carina, respectively, for resection of tracheal or bronchial malignancies. The technique avoided longitudinal tension and anastomosis stenosis and preserved the lung tissue intact.

Indication 3

Krishna Khargi et al. performed lobectomy with bronchial wedge resection in eight patients with lung malignancies involving the main bronchus, including four right upper lobectomies, two left upper lobectomies, and two left lower lobectomies. Postoperative histopathological results revealed seven cases of squamous cell carcinoma and one case of carcinoid. They believe it is feasible to remove one-third to one-half of the circumference of the main bronchus in the wedge resection (1). However, three patients experienced varying degrees of bronchial stenosis after the operation. Therefore, Florian Augustin et al. suggested that the maximum distance between the upper and lower edges of the bronchus in wedge resection should be less than the transverse diameter of the bronchus, which is more conducive to avoiding anastomotic stenosis (14).

In 16 patients with right lung malignancies, Christophoros Kotoulas et al. performed 12 right upper lobectomies and four right upper and middle lobectomies combined with main bronchial wedge resection. They dissected the inferior pulmonary ligament and released the hilum, allowing the trachea and main bronchi to move 1–2 cm (6). None of the 16 patients had anastomotic stenosis and distortion after surgery, and the long-term prognosis was satisfactory.

Although Krishna Khargi et al. thought that local tumor infiltration of the cranial and the caudal parts of adjoining main bronchus was the indication for wedge bronchoplasty (1), the use

of wedge resection has many limitations. First, although the wedge bronchoplasty can be performed on either lobe, the right upper lobe is more suitable for anatomical reasons (6, 18) (Figure 4). In addition, the mobilization of the trachea and main bronchus, the limitation of resection range of main bronchus, and the determination of resection margin are all necessary to ensure the safety of wedge bronchoplasty.

Similarly, for benign tracheal or bronchial tumors, we recommend lobectomy or segmentectomy with bronchial wedge resection rather than sleeve resection if the obstruction of the bronchus has resulted in irreversible destruction of the lung tissue and lobectomy or segmentectomy alone cannot resolve the problem. For example, Azevedo-Pereira AE (19), Galvez C (20), and Maeda M (21) used lobectomy or segmentectomy with wedge bronchoplasty for the treatment of bronchial glomus tumor, bronchial lipomas, and bronchial inflammatory pseudotumors, respectively.

These demonstrate that tracheal or bronchial wedge resection is a feasible and excellent technique when the indications for wedge resection are understood, particularly for some benign and malignant tumors with guaranteed margins. The indications for wedge resection include (1) Tumors with a base diameter smaller than the diameter of trachea or bronchus. (2) Tumors that are confined to the carina or bronchial corner. (3) Local tumor infiltration in the cranial and the caudal parts of adjoining main bronchus.

In addition, wedge resection requires the dissection of the inferior pulmonary ligament, the hilum release, the dissociation of intrapericardial pulmonary vein attachments, the mobilization of the trachea and main bronchus, the limitation of resection range, the determination of resection margin, and suturing from low tension area to high tension area. These are effective measures for preventing anastomotic stenosis and ensuring the safety of wedge resection.

Compared with sleeve resection, wedge resection preserves the continuity and blood supply of the trachea or bronchus (22, 23). It significantly reduces the difficulty and trauma of surgery and is easier to be performed under thoracoscopy without conversion to thoracotomy (22). It also reduces the incidence of postoperative complications such as bronchopleural fistula (24). For benign and

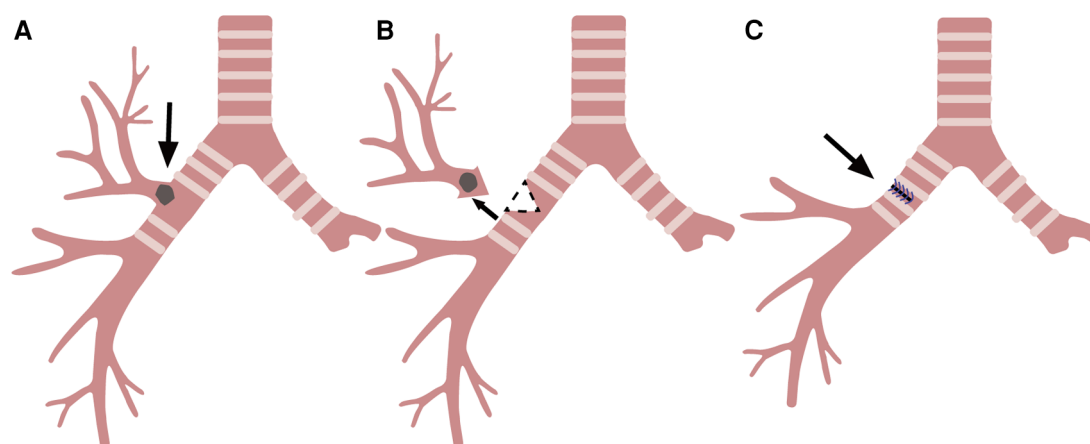


FIGURE 4

Right upper lobectomy with wedge resection and reconstruction of the bronchus. (A) Right upper lung malignancy involving the main bronchus (arrow). (B) Resection of the right superior lobar bronchus along the dotted line (arrow). (C) Right main bronchus wall after suture (arrow).

low-grade malignant tumors of the trachea or bronchus, the preferred surgical approach should be video-assisted thoracoscopic wedge resection. For tumors such as non-small cell lung cancer, Park et al. found that wedge bronchoplastic lobectomy should be an appropriate alternative to sleeve lobectomy regardless of lymph node status (23).

However, we found that there is a debate about which technique is more likely to cause postoperative anastomotic complications. Although Krüger et al. believe that sleeve resection is more prone to result in anastomotic complications and pneumonia (24), many believe that wedge resection is more prone to result in various degrees of anastomotic stenosis (1, 2). Anastomotic stenosis can cause postoperative complications such as secretion retention, pneumonia, atelectasis, respiratory distress, and complete anastomotic obstruction (1–8, 14, 22, 23). It may result in the patient requiring bronchoscopic toileting or mechanical ventilation support after surgery (1, 23). When stricture is severe, a second operation is required to perform sleeve resection to relieve the anastomotic stenosis (6). However, according to our references, anastomotic stenosis after wedge resection is more of a technical problem. When the indications and precautions of wedge resection are strictly grasped, the probability of anastomotic stenosis after wedge resection is no greater than after sleeve resection.

In conclusion, we believe that tracheal or bronchial wedge resection is a significantly superior technique under the appropriate conditions. Video-assisted thoracoscopic wedge resection of trachea or bronchus should be a new and excellent development direction of minimally invasive bronchial surgery.

Data availability statement

The original contributions presented in the study are included in the article/[Supplementary Material](#), further inquiries can be directed to the corresponding author/s.

Ethics statement

Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

Author contributions

ZHJ drafted and edited this manuscript, assisted in the surgery, and analyzed patient data. JY and ZT performed the surgery, edited this manuscript, and analyzed patient data. All authors contributed to the article and approved the submitted version.

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Supplementary material

The Supplementary Material for this article can be found online at: <https://www.frontiersin.org/articles/10.3389/fsurg.2023.1122075/full#supplementary-material>.

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