Zhang *et al. Holistic Integrative Oncology* (2023) 2:30
https://doi.org/10.1007/s44178-023-00051-y

Holistic Integrative Oncology

ORIGINAL RESEARCH

Open Access

Results of robot-assisted minimally invasive esophagectomy in 111 consecutive patients: an Asia cohort study

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Abstract

Background Robot-assisted minimally invasive esophagectomy (RAMIE) is becoming increasingly popular as a treatment for esophageal cancer. The purpose of this study was to use the da Vinci robotic system (Intuitive Surgical, Sunnyvale, CA, USA) to perform 111 consecutive cases of radical esophageal cancer and report the perioperative data of surgery and postoperative complications and short-term oncological outcomes.

Methods We retrospectively analyzed 111 patients who underwent RAMIE conducted at Fujian Medical University Union Hospital from August 2016 to January 2021. Each patient's characteristics, clinicopathological stage, postoperative pathological stage, surgery outcome, postoperative recovery, and short-term oncological outcomes were analyzed.

Results Of the 111 patients who underwent RAMIE, 77 were male and 34 were female, and the mean age was 62.1 ± 8.8 years. Twenty-seven patients (24.3%) received preoperative neoadjuvant therapies, the most popular of which was preoperative induction chemotherapy in 16 cases (14.4%), followed by preoperative induction radiotherapy in 8 cases (7.2%) and preoperative induction chemotherapy plus immunization in 3 cases (2.7%). The vast majority of patients (110/111, 99.1%) underwent radical resection, with a mean intraoperative bleeding amount of 99.9 ± 68.4 mL and a mean operative time of 271.9 ± 70.0 min. The mean total number of lymph nodes removed was 40.9 ± 16.7, including 21.8 ± 9.0 thoracic lymph nodes. Fifty-five (49.6%) patients had lymph node metastases, including 17 (15.3%) with lymph node metastases in the left recurrent laryngeal nerve, 24 (21.6%) with lymph node metastases in the right recurrent laryngeal nerve, and 7 (6.3%) with lymph node metastases in the bilateral recurrent laryngeal nerve. The positive rate of left recurrent nerve lymph nodes was 4.77%, and he positive rate of right recurrent nerve lymph nodes was 8.38%. The main postoperative complications included pulmonary infection in 24 cases (21.6%), celiac disease in 3 cases (2.7%), tracheoesophageal fistula in 1 case (0.9%), anastomotic fistula in 3 cases (2.7%), postoperative cardiac arrhythmias in 11 cases (9.9%), VTE in 3 cases (2.7%), and pleural effusion (requiring postoperative tube drainage) in 13 cases (11.7%). Additionally, 2 cases of postoperative pneumothorax (1.8%), 1 case of poor incision healing (0.9%), 1 case of incomplete bowel obstruction (0.9%), 1 case of neck hematoma (0.9%), and 1 case of postoperative admission to the intensive care unit (0.9%) occurred. The median length of stay was 10.9 ± 6.1 days, and there were no cases of perioperative death.

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Conclusions Robotic esophageal cancer radical surgery is safe and feasible. The surgeon can be proficient in thoracic robotic surgery and mediastinal lymph node dissection and achieve high levels of perioperative safety and short-term efficacy.

Keywords Robot-assisted surgery, esophageal cancer, Minimally invasive surgery, Complications, Short-term outcomes

1 Background

Esophageal cancer is a prevalent disease in thoracic surgery, with an estimated 456,000 incident cases and 400,200 deaths in the year 2012 worldwidely [1]. Conventional open transthoracic esophagectomy is the preferred surgical approach, allowing for optimal resection of the tumor and the surrounding lymph nodes; however, it has been found to lead to considerable morbidity and mortality[2]. Minimally invasive esophagectomy (MIE), which is less invasive with a similar long-term survival rate compared to open surgery, has become increasingly common in the treatment of resectable esophageal cancer [3–5]. However, MIE is a complex procedure with a long learning curve, requiring the surgeon to perform more than 60 cases to obtain lower morbidity [6, 7]. With the development of minimally invasive techniques, RAMIE has been recognized for its efficacy and safety, especially for the clearance of recurrent laryngeal nerve lymph nodes of the recurrent laryngeal nerve, in a manner nearly equal to or better than open surgery [8–10]. Compared to minimally invasive esophagectomy, RAMIE decreases postoperative complications without compromising short-term postoperative functional recovery and oncological outcomes [11–13]. With the proven advantages of RAMIE over conventional MIE for better lymph node clearance and organ protection with a high-definition 3-dimensional view and a wrist-like flexible robotic arm system [10, 14–16].

However, to date, few studies offering large volumes of data exist. In this study, the clinical characteristics and short-term survival of 111 patients who underwent robot-assisted surgery for esophageal cancer using the da Vinci robotic system (Intuitive Surgical, Sunnyvale, CA, USA) were analyzed. In particular, we focused on the perioperative safety, efficacy, and short-time oncological outcomes of patients treated with RAMIE.

2 Methods

2.1 Patients

A total of 111 patients undergoing radical surgery for RAMIE from August 2016 to January 2021 at Fujian Medical University Union Hospital were reviewed. All of the patients underwent esophagectomy, including esophagectomy and lymph node dissection, with the Xi da Vinci robotic system. We then reviewed patients' general information, induction treatment, surgical procedure, postoperative statistics, functional recovery after discharge, and short-time oncological outcomes.

Each patient's preoperative evaluation included computed tomography (CT) imaging of the chest and abdomen, ultrasound of the cervical lymph nodes, gastrointestinal endoscopy, endoscopic ultrasound, and fiberoptic bronchoscopy. Positron-emission CT (PET-CT) is used routinely as an imaging modality, but it may not be used in some patients with limited finances or those with a preoperative pathology of high-grade intraepithelial neoplasia of the squamous epithelium. Preoperative induction therapy was given to patients with suspected lymph node metastases and/or $\geq$ T3 stage on preoperative evaluation. All of the patients underwent radical 2-field lymph node dissection or 3-field lymph node dissection (when preoperative lymph node ultrasound, cervical CT, or PET-CT showed suspected cervical lymph node metastases, or cervical or upper thoracic esophageal cancer, or positive intraoperative frozen pathological results of recurrent laryngeal nerve lymph nodes, 3-field lymph node dissection was conducted). As long as the imaging assessment suggested the tumor was surgically resectable, the patient was considered a candidate for robotic esophageal surgery. Clinicopathological factors were noted with reference to the Japanese Classification of Esophageal Cancer [17, 18]. Outcome data included operative time, lymph node dissection, blood loss, postoperative hospital stay, and mortality at 90 days. Intraoperative and postoperative complications were graded according to the Esophagectomy Complication Consensus Group (ECCG) definitions [19].

The standard neoadjuvant treatment for patients with esophageal cancer is perioperative chemotherapy (2 cycles preoperatively and 2–4 cycles postoperatively of paclitaxel [75 mg/m$^{2]}$ and intravenous cisplatin [80–120 mg/m2] or carboplatin [300–500 mg/m2]); patients treated with concurrent preoperative radiotherapy were treated with radiotherapy for 5 weeks (41.4 Gy in 23 fractions, 5 days per week). Immunotherapy was administered in 2 or 3 cycles of pembrolizumab (2 mg/kg, every 3 weeks). All of the patients with cT1N0 undergoing esophagectomy or with a preoperative pathology of high-grade intraepithelial neoplasia underwent a preoperative

ultrasound endoscopic evaluation, incomplete endoscopic mucosal resection (R1), or endoscopic submucosal dissection.

2.2 Surgical procedures

Each patient was placed in a left lateral recumbent position at an angle of 135 degrees (Fig. 1). A 1.0-cm incision was made in the fourth intercostal space between the right mid-axillary line and the posterior axillary line, a 1.0-cm incision was made in the eighth intercostal space at the subscapular angle as the operating hole, a 1.0-cm incision was made in the sixth intercostal space at the anterior border of the latissimus dorsi muscle as the observation hole, and a 1.2-cm incision was made in the fifth intercostal space at the mid-axillary line as the secondary operating hole.

The artificial pneumothorax pressure was 6–8 mmHg (1 mmHg = 0.133 kPa). The surgical procedure was identical to that of thoracoscopy, as follows:

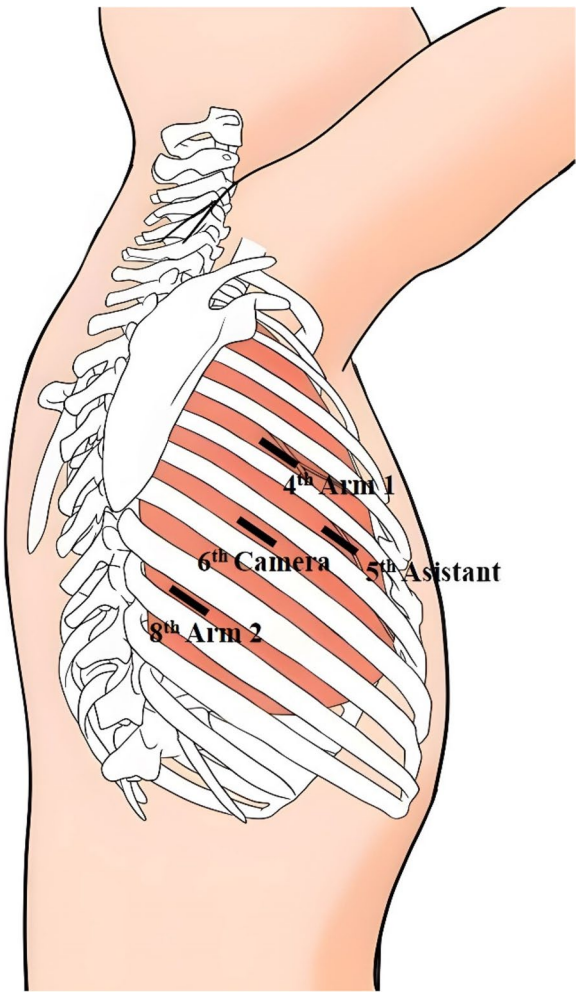

Fig.1 Port positions for right robot-assisted intrathoracic procedures

first, the lower esophagus was separated up to the esophageal hiatus, and the odd vein arch was then dissected. Next, the esophagus is dissected upwards to the level of T2 of the thorax. The right and left recurrent lymph nodes are cleared to the bilateral inferior thyroid artery (Fig. 2.), i.e., 2.5-field lymph node dissection, which is described in detail in our previous publication [20]. The patient's position was reversed to a supine split-legged position, and the stomach was laparoscopically freed. A linear cutting suture was made to shape the tubular stomach along the lateral side of the gastric lesser curvature. A routine jejunostomy was performed. During the neck procedure (3-field lymph node dissection was performed when preoperative cervical lymph node ultrasound, cervical CT, or PET-CT for suspected cervical lymph node metastases, or upper thoracic esophageal cancer patients, or positive lymph node cryopathology in the right and left recurrent laryngeal nerves), a left cervical incision was made at the medial border of the sternocleidomastoid muscle. The tubular stomach was lifted through the esophageal bed to the left neck and mechanically anastomosed with a tubular anastomosis.

2.3 Statistical analysis

The SPSS version 21.0 software (IBM Corporation, Armonk, NY, USA) was used for statistical processing. The measures were expressed using mean ± standard deviation (x ± s) or median values. Depending on the situation, an independent-samples *t*-test or chi-squared test was chosen to compare the data of different subgroups. Overall and progression-free survival curves were estimated with the Kaplan–Meier method and compared with the log-rank test. All of the reported *P* values were 2-sided, and the level of significance was set at 0.05.

3 Results

3.1 Patient characteristics

Baseline data, demographic data, and tumor characteristics are shown in Table 1**.** We had a total of 77 male and 34 female patients, with a median age of 62 years (range, 44–85 years). A total of 49 patients were preoperatively staged as having cT1–cT2 tumors, 59 of the remaining 62 were staged as having cT3 tumors, and the other 3 were staged as having cT4 tumors. During preoperative staging, 55 patients presented with positive lymph node disease. The majority of tumors were localized in the middle esophagus in 75 cases (67.6%). Approximately 66% of the patients did not present with comorbidities. Fifteen patients had a previous thoracic or abdominal surgery. None of the patients underwent esophageal or gastric surgery. Twenty-seven patients received neoadjuvant therapy, including preoperative induction radiotherapy

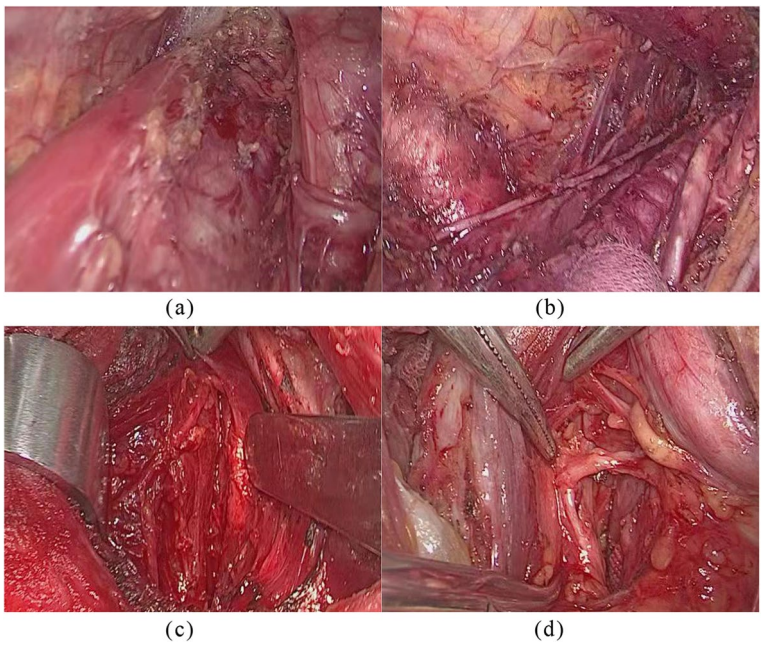

Fig.2 Right and left recurrent laryngeal nerve in robotic thoracoscopy and cervical incision

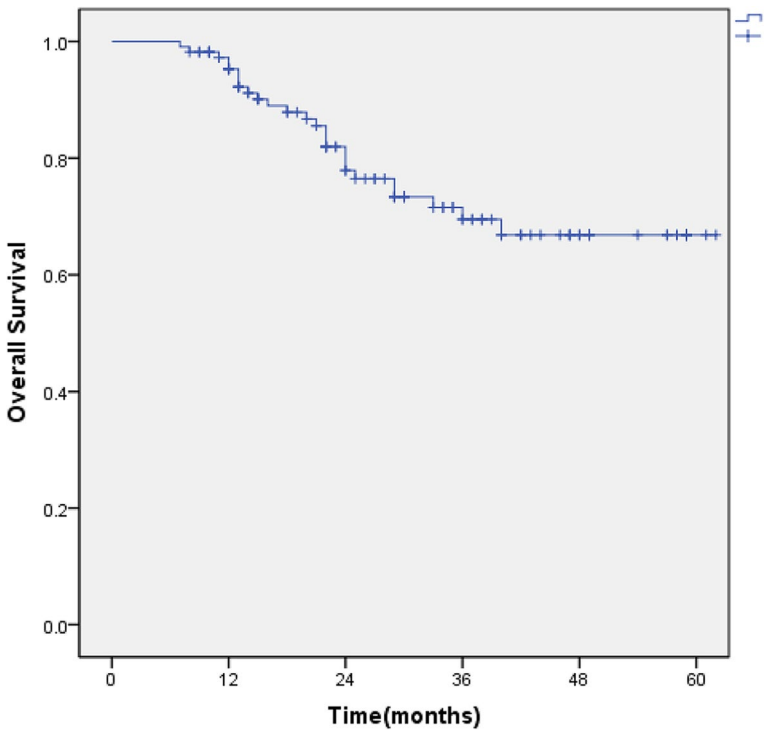

Fig.3 Overall survival of 111 patients who underwent Robot-Assisted Minimally Invasive Esophagectomy

Table 1 Demographics and tumor characteristics of the patients(n = 110)

n **= 111**	
Age (y) (Median-range)	(62.1 ± 8.8) (44–85)
gender(n(%))	
Male	77 (69.3)
Female	34 (30.6)
Comorbidity (n(%))	
No comorbidity	59(79.3)
Vascular	13 (11.7)
Cardiac	7 (6.3)
Diabetes	10 (9.0)
Pulmonal	23(20.7)
Oncologic	3 (2.7)
Previous thoracic/abdominal operation	15(13.5)
ASA score (n (%))	
1	64 (57.7)
2	42 (37.8)
3	5(4.5)
Clinical stage (TNM 8) (n (%))	
cT1N0	22 (19.8)
cT1N1	8 (7.2)
cT2N0	10 (9.0)
cT2N1	7 (6.3)
cT2N2	2 (1.8)
cT3N0	22 (19.8)
cT3N1	26 (23.4)
cT3N2	10 (9.0)
cT3N3	1(0.9)
cT4aN0	2(1.8)
cT4aN1	1(0.9)
cT4aN2	0(0)
Tumor location (n (%))	
Upper esophageal	10 (9.0)
Middle esophageal	75 (67.6)
Lower esophageal	26 (23.4)
Tumor type (n (%))	0 (0)
Adenocarcinoma	102 (91.9)
Squamous cell carcinoma	8 (7.2)
High-grade intraepithelial neoplasiaNeuroendocrine	1 (0.9)
Neoadjuvant treatment (n (%))	
No therapy	84(75.7)
Chemotherapy	16 (14.4)
Chemoradiotherapy	8 (7.2)
Immunotherapyand chemotherapy	3 (2.7)

in 8 (7.2%), preoperative induction chemotherapy with immunization in 3 (2.7%), and preoperative induction chemotherapy alone in 16 (14.4%), respectively.

Table 2 Operative details (*n* = 110)

n **= 110**	
Operating time (min)(mean ± SD)	(271.9 ± 69.7) min
Blood loss (ml)(mean ± SD)	(99.9 ± 68.4) ml
Intraoperative complications	
Conversion thoracic phase	0
Conversion abdominal phase	3
Lymph nodes (number) (median – range)	(40.9 ± 16.7)
Thoracic lymph node (number)	(21.8 ± 9.0)
Positive lymph nodes (number)	55(49.5%)
106recLPositive lymph nodes n(%)	17(15.3%)
106recRPositive lymph nodes n(%)	24(21.6%)
106rec Positive lymph nodes n(%)	7(6.3%)

3.2 Operative data

The thoracic portion of the surgery was performed robotically in all of the patients, while the abdominal phase was performed by conventional laparoscopy. There were no conversions to an open chest approach during thoracic surgery, but 3 patients were converted to open surgery during the abdominal phase of surgery, including 1 because of intraoperative bleeding and another 2 because of abdominal adhesions. Data on operative details are shown in Table 2. The mean total operative time was 271.9 ± 69.7 min. The mean total number of lymph nodes removed was 40.9 ± 16.7, and the number of lymph nodes removed from the chest was 21.8 ± 9.0. The number of lymph node dissections and the rate of positive lymph nodes at each station are shown in Table 3.

3.3 Complications

In total, 72 of 111 patients recovered without complications, while 39 patients had an uneventful postoperative course. The most common complication was pulmonary complication (21.6%). Three cases of anastomotic leakage were found during esophagogastrostomy. All of the patients with anastomotic insufficiency were treated mainly conservatively, without reoperation. Nine patients (8.1%) were clinically diagnosed with laryngeal recurrent nerve palsy, which was unilateral and temporary. Three patients were found to have celiac disease postoperatively and were treated conservatively with dietary modification. One patient was found to have a chest wound infection. Two patients were readmitted for pulmonary complications or for treatment of anastomotic fistula. The 90-day mortality rate was 0%. The median length of stay was 10.9 ± 6.1 days (range, 6–50 days), and 3 patients were

Table 3 The number of lymph node dissections and the rate of positive lymph nodes at each station

The station of lymph nodes dissections	Average of lymph node dissections (*n* = cases)	Rate of positive lymph nodes *n*(%)
Left superclavicular lymph nodes(104L)	7.2 ± 4.0 (n = 30)	0 (0)
Right superclavicular lymph nodes(104R)	6.46 ± 3.5 (n = 26)	3 (1.79)
Left cervical paraesophageal lymp nodes(101L)	2.93 ± 2.0 (n = 43)	7 (5.56)
Right cervical paraesophageal lymp nodes(101R)	2.46 ± 1.8 (n = 68)	10 (5.99)
Main bronchus lymph nodes(109)	2.67 ± 1.0 (n = 12)	0 (0)
Left recurrent nerve lymph nodes (106recL)	4.37 ± 3.1 (n = 91)	19 (4.77)
Right recurrent nerve lymph nodes (106recR)	3.48 ± 2.8 (n = 96)	28 (8.38)
Upper thoracic paraesophageal lymph nodes (105)	2.3 ± 1.6 (n = 37)	4 (4.71)
Middle thoracic paraesophageal lymph nodes (108)	2.83 ± 2.4 (n = 81)	18 (7.86)
Lower thoracic paraesophageal lymph nodes (110)	2.32 ± 1.6 (n = 81)	10 (5.32)
Subcarinal lymph nodes (107)	5.2 ± 3.7 (n = 103)	12 (2.24)
Left cardiac lymph nodes (2)	2.39 ± 1.6 (n = 87)	19 (9.13)
Right cardiac lymph nodes (1)	2.45 ± 1.9 (n = 71)	4 (2.30)
Lymph nodes along the lesser curvature (3)	3.57 ± 3.0 (n = 69)	11 (4.47)
Lymph nodes along the left gastric artery (7)	3.8 ± 2.7 (n = 91)	17 (4.91)
Lymph nodes along the left gastric artery (8)	1.86 ± 0.5 (n = 7)	1 (7.70)

Table 4 Postoperative data (*n* = 111)

n **= 111**	
Complicated procedures (n (%))	39(35.1)
Pulmonary complications (n (%))	33(29.7)
Pneumonia (n (%))	24(21.6)
Pneumothorax (n (%))	2(1.8)
Pleural effusion (n (%))	13(11.7)
ARDS (n(%))	3(2.7)
Cardiac complications (n (%))	11(9.9)
Anastomotic leakage type II (n (%))	3(2.7)
tracheoesophageal fistula (n(%))	1(0.9%)
Chylothorax (n (%))	3(2.7)
Recurrent laryngeal nerve paralysis (n (%))	9(8.1)
VTE(n(%))	3(2.7%)
Wound infection (n (%))	1(0.9)
30-day mortality	0(0)
90-day-mortality	0(0)
Readmission ICU (n (%))	3(2.7)
Hospital stay (days) (mean – range)	(10.9 ± 6.1) (6–50)
Readmission in 30 days after discharge (n (%))	2(1.8)

admitted to the intensive care unit. The data of postoperative complications are shown in Table 4.

3.4 Histopathological outcome and short-term oncological outcomes

Table 5 provides a summary of the histopathological findings. The majority of tumors were squamous (94.6%). Two patients had no viable tumor cells found in the resection specimens. The median number of lymph nodes collected was 41. Metastatic lymph nodes were identified in 55 patients. All 110 patients underwent radical (R0) tumor resection. One patient underwent R1 resection, which was positive for cut ends. The median follow-up time was 48.9 months, and the median overall survival was not reached. The overall survival is shown in Fig. 3.

4 Discussion

In this article, we present the results of 110 patients with da Vinci robotic esophageal cancer (single-institution experience). RAMIE has been reported to be technically feasible and safe and shown to reduce pulmonary complications, postoperative pain levels, and hospital length of stay compared to open esophagectomy, without compromising oncologic outcomes, in recent Asian and European literature [21, 22].

Although open transthoracic esophagectomy is considered the first-choice procedure for patients with resectable esophageal carcinoma, minimally invasive techniques have gained popularity over the last decade as studies have confirmed faster recovery rates and a decrease in pulmonary complications [3, 4, 23]. However, conventional minimally invasive esophageal cancer surgery is complicated and difficult to master, resulting in a long learning curve and a high level of postoperative complications when the plateau stage has

Table 5 Histopathological data

Histological type (n (%))	
R0	110 (99.10)
R1	1 (0.90)
Lymph nodes (number) (median – range)	(40.88 ± 16.7)
Positive lymph nodes (number)	55(49.55%)
Pathological stage (TNM 8) (n (%))	
pTisN0M0	3(2.70)
pT0N0	4(3.60)
pT0N1	1(0.90)
pT0N3	1(0.90)
pT1N0	2(1.80)
pT1aN0	4(3.60)
pT1bN0	14(12.61)
pT1bN1	2(1.80)
pT1bN2	2 (1.80)
pT1N1	3(2.70)
pT2N0	9(8.11)
pT2N1	6(5.40)
pT2N2	2(1.80)
pT3N0	17(15.32)
pT3N1	17(15.32)
pT3N2	13(11.71)
pT3N3	6(5.40)
pT4aN0	2(1.80)
pT4aN3	1(0.90)
pT4bN0	1(0.90)
neuroendocrine carcinoma (ypT0N1M0)	1(0.90)
Histological type (n (%))	
Adenocarcinoma	0(0)
Squamous cell carcinoma	105(94.60)
No viable tumor cells	2 (1.80)
neuroendocrine carcinoma	1 (0.90)
High-grade intraepithelial	3 (2.70)

not been reached [6, 7, 24]. In addition, conventional thoracoscopic surgery has some important limitations, such as 2-dimensional views, disordered eye-hand coordination, and limited freedom, which may limit the surgeon's ability to perform optimal radical esophageal and mediastinal lymph node dissection.

The first series of patients treated with robotic-assisted minimally invasive esophagectomy was reported in 2005 and has been proven to be safe and effective in subsequent studies [11, 25, 26]. RAMIE might help overcome technical difficulties by providing high-definition 3-dimensional vision, better ergonomics, and precise surgical maneuvers [27]. The results of Guo et al. showed that at least 30 cases were needed to reach the plateau of thoracoscopic esophagectomy, and a lower morbidity rate was obtained after at least 60 cases of thoracoscopic esophagectomy [6]. Some studies suggest that robotic esophagectomy learning curves can reach a plateau by 22 cases and that postoperative complications and oncologic outcomes are comparable to the highest international standards [21, 28, 29].

The incidence of postoperative complications observed in our study is comparable to the results described above [26, 30–33]. In our study, 72% of the patients experienced a smooth postoperative recovery without complications. The main postoperative complications included pulmonary infection in 24 cases (21.62%), celiac disease in 3 cases (2.70%), tracheoesophageal fistula in 1 case (0.90%), anastomotic fistula in 3 cases (2.70%), postoperative arrhythmia in 11 cases (9.91%), VTE in 3 cases (2.70%), and pleural effusion (requiring postoperative tube drainage) in 13 cases (11.71%)—including left pleural effusion in 11 cases and bilateral pleural effusion in 2 cases (1.80%). Additionally, 2 cases of postoperative pneumothorax (1.80%), and 3 cases admitted to the postoperative intensive care unit for pulmonary infection (2.70%), which were cured after treatment, occurred. The median length of stay of the patients was 10.93 ± 6.1 days, and there were no cases of death within 90 days after surgery.

Short-term oncologic outcomes were reported for patients treated with RAMIE at our institution. Overall, 99.1% of patients with a median of 41 lymph nodes underwent radical (R0) resection. All of the patients were followed up with for at least 9 months, with a median follow-up length of 48.89 months. To date, the median overall survival has not been achieved. Short-term oncologic outcomes and short-term survival data are comparable to those of studies describing (minimal) esophagectomy [34, 35].

In conclusion, RAMIE is technically feasible and safe in the treatment of esophageal cancer. Postoperative complications and short-term oncologic outcomes are comparable to the highest current international standards [18]. The advantages of robotic versus MIE are currently being studied in multiple randomized controlled trials. The results of these trials will define the role of robotic treatment of patients with esophageal cancer. RAMIE radical surgery currently appears to be safe and reliable, and mediastinal lymph node dissection—especially bilateral recurrent nerve—can be significantly improved, while the rate of laryngeal recurrent nerve injury can be significantly reduced. As such, the use of RAMIE deserves to be promoted.

Acknowledgements
Not applicable.

Authors' contributions
ZB and CC conceived the idea of the study; ZSL and CMH analysed the data; ZTD, HGL, LW and ZW interpreted the results; CMH and HYZ wrote the paper; all authors discussed the results and revised the manuscript.

Funding
This work was supported by the National key clinical specialty of Thoracic Surgery.

Availability of data and materials
The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
Not applicable.

Consent for publication
Not applicable.

Competing interests
None declared.

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Received: 16 November 2022 Accepted: 24 July 2023
Published online: 22 August 2023

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