Original Article

Surgical outcomes of 500 robot-assisted minimally invasive esophagectomies for esophageal carcinoma

Yun-Ho Jeon[1#]^, Jae Kwang Yun[2#]^, Yong Ho Jeong[3], Chung-Sik Gong[4], Yoon Se Lee[5], Yong-Hee Kim[2]^

[1]Department of Thoracic and Cardiovascular Surgery, Daegu Catholic University School of Medicine, Daegu, Republic of Korea; [2]Division of Thoracic Surgery, Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [3]Division of Thoracic Surgery, Department of Thoracic and Cardiovascular Surgery, Hanyang University Seoul Hospital, Hanyang University College of Medicine, Seoul, Republic of Korea; [4]Division of Stomach Surgery, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; [5]Department of Otolaryngology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea

Contributions: (I) Conception and design: YH Jeon, JK Yun, YH Kim; (II) Administrative support: YH Jeon; (III) Provision of study materials or patients: YH Jeon, JK Yun, YH Kim; (IV) Collection and assembly of data: YH Jeon, JK Yun, YH Jeong; (V) Data analysis and interpretation: YH Jeon, JK Yun; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

[#]These authors contributed equally to this work.

Correspondence to: Yong-Hee Kim, MD, PhD. Division of Thoracic Surgery, Department of Thoracic and Cardiovascular Surgery, Asan Medical Center, University of Ulsan College of Medicine, 88 Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Republic of Korea. Email: kimyh67md@hotmail.com.

Background: In 2003, robot-assisted minimally invasive esophagectomy (RAMIE) was first reported to overcome the technical limitations of minimally invasive esophagectomy. RAMIE requires repeated modifications to set up the robotic system, and sufficient experience is required to gain technical proficiency. This study aimed to identify the learning periods and the outcomes of RAMIE for esophageal carcinoma.

Methods: We retrospectively reviewed 500 consecutive RAMIE cases for esophageal cancer from December 2008 to February 2021. The learning curve for RAMIE was identified using cumulative sum analysis.

Results: In a total of 500 RAMIE patients, the Ivor Lewis and McKeown operation were performed in 267 patients (53.4%) and 192 patients (38.4%), respectively. We classified learning periods into the learning phase (first 50 cases), the developing phase (51–150 case), and the stable phase (151–500 case). The rates of vocal cord palsy (42.0% *vs.* 28.4%) and anastomotic leakage (10.0% *vs.* 6.4%) were reduced after the learning phase. The mean total operative time (420 *vs.* 373 min), the mean length of stay (21.6 *vs.* 16.7 days), and the rate of anastomotic stricture (27.0% *vs.* 12.4%) were significantly reduced after reaching stable phase. In the stable phase, the proportion of the Ivor Lewis operation (26.0% *vs.* 67.1%), neoadjuvant chemoradiation therapy (14.0% *vs.* 25.7%), and bilateral cervical node dissection cases (12.0% *vs.* 22.0%) were significantly increased.

Conclusions: Fifty procedures might be needed to achieve early proficiency, and extensive experience of more than 150 procedures is needed for quality stabilization.

Keywords: Esophageal cancer; robotic surgery; esophagectomy; learning curve

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^ ORCID: Yun-Ho Jeon, 0000-0002-5283-3261; Jae Kwang Yun, 0000-0001-5364-5548; Yong-Hee Kim, 0000-0003-2177-4876.

Introduction

Radical esophagectomy with lymphadenectomy is the main therapeutic modality for localized esophageal cancer. However, open esophagectomy (OE) with lymphadenectomy has considerably high rates of morbidity (26–41%) and mortality (4–10%) (1).

Recently, robot-assisted minimally invasive esophagectomy (RAMIE) has increasingly been applied to surgery for esophageal cancer (2). RAMIE provides convenience to the operator by enabling precise and meticulous dissection with a 10-time magnified three-dimensional field view and an ambidextrous articulated instrument. It also enables dissection of the entire mediastinum through a superior surgical view at the hiatus and thoracic inlet level in esophageal cancer surgery, which is helpful especially for upper mediastinal lymph node (LN) dissection involving the recurrent laryngeal nerve (RLN) (3). Additionally, it enables robot-sewn anastomosis within the thoracic cavity. However, intrathoracic robot-sewn anastomosis is a highly challenging procedure, and a multicenter study demonstrated a disappointing anastomotic leakage (AL) rate of 33% (4). Oncologic outcomes of RAMIE are comparable to outcomes of open surgical methods (5,6), with lower postoperative morbidity, better short-term quality of life and functional recovery, and lesser postoperative pain than with OE (6).

However, RAMIE requires sufficient experience to gain technical proficiency. Studies on the learning curve of RAMIE have shown that at least 20 to 80 procedures are required to achieve proficiency (7-9).

In this study, we aimed to identify the experience needed to reduce complications and become technically proficient in RAMIE through the learning curves. In addition, we described the surgical and oncologic outcomes after RAMIE based on an experience of 500 cases. We present this article in accordance with the STROBE reporting checklist (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-637/rc).

Highlight box

Key findings

- We evaluated 500 cases of robot-assisted minimally invasive esophagectomy (RAMIE) for esophageal carcinoma to identify the learning periods and the surgical outcomes.

What is known and what is new?

- Previous studies on the learning curve of RAMIE have shown that at least 20 to 80 procedures are required to achieve proficiency.
- In this study, approximately 50 procedures are required to achieve early proficiency, and extensive experience of more than 150 procedures is needed for quality stabilization.

What is the implication, and what should change now?

- Appropriate anastomosis according to the cancer location can reduce patient morbidity and mortality. Specifically for the Ivor-Lewis RAMIE, the damage caused by additional cervical incision was reduced, and the required conduit length was reduced, resulting in a decrease in tight conduit, which was thought to be related to better outcomes.

Methods

Patients

We retrospectively reviewed 503 consecutive patients with primary esophageal cancer who underwent the RAMIE procedure, performed by Kim YH for esophageal cancer, from December 2008 to February 2021. Patients with histology other than esophageal carcinoma (n=3) were excluded. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of Asan Medical Center approved this study (IRB No. 2021-1812; approval date: December 24, 2021). The need for informed consent was waived owing to the retrospective nature of study and patient data anonymization.

The contraindications for RAMIE procedure were patients with expected severe lung adhesion, and with highly suspected direct adjacent structural invasion of tumors and metastatic LNs in preoperative imaging modalities. However, if re-evaluation of imaging tests performed 1 month after neoadjuvant chemoradiotherapy (nCRT) showed remarkable remission and clear boundaries between adjacent structures, we included them as candidates for RAMIE. Finally, we reviewed 500 patients who underwent RAMIE to identify the learning curves, the surgical and oncologic outcomes.

Surgical technique of RAMIE

RAMIE was initiated using the da Vinci S system in 2008. Since the introduction of the da Vinci Xi system, RAMIE has been mainly carried out using the da Vinci Xi surgical system (Intuitive Surgical, Inc., Sunnyvale, CA, USA).

The RAMIE procedure consists of thoracic esophagectomy by robotic system, abdominal, and with or without cervical procedure. During the abdominal procedure, conduit was formed using the stomach, jejunum, or colon. Gastric conduit formation using a minimally invasive technique was performed by an experienced gastric surgeon. However, during the learning phase, there were instances of conduit-related issues, leading to the temporary use of an open laparotomy approach by the thoracic surgeon for conduit formation. In the developing phase, a change in the conduit formation strategy was introduced. The thoracic surgeon provided instructions to the gastric surgeon to create a gastric conduit using the same strategy and perform laparoscopic or robotic surgery entirely starting from the 82nd case.

The sequential thoracic procedure was performed in the left semi-prone position. Three 8-mm ports were utilized for the robotic arms, while one 12-mm port was designated for the first assistant. Carbon dioxide (CO_2) gas insufflation into the thoracic cavity was carried out as a standard procedure, maintaining a CO_2 pressure of 6 mmHg. For intra-thoracic anastomosis, the camera port at the 5th intercostal space was extended by approximately 4 cm to allow for the insertion of a circular stapler into the thoracic cavity. The specimen was subsequently extracted through this port. Following partial transection of the esophagus at the highest level of the thoracic esophagus, a purse-string suture was performed using a robotic arm equipped with Maryland forceps and a needle holder. The anvil of the stapler was inserted into the proximal esophagus, and the purse-string suture was secured. The conduit in the abdomen was then pulled up into the thoracic cavity, and an esophago-gastric anastomosis was performed. Routinely, anastomosis of the conduit and proximal thoracic esophagus was performed at the level of the brachiocephalic artery. For anastomosis, the 25 mm sized circular stapler was routinely considered first, while manual suture anastomosis was considered for relatively short conduits. There is no specific definition for “relatively short” in terms of a precise length. When a thoracic surgeon pulls up the conduit to the anastomosis site and there is a lack of length and a tight sensation, it is described as “relatively short”. When the surgeon perceived the conduit to be “relatively short”, we documented this in the surgical records. Fuchs *et al.* also showed that intra-thoracic esophagogastrostomy is possible by extending the incision of the previously used port without rib cutting (10). Intra-thoracic anastomosis was performed if the tumor was located below the carina. Otherwise, the anastomosis was performed at the cervical esophagus or above. The description of the anastomosis site can be found in Table S1. Bilateral cervical node dissection (CND) was performed by a head and neck surgeon. The indications of CND are as follows; advanced T-stage upper thoracic esophageal cancer, cervical esophageal cancer, or a suspected/confirmed cervical/highest mediastinal LN metastases. The detailed technique of RAMIE in our center has been previously reported (3).

Postoperative management

Sips of water were commenced from postoperative day 3, and if there were no significant events during the surgery, the resection margin of the anastomosis exhibited a complete donut shape, there are no signs of aspiration or leakage, and there is no sudden high fever, then the diet was advanced on the next day. Esophagography is a crucial examination for detecting postoperative anastomotic leakage. However, there have been instances where esophagography could not be conducted on time due to scheduling constraints, leading to delayed initiation of oral intake or potential complications such as aspiration pneumonia caused by the contrast medium. Esophagography to evaluate anastomosis site leakage and conduit was only performed on patients with suspected leakage because in patients with no intraoperative event, the sensitivity to detect AL may be low (5).

If symptoms of hoarseness were observed in the patient and vocal cord palsy (VCP) was suspected, a vocal cord examination was performed by head and neck specialist. In the case of unilateral VCP, hyaluronic acid (HA) injection was recommended regardless of whether the patients’ aspirated or not, to reduce respiratory complications following surgery and to reduce the anxiety of hoarseness. In the case of bilateral VCP, if the airway was well preserved, the patient was carefully observed, and the diet was proceeded with caution; otherwise, tracheostomy was performed.

Postoperative complications and outcome assessment

Most complications were evaluated based on the joint definitions of the Society of Thoracic Surgeons and the European Society of Thoracic Surgeons (11). The complications of AL were evaluated according to the Esophageal Complication Consensus Group guidelines (ECCG) (12). Minor leak of anastomotic leakage that does not require surgical therapy corresponds to anastomotic leak type I and type II of ECCG, and major leak that requires surgical therapy corresponds to type III of ECCG (12).

Table 1 Patient characteristics

Variables	Value, n=500
Age (years)	63.3±8.2
Male	447 (89.4)
Weight (kg)	65.8±10.5
Height (cm)	165.7±6.8
BMI (kg/m^2)	23.9±3.2
Pulmonary function test	
FEV1 (%)	88.7±14.6
DLCO (%)	83.7±18.6
Comorbidity	
Diabetes mellitus	99 (19.8)
Hypertension	206 (41.2)
Arrhythmia	20 (4.0)
Coronary artery disease	45 (9.0)
Cerebrovascular accident history	23 (4.6)
Pulmonary Tb history	21 (4.2)
Hepatic disease	34 (5.4)
Chronic renal failure	7 (1.4)
Gastrointestinal disease	29 (5.8)
Previous malignancy	50 (10.0)
Coincidental malignancy	30 (6.0)
Smoking status	
Never smoker	125 (25.0)
Ex-smoker/current smoker	308 (61.6)/67 (13.4)
Pack-year	30.1±19.6
Histology	
Squamous cell carcinoma	486 (97.2)
Others	14 (2.8)
Neoadjuvant CCRT	113 (22.6)
Tumor location	
Cervical esophagus	17 (3.4)
Upper thoracic esophagus	65 (13.0)
Mid-thoracic esophagus	169 (33.8)
Lower thoracic esophagus	249 (49.8)
Clinical stage	
T stage (cT1/cT2/cT3)	335 (67.0)/100 (20.0)/65 (13.0)
N stage (cN0/cN+)	375 (75.0)/125 (25.0)

Values were presented as number (%), or means ± deviation. BMI, body mass index; FEV1, forced expiratory volume at 1 second; DLCO, diffusion capacity of carbon monoxide; Tb, tuberculosis; CCRT, concurrent chemoradiation therapy.

Statistical analysis

Statistical analysis was performed using SPSS, version 18.0 for Windows (IBM Corp, Armonk, NY, USA). All P values <0.05 were considered statistically significant. The χ^2 test or Fisher's exact test were used to compare categorical variables. The Student's *t*-test was used for comparisons of continuous variables between two groups. To compare continuous variables among groups, the one-way analysis of variance was used.

To evaluate oncologic outcome, overall survival and disease-free survival of RAMIE were obtained using Kaplan-Meier analysis. The definition of disease-free survival is the length of time a patient survives without signs or symptoms of cancer after operation. A cumulative sum (CUSUM) curve was created to calculate the learning curve (13). The significant change point on this curve was the highest or lowest peak. A positive slope indicates that the value corresponding to this point is greater than the average, and a negative slope corresponds to a value lower than the average.

Results

Patient characteristics

Between December 2008 and February 2021, 500 consecutive patients who underwent RAMIE were evaluated. The baseline patient characteristics are presented in *Table 1*. The mean age was 63.3±8.2 years. Most of the patients were male (n=447, 89.4%). Most histology types were squamous cell carcinoma (n=486, 97.2%). There were 17 (3.4%), 65 (13.0%), 169 (33.8%), and 249 (49.8%) patients with cervical, upper thoracic, mid thoracic, and lower thoracic esophageal tumors, respectively. The nCRT was administered to 113 patients (22.6%). In the clinical stage, cT1 was the most common with 335 cases (67.0%), and clinical N positive was 125 cases (25.0%).

Operative and pathologic outcomes

Operative and pathologic outcomes are summarized in *Table 2*. The mean total operation time and thoracic phase time were 391±81 and 146±43 minutes, respectively. The sites of anastomosis varied the thoracic esophagus, and the cervical esophagus, accounting for 282 cases (56.4%), and 202 cases (41.4%), respectively. Regarding conduits, the stomach accounted for the most with 479 cases (95.8%). Regarding the anastomosis method, circular end-to-end

Table 2 Operative and pathologic outcomes

Variables	Value, n=500
Total operation time (min)	391±81
Thoracic procedure time (min)	146±43
Length of stay (days)	
Mean ± SD	18.5±17.8
Median [lower quartile, upper quartile]	14 [12–18]
Anastomosis	
Thoracic esophagus	282 (56.4)
Cervical esophagus	202 (41.4)
Pharynx/oropharynx	12 (2.4)/4 (0.8)
Conduit	
Stomach	479 (95.8)
Colon/jejunum	19 (3.8)/2 (0.4)
Conduit length	
Relatively short	46 (9.2)
Anastomosis method	
Circular stapler/manual	467 (93.4)/33 (6.6)
Circular stapler 25 mm/28 mm/29 mm	456 (97.6)/4 (0.9)/7 (1.5)
Abdominal approach	
Laparoscopic	345 (69.0)
Robotic	96 (19.2)
Laparotomy	59 (11.8)
LN dissection	
2 field/3 field	411 (82.2)/89 (17.8)
RLN LN dissection	
Unilaterally/bilaterally	213 (42.6)/245 (49.0)
None	42 (8.4)
Number of harvested LNs	34.4±13.6
Pathologic LN metastasis	128 (25.6)
R0 resection	483 (96.6)
Pathologic stage	
Stage 0	3 (0.6)
Stage I	332 (66.4)
Stage II	95 (19.0)
Stage III	67 (13.4)
Stage IV	3 (0.6)
Complete remission	54 (47.8)
Adjuvant therapy	108 (21.6)
Recurrence	104 (20.8)
Thoracotomy conversion	5 (1.0)

Values were presented as numbers (%), or means ± standard deviation. SD, standard deviation; LN, lymph node; RLN, recurrent laryngeal nerve.

anastomosis (EEA) was used in 467 cases (93.4%). Three-field LN dissection was done in 89 cases (17.8%). The mean number of harvested LNs was 34.4±13.6.

Postoperative complications

The postoperative morbidity and mortality are presented in *Table 3*. The median length of hospital stay was 14 [12–18] days. VCP occurred in 148 (29.6%) cases. Most of the VCPs were transient (89.1%). The rates of AL and anastomotic stricture (AS) were 6.6% and 17.6%, respectively.

Variables related to AL and AS are shown in Tables S2,S3, respectively. The rate of AL was lower in the cervical esophagus (4.0%), than in the thoracic esophagus (7.8%). Regarding the conduit, the stomach showed the lowest leakage rate (5.6%), and nCRT increased the leakage rate (12.4%). When intra-thoracic anastomosis was performed, the incidence rate was the lowest (9.9%), and the short conduit length increased the incidence of stricture (34.8%). The rate of stricture was low in patients receiving nCRT (7.1%). VCP was associated with anastomosis site, and CND (Table S4). The incidence of VCP was lower in intra-thoracic anastomosis (23.4%) than in other sites. CND increased the incidence of VCP (26.4%). Re-operation within 90 days was performed in 38 (7.6%) patients. The most common re-operation was thoracic duct ligation (n=10) (Table S5).

Assessment of learning periods

The CUSUM curve for variables showed each significant change point, which is shown in *Table 4* and *Figures 1,2*. The change points for the number of harvested LNs, and the rate of VCP and AL were about 50^{th} case. After 150 cases, significant improvements in thoracic and total procedure time, reoperation within 90 days, length of stay, and AS were observed. Through these change points, the learning period could be classified into the learning, the developing, and the stable phase.

Surgical outcomes according to learning periods

With increasing proficiency, the total operation time, thoracic procedure time, and length of stay were significantly reduced, and the incidence of intraoperative transfusion, re-operation within 90 days, and AS decreased. As experience accumulated, the number of patients receiving nCRT and CND increased gradually. As the phase changed, the main operation type changed from the McKeown operation to the Ivor Lewis operation (*Table 5*).

Table 3 Postoperative morbidity and mortality

Variables	Value, n=500
Intraoperative transfusion	9 (1.8)
Vocal cord palsy	148 (29.6)
Unilateral/bilateral	135 (91.2)/13 (8.8)
Transient/permanent	132 (89.1)/16 (10.9)
Hyaluronic acid injection	98 (66.2)
Overall morbidity	208 (41.6)
Atrial fibrillation	22 (4.4)
Chylothorax	19 (3.8)
Empyema	5 (1.0)
Respiratory complication	43 (8.6)
Anastomotic leakage	33 (6.6)
Minor leaks (Type I/II)	3 (0.6)/21 (4.2)
Major leaks (Type III)	10 (2.0)
Conduit necrosis	5 (1.0)
Anastomotic stricture	88 (17.6)
Re-operation within 90days	38 (7.6)
30-day mortality	1 (0.2)
90-day mortality	5 (1.0)

Values were presented as numbers (%).

Oncologic outcomes

Median follow-up period was 35 months (range, 17–57 months). The 5-year overall survival rate was 70.6%, and the 5-year disease-free survival rate was 70.6% (Figure S1).

Discussion

In the current study, we described the surgical and oncologic outcomes of 500 cases of RAMIE. The learning period for RAMIE was divided into 3 phases according to CUSUM analysis. As the most important factors for beginners, improvement of VCP, AL and an increase in the number of harvested LNs were evident at the beginning of 50 cases. After experience was sufficiently accumulated, change points of operation time, reoperation within 90 days, length of stay, and AS appeared after 150 cases.

Previously, there have been excellent studies on the learning curve and surgical outcomes of RAMIE. Sarkaria *et al.* demonstrated tips that were useful during surgery and management of critical complications from 100 cases of totally minimally invasive RAMIE (14). Han *et al.* analyzed the learning curve in 124 cases of Ivor Lewis RAMIE and it demonstrated that 51 cases were required to gain technical proficiency (15). Yang *et al.* analyzed the experience of 400 McKeown RAMIE and demonstrated that the 40 cases comprised the learning phase and the quality outcomes improved after 80 cases (9). To our knowledge, our 500 cases of RAMIE performed by a single surgeon constitute one of the largest experiences. Our study showed changes in the type of operation performed by a surgeon as he became proficient in RAMIE and the flow of changes in surgical outcomes.

Table 4 Comparison of outcomes according to change point

Variables	Change points†	Comparison by change point	P value
Harvested lymph nodes (number)	43rd case	27.5 *vs.* 35.0	0.001
Vocal cord palsy rate	50th case	42.0% *vs.* 28.4%	0.047
Anastomotic leakage rate	50th case	10.0% *vs.* 6.4%	0.34
Thoracic procedure time (min)	151st case	169 *vs.* 135	<0.001
The rate of reoperation within 90 days	176th case	13.1% *vs.* 4.6%	0.001
Length of stay (days)	183rd case	21.6 *vs.* 16.7	0.003
Anastomotic stricture rate	185th case	27.0% *vs.* 12.4%	0.001
Total operation time (min)	193rd case	420 *vs.* 373	<0.001

†, change points were identified in cumulative sum curves.

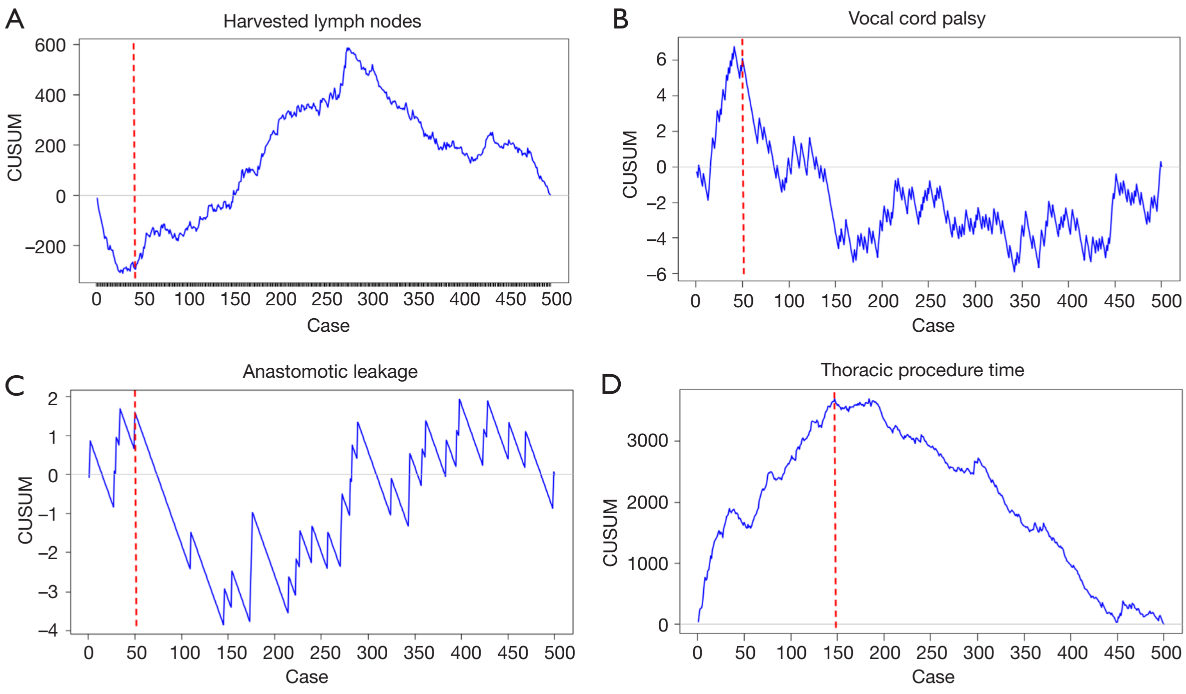

Figure 1 Cumulative sum analysis curves for RAMIE. (A) Harvested lymph nodes, (B) vocal cord palsy, (C) anastomotic leakage, and (D) thoracic procedure time. Approximately 50 procedures are required to achieve early proficiency. CUSUM, cumulative sum analysis; RAMIE, robot-assisted minimally invasive esophagectomy.

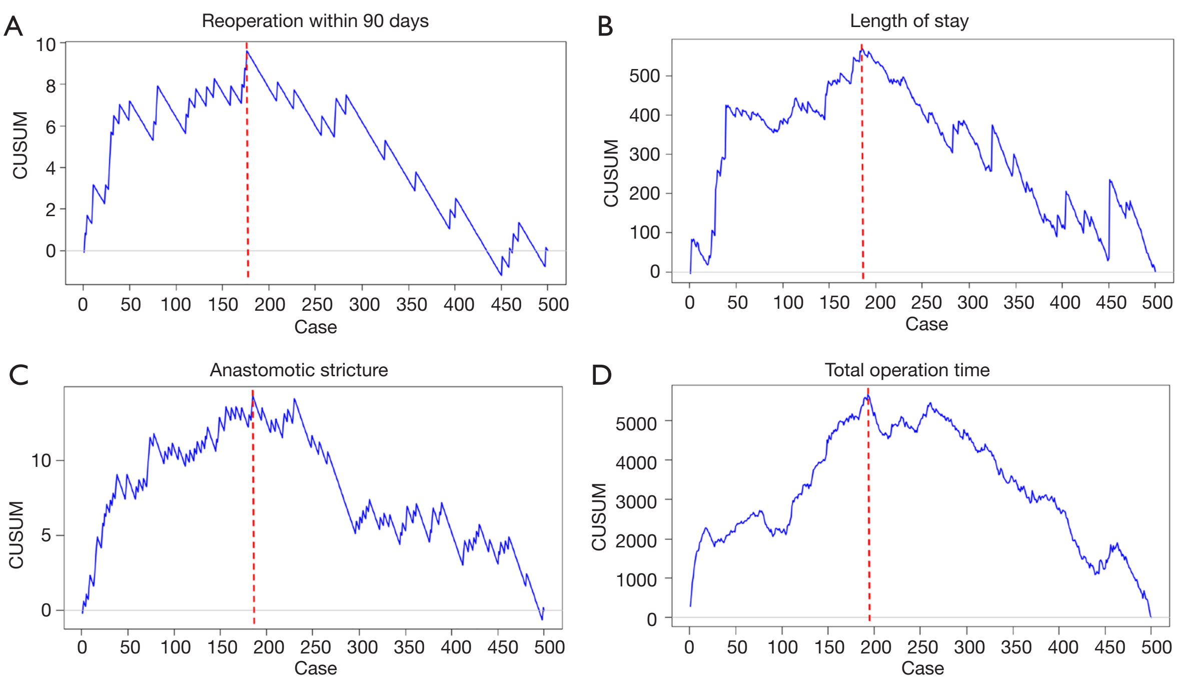

Figure 2 Cumulative sum analysis curves for RAMIE. (A) Reoperation within 90 days, (B) length of stay, (C) anastomotic stricture, and (D) total operation time. Extensive experience of more than 150 procedures is needed for quality stabilization. CUSUM, cumulative sum analysis; RAMIE, robot-assisted minimally invasive esophagectomy.

Table 5 Surgical outcomes according to learning periods

Variables	Learning phase (Case 1–50)	Developing phase (Case 51–150)	Stable phase (Case 151–500)	P value
Age (years)	63.6 (±7.6)	63.9 (±8.5)	63.3 (±8.2)	0.76
Harvested lymph nodes	29.3 (±13.1)	36.6 (±12.9)	34.5 (±13.6)	0.007
Total operation time	438 (±97.8)	412 (±74.2)	378 (±77.2)	<0.001
Thoracic procedure time	179 (±66)	165 (±43)	135 (±35)	<0.001
Length of stay	26.8 (±30.2)	19.1 (±9.8)	17.1 (±16.8)	0.001
Neoadjuvant therapy	9 (18.0)	14 (14.0)	90 (25.7)	0.035
Cervical node dissection	0 (0.0)	12 (12.0)	77 (22.0)	<0.001
Intraoperative transfusion	4 (8.0)	2 (1.6)	2 (0.6)	0.002
Respiratory complication	6 (12.0)	9 (9.0)	28 (8.0)	0.63
30-day mortality	1 (2.0)	0 (0.0)	0 (0.0)	0.10
90-day mortality	2 (4.0)	0 (0.0)	3 (0.9)	0.098
Re-operation within 90days	11 (22.0)	8 (8.0)	19 (5.4)	<0.001
Vocal cord palsy	21 (42.0)	20 (20.0)	107 (30.6)	0.016
Transient	17 (80.9)	18 (90.0)	97 (90.7)	
Permanent	4 (19.1)	2 (10.0)	10 (9.3)	
Anastomotic stricture	20 (40.0)	22 (22.0)	46 (13.1)	<0.001
Anastomotic leakage	5 (10.0)	2 (2.0)	26 (7.4)	0.086
Pathologic stage				0.077
0–I	37 (74.0)	62 (62.0)	237 (67.7)	
II	12 (24.0)	19 (19.0)	64 (18.3)	
III	1 (2.0)	18 (18.0)	47 (13.4)	
IV	0 (0.0)	1 (1.0)	2 (0.6)	
Operation type				<0.001
Ivor Lewis	6 (12.0)	26 (26.0)	235 (67.1)	
McKeown	43 (86.0)	71 (71.0)	78 (22.3)	
Colon interposition	1 (2.0)	1 (1.0)	17 (4.9)	
Oro-gastrostomy	0 (0.0)	1 (1.0)	2 (0.6)	
Pharyngo-gastrostomy	0 (0.0)	1 (0.0)	11 (3.1)	
Esophago-jejunostomy	0 (0.0)	0 (0.0)	1 (0.3)	
Trans-hiatal esophagectomy	0 (0.0)	0 (0.0)	6 (1.7)	

Values were presented as numbers (%), or means (± standard deviation).

There were three notable changes in the stable phase. First, the increase in the Ivor Lewis operation in the stable phase indicates that it was possible to apply an appropriate surgical method according to the location of esophageal cancer. It means that unnecessary incisions and damage to the patient can be reduced at the cervical level, thereby reducing complications (16,17). The VCP rate was 23.4% for intra-thoracic anastomosis and 37.8% for anastomosis at cervical level or above, with the intra-thoracic anastomosis rate being significantly lower (P=0.001). Compared to previous studies, the rate of vocal cord palsy in this study is higher at 29.6%. This elevated rate can be attributed to the extensive en bloc lymph node dissection in the superior mediastinum. The improved accessibility afforded by RAMIE enables surgeons to reach deeper regions of the thoracic cavity, which would not have been possible with conventional surgery. As a result, we performed nearly 35 lymph node harvesting procedures during RAMIE, a significantly higher number compared to other studies where the average ranged from 18 to 30 lymph nodes (18,19). Similar findings have been reported in other studies, where vocal cord palsy occurred in 26% and 29% of cases after 44 and 38 lymph node harvesting procedures, respectively (20,21). Compared to anastomosis at cervical or above level group (20.4±20.0 d), the intra-thoracic anastomosis group (16.9±15.5 d) had a significantly shorter mean length of hospital stay (P=0.029). In this study, as the rate of the Ivor Lewis operation increased, conduit related complications decreased. Intra-thoracic anastomosis has a benefit in terms of the length of the conduit, which can reduce the incidence of stricture. In contrast to general expectations, our study revealed a higher rate of intrathoracic AL compared to cervical anastomosis (7.8% *vs.* 4.0%). Performing intrathoracic anastomosis in the context of RAMIE can be a challenging procedure. During the learning phase, the implementation rate of RAMIE Ivor-Lewis was low due to a lack of proficiency, resulting in a higher incidence of AL. However, the cervical procedure of RAMIE McKeown, which was similar to open McKeown, was performed with proficiency, leading to a lower incidence of AL. As the proficiency in RAMIE increased, we observed a gradual increase in the number of intrathoracic anastomoses and a decrease in the incidence of intrathoracic AL. This finding was evident in the stable phase, where despite a rise in the proportion of Ivor-Lewis RAMIE (67%), there was a decrease in the overall occurrence of AL. Nevertheless, we consider the 7.8% rate of intrathoracic AL to be an acceptable outcome (Table S6).

Second, the number of patients who received nCRT for locally advanced esophageal cancer increased in the stable phase. Due to the dense adhesion between the esophagus and surrounding tissues induced by nCRT (22), it might be difficult to find the surgical plane, especially between the trachea, left main bronchus and esophagus. As the surgeon's experience grew, the number of challenging cases with RAMIE also increased. In patients with suspected T4 invasion, if there was a therapeutic response after nCRT and the tumor was deemed resectable, OE was initially recommended to address the injury to the surrounding structures during dissection when the experience with RAMIE was insufficient. As experience with RAMIE increased, the ability to perform meticulous and precise dissection improved, thanks to the magnified surgical view and articulated surgical arm, which minimized damage to surrounding structures. This can be attributed to the ease of accessing and the enhanced accuracy in performing mediastinal lymph node harvest during RAMIE. Weindelmayer *et al.* demonstrated that RAMIE allows for a more accurate lymphadenectomy, resulting in a higher number of thoracic lymph nodes compared to OE, without an increase in other complications (23). Therefore, based on these experiences, it can be concluded that RAMIE is a feasible approach for locally advanced esophageal cancer.

Third, the number of patients receiving CND in the stable phase increased, which was associated with the increased number of patients with locally advanced esophageal cancer described above. This is the reason why the rate of VCP increased in the stable phase. However, when it comes to long-term outcome, the permanent VCP rate decreased in the stable phase, suggesting that most nerve injuries were transient palsy due to traction or thermal injury (*Table 5*). However, in terms of long-term outcomes, the rate of permanent VCP decreased during the stable phase, suggesting that the majority of nerve injuries were transient and likely caused by traction or thermal injury (*Table 5*). The relatively high rate of vocal cord palsy in our technique highlights an area that requires improvement, and we are currently making efforts to perform a more meticulous recurrent laryngeal nerve lymph node dissection.

The rate of AL and the details of conduit formation should be taken note of. The rate of AL decreased from 10% in the learning phase to 2% in the developing phase, which might be due to several procedures applied during conduit formation. Gentle manipulation was performed to preserve the serosa of the gastric conduit, and at least 2 cm of omental fat tissue was left in the great curvature (up to the fundus level) to preserve vascular flow. However, the AL rate increased to 7.4% again in the stable phase. We carried out additional analysis to identify the risk factors for AL (see Table S2). As a result, the nCRT was significantly associated with an increase in the incidence rate of AL, which is also reported in several studies (24,25), The increased rate of AL in the stable phase might be attributed to the increase in patients with nCRT. Unlike previous studies (25,26), the rate of AL was higher with intrathoracic anastomosis than with cervical anastomosis. We believe this is related to the high proportion of intrathoracic anastomosis among patients who received nCRT (64.6%, 73/113).

In our study, the rate of AS gradually decreased (*Table 5*). The incidence of AS was significantly lower when the site of anastomosis was the intra-thoracic esophagus, when the conduit length was not short, and when nCRT was performed (Table S3). Ischemia is an important risk factor for AS (27). If the conduit is short, tension occurs in the conduit at the anastomosis site, which leads to a decrease in the vascular flow. Based on these findings, the decrease in stricture occurrence in the stable phase seems to be influenced not only by the improvement in surgical technique but also by the proportion of the Ivor Lewis operation increases. Most patients who received nCRT underwent intrathoracic anastomosis (64.6%, 73/113), which is thought to be the reason for association of nCRT with lower incidence of AS.

This study had notable limitations. First, selection bias is inherent in a retrospective study conducted at a single institution. Second, RAMIE was performed by a single thoracic surgeon. Therefore, it may be challenging to generalize the learning curve and surgical outcomes of this study to other settings. Third, the clinical outcomes in this study were obtained through a well-established collaborative system involving highly experienced surgeons in their respective fields. Therefore, we believe that the impact of collaboration on the learning curve in our study is likely to be minimal. However, it may be challenging to generalize our learning curves to surgeons who do not have access to a similar collaborative system. Fourth, the patient population in our study has different characteristics compared to esophageal cancer patients in the Western world. Therefore, it may be challenging to generalize our research findings. Fifth, we do not have data on the learning curve or surgical outcomes specifically related to robotic-sewn anastomosis. However, a recent study by Huscher *et al.* demonstrated excellent results with an AL rate of 10% in 40 patients who underwent intrathoracic robotic-sewn anastomosis (28). This indicates that as proficiency with RAMIE increases, complete robotic Ivor Lewis esophagectomy becomes feasible. Last, it should be noted that the patient population in our study consisted predominantly of early-stage patients who did not receive nCRT. It is important to recognize that as the proportion of patients receiving nCRT increases, the learning curve may be longer, and the surgical outcomes may not be as favorable.

Conclusions

Approximately 50 procedures are required to achieve early proficiency, and extensive experience of more than 150 procedures is needed for quality stabilization. Appropriate anastomosis according to the cancer location can reduce patient morbidity and mortality. Specifically for the Ivor-Lewis operation, the damage caused by additional cervical incision was reduced, and the required conduit length was reduced, resulting in a decrease in tight conduit, which was thought to be related to better outcomes. For surgeons beyond the learning curve, RAMIE could be a safe and feasible option for patients with locally advanced-stage esophageal cancer.

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Footnote

Reporting Checklist: The authors have completed the STROBE reporting checklist. Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-637/rc

Data Sharing Statement: Available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-637/dss

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://jtd.amegroups.com/article/view/10.21037/jtd-23-637/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The Institutional Review Board of Asan Medical Center approved this study (IRB No. 2021-1812; approval date: December 24, 2021). The need for informed consent was waived owing to the retrospective nature of study and patient data anonymization.

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Supplementary

Table S1 The description of the anastomosis site

Anastomosis site	Description
Oropharynx	The oropharynx is behind the oral cavity, below the soft palate and above the epiglottis. Anastomosis in the oropharynx is performed at the tongue base level, resulting in the removal of the tracheal inlet, which necessitates the need for a permanent tracheostomy
Pharynx	It refers to the hypopharynx or laryngopharynx. The hypopharynx is located behind the larynx and extends to the esophagus. Anastomosis in the hypopharynx is performed at the commencement site of the esophagus, beyond the epiglottis and tracheal inlet. This surgical procedure does not require a permanent tracheostomy; however, it necessitates a more extensive dissection for adequate exposure of the target area
Cervical esophagus	Anastomosis in the cervical esophagus involves pulling out the esophagus through a standard cervical incision and performing an anastomosis without the need for deep dissection towards the proximal portion of the esophagus
Thoracic esophagus	It refers to the esophagus located within the thoracic cavity

Table S2 Anastomotic leakage rate according to anastomosis site, conduit, conduit length, neoadjuvant therapy, abdominal approach, and pathologic stage

Variables	Leakage (–)	Leakage (+)	%	P value
Anastomosis site				0.042
Thoracic esophagus	260	22	7.8	
Cervical esophagus	194	8	4.0	
Pharynx	10	2	16.7	
Oropharynx	3	1	25.0	
Conduit				<0.001
Stomach	452	27	5.6	
Colon	13	6	31.6	
Jejunum	2	0	0.0	
Conduit length				0.55
Not short	425	29	6.4	
Short	42	4	8.7	
Neoadjuvant therapy				0.007
(–)	368	19	4.9	
(+)	113	14	12.4	
Abdominal approach				0.26
Laparoscopic	325	20	5.8	
Robotic	90	6	6.3	
Laparotomy	52	7	11.9	
Pathologic stage				0.63
0–I	312	24	7.1	
II	89	6	6.3	
III–IV	92	4	4.3	

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Table S3 Anastomotic stricture rate according to anastomosis site, conduit, conduit length, neoadjuvant therapy, abdominal approach, and pathologic stage

Variables	Stricture (–)	Stricture (+)	%	P value
Anastomosis site				<0.001
Thoracic esophagus	254	28	9.9	
Cervical esophagus	152	50	24.8	
Pharynx	5	7	58.3	
Oropharynx	1	3	75.0	
Conduit				0.69
Stomach	393	86	18	
Colon	17	2	10.5	
Jejunum	2	0	0.0	
Conduit length				0.001
Not short	382	72	15.9	
Short	30	16	34.8	
Neoadjuvant therapy				0.001
(–)	307	80	20.7	
(+)	105	8	7.1	
Abdominal approach				0.98
Laparoscopic	285	60	17.4	
Robotic	79	17	17.7	
Laparotomy	48	11	18.6	
Pathologic stage				0.65
0–I	279	57	17.0	
II	79	16	16.7	
III–IV	51	15	21.7	

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Table S4 Vocal cord palsy rate according to anastomosis site, conduit, cervical node dissection (CND), neoadjuvant therapy, recurrent laryngeal lymph node (RLN LN) dissection and pathologic stage

Variables	VCP (–)	VCP (+)	%	P value
Anastomosis site				<0.001
Thoracic esophagus	216	66	23.4	
Cervical esophagus	129	73	36.1	
Pharynx	4	8	66.7	
Oropharynx	3	1	25.0	
Conduit				0.57
Stomach	338	141	29.4	
Colon	12	7	36.8	
Jejunum	2	0	0.0	
CND				0.001
(–)	302	109	14.2	
(+)	50	39	26.4	
Neoadjuvant therapy				0.41
(–)	276	111	28.7	
(+)	76	37	32.7	
Harvested RLN LN				0.22
None	30	12	28.6	
Unilateral	158	55	25.8	
Bilateral	163	81	33.2	
Pathologic stage				0.74
0–I	240	96	28.6	
II	64	31	32.6	
III–IV	48	21	30.4	

VCP, vocal cord palsy; CND, cervical node dissection; RLN, recurrent laryngeal nerve; LN, lymph node.

Table S5 Re-operation within 90 days according to learning periods

Re-operation within 90 days	Learning phase (Case 1–50)	Developing phase (Case 51–150)	Stable phase (Case 151–500)
Thoracic duct ligation	2 (4.0)	6 (6.0)	2 (0.6)
Primary closure of leakage or fistula	4 (8.0)	0 (0.0)	5 (1.4)
Neck wound debridement and revision	2 (4.0)	1 (1.0)	5 (1.4)
Conduit take-down	4 (8.0)	0 (0.0)	2 (0.6)
Empyemectomy	0 (0.0)	0 (0.0)	5 (1.4)
Bleeding control	2 (4.0)	1 (1.0)	0 (0.0)
Diaphragmatic hernia repair	1 (2.0)	0 (0.0)	1 (0.3)
Bullectomy due to pneumothorax	0 (0.0)	0 (0.0)	2 (0.6)

Values were presented as numbers (%).

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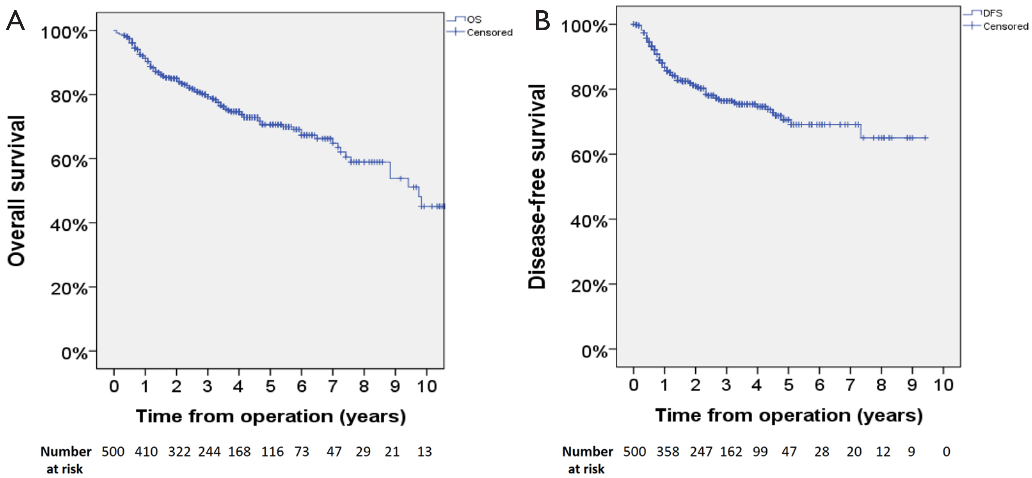

Figure S1 Kaplan-Meier curves for overall survival and disease-free survival for robot-assisted minimally invasive esophagectomy. The rate of 5-year overall survival and 5-year disease-free survival were 70.6% and 70.2%, respectively.

Table S6 Anastomotic leakage rates for intrathoracic and cervical anastomosis according to the learning periods

Anastomosis site	Learning period	Anastomotic leakage event/total
Intrathoracic anastomosis	Learning phase	3/6 (50.0%)
	Developing phase	2/25 (8.0%)
	Stable phase	17/251 (6.8%)
	Total	22/282 (7.8%)
Cervical anastomosis	Learning phase	2/44 (4.5%)
	Developing phase	0/73 (0.0%)
	Stable phase	6/85 (7.1%)
	Total	8/202 (4.0%)

Values were presented as numbers (%).

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