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# Will robot-assisted minimally invasive esophagectomy improve patient outcomes compared to conventional minimally invasive esophagectomy?

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## Abstract

**Aim:** To determine if introducing a standardized minimally invasive esophagectomy (MIE) to robot-assisted MIE (RAMIE) improves the short-term patient outcomes.

**Methods:** A total of 292 patients with esophageal cancer underwent thoracic esophagectomy [MIE ($n$ = 208); RAMIE ($n$ = 84)] at Aichi Cancer Center Hospital between January 2019 and August 2022. The cumulative sum (CUSUM) method was used to analyze the learning curve for RAMIE. The MIE and RAMIE surgical and postoperative outcomes were also analyzed retrospectively. Propensity score matching was used to compensate for the selection bias.

**Results:** The CUSUM plot of the console time reached a plateau in the 29th case and began to decrease in the 43rd case. Therefore, we defined phase I (introductory phase) up to the 28th case, phase II from the 29th - 42nd case, and phase III from the 43rd case onward. The median thoracic operative time was significantly longer in the RAMIE group than the MIE group in phase I ($P$ < 0.001); however, the median RAMIE console time was 227.5, 212, and 182 min in phases I-III, respectively, compared to a median MIE thoracic operative time of 232 min. The incidence of recurrent laryngeal nerve (RLN) palsy was significantly less after phase II for RAMIE (12.5%) compared to MIE (25%; $P$ = 0.04). The incidence of RLN palsy was also decreased in phases II and III for RAMIE after matching (13%; $P$ = 0.04).

**Conclusion:** Standardization of RAMIE may decrease the incidence of RLN palsy in patients compared to MIE.

**Keywords:** Robotic surgery, esophageal cancer, learning curve, recurrent laryngeal nerve palsy

## INTRODUCTION

Although preoperative chemotherapy or chemoradiotherapy (CRT) followed by esophagectomy with radical lymph node dissection has a major role in the standard treatment of resectable esophageal cancer, radical esophagectomy is a highly-invasive procedure with high morbidity and mortality rates[1-3]. Therefore, the global demand for minimally invasive esophageal cancer surgery has resulted in the rapid spread of thoracoscopic esophagectomy [minimally invasive esophagectomy (MIE)] as a minimally invasive surgical treatment in recent years[4]. Recently, robot-assisted MIE (RAMIE) has been introduced and rapidly standardized for esophageal cancer surgery at various institutions in Japan. RAMIE has the advantages of recognizing microanatomy based on 3D high-definition images, multi-joint function, and vibration filtering, thereby improving operability, especially for superior mediastinal dissection, and enabling precise surgical manipulation[5-7]. However, whether the introduction of RAMIE improves patient outcomes compared to conventional MIE is controversial.

The aim of this study was to evaluate the surgical outcomes of RAMIE compared to standardized MIE and to determine if RAMIE improves short-term patient outcomes.

## METHODS

### Patients

This was a single-center retrospective cohort study. Consecutive patients who underwent MIE or RAMIE for thoracic esophageal cancer at the Aichi Cancer Center Hospital between 2012 and 2022 were identified from an institutional prospectively maintained database of patients with thoracic esophageal cancer who underwent esophagectomy. The inclusion criterion for this study was thoracoscopic esophagectomy or robot-assisted thoracoscopic esophagectomy [full minimally invasive or hybrid (laparoscopic or open gastric mobilization) Mckeown procedure] with gastric tube reconstruction. The exclusion criteria were as follows: patients who underwent the Mckeown esophagectomy via a right thoracotomy or mediastinoscopic esophagectomy or those with a history of gastrectomy. MIE was introduced in our center in 2012, and MIE has been the standard procedure for resectable esophageal cancer since 2015, when the surgical technique was standardized. RAMIE was introduced in our center for resectable esophageal cancer in March 2019. MIE was performed by four skilled esophageal surgeons; RAMIE was performed by two skilled esophageal surgeons.

### RAMIE and MIE operative procedures

*MIE and RAMIE preparation*

The patients were intubated with a single-lumen spiral tube with bilateral lung ventilation in preparation for MIE and RAMIE. An artificial pneumothorax was established with 8 mmHg carbon dioxide gas using the Airseal® Intelligent Flow System (ConMed, Utica, NY, USA) to secure the visual field.

A pneumothorax was initiated during MIE by puncturing the Airseal® 12-mm port using the optical view technique at the extension of the 9th intercostal space (ICS) at the subscapular angle. This port was used as a camera port with a 3D high-definition flexible scope. Next, five ports were inserted as follows: a 12-mm port was inserted in the posterior axillary line of the 5th and 7th ICSs; a 5-mm port was inserted in the mid-axillary line of the 3rd and 8th ICSs; and a 5-mm port was inserted in the 6th ICS slightly midline of the subscapular angle [Figure 1A]. The energy devices used are mainly electrocautery or vessel sealing systems.

RAMIE was performed using a robotic system (da Vinci Xi System; Intuitive Surgical Inc., Sunnyvale, CA, USA). The da Vinci Xi System ports for arms 1, 2, 3, and 4 were used for the 9th ICS at the subscapularis line, the 7th ICS behind the axillary line, the 5th ICS behind the axillary line, and the 3rd ICS at the mid-axillary line, respectively. In addition, an assistant port was placed at the 6th ICS slightly anterior to the mid-axillary line. Because an artificial pneumothorax with an 8-mmHg carbon dioxide gas was used with the Airseal® Intelligent Flow System, we used an Airseal® 5-mm port on the dorsal aspect of the 8th ICS [Figure 1B]. During RAMIE, we primarily used a 30°-angle thoracoscope. The primary instruments used by the surgeon during RAMIE were sharp monopolar cutting scissors, which were used to dissect, coagulate, and cut tissue during the procedure.

The surgical procedures for MIE and RAMIE were similar, although the port placement and the surgical devices used were different [Supplementary Video 1A and B].

### Surgical procedure

*Middle and lower mediastinal dissection*

The right pulmonary ligament was dissected, the pericardial surface was exposed, the pericardial side of the tracheal bifurcation lymph node was dissected, and the membranous part of the left main bronchus was identified. The lower pulmonary branch of the right vagal nerve was sacrificed; only the right upper pulmonary branch was preserved. During dissection of the tracheal bifurcation, it is important to be aware of the tracheal sheath [Figure 2A]. The azygos arch was also divided using a linear stapler. Next, a descending peri-aortic dissection was performed. At this time, we were aware of the ligament interpleural de Morosow[8] [Figure 2B]. Patients with cT3 or more disease in our department were treated with combined resection of the thoracic duct, while patients with cT1-2 disease were treated with preservation of the thoracic duct. In cases involving thoracic duct preservation, the ligament interpleural de Morosow was preserved, but in cases involving combined resection of thoracic ducts, the ligament interpleural de Morosow was incised, and the thoracic duct and surrounding lymph nodes were excised [Figure 2B].

*Dissection of the right laryngeal nerve lymph nodes*

It is important to be aware of the tracheoesophageal sheath and right tracheoesophageal artery (TEA) during right recurrent laryngeal nerve (RLN) lymph node dissection[9]. The mediastinal pleura was incised up to the right subclavian artery (SCA) while preserving the epineurium of the right vagal nerve. The level of the vagal nerve epineurium, the tracheoesophageal sheath, and the right RLN were identified at the recurrent part [Figure 2C]. The upper thoracic esophagus was mobilized from the trachea and vertebral side, and the dissected right RLN lymph nodes were detached from the tracheal sheath at the right wall of the trachea. Next, three to five esophageal branches of the right RLN were dissected, and then the right RLN was dropped ventrally, continuing the dissection of the tissue to the pre-tracheal region as far ventrally as possible [Figure 2D]. The right RLN lymph nodes were dissected as far as possible into the neck. In some cases, it was possible to identify the pulsation of the right inferior thyroid artery and the lower pole of the thyroid gland [Figure 2E].

*Dissection of the left RLN nodes*

It is also important to be aware of the microanatomy of the tracheoesophageal sheath and left TEA, as well as the left RLN lymph node dissection[9] [Figure 2F]. After taping the upper thoracic esophagus, the trachea was expanded ventrally. From the left aspect of the trachea, the dissected tissues of the left RLN lymph

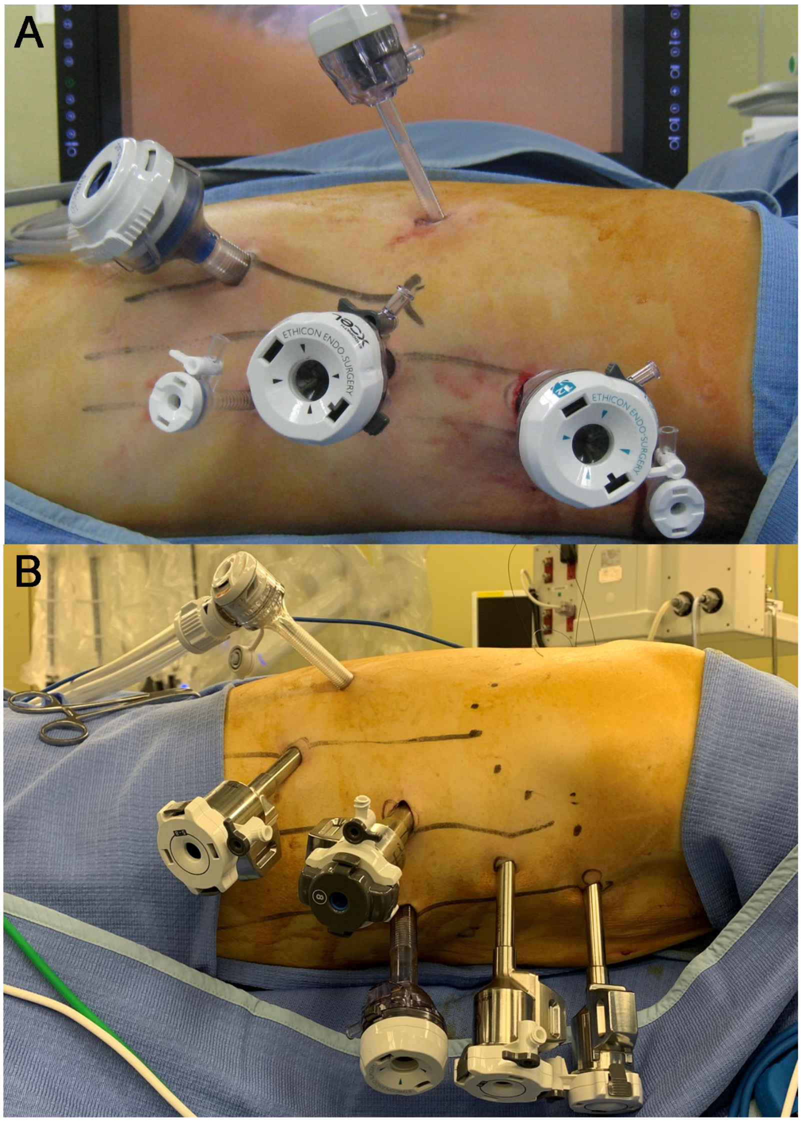


**Figure 1.** (A) Port placement of MIE. The Airseal® 12-mm port, used as the camera port, was inserted at the extension of the 9th intercostal space (ICS) at the subscapular angle. Next, five ports were inserted as follows: a 12-mm port was inserted in the posterior axillary line of the 5th and 7th ICSs; a 5-mm port was inserted in the mid-axillary line of the 3rd and 8th ICSs; and a 5-mm port was inserted in the 6th ICS slightly midline of the subscapular angle; (B) Port placement of RAMIE. The da Vinci Xi System ports for arms 1, 2, 3, and 4 were used for the 9th ICS at the subscapularis line, the 7th ICS behind the axillary line, the 5th ICS behind the axillary line, and the 3rd ICS at the mid-axillary line, respectively. In addition, an assistant port was placed at the 6th ICS slightly anterior to the mid-axillary line. An Airseal® 5-mm port was inserted on the dorsal aspect of the 8th ICS for use with the Airseal® Intelligent Flow System.

nodes were temporarily gathered on the esophageal side [Figure 2F]. Next, dissecting forceps were inserted into the anterior surface of the left RLN along the epineurium, and the tracheoesophageal arteriovenous branch and the tracheal branch of the left RLN were dissected. Thereafter, separating the lymphatic chain from the left RLN on the ventral side allowed subsequent manipulation without any traction to the left RLN. The ventrally-dropped lymphatic chain was explored to the pre-tracheal border and then clipped and dissected [Figure 2G]. Next, the esophageal branch of the left RLN was cut from the caudal-to-cephalic side, and the recurrent nerve was freed ventrally, then the tracheoesophageal sheath was incised, the esophageal branch of the TEA from the dorsal tracheoesophageal sheath to the esophagus was dissected, and the remaining dissected tissue was gathered to the esophagus and removed with the esophagus [Figure 2H].

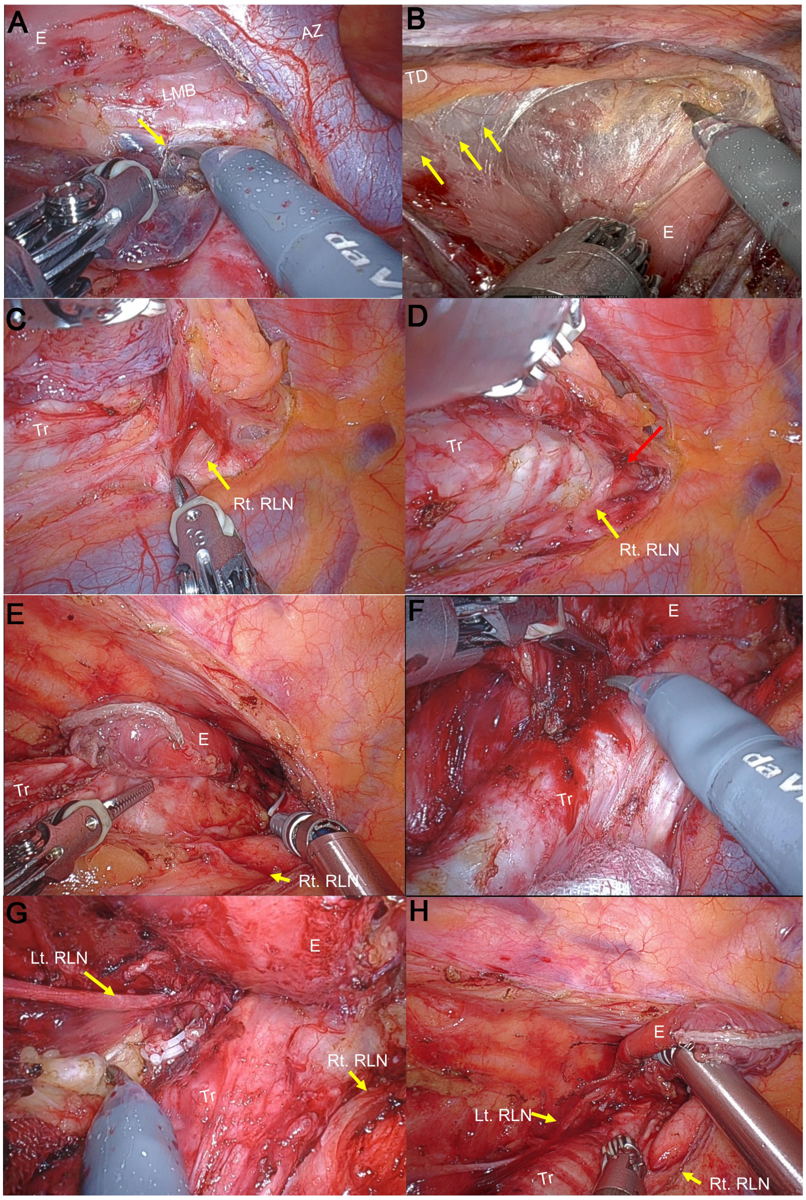


**Figure 2.** (A) Lymph node dissection of the tracheal bifurcation. The yellow arrow indicates the tracheal sheath; (B) Peri-aortic dissection of the descending aorta. Yellow arrows indicate the ligament interpleural de Morosow; (C) Lymph node dissection around the right recurrent laryngeal nerve. The right recurrent laryngeal nerve was identified at the recurrent part (yellow arrow); (D) Lymph node dissection around the right recurrent laryngeal nerve. The red arrow indicates the tracheoesophageal sheath; (E) Intraoperative view after lymph node dissection around the right recurrent laryngeal nerve; (F) Lymph node dissection around the left recurrent laryngeal nerve. The dissected tissues were temporarily gathered on the esophageal side along the inner surface of the tracheoesophageal sheath; (G) Lymph node dissection around the left recurrent laryngeal nerve. The ventrally-dropped lymphatic chain was explored to the pre-tracheal border, then clipped and dissected; (H) Intraoperative view after lymph node dissection around the left recurrent laryngeal nerve. AZ: Azygos arch; E: esophagus; Lt. RLN: left recurrent laryngeal nerve; Rt. RLN: right recurrent laryngeal nerve; TD: thoracic duct; Tr: trachea.

*Abdominal procedure and reconstruction*

Gastric mobilization and upper abdominal lymph node dissection were performed using a hand-assisted laparoscopic approach, with the exception of cases with massive metastases of abdominal lymph nodes or a history of a laparotomy. Bowel continuity was principally reconstructed using a gastric conduit via the retrosternal route. Cervical esophagogastric anastomosis was performed using the modified Collard technique[10] or a hand-sewn anastomosis. Both MIE and RAMIE abdominal manipulations were performed in the same way.

### Recording of clinical data and postoperative complications

Patient demographic data and clinical outcomes were compared between the MIE and RAMIE groups. Data included age, gender, body mass index (BMI), American Society of Anesthesiologists (ASA) score, Charlson comorbidity index (CCI), preoperative therapy (chemotherapy or CRT), tumor characteristics, operative procedure, operative time, console time, intraoperative blood loss, duration of hospital stay, incidence of postoperative complications, and short-term outcomes. The clinical staging of tumors was performed according to the 8th edition of the TNM classification[11]. Postoperative complications were classified according to the Clavien-Dindo classification[12].

### Propensity score matching

To control potential differences in patient characteristics between the two groups, we used propensity score matching to assemble comparable groups. After estimating the propensity score of patients in the RAMIE group, we matched each patient sequentially to a patient in the MIE group who had the closest propensity score using simple 1:1 nearest neighbor matching. We imposed a 0.20 caliper of the propensity score logit standard deviation. We included age, gender, cStage, CCI, ASA-physical status (ASA-PS), main tumor location, neoadjuvant therapy, dissection field, and abdominal procedure as covariates.

### Statistical analysis

The results are expressed as the median with a range for continuous variables. Differences between groups were analyzed using the Fisher exact test or the Mann-Whitney U test, as indicated. A $P$-value $< 0.05$ was considered statistically significant. All statistical computations, including propensity scores, were carried out with SAS software (version 12; SAS Institute, Inc., Cary, NC, USA).

The cumulative sum (CUSUM) method was used to quantify the effect on the operative time learning curve. We used CUSUM plots to analyze the RAMIE learning curve in patients with esophageal cancer[13]. A learning curve was considered complete at the point at which the surgical time decreased on the CUSUM plot.

## RESULTS

MIE was introduced in 2012, and 535 cases were performed until August 2022. RAMIE was started in 2019, and 84 cases were performed by August 2022. Of the 535 MIE cases, 208 cases of MIE were performed from January 2019 to August 2022.

To analyze the number of cases required for RAMIE standardization, the console time was calculated using CUSUM analysis. The calculated CUSUM learning curve was identified graphically to consist of three phases: phase I (28 initial cases), phase II (14 mid-term cases), and phase III (42 final cases; Figure 3). The slope of the CUSUM for phase I was positive, indicating insufficient procedural proficiency. The slope for phase II was variable but generally plateaued, suggesting that the console surgeon had achieved the learning point. In contrast, the slope of CUSUM in phase III tended to decrease, indicating that the surgeon has acquired technical proficiency.

### Patient demographics

To compare the outcomes of MIE and RAMIE, we compared 208 MIE and 84 RAMIE cases performed from 2019, at the time when RAMIE was introduced, to September 2022. Table 1 shows the background factors between the MIE and RAMIE groups. There were no differences in background factors between the

**Table 1. Baseline clinical characteristics between the groups**

| Variables | Total | MIE | RAMIE | | | | *P* value | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | All phase | Phase I | Phase II | Phase III | MIE *vs.* RAMIE | | |
| | *n* = 292 | *n* = 208 | *n* = 84 | *n* = 28 | *n* = 14 | *n* = 42 | All phase | Phase I | Phase II & III |
| Age, years, median | 68 | 69 | 67 | 68.5 | 67 | 66 | 0.379 | 0.974 | 0.286 |
| [range] | [28-84] | [28-83] | [42-84] | [46-83] | [56-77] | [42-84] | | | |
| Gender, *n* (%) | | | | | | | 0.754 | 0.539 | 0.461 |
| Male | 226 (77%) | 162 (78%) | 64 (76%) | 23 (82%) | 10 (71%) | 31 (74%) | | | |
| Female | 66 (23%) | 46 (22%) | 20 (24%) | 5 (18%) | 4 (29%) | 11 (26%) | | | |
| BMI (kg/m$^2$), *n* (%) | | | | | | | 0.551 | 0.101 | 0.461 |
| < 18.5 | 50 (17%) | 34 (16%) | 16 (19%) | 2 (7%) | 3 (21%) | 11 (26%) | | | |
| 18.5-25 | 213 (73%) | 151 (73%) | 62 (74%) | 26 (93%) | 10 (71%) | 26 (62%) | | | |
| > 25 | 29 (10%) | 23 (11%) | 6 (7%) | 0 (0%) | 1 (7%) | 5 (12%) | | | |
| CCI, *n* (%) | | | | | | | 0.171 | 0.72 | 0.038 |
| 0 | 113 (39%) | 83 (40%) | 30 (36%) | 9 (32%) | 3 (21%) | 18 (43%) | | | |
| 1 | 69 (24%) | 45 (22%) | 24 (29%) | 8 (29%) | 5 (36%) | 11 (26%) | | | |
| 2 | 50 (17%) | 32 (15%) | 18 (21%) | 4 (14%) | 5 (36%) | 9 (21%) | | | |
| > 3 | 60 (21%) | 48 (23%) | 12 (14%) | 7 (25%) | 1 (7%) | 4 (9%) | | | |
| ASA-PS, *n* (%) | | | | | | | 0.131 | 0.639 | 0.143 |
| 1 | 51 (17%) | 31 (15%) | 20 (24%) | 5 (18%) | 3 (21%) | 12 (29%) | | | |
| 2 | 176 (60%) | 132(63%) | 44 (52%) | 15 (54%) | 8 (57%) | 21 (50%) | | | |
| 3 | 65 (22%) | 45 (22%) | 20 (24%) | 8 (29%) | 3 (21%) | 9 (21%) | | | |
| Main tumor location, *n* (%) | | | | | | | 0.161 | 0.018 | 0.448 |
| Cervix | 12 (4%) | 10 (5%) | 2 (2%) | 0 (0%) | 1 (7%) | 1 (3%) | | | |
| Upper | 35 (12%) | 25 (12%) | 10 (12%) | 0 (0%) | 2 (14%) | 8 (19%) | | | |
| Middle | 135 (46%) | 102 (49%) | 33 (39%) | 10 (36%) | 5 (36%) | 18 (43%) | | | |
| Lower | 85 (29%) | 52 (25%) | 33 (39%) | 15 (54%) | 6 (43%) | 12 (29%) | | | |
| Abdomen | 25 (9%) | 19 (9%) | 6 (7%) | 3 (11%) | 0 (0%) | 3 (7%) | | | |
| Clinical depth of tumor invasion, *n* (%) | | | | | | | 0.838 | 0.781 | 0.705 |
| cT1 | 77 (26%) | 56 (27%) | 21 (25%) | 7 (25%) | 1 (7%) | 13 (31%) | | | |
| cT2 | 42 (14%) | 30 (14%) | 12 (14%) | 6 (21%) | 1 (7%) | 5 (12%) | | | |
| cT3 | 158 (54%) | 110 (53%) | 48 (57%) | 14 (50%) | 12 (86%) | 22 (52%) | | | |
| cT4 | 15 (5%) | 12 (6%) | 3 (4%) | 1 (4%) | 0 (0%) | 2 (5%) | | | |
| Clinical lymph node metastasis, *n* (%) | | | | | | | 0.856 | 0.627 | 0.741 |
| cN0 | 76 (26%) | 56 (27%) | 20 (24%) | 9 (32%) | 4 (29%) | 7 (17%) | | | |
| cN1 | 121 (41%) | 83 (40%) | 38 (45%) | 13(46%) | 3 (21%) | 22 (52%) | | | |
| cN2 | 85 (29%) | 62 (30%) | 23 (27%) | 5 (18%) | 6 (43%) | 12 (29%) | | | |
| cN3 | 10 (3%) | 7 (3%) | 3 (4%) | 1 (4%) | 1 (7%) | 1 (2%) | | | |
| Neoadjuvant therapy, *n* (%) | | | | | | | 0.722 | 0.401 | 0.271 |
| None | 71 (24%) | 53 (25%) | 18 (21%) | 5 (18%) | 2 (14%) | 11 (26%) | | | |
| NAC | 204 (70%) | 140 (68%) | 64 (77%) | 23 (82%) | 1 2(86%) | 29 (69%) | | | |
| CRT | 17 (6%) | 15 (7%) | 2 (2%) | 0 (0%) | 0 (0%) | 2 (5%) | | | |

ASA-PS: American Society of Anesthesiologists-physical status; BMI: body mass index; CCI: charlson comorbidity index; CRT: chemoradiotherapy; NAC: neoadjuvant chemotherapy.

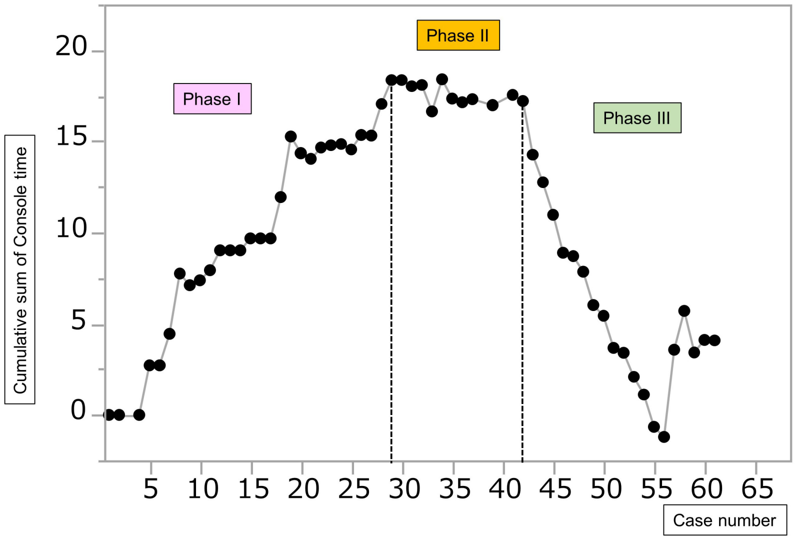


**Figure 3.** The CUSUM plot of console time. A plateau was reached after the 29th case, followed by a further decrease after 43 cases. Therefore, we defined the period up to the 28th case as phase I, the period from the 29th-42nd cases as phase II, and the period after the 43rd case as phase III.

two groups during the entire study period. In the introductory phase (phase I), there were no cases requiring salvage surgery after CRT. Patients who had lower or abdominal esophageal cancer tended to be more common in the RAMIE group. There were more cT3 cases in phase II than the other phases. There were more cases of middle and lower thoracic esophagus in phase I compared to the other phases, indicating that more typical cases tended to be selected in the introductory phases.

### Surgical outcomes

Table 2 shows the surgical outcomes. The median thoracic procedure time was 232 min for MIE and 239 min for RAMIE, with no difference between the two groups. The R0 resection rate was 92% for MIE and 90% for RAMIE, with no significant difference between the groups.

### Postoperative mortality, morbidity, and short-term outcomes

Table 3 shows the postoperative short-term outcomes. There were no postoperative in-hospital mortalities in the MIE or RAMIE groups. The 90-day mortality rates for MIE and RAMIE were 1.4% and 0, respectively. All patients were discharged to home. The RLN palsy rate was 25% in the MIE group compared to 18% in the RAMIE group. Although the incidence of RLN palsy was slightly higher in the RAMIE group (29%) in the introductory phase (phase I) compared to the MIE group, the incidence was lower in the RAMIE group (12.5%) in phases II and III, at which time RAMIE became more standardized. The incidence of postoperative pneumonia was 20% in the MIE group and 18% in the RAMIE group, with no difference between the groups. The incidence of anastomotic leakage was 8% in the MIE group and 1% in the RAMIE group ($P = 0.029$). No difference was detected between MIE and RAMIE in surgical technique in the gastric tube reconstruction, and we believe that the MIE group incidentally had more anastomotic leakage cases. The incidence of chylothorax was 32% higher in phase I compared to MIE ($P = 0.01$), which decreased to 16% in phase II/III ($P = 0.618$).

The median postoperative hospital stay was 18 days in the MIE group compared to 15 days in the RAMIE group ($P < 0.001$). Notably, the median postoperative hospital stay was significantly reduced to 14.5 days in the RAMIE during phases II and III. We believe that the difference between the groups may be influenced

**Table 2. Surgical outcomes between the groups**

| Variables | MIE | RAMIE | | | | *P* value | | |
|---|---|---|---|---|---|---|---|---|
| | | All phase | Phase I | Phase II | Phase III | MIE *vs.* RAMIE | | |
| | *n* = 208 | *n* = 84 | *n* = 28 | *n* = 14 | *n* = 42 | All phase | Phase I | Phase II & III |
| Operative time, median [range], min | 485 [331-1045] | 491.5 [310-766] | 504.5 [386-663] | 505 [401-766] | 486.5 [310-656] | 0.86 | 0.537 | 0.853 |
| Thoracic procedure time, median [range], min | 232 [89-425] | 239 [126-426] | 268.5 [221-426] | 248 [183-359] | 208 [126-379] | 0.244 | <0.001 | 0.292 |
| Console time, median [range], min | | 208.5 [105-354] | 227.5 [180-337] | 212 [136-279] | 182 [105-354] | | | |
| Estimated intraoperative blood loss, median [range], min | 100 [0-1550] | 110 [0-550] | 100 [20-550] | 120 [35-300] | 105 [0-550] | 0.347 | 0.558 | 0.413 |
| Number of harvested mediastinal lymph nodes, median [range] | 24 [2-58] | 22 [10-60] | 21 [11-40] | 26.5 [14-51] | 22 [10-60] | 0.715 | 0.403 | 0.929 |
| R0 resection, *n* (%) | 192 (92%) | 76 (90%) | 26 (93%) | 12 (86%) | 38 (91%) | 0.365 | 0.585 | 0.458 |

MIE: Minimally invasive esophagectomy; RAMIE: robot-assisted minimally invasive esophagectomy.

**Table 3. Surgical mortality, morbidity, and short-term outcomes between the groups**

| Variables | MIE | RAMIE | | | | *P* value | | |
|---|---|---|---|---|---|---|---|---|
| | | All phase | Phase I | Phase II | Phase III | MIE *vs.* RAMIE | | |
| | *n* = 208 | *n* = 84 | *n* = 28 | *n* = 14 | *n* = 42 | All phase | Phase I | Phase II & III |
| In-hospital death, *n* (%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | NA | NA | NA |
| Death within 90 days, *n* (%) | 3 (1.4%) | 0 (0%) | | | | 0.56 | NA | NA |
| Duration of hospital stay, day, median | 18 | 15 | 16 | 14.5 | 14.5 | < 0.001 | 0.08 | 0.002 |
| [range] | [9-100] | [8-78] | [8-36] | [10-78] | [10-59] | | | |
| Postoperative pneumonia, *n* (%) | | | | | | | | |
| CD > 2 | 41 (20%) | 15 (18%) | 8 (29%) | 3 (21%) | 4 (10%) | 0.716 | 0.278 | 0.214 |
| Recurrent laryngeal nerve palsy, *n* (%) | | | | | | | | |
| CD > 1 | 53 (25%) | 15 (18%) | 8 (29%) | 1 (7%) | 6 (14%) | 0.163 | 0.726 | 0.04 |
| Anastomotic leakage, *n* (%) | | | | | | | | |
| CD > 2 | 17 (8%) | 1 (1%) | 0 (0%) | 0 (0%) | 1 (2%) | 0.029 | 0.234 | 0.134 |
| Chylothorax, *n* (%) | | | | | | | | |
| CD > 2 | 28 (13%) | 18 (21%) | 9 (32%) | 3 (21%) | 6 (14%) | 0.081 | 0.01 | 0.618 |
| ARDS, *n* (%) | | | | | | | | |
| CD > 2 | 9 (4%) | 1 (1%) | 1 (4%) | 0 (0%) | 0 (0%) | 0.291 | 1 | 0.212 |

ARDS: Acute respiratory distress syndrome; CD: clavien-Dindo classification; MIE: minimally invasive esophagectomy; NA: not available; RAMIE: robot-assisted minimally invasive esophagectomy.

by the incidence of anastomotic leakage. To compensate for the differences in baseline characteristics between the groups, we carried out a propensity score matching analysis in the assessment of postoperative outcomes. Eventually, 77 paired cases were matched from the cohort, and the two groups were comparable with respect to patient characteristics [Supplementary Table 1]. Table 4 shows the postoperative short-term outcomes after matching. Even after propensity score matching, the incidence of left RLN palsy in phases II

**Table 4. Surgical mortality, morbidity, and short-term outcomes between the groups after matching**

| Variables | MIE | RAMIE | | | | *P* value | | |
|---|---|---|---|---|---|---|---|---|
| | | All phase | Phase I | Phase II | Phase III | MIE *vs.* RAMIE | | |
| | *n* = 77 | *n* = 77 | *n* = 27 | *n* = 13 | *n* = 37 | All phase | Phase I | Phase II & III |
| Mortality, *n* (%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | 0 (0%) | NA | NA | NA |
| Duration of hospital stay, day, median | 17 | 15 | 16 | 15 | 15 | 0.103 | 0.369 | 0.103 |
| [range] | [9-100] | [8-78] | [8-36] | [10-78] | [10-59] | | | |
| Postoperative pneumonia, *n* (%) | | | | | | 0.161 | 0.21 | 0.535 |
| CD > 2 | 14 (18%) | 15 (19%) | 8 (30%) | 3 (23%) | 4 (11%) | | | |
| Recurrent laryngeal nerve palsy, *n* (%) | | | | | | 0.233 | 0.613 | 0.039 |
| CD > 1 | 19 (25%) | 13 (17%) | 8 (29%) | 1 (8%) | 4 (11%) | | | |
| Anastomotic leakage, *n* (%) | | | | | | 0.033 | 0.108 | 0.087 |
| CD > 2 | 8 (10%) | 1 (1%) | 0 (0%) | 0 (0%) | 1 (3%) | | | |
| Chylothorax, *n* (%) | | | | | | 0.149 | 0.031 | 0.575 |
| CD > 2 | 12 (16%) | 18 (23%) | 9(33%) | 3 (23%) | 6 (16%) | | | |
| ARDS, *n* (%) | | | | | | 1 | 1 | 0.519 |
| CD > 2 | 4 (5%) | 1 (1%) | 1 (4%) | 0 (0%) | 0 (0%) | | | |

ARDS: Acute respiratory distress syndrome; CD: clavien-Dindo classification; NA: not available; MIE: minimally invasive esophagectomy; RAMIE: robot-assisted minimally invasive esophagectomy.

and III was significantly reduced compared to MIE, whereas the duration of hospital stay was similar between the groups.

## DISCUSSION

In the present study, it was found that RAMIE required 29 cases to achieve surgical proficiency. Moreover, the console time tended to decrease further after 43 cases. In addition, although the incidence of RLN palsy increased in phase I immediately after the introduction of RAMIE, the incidence of RLN palsy decreased significantly after proficiency was acquired.

Several reports have focused on learning curves for robotic-assisted esophagectomy. Hernandez *et al.*[13] reported that the learning curve for robotic Ivor-Lewis surgery required a minimum of 20 cases to become proficient with respect to operative time and incidence of postoperative complications. In addition, de la Fuente *et al.*[14] observed a trend toward lower complication rates after the first 29 surgeries using the robotic Ivor-Lewis system. In contrast, Park *et al.*[15] reported that serving as an assistant surgeon in 50 cases prior to performing robotic surgery did not require a learning curve with respect to operative time or the number of lymph nodes dissected, whereas the postoperative results were similar to previous studies involving robotic esophagectomy outcomes[15]. Although we implemented RAMIE without any experience in robotic surgery, the learning curve and postoperative outcomes were similar to reports by other authors after 29 cases. Moreover, we found an improvement in the incidence of RLN palsy and the duration of hospital stay, while other outcome measures were similar to reports by other authors. We conclude that these results could have been obtained by extrapolating the standardized MIE technique to robotic surgery. Moreover, the console operative time was shortened after 43 cases in our department. One reason for the robotic surgery biphasic learning curve in our hands, which differs from previous reports[13-15], is that the proportion of cT3 cases was increased in phase II and the number of cases with combined thoracic duct resection increased. In addition, the indication for salvage surgery was expanded to robot-assisted esophagectomy, which may have resulted in a longer console operative time.

Several single-center studies have reported that robotic surgery tends to increase thoracic operative time compared to MIE[16,17]; however, a recent RAMIE study showed that robotic-assisted surgery significantly reduces the operative time[7]. These conflicting results may reflect the fact that most of the previous single-center studies tended to show longer operative times for robot-assisted surgery because of learning curves in the early phases after introduction. Therefore, we believe that if RAMIE is standardized at each institution, the console operative time will improve, as we have reported in our department.

The efficacy of robotic-assisted surgery compared to MIE has not been fully validated. Several systematic reviews have shown reduced blood loss, an increased number of lymph nodes dissected, and shorter hospital stays, but most of the reports were single-center studies with a small number of patients; large multicenter studies are lacking[18]. The results of ongoing multicenter prospective studies, such as the RAMIE[15] and REVATE trials[19], are warranted.

Our results showed that the incidence of RLN palsy was reduced in the cases in which standardized RAMIE was performed. While there have been recent reports that RAMIE reduces the incidence of RLN palsy compared to MIE[7,16,20], several studies have demonstrated conflicting results[21-24].

Therefore, whether RAMIE is superior to MIE in reducing the incidence of RLN palsy is debatable; however, because the microanatomy detail provided by the multi-joint capabilities and 3D high-definition images in robotic surgery contributes to improving the accuracy of superior mediastinal lymph node dissection, we are of the opinion that standardized robotic surgery may contribute to a reduction in the incidence of RLN palsy. The results of the ongoing REVATE study, in which the primary endpoints are successful lymph node harvesting around the left RLN and the incidence of left RLN palsy, are very interesting and eagerly awaited.

Because RLN palsy is a risk factor for postoperative pneumonia[20,25,26], a reduction in the incidence of RLN palsy has the potential to decrease the risk of postoperative pneumonia and thereby improve the prognosis. Therefore, it is important to determine whether robotic-assisted surgery reduces the incidence of RLN palsy. Our results showed a trend toward a decrease in the incidence of RLN palsy with standardization of RAMIE but no decrease in the incidence of postoperative pneumonia. These results are similar to previous studies, and few studies have reported that RAMIE reduces the incidence of pneumonia compared to MIE[7,16,20]. Because risk factors for postoperative pneumonia vary widely, including intraoperative position[27], postoperative antibiotic management[28], and the presence of sarcopenia[29], it may be difficult to demonstrate a reduction in the incidence of pneumonia simply by a reduction in the incidence of RLN palsy alone.

The incidence of chylothorax tended to be higher in the RAMIE group, at 21%, compared to 13% in the MIE group ($P = 0.081$). The reason for the slightly higher incidence of chylothorax compared to other centers may be attributed to the use of early enteral feeding, which started four hours postoperatively, for postoperative management at our institution. In addition, the difference in surgical devices used between MIE and RAMIE may have also affected the incidence of chylothorax: in MIE, the vessel sealing system was used during periaortic lymph node dissection, whereas in RAMIE, only a monopolar electrocautery scalpel was initially used. This may have resulted in incomplete closure of lymphatic branches during the periaortic dissection in the RAMIE group. Therefore, the use of bipolar coagulation method during periaortic lymph node dissection resulted in a reduced incidence of chylothorax in the RAMIE group (MIE *vs*. phases II and III, $P = 0.618$). Moreover, all patients who developed chylothorax were healed conservatively by discontinuing enteral nutrition, with no significant impact on the postoperative course.

The incidence of RLN palsy was reduced in the RAMIE group, and the number of retrieved mediastinal lymph nodes and estimated intraoperative blood loss did not differ between groups. However, it is the surgeon, not the robot, who performs better lymph node dissection. We should not confuse the surgeon operating the robot with the robot[30]. We believe that the fact that this study was performed by two surgeons experienced in both esophageal cancer surgery and robotic surgery contributed to these favorable results.

This study had several limitations. First, this was a retrospective study. Therefore, additional multicenter prospective studies are needed to fully clarify the superiority of RAMIE compared to MIE. Second, this study was ≤ 4 years in duration, and although the surgical technique and perioperative patient management were consistent, some of the surgical instruments differed. Third, although console operating time is one of the most important factors for achieving the learning curve, there are other important factors, such as the amount of blood loss, the number of retrieved mediastinal lymph nodes, and the time density of the surgical volume and operation frequency. This study did not consider all these factors in the learning curve. Regarding the amount of blood loss and the number of retrieved mediastinal lymph nodes, no difference was observed between the two groups in this study, and similar reports are available in the literature[7,31]. However, we believe that one of the limitations of this study is the fact that the time density of surgical volume and operation frequency were not considered in the study.

In conclusion, RAMIE required 29 cases to achieve surgical proficiency. Our results suggest that the introduction and standardization of prone robot-assisted esophagectomy may decrease the incidence of RLN palsy in patients compared to MIE. Further analysis of more cases in future multicenter studies will clarify the potential impact of RAMIE in esophageal cancer.

## DECLARATIONS

### Authors' contributions

Conception and design: Abe T
Data collection: Abe T
Establishment of study materials or enrolment of patients: Abe T, Higaki E, Fujieda H, Shimizu Y
Data scrutiny, analysis, and clarification: Abe T
Writing and revision of the manuscript: Abe T
Study supervision: Shimizu Y
Read and agree with the final manuscript: Abe T, Higaki E, Fujieda H, Saito H, Narita K, Komori K, Ito S, Shimizu Y

### Availability of data and materials

Not applicable.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

All patients provided written informed consent before treatment, and the study was approved by the Ethics Committee of Aichi Cancer Center Hospital. This work conformed to the guidelines set forth in the Helsinki Declaration of 1975 and later versions. The Review Board of the Aichi Cancer Center Hospital approved this study (Approval No. ACC 2021-0-046).

### Consent for publication

We have obtained patient consent for the publication of the data and research.

### Copyright



## REFERENCES


1. Takeuchi H, Miyata H, Gotoh M, et al. A risk model for esophagectomy using data of 5354 patients included in a japanese nationwide web-based database. *Ann Surg* 2014;260:259-66. DOI
2. Matsubara T, Ueda M, Yanagida O, Nakajima T, Nishi M. How extensive should lymph node dissection be for cancer of the thoracic esophagus? *J Thorac Cardiovasc Surg* 1994;107:1073-8. DOI PubMed
3. Igaki H, Tachimori Y, Kato H. Improved survival for patients with upper and/or middle mediastinal lymph node metastasis of squamous cell carcinoma of the lower thoracic esophagus treated with 3-field dissection. *Ann Surg* 2004;239:483-90. DOI PubMed PMC
4. Oshikiri T, Goto H, Horikawa M, et al. Robot-assisted minimally invasive esophagectomy reduces the risk of recurrent laryngeal nerve palsy. *Ann Surg Oncol* 2021;28:7258. DOI
5. Ninomiya I, Okamoto K, Yamaguchi T, et al. Optimization of robot-assisted thoracoscopic esophagectomy in the lateral decubitus position. *Esophagus* 2021;18:482-8. DOI
6. Daiko H, Oguma J, Fujiwara H, et al. Robotic esophagectomy with total mediastinal lymphadenectomy using four robotic arms alone in esophageal and esophagogastric cancer (RETML-4): a prospective feasibility study. *Esophagus* 2021;18:203-10. DOI
7. Fujita T, Sato K, Ozaki A, et al. Propensity-matched analysis of the short-term outcome of robot-assisted minimally invasive esophagectomy versus conventional thoracoscopic esophagectomy in thoracic esophageal cancer. *World J Surg* 2022;46:1926-33. DOI
8. Meyer P, Sublon R. [Considerations on the interpleural ligament (De Morosow)]. *Arch Anat Pathol* 1961;9:111-5. PubMed
9. Matsubara T, Ueda M, Nagao N, Takahashi T, Nakajima T, Nishi M. Cervicothoracic approach for total mesoesophageal dissection in cancer of the thoracic esophagus. *J Am Coll Surg* 1998;187:238-45. DOI PubMed
10. Hosoi T, Abe T, Higaki E, et al. Circular stapled technique versus modified collard technique for cervical esophagogastric anastomosis after esophagectomy: a randomized controlled trial. *Ann Surg* 2022;276:30-7. DOI
11. Rice TW, Ishwaran H, Hofstetter WL, et al. Recommendations for pathologic staging (pTNM) of cancer of the esophagus and esophagogastric junction for the 8th edition AJCC/UICC staging manuals. *Dis Esophagus* 2016;29:897-905. DOI PubMed PMC
12. Clavien PA, Barkun J, de Oliveira ML, et al. The Clavien-Dindo classification of surgical complications: five-year experience. *Ann Surg* 2009;250:187-96. DOI
13. Hernandez JM, Dimou F, Weber J, et al. Defining the learning curve for robotic-assisted esophagogastrectomy. *J Gastrointest Surg* 2013;17:1346-51. DOI PubMed
14. de la Fuente SG, Weber J, Hoffe SE, Shridhar R, Karl R, Meredith KL. Initial experience from a large referral center with robotic-assisted Ivor Lewis esophagogastrectomy for oncologic purposes. *Surg Endosc* 2013;27:3339-47. DOI PubMed
15. Park SY, Kim DJ, Kang DR, Haam SJ. Learning curve for robotic esophagectomy and dissection of bilateral recurrent laryngeal nerve nodes for esophageal cancer. *Dis Esophagus* 2017;30:1-9. DOI PubMed
16. Tsunoda S, Obama K, Hisamori S, et al. Lower incidence of postoperative pulmonary complications following robot-assisted minimally invasive esophagectomy for esophageal cancer: propensity score-matched comparison to conventional minimally invasive esophagectomy. *Ann Surg Oncol* 2021;28:639-47. DOI
17. Yang Y, Li B, Yi J, et al. Robot-assisted versus conventional minimally invasive esophagectomy for resectable esophageal squamous cell carcinoma: early results of a multicenter randomized controlled trial: the RAMIE trial. *Ann Surg* 2022;275:646-53. DOI
18. Angeramo CA, Bras Harriott C, Casas MA, Schlottmann F. Minimally invasive Ivor Lewis esophagectomy: robot-assisted versus laparoscopic-thoracoscopic technique. Systematic review and meta-analysis. *Surgery* 2021;170:1692-701. DOI PubMed
19. Chao YK, Li ZG, Wen YW, et al. Robotic-assisted esophagectomy vs video-assisted thoracoscopic esophagectomy (REVATE): study protocol for a randomized controlled trial. *Trials* 2019;20:346. DOI PubMed PMC
20. Oshikiri T, Takiguchi G, Hasegawa H, et al. Postoperative recurrent laryngeal nerve palsy is associated with pneumonia in minimally invasive esophagectomy for esophageal cancer. *Surg Endosc* 2021;35:837-44. DOI
21. He H, Wu Q, Wang Z, et al. Short-term outcomes of robot-assisted minimally invasive esophagectomy for esophageal cancer: a propensity score matched analysis. *J Cardiothorac Surg* 2018;13:52. DOI PubMed PMC
22. Deng HY, Luo J, Li SX, et al. Does robot-assisted minimally invasive esophagectomy really have the advantage of lymphadenectomy over video-assisted minimally invasive esophagectomy in treating esophageal squamous cell carcinoma? A propensity score-matched analysis based on short-term outcomes. *Dis Esophagus* 2019;32:doy110. DOI
23. Zhang Y, Han Y, Gan Q, et al. Early outcomes of robot-assisted versus thoracoscopic-assisted ivor lewis esophagectomy for

esophageal cancer: a propensity score-matched study. *Ann Surg Oncol* 2019;26:1284-91. DOI

24. Chao YK, Hsieh MJ, Liu YH, Liu HP. Lymph node evaluation in robot-assisted versus video-assisted thoracoscopic esophagectomy for esophageal squamous cell carcinoma: a propensity-matched analysis. *World J Surg* 2018;42:590-8. DOI PubMed
25. Kataoka K, Takeuchi H, Mizusawa J, et al. Prognostic impact of postoperative morbidity after esophagectomy for esophageal cancer: exploratory analysis of JCOG9907. *Ann Surg* 2017;265:1152-7. DOI
26. Huang CL, Chen CM, Hung WH, et al. Clinical outcome of intraoperative recurrent laryngeal nerve monitoring during thoracoscopic esophagectomy and mediastinal lymph node dissection for esophageal cancer. *J Clin Med* 2022;11:4949. DOI PubMed PMC
27. Okamura A, Endo H, Watanabe M, et al. Influence of patient position in thoracoscopic esophagectomy on postoperative pneumonia: a comparative analysis from the National Clinical Database in Japan. *Esophagus* 2023;20:48-54. DOI
28. Higaki E, Abe T, Fujieda H, et al. Significance of antimicrobial prophylaxis for the prevention of early-onset pneumonia after radical esophageal cancer resection: a retrospective analysis of 356 patients undergoing thoracoscopic esophagectomy. *Ann Surg Oncol* 2022;29:1374-87. DOI
29. Fukushima T, Watanabe N, Okita Y, et al. The evaluation of the association between preoperative sarcopenia and postoperative pneumonia and factors for preoperative sarcopenia in patients undergoing thoracoscopic-laparoscopic esophagectomy for esophageal cancer. *Surg Today* 2023;53:782-90. DOI
30. Lerut T. The surgeon as a prognostic factor. *Ann Surg* 2000; 232:729-32. DOI PubMed PMC
31. Shirakawa Y, Noma K, Maeda N, Tanabe S, Sakurama K, Fujiwara T. Standardization of bilateral upper mediastinal lymph node dissection using microanatomical concepts in minimally invasive esophagectomy. *Mini-invasive Surg* 2020;4:33. DOI