



Incidence of Recurrent Laryngeal Nerve Palsy in Robot-Assisted Versus Conventional Minimally Invasive McKeown Esophagectomy in Prone Position: A Propensity Score-Matched Study

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Incidence of recurrent laryngeal nerve palsy in robot-assisted versus conventional minimally invasive McKeown esophagectomy in prone position: A propensity score-matched study

Short running head: RLN palsy in RAMIE

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Synopsis: RAMIE is superior to C-MIE in prone position in decreasing the incidence of left RLN palsy.

Abstract

Background

Esophagectomy with lymphadenectomy is the principal treatment for localized esophageal cancer. Conventional minimally invasive esophagectomy (C-MIE) in prone position has spread worldwide as it less invasive. However, its efficacy remains controversial. Robot-assisted MIE (RAMIE) can have more advantages than C-MIE. Therefore, the current study aimed to validate whether RAMIE is associated with a lower incidence of left recurrent laryngeal nerve (RLN) palsy compared with C-MIE in prone position.

Methods

In total, 404 patients with esophageal carcinoma underwent MIE (353 C-MIEs and 51 RAMIEs) in prone position at Kobe University between 2010 and 2020. Then, propensity score matching was performed, and results showed that 51 patients should be included in each group. Thereafter, the perioperative outcomes between the two groups were compared.

Results

The RAMIE group had a significantly longer operative time than the C-MIE group ($P < 0.0001$). However, the number of lymph nodes resected along the left RLN was similar in both groups. Moreover, the incidence of left RLN palsy was significantly lower in the RAMIE group than in the C-MIE [Clavien-Dindo classification Grade II; 0 (0%) versus 32 (9%), $P = 0.022$ in entire cohort, and 0 (0%) versus 5 (10%), $P = 0.022$ in matched cohort. Esophagectomy Complications Consensus Group definitions type I; 8 (16%) versus 101 (29%), $P = 0.041$ in entire cohort and 8 (16%) versus 18 (35%) in matched cohort ($P = 0.023$).

Conclusions

RAMIE is superior to C-MIE in prone position in decreasing the incidence of left RLN palsy.

Key words: conventional minimally invasive esophagectomy (C-MIE), robot-assisted MIE (RAMIE), prone position, recurrent laryngeal nerve (RLN) palsy

Background

Esophageal cancer ranks seventh in terms of incidence (57,000 new cases annually worldwide),¹ and it is the sixth most common cause of cancer-related deaths.² Esophagectomy with extended lymphadenectomy is the principal treatment for localized esophageal cancer.^{3,4}

During the last two decades, conventional minimally invasive esophagectomy (C-MIE) with thoracoscopy in prone position has been widely used worldwide as it is less invasive.^{5,6} In terms of complications after esophagectomy, pneumonia is associated with a worse overall prognosis.⁷ Recurrent laryngeal nerve (RLN) palsy is an independent risk factor of pneumonia.⁸ To reduce the incidence of RLN palsy, a few novel techniques for lymphadenectomy along the RLN during C-MIE have been reported.^{9,10} However, data about these methods are still limited.

Robot-assisted MIE (RAMIE) has more advantages than C-MIE. That is, it can facilitate a magnified three-dimensional visualization and seven degrees of freedom in ambidexterity due to the use of a manipulator with a wrist and tremor filtration. Some studies have compared the incidence rates of RLN palsy between RAMIE and C-MIE using propensity score matching.¹¹⁻¹⁶ However, whether RAMIE is superior to C-MIE in decreasing the incidence of RLN palsy has not been validated. In addition, only few studies have assessed RAMIE and C-MIE in prone position because the latter is commonly performed in left lateral decubitus or semi-prone position.¹¹⁻¹⁵ In a recent study, the modified Bascule method, which is a novel technique, for lymphadenectomy along the left RLN during RAMIE has been used. This strategy is based on a logical

and simple understanding of the left upper mediastinum anatomy.¹⁷

The current study aimed to validate whether the modified Bascule method during RAMIE is correlated with a lower incidence of left RLN palsy compared with C-MIE in prone position.

Materials and Methods

Patient population

We performed a propensity score-matched study including patients with esophageal cancer who underwent minimally invasive McKeown esophagectomy (n = 472) at Kobe University between 2010 and 2020.¹⁸ In our institution, all surgical candidates with esophageal carcinoma undergo C-MIE or RAMIE in prone position.

The diagnosis of esophageal carcinoma was based on the eighth edition of the Union for International Cancer Control tumor–node–metastasis cancer staging system.¹⁹ Preoperative chemoradiotherapy was not provided. The inclusion criteria were as follows: age 18–85 years, cT1–3 and cN0–3 disease,¹⁹ histologically confirmed thoracic ESCC or adenocarcinoma, upper mediastinal lymphadenectomy, and simultaneous esophagectomy and reconstruction.¹⁷

All data were extracted from a prospectively registered database. This study was approved by the Institutional Review Board and Ethics Committee of Kobe University.

Thoracic procedure criteria

Until 2018, all patients with esophageal carcinoma underwent C-MIE in prone

position. Then, RAMIE was approved by the Japanese insurance system in 2018, and its application was introduced in the same year. Hence, procedures performed between 2010 and 2018 commonly comprised C-MIE. Subsequently, RAMIE had been often conducted.

Thoracic procedure

All patients underwent either C-MIE or RAMIE (da Vinci® Xi Surgical System, Intuitive Surgical, Inc., Sunnyvale, CA) in prone position. Under single-lumen tracheal tube intubation, a blocker was inserted into the right bronchus for one-lung ventilation anesthesia. Five ports were inserted into the intercostal space (ICS). In RAMIE, four 8- or 12-mm ports were inserted into the third, fifth, seventh, and ninth ICSs along the middle axillary line. Meanwhile, an assistant port was inserted into the sixth ICS on the anterior axillary line. The chest cavity was inflated using carbon dioxide insufflation at a pressure of 8 mmHg. The surgical techniques for RAMIE and C-MIE have been published in detail in previous studies.^{9,10,17}

Neck procedure

Lymphadenectomy around the trachea and left RLN via the cervical wound had been performed in both two- and three-field lymphadenectomies. In three-field lymphadenectomy, clinically positive supraclavicular lymph nodes were dissected additionally.

Abdominal procedure

Laparoscopic surgery or open laparotomy (OL) was performed. Laparoscopic surgery was the primary choice. Then, OL was considered in some patients with a previous medical history of laparotomy. Gastric mobilization and abdominal lymphadenectomy were initially performed. Next, a gastric conduit with a width of 3–4 cm was typically created outside of the wound and was raised via the posterior mediastinum or retrosternal route. In some patients without gastric conduits due to previous gastric resection or synchronous gastric cancer, pedicled jejunum reconstruction via the presternal route was performed.⁸

Outcome

Postoperative clinical course evaluation

The following parameters were assessed: operative time of thoracic procedure including console time; number of harvested lymph nodes from the mediastinum and along the left RLN; volume of blood loss; incidence rates of left RLN palsy, pneumonia, and anastomotic leakage; and postoperative hospital stay. Postoperative morbidity was analyzed according to the Clavien–Dindo (C–D) classification system.²⁰ In addition, RLN palsy and anastomotic leakage were evaluated using the Esophagectomy Complications Consensus Group (ECCG) definitions.²¹ In the assessment of pneumonia, the Uniform Pneumonia Score was used. A score of ≥ 2 with at least 1 point based on pulmonary radiography indicated that suspected pneumonia must be treated.²² All patients were assessed for RLN palsy by evaluating vocal cord

mobility under laryngoscopy on postoperative day 7.

Two definitions of RLN palsy

Clavien–Dindo (C–D) classification system²⁰

Grade I: Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical, endoscopic, and radiological interventions.

Grade II: Requiring pharmacological treatment with drugs.

Grade III: Requiring surgical, endoscopic or radiological intervention.

IIIa: Intervention not under general anesthesia

IIIb: Intervention under general anesthesia

Grade IV: Life-threatening complication requiring IC/ICU management.

Grade V: Death of a patient.

Esophagectomy Complications Consensus Group (ECCG) definitions²¹

Type I: Transient injury requiring no therapy.

Type II: Injury requiring elective surgical procedure, for example, thyroplasty or medialization procedure.

Type III: Injury requiring acute surgical intervention (due to aspiration or respiratory issues), for example, thyroplasty or medialization procedure.

Severity Level; (A) Unilateral, (B) Bilateral

Statistical analysis

To generate two comparable groups, this study performed propensity score (simple 1:1 nearest-neighbor) matching using covariates such as age, sex, tumor location, histology, clinical depth of tumor invasion, clinical lymph node metastasis, neoadjuvant chemotherapy, abdominal procedure, and lymph node dissection.¹⁸ These variables were utilized as common factors in medical practice to adjust the characteristics of both groups. A caliper equal to 0.20 for the standard deviation of the logit of the propensity score was used to prevent poor matches.

All continuous data were presented as medians and categorical data as numbers (percentage). Between-group differences were determined using the χ^2 test, Fisher's exact test, or Mann–Whitney U test, as appropriate. A *P* value of < 0.05 was considered statistically significant. All statistical analyses were performed using JMP® 11 (SAS Institute, Cary, NC, the USA).

Results

Characteristics of patients

In total, 404 patients with esophageal carcinoma who met the inclusion criteria underwent MIE in prone position (*n* = 353, C-MIEs and *n* = 51, RAMIEs) between 2010 and 2020. The characteristics of patients are depicted in Table 1. The propensity score matching showed that 51 patients should be included in each group (Figure 1). There were significant differences in baseline characteristics, sex, abdominal procedure, and lymph node dissection before adjustment. All differences disappeared after propensity score matching (Table 1).

Operative outcomes

The operative outcomes after propensity score matching are summarized in Table

2. Accordingly, the RAMIE group had a significantly longer overall (808 vs 679 min in the entire cohort [$P < 0.0001$] and 808 vs 655 min in the matched cohort [$P < 0.0001$]) and thoracic (440 vs 300 min in the entire cohort [$P < 0.0001$] and 440 vs 300 min in the matched cohort [$P < 0.0001$]) procedure times compared with the C-MIE group.

The number of lymph nodes resected along the left RLN was similar in both the RAMIE and C-MIE groups (4 vs 4 in the entire cohort [$P = 0.371$] and 4 vs 4 in the matched cohort [$P = 0.324$]). The volume of blood loss was significantly lower in the RAMIE group than in the C-MIE group (35 vs 200 in the entire cohort [$P < 0.0001$] and 35 vs 100 in the matched cohort [$P = 0.0012$]) (Table 2).

Regarding postoperative complications, the incidence rate of each grade or type of right RLN palsy was similar in the RAMIE and C-MIE groups. By contrast, the incidence of left RLN palsy was significantly lower in the RAMIE group than in the C-MIE group. Some patients presented with grade II complications based on the C–D classification²⁰ system (0 [0%] vs 32 [9%] in the entire cohort [$P = 0.022$] and 0 [0%] vs 5 [10%] in the matched cohort [$P = 0.022$]). Then, type I left RLN palsy according to the ECCG definitions was observed in 8 (16%) versus 101 (29%) patients in the entire cohort ($P = 0.041$) and 8 (16%) versus 18 (35%) patients in the matched cohort ($P = 0.023$) (Table 3). The proportion of patients with a Uniform Pneumonia Score²² of ≥ 4 was significantly lower in the RAMIE group than in the C-MIE group in the entire

cohort. However, there was no significant difference between the two groups in terms of grade or type in the matched cohort (Table 4). The proportion of patients with anastomotic leakage based on the ECCG definition²¹ was significantly higher in the RAMIE group than in the C-MIE group in the entire cohort. However, there was no significant difference between the two groups in terms of grade or type in the matched cohort (Table 5).

Discussion

This study showed that the incidence rate of left RLN palsy was significantly lower in the RAMIE group than in the C-MIE group even though the number of resected lymph nodes was similar in both groups. There is only one randomized prospective trial comparing RAMIE and open esophagectomy.²³ In this research, there was no significant difference in terms of the incidence of RLN palsy between the two groups. By contrast, whether RAMIE is superior to C-MIE in decreasing the incidence of RLN palsy remains controversial. Chen et al. revealed that the incidence of RLN palsy was lower in the RAMIE group than in the C-MIE group.¹⁶ However, other studies have contrasting results. That is, RLN palsy was more common in the RAMIE group than in the C-MIE group.¹¹ Hence, some reports showed that there were no significant differences between the two groups.¹²⁻¹⁵ In terms of synthetic analysis, there were two meta-analyses. Jin et al. revealed that the risk for RLN palsy in the RAMIE group was lower than that in the C-MIE group (odds ratio [OR]: 0.57, 95% confidence Interval (CI): 0.33–0.99, and $P = 0.04$).²⁴ Li et al. reported that RAMIE was superior to

C-MIE in decreasing the incidence of RLN palsy (OR: 0.62, 95% CI: 0.41–0.95, $P = 0.027$).²⁵ This finding is attributed to the fact that it can facilitate a magnified three-dimensional imaging and seven degrees of freedom in ambidexterity due to the use of a manipulator with a wrist and tremor filtration. Therefore, surgeons can accurately perform a procedure and can protect the RLN, which must be preserved. Otsuka et al. showed that touching or stretching the RLN can be a risk factor for palsy. Thus, the left RLN must be maintained in its normal anatomical position to prevent touching and stretching.²⁶ Conversely, Kim et al. showed that the skeletonization of RLN during RAMIE, which leads to the unfixed status of RLN, should be prevented. In this study, the incidence rate of RLN palsy in the skeletonization group was six times higher than that in the non-skeletonization group.²⁷ A recent study showed the use of the modified Bascule method, which is well-thought-out procedure developed in 2018. This method can safely maintain the left RLN in its normal anatomical position and may possibly be indicated for not only RAMIE but also C-MIE. However, RAMIE using articulated robot arms preferably embodies the concept of the “modified Bascule method,” which requires finer techniques.¹⁷ Thus, the nerve stretching or thermal injury leading to RLN palsy are more likely to occur in C-MIE even if it was done with modified Bascule method. Additionally, most old C-MIEs were done without this method despite the fact that RAMIEs in this study were performed using the modified Bascule method. Consequently, the incidence of left RLN palsy was significantly lower in the RAMIE group than in the C-MIE group.

In the current research, there was no significant difference between the two

groups in terms of the incidence of pneumonia. A meta-analysis comparing RAMIE and C-MIE has obtained similar results.²⁴ By contrast, the incidence of pneumonia was significantly lower in the RAMIE than in the open esophagectomy in the ROBOT trial.²³ Positions during surgery significantly affect the incidence of respiratory complications. Any compression and mechanical damage to the right lung can be prevented in prone position, compared with left lateral decubitus position, via artificial pneumothorax and gravity. Moreover, the risk of airway secretions flowing into the left lung is lower in prone position than in left lateral decubitus position. In addition, the functional residual capacity is higher in prone position due to decreased cephalad pressure in the diaphragm.²⁸ In our previous study, the partial pressure of oxygen/fraction of inspired oxygen ratio was significantly better in the prone group than in the left lateral decubitus group.²⁹ Hence, prone position is superior to left lateral decubitus position in decreasing the incidence of pneumonia. RAMIE is performed in prone position. However, open esophagectomy is conducted in left lateral decubitus position. Thus, there might be significant differences in the incidence of pneumonia in the ROBOT trial. However, in our study and some previous reports, C-MIE was conducted in prone position. Therefore, we could not find any significant difference in terms of the incidence of pneumonia between RAMIE and C-MIE. However, as we reported previously, improvement of RLN palsy should contribute to the decrease of pneumonia.⁸ Indeed, in both cohorts, pneumonia more than C-D grade IIIa or Uniform Pneumonia Score 4 occurred in C-MIE group only. Storage of cases might be necessary to prove the significant differences in occurrence of pneumonia between RAMIE and

1 C-MIE.

2 Differences between institutions in estimating the grade of complications remains
3 a challenge. To address this issue, some criteria, such as the C–D classification, ECCG,
4 and Uniform Pneumonia Score, were used. Thus, we could obtain reliable data
5 evaluated from different angles. However, the current study had several limitations.
6 That is, the number of participants was small, and the study was performed at one
7 institution only. Moreover, there might be a bias in terms of therapeutic period. To
8 obtain further evidence, a prospective study, similar to the ROBOT trial, comparing
9 RAMIE and C-MIE should be conducted.

11 **Conclusions**

12 RAMIE using a well-thought-out procedure is superior to C-MIE in prone
13 position in decreasing the incidence of left RLN palsy.

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1 **Figure legends**

2 Fig. 1 Flow of patient recruitment.

3 Of 472 patients who underwent MIE with either C-MIE or RAMIE between 2010 and

4 2020, 68 were excluded. Then, 51 patients were included in each group after propensity

5 score matching.

6

Patients and Methods

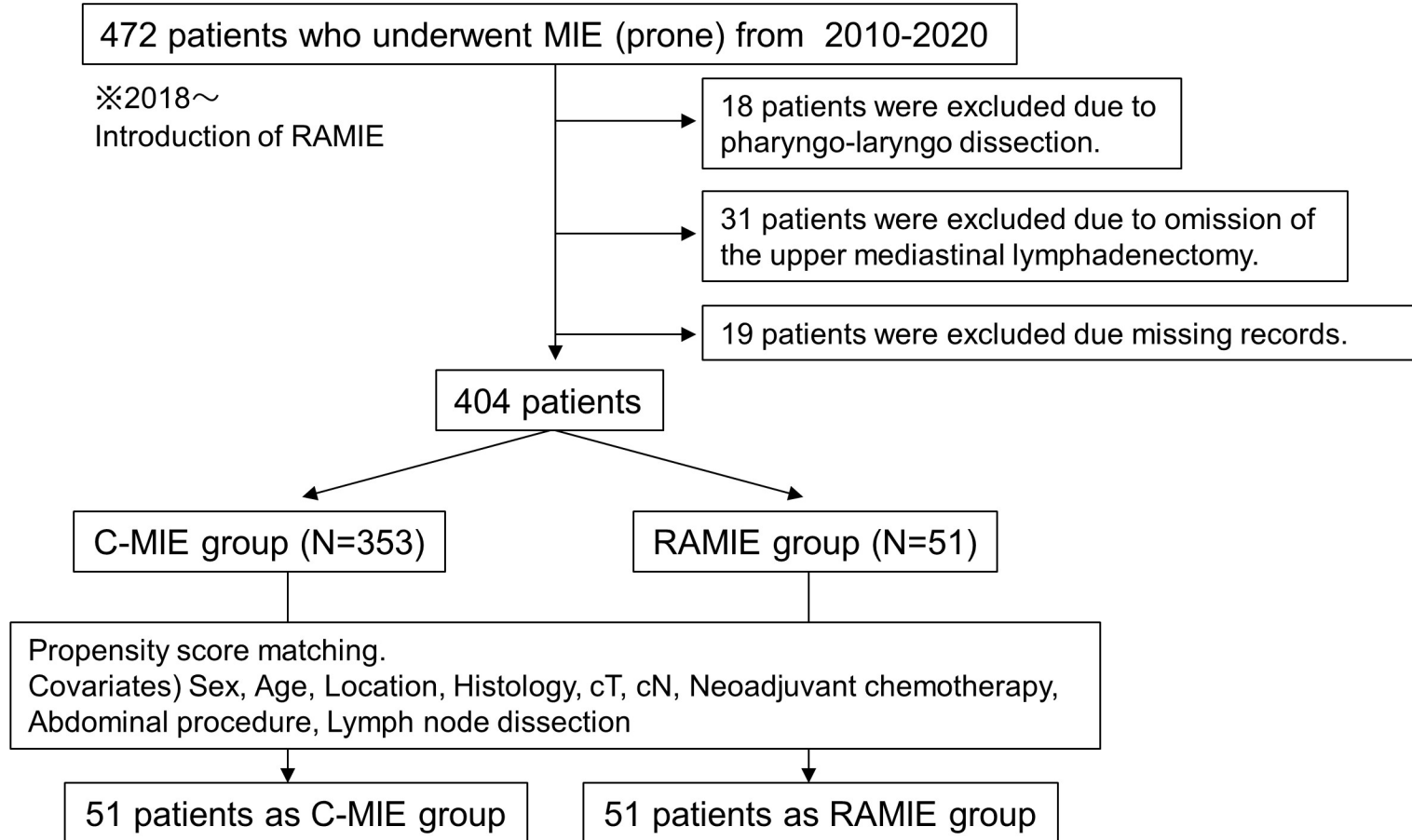


Table 1. Demographic and clinical characteristics of patients who underwent conventional or robot-assisted minimally invasive esophagectomy.

	Whole cohort		<i>P</i> value	Matched cohort		<i>P</i> value
	Conventional MIE group (n = 353)	RAMIE group (n = 51)		Conventional MIE group (n = 51)	RAMIE group (n = 51)	
Age ^{a)}	67 (27–82)	67 (45–80)	0.817 ^{b)}	67 (27–80)	67 (45–80)	0.763 ^{b)}
Sex			0.0010 ^{c)}			0.537 ^{c)}
Male/female	301 (85%)/52 (15%)	34 (67%)/17 (33%)		31 (61%)/20 (39%)	34 (67%)/17 (33%)	
Tumor location			0.529 ^{c)}			0.664 ^{c)}
Ut	62 (18%)	12 (24%)		9 (18%)	12 (24%)	
Mt	161 (45%)	20 (39%)		24 (47%)	20 (39%)	
Lt	130 (37%)	19 (37%)		18 (35%)	19 (37%)	
Histology			0.357 ^{c)}			0.207 ^{c)}
SCC/adeno ca.	325 (92%)/28 (8%)	45 (88%)/6 (12%)		41 (80%)/10 (20%)	45 (88%)/6 (12%)	
Depth of tumor invasion			0.712 ^{c)}			0.541 ^{d)}
cT1	131 (37%)	21 (41%)		23 (45%)	21 (41%)	
cT2	57 (16%)	7 (14%)		10 (20%)	7 (14%)	
cT3	158 (45%)	23 (45%)		18 (35%)	23 (45%)	
cT4	7 (2%)	0 (0%)		0 (0%)	0 (0%)	
Lymph node metastasis			0.407 ^{c)}			0.553 ^{c)}
cN+/cN-	188 (53%)/165 (47%)	24 (47%)/27 (53%)		27 (53%)/24 (47%)	24 (47%)/27 (53%)	
UICC-cStage ^a			0.849 ^{c)}			0.732 ^{d)}

I	122 (35%)	21 (41%)		21 (41%)	21 (41%)
II	86 (24%)	11 (22%)		7 (14%)	11 (22%)
III	117 (33%)	16 (31%)		19 (37%)	16 (31%)
IV	28 (8%)	3 (6%)		4 (8%)	3 (6%)
NAC			0.119 ^{c)}		0.841 ^{c)}
Yes/no	246 (70%)/107 (30%)	30 (59%)/21 (41%)		29 (57%)/22 (43%)	30 (59%)/21 (41%)
Abdominal procedure			0.0002 ^{d)}		0.678 ^{d)}
Laparoscopy/open	263 (74%)/90 (26%)	49 (96%)/2 (4%)		47 (92%)/4 (8%)	49 (96%)/2 (4%)
conduit			0.336 ^{d)}		1.000 ^{d)}
Stomach/others	331 (94%)/22 (6%)	50 (98%)/1 (2%)		51 (100%)/0 (0%)	50 (98%)/1 (2%)
Lymph node dissection			< 0.0001 ^{d)}		1.000 ^{d)}
3-/2-field	119 (34%)/234 (66%)	4 (8%)/47(92%)		3 (6%)/48 (94%)	4 (8%)/47(92%)

SCC, squamous cell carcinoma; adeno ca, adenocarcinoma; NAC, neoadjuvant chemotherapy; MIE, minimally invasive esophagectomy

- a) Data were expressed as median (range).
- b) Mann–Whitney U test.
- c) χ^2 test.
- d) Fisher's exact test.

Table 2. Operative outcomes of patients who underwent conventional or robot-assisted minimally invasive esophagectomy.

	Whole cohort		<i>P</i> value	Matched cohort		<i>P</i> value
	Conventional MIE group (n = 353)	RAMIE group (n = 51)		Conventional MIE group (n = 51)	RAMIE group (n = 51)	
Operative time ^{a)}						
Overall procedure	679 (302–1215)	808 (360–1327)	< 0.0001 ^{b)}	655 (452–957)	808 (360–1327)	< 0.0001 ^{b)}
Thoracic procedure	300 (113–600)	440 (180–600)	< 0.0001 ^{b)}	300 (180–464)	440 (180–600)	< 0.0001 ^{b)}
Console time		358 (244–518)			358 (244–518)	
Number of resected mediastinal lymph nodes ^{a)}	22 (10–74)	22 (11–34)	0.397 ^{b)}	23 (12–37)	22 (11–34)	0.556 ^{b)}
Number of resected lymph nodes along the left RLN ^{a)}	4 (0–18)	4 (0–10)	0.371 ^{b)}	4 (0–12)	4 (0–10)	0.324 ^{b)}
Volume of blood loss (mL)	200 (0–10000)	35 (0–380)	< 0.0001 ^{b)}	100 (0–1485)	35 (0–380)	0.0012 ^{b)}
Duration of postoperative hospital stay ^{a)}	30 (9–583)	24 (15–96)	0.013 ^{b)}	27 (14–149)	24 (15–96)	0.615 ^{b)}

MIE, minimally invasive esophagectomy; RAMIE, robot-assisted minimally invasive esophagectomy

a) Data were expressed as median (range).

b) Mann–Whitney U test.

Table 3. RLN palsy in patients who underwent conventional or robot-assisted minimally invasive esophagectomy.

	Whole cohort		<i>P</i> value	Matched cohort		<i>P</i> value
	Conventional MIE group (n = 353)	RAMIE group (n = 51)		Conventional MIE group (n = 51)	RAMIE group (n = 51)	
RLN palsy						
Right side						
C–D classification ^{a)}						
Grade I	10 (3%)	0 (0%)	0.622 ^{d)}	3 (6%)	0 (0%)	0.243 ^{d)}
Grade II	2 (1%)	0 (0%)	1.000 ^{d)}	0 (0%)	0 (0%)	-
Grade III	12 (3%)	0 (0%)	0.377 ^{d)}	0 (0%)	0 (0%)	-
Grades IV, V	0 (0%)	0 (0%)	-	0 (0%)	0 (0%)	-
ECCG definitions ^{b)}						
Type I	12 (3%)	0 (0%)	0.377 ^{d)}	3 (6%)	0 (0%)	0.243 ^{d)}
Type II	10 (3%)	0 (0%)	0.622 ^{d)}	0 (0%)	0 (0%)	-
Type III	2 (1%)	0 (0%)	1.000 ^{d)}	0 (0%)	0 (0%)	-
Left side						
C–D classification ^{a)}						
Grade I	66 (19%)	8 (16%)	0.603 ^{c)}	13 (25%)	8 (16%)	0.221 ^{c)}
Grade II	32 (9%)	0 (0%)	0.022 ^{d)}	5 (10%)	0 (0%)	0.022 ^{d)}
Grade III	19 (5%)	0 (0%)	0.149 ^{d)}	3 (6%)	0 (0%)	0.243 ^{d)}
> Grades IV, V	0 (0%)	0 (0%)	-	0 (0%)	0 (0%)	-
ECCG definitions ^{b)}						

Type I	101 (29%)	8 (16%)	0.041 ^{c)}	18 (35%)	8 (16%)	0.023 ^{c)}
Type II	4 (1%)	0 (0%)	1.000 ^{d)}	1 (2%)	0 (0%)	1.000 ^{d)}
Type III	12 (3%)	0 (0%)	0.377 ^{d)}	2 (4%)	0 (0%)	0.495 ^{d)}

RLN, recurrent laryngeal nerve; MIE, minimally invasive esophagectomy; RAMIE, robot-assisted minimally invasive esophagectomy

- a) Grades were based on the Clavien–Dindo classification of surgical complications.
- b) Types were based on the Esophagectomy Complications Consensus Group definitions.
- c) χ^2 test.
- d) Fisher's exact test.

Table 4. Pneumonia in patients who underwent conventional or robot-assisted minimally invasive esophagectomy.

	Whole cohort		<i>P</i> value	Matched cohort		<i>P</i> value
	Conventional MIE group (n = 353)	RAMIE group (n = 51)		Conventional MIE group (n = 51)	RAMIE group (n = 51)	
Pneumonia						
C–D classification ^{a)}						
Grade I	3 (1%)	2 (4%)	0.122 ^{d)}	1 (2%)	2 (4%)	1.000 ^{d)}
Grade II	44 (12%)	7 (14%)	0.064 ^{c)}	6 (12%)	7 (14%)	0.767 ^{c)}
Grade IIIa	7 (2%)	0 (0%)	0.603 ^{d)}	2 (4%)	0 (0%)	0.495 ^{d)}
Grade IIIb	15 (4%)	0 (0%)	0.234 ^{d)}	2 (4%)	0 (0%)	0.495 ^{d)}
Grade IV	4 (1%)	0 (0%)	1.000 ^{d)}	0 (0%)	0 (0%)	-
Grade V	1 (0.3%)	0 (0%)	1.000 ^{d)}	0 (0%)	0 (0%)	-
Uniform Pneumonia Score ^{b)}						
0	279 (79%)	42 (82%)	0.300 ^{c)}	40 (78%)	42 (82%)	0.618 ^{c)}
1	3 (1%)	1 (2%)	0.418 ^{d)}	1 (2%)	1 (2%)	1.000 ^{d)}
2	22 (6%)	4 (8%)	0.539 ^{d)}	3 (6%)	4 (8%)	1.000 ^{d)}
3	23 (7%)	4 (7%)	0.763 ^{d)}	3 (6%)	4 (8%)	1.000 ^{d)}
≥ 4	27 (8%)	0 (0%)	0.035 ^{d)}	4 (8%)	0 (0%)	0.118 ^{d)}

MIE, minimally invasive esophagectomy; RAMIE, robot-assisted minimally invasive esophagectomy

a) Grades were based on the Clavien–Dindo classification of surgical complications.

b) Scores were based on the Uniform Pneumonia Score. The definition is used for hospital-acquired pneumonia after esophagectomy.

* A score of ≥ 2 with at least 1 point on pulmonary radiography indicates that suspected pneumonia must be treated.

c) χ^2 test.

d) Fisher's exact test.

Table 5. Anastomotic leakage in patients who underwent conventional or robot-assisted minimally invasive esophagectomy.

	Whole cohort		<i>P</i> value	Matched cohort		<i>P</i> value
	Conventional MIE group (n = 353)	RAMIE group (n = 51)		Conventional MIE group (n = 51)	RAMIE group (n = 51)	
Anastomotic leakage						
C–D classification ^{a)}						
Grade I	0 (0%)	0 (0%)	-	0 (0%)	0 (0%)	-
Grade II	15 (4%)	1 (2%)	0.705 ^{d)}	3 (6%)	1 (2%)	0.618 ^{d)}
Grade III	51 (15%)	13 (25%)	0.056 ^{c)}	9 (18%)	13 (25%)	0.336 ^{c)}
Grade IV		0 (0%)		0 (0%)	0 (0%)	-
Grade V		0 (0%)		0 (0%)	0 (0%)	-
ECCG definitions ^{b)}						
Type I	15 (4%)	1 (2%)	0.705 ^{d)}	3 (6%)	1 (2%)	0.618 ^{d)}
Type II	45 (13%)	13 (25%)	0.024 ^{c)}	8 (16%)	13 (25%)	0.221 ^{c)}
Type III	9 (3%)	0 (0%)	0.610 ^{d)}	1 (2%)	0 (0%)	1.000 ^{d)}

MIE, minimally invasive esophagectomy; RAMIE, robot-assisted minimally invasive esophagectomy

a) Grades were based on the Clavien–Dindo classification of surgical complications.

b) Types were based on the Esophagectomy Complications Consensus Group definitions.

c) χ^2 test.

d) Fisher's exact test.