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Impact of Robot-Assisted Minimally Invasive Esophagectomy for Esophageal Cancer: A Propensity Score-Matched Short-Term Analysis

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ABSTRACT

Background We compared short-term clinical outcomes between robotic-assisted minimally invasive esophagectomy (RAMIE) and video-assisted thoracic esophagectomy (VATS-E) using propensity score-matched analysis.

Methods We enrolled 114 patients with esophageal cancer who underwent esophagectomy at our institution from January 2013 to January 2022. Propensity score matching was performed to minimize selection bias between the RAMIE and VATS-E groups.

Results After propensity score matching, 72 patients (RAMIE group, n = 36; VATS-E group, n = 36) were selected for analysis. No significant differences in clinical variables were observed between the two groups. The RAMIE group had a significantly longer thoracic operation time (313 ± 40 vs. 295 ± 35 min, P = 0.048), a higher number of right recurrent laryngeal nerve lymph nodes (4.2 ± 2.7 vs. 2.9 ± 1.9, P = 0.039), and a shorter postoperative hospital stay (23.2 ± 12.8 vs. 30.4 ± 18.6 days, P = 0.018) than the VATS-E group. The RAMIE group tended to have a lower rate of anastomotic leakage (13.9% vs. 30.6%) than the VATS-E group, although the difference was not statistically significant (P = 0.089). No significant differences were found in recurrent laryngeal nerve paralysis (11.1% vs. 13.9%, P = 0.722) or pneumonia (13.9% vs. 13.9%, P = 1.000) between the RAMIE group and the VATS-E group.

Conclusion Although RAMIE for esophageal cancer requires a longer thoracic surgery time, it might be a feasible and safe alternative to VATS-E for treating esophageal cancer. Further analysis is needed to clarify the advantages of RAMIE over VATS-E, especially in terms of long-term surgical outcomes.

Key words esophageal cancer; robotic esophagectomy

Esophageal cancer has a poor prognosis and is the sixth leading cause of cancer-related death worldwide.[1, 2] The treatment strategy for esophageal cancer involves surgery, and both thoracic and abdominal operations are required. Esophagectomy is one of the most invasive gastrointestinal surgeries, with higher complication and mortality rates than surgery for other diseases.[3, 4] Very important complications in esophagectomy include recurrent laryngeal nerve palsy, pneumonia, and anastomotic leakage.[5, 6] Although lymph node dissection around the recurrent laryngeal nerve is important in esophageal cancer surgery, it is associated with unique complications such as recurrent laryngeal nerve palsy. Several studies have shown that complications worsen the prognosis of esophageal cancer,[7, 8] and various attempts are being made to reduce complications. The performance of video-assisted thoracoscopic esophagectomy (VATS-E) has been increasing in recent years as a minimally invasive procedure to reduce complications, and the use of robot-assisted minimally invasive esophagectomy (RAMIE) is also increasing to achieve more accurate surgery.[9–12] Robotic surgery has been shown to be useful in a variety of fields,[13–15] and various reports have described its use in the treatment of esophageal cancer. However, the short-term results of RAMIE still remain insufficient.

This study examined the short-term results of VATS-E and RAMIE performed at our institution using propensity score matching (PSM).

SUBJECTS AND METHODS

Patients

This retrospective study involved 130 patients with esophageal cancer who underwent RAMIE or VATS-E at our institution from January 2013 to January 2022. Patients who underwent total pharyngo-laryngo-esophagectomy, patients who underwent two-stage

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Abbreviations: PSM, propensity score matching; RAMIE, robot-assisted minimally invasive esophagectomy; VATS-E, video-assisted thoracoscopic esophagectomy; 106recR, right recurrent laryngeal nerve lymph node station

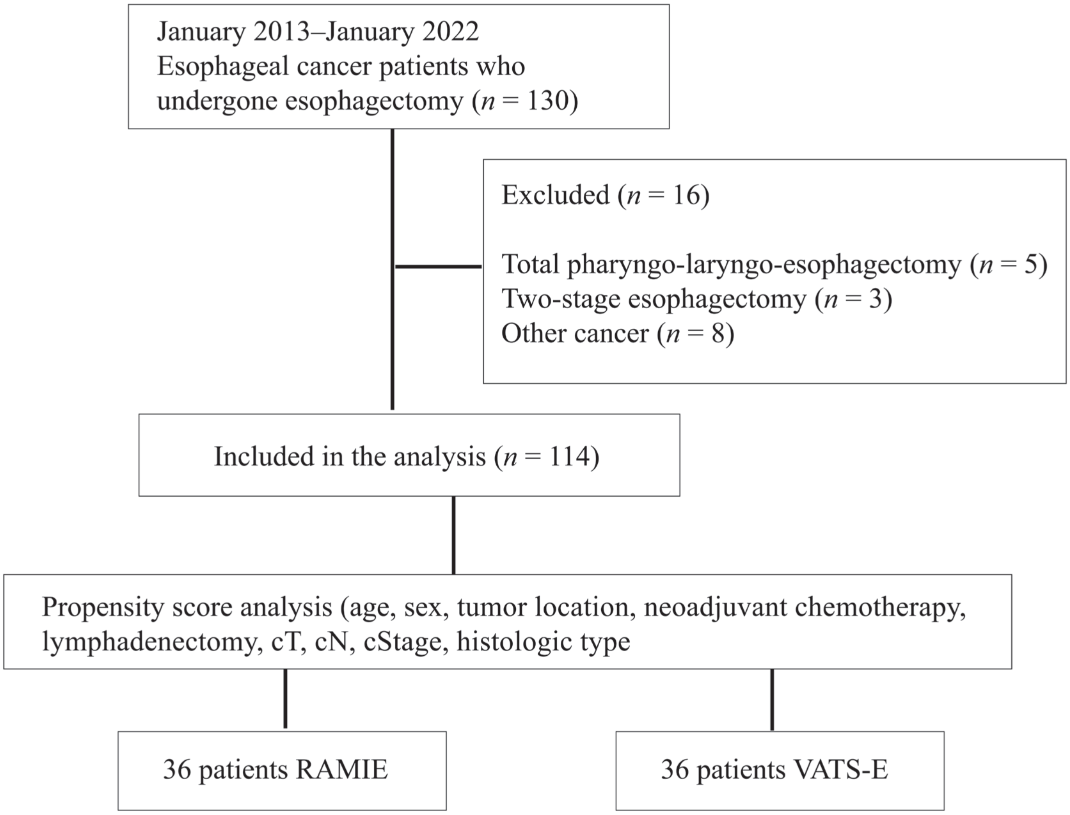

Fig. 1. CONSORT diagram.

esophagectomy, and patients with other cancer were excluded. Finally, 114 patients were included in this study (Fig. 1). We began performing RAMIE in February 2020; since then, we have treated all patients with esophageal cancer by RAMIE. In this study, there were three surgeons for VATS-E, one of them also being a surgeon for RAMIE. The clinicopathological findings were determined according to the Japanese Classification of Esophageal Cancer (11th edition).[16, 17] PSM was performed to minimize selection bias between the two groups. The following variables were selected and matched because they were determined to have a significant survival impact: age, sex (male, female), tumor location (upper, middle, lower), neoadjuvant chemotherapy (present, absent), lymphadenectomy (two-field, three-field), clinical depth of tumor invasion (T1, T2, T3, T4), clinical lymph node metastasis (N0, N1, N2, N3), histologic type (squamous cell carcinoma, adenocarcinoma), and clinical stage (I, II, III).

Treatment strategy

Our treatment strategy for esophageal cancer was as follows: patients with T1 tumors who did not have lymph node metastasis underwent surgery without preoperative treatment; patients with ≥ T2, non-T4b, or node-positive tumors (Stage ≥ 2) received neoadjuvant chemotherapy followed by esophagectomy; and patients with T4 tumors suspected to have invaded other organs (T4b) received chemoradiation therapy. The standard surgical approach was subtotal esophagectomy and reconstruction using a gastric tube. Either two- or three-field lymphadenectomy was performed. Cervical lymph node dissection was not performed in patients with lower thoracic or abdominal esophageal cancer without cervical or upper mediastinal lymph node metastasis.

Surgical procedures

We performed thoracoscopic subtotal esophagectomy with mediastinal lymph node dissection in the prone position under right pneumothorax in all patients in both the VATS-E and RAMIE groups. Lymphadenectomy was performed for the mediastinal lymph nodes, including the right and left recurrent laryngeal nerve nodes, tracheal bifurcation nodes, thoracic paraesophageal nodes, and diaphragmatic nodes. After completion of the thoracic procedure, the patients were repositioned in the supine position, and the cervical and abdominal procedures were started simultaneously. The abdominal procedure was basically performed by hand-assisted laparoscopic surgery except in patients with massive metastasis of abdominal lymph nodes or a history of major abdominal surgery such as laparotomy. In cases of hand-assisted laparoscopic surgery, an 8-cm small laparotomy was performed in the upper abdomen after completion of abdominal lymph node dissection, and the gastric tube was created under direct vision in all cases. From July 2018, we standardized the surgical anastomotic technique using indocyanine green fluorescence imaging as previously reported.[18] The gastric tube was pulled up to the neck through the posterior mediastinal route, and esophagogastric anastomosis was performed on the left side of the neck.

Definitions of perioperative complications

Anastomotic leakage was defined as saliva leakage from the cervical wound, contrast leakage outside the gastrointestinal tract on gastrointestinal series, and abnormal air or fluid accumulation around the anastomosis on computed tomography. Pneumonia was defined as the appearance of consolidation on chest X-ray or computed tomography and the detection of bacteria on sputum culture. Recurrent laryngeal nerve paralysis was diagnosed in patients who complained of hoarseness and dysphagia and when insufficient movement of the vocal cords was observed by laryngofiberscopy.

Statistical analysis

Continuous variables were compared using the Mann–Whitney *U* test. Categorical variables were compared using Fisher's exact test or the χ^2 test. PSM was performed with a logistic regression model and 1:1 nearest neighbor matching (caliper width = 0.2). SPSS for Windows Version 24 (IBM Corp., Armonk, NY) was used for all statistical analyses.

RESULTS

The RAMIE group comprised 46 patients, and the VATS-E group comprised 68 patients (Table 1). The patients' mean age was 65.4 ± 8.0 years, and the study population comprised 99 men and 15 women. Neoadjuvant chemotherapy was performed in 41 patients, and the histology was squamous cell carcinoma in almost all patients. The clinical disease stage was I, II, III, and IV in 39, 36, 38, and 1 patient, respectively.

The patients' clinical variables are shown in Table 1. No significant differences were observed in age, sex, American Society of Anesthesiologists physical status, body mass index, tumor location, neoadjuvant chemotherapy, histology, clinical depth of tumor invasion, clinical lymph node metastasis, or clinical stage between the RAMIE group and the VATS-E group. The patients' surgical variables are shown in Table 2. The RAMIE group had a significantly longer thoracic operation time, lower proportion of abdominal open procedures, higher number of right recurrent laryngeal nerve lymph nodes (lymph node station 106recR), and shorter postoperative hospital stay than the VATS-E group. The postoperative complications are shown in Table 3. No 30-day mortality was observed in either group, but 90-day mortality occurred in one patient in the VATS-E group. The RAMIE group had a significantly lower rate of anastomotic leakage than the VATS-E group. No significant differences in recurrent laryngeal nerve paralysis or pneumonia were observed between the RAMIE group and the VATS-E group.

After PSM, 72 patients (RAMIE group, $n = 36$; VATS group, $n = 36$) were selected for analysis. No significant differences in the clinical variables were observed between the two groups (Table 1). The RAMIE group had a significantly longer thoracic operation time, higher number of 106recR lymph nodes, and shorter postoperative hospital stay than the VATS-E group (Table 2). The RAMIE group tended to have a lower rate of anastomotic leakage than the VATS-E group, although the difference was not statistically significant ($P = 0.089$) (Table 3). No significant differences in recurrent laryngeal nerve paralysis or pneumonia were observed between the RAMIE group and the VATS-E group.

DISCUSSION

This study examined the short-term results of RAMIE and VATS-E and showed that the RAMIE group had a significantly longer thoracic operation time, higher number of 106recR lymph nodes, and shorter postoperative hospital stay than the VATS-E group. In terms of postoperative complications, the RAMIE group tended to have a lower rate of pneumonia and recurrent laryngeal nerve palsy than the VATS-E group; however, there was no significant difference between the two groups after PSM. The RAMIE group had a significantly lower rate of anastomotic leakage than the VATS group before PSM, and the RAMIE group tended to have a lower rate of anastomotic leakage than the VATS-E group after PSM.

Recurrent laryngeal nerve palsy is an important complication in esophagectomy. It is caused by intraoperative damage to the recurrent laryngeal nerve secondary to heat injury or nerve traction. RAMIE has the potential to reduce the incidence of recurrent laryngeal nerve palsy through precise surgical techniques. In the present study, the frequency of recurrent

Table 1. Patient characteristics

		Before PSM			After PSM		
	All	RAMIE	VATS-E		RAMIE	VATS-E	
	(*n* = 114)	(*n* = 46)	(*n* = 68)	*P* value	(*n* = 36)	(*n* = 36)	*P* value
Age (years)	65.4 ± 8.0	65.8 ± 8.2	65.0 ± 7.8	0.575	65.8 ± 8.1	65.1 ± 8.0	0.591
Sex				0.552			0.527
Male	99 (86.8)	41 (89.1)	58 (85.3)		31 (86.1)	29 (80.6)	
Female	15 (13.2)	5 (10.9)	10 (14.7)		5 (13.9)	7 (19.4)	
ASA PS				0.059			0.149
1	10 (8.8)	1 (2.2)	9 (13.2)		1 (2.8)	5 (13.9)	
2	82 (71.9)	33 (71.7)	49 (72.1)		26 (72.2)	26 (72.2)	
3	22 (19.3)	12 (26.1)	10 (14.7)		9 (25.0)	5 (13.9)	
BMI, kg/m^2	21.5 ± 3.3	22.2 ± 3.5	21.1 ± 3.0	0.12	21.9 ± 3.1	21.0 ± 3.4	0.203
Tumor location				0.5			0.929
Upper	26 (22.8)	5 (10.9)	21 (30.9)		4 (11.1)	5 (13.9)	
Middle	59 (51.8)	22 (47.8)	37 (54.4)		18 (50.0)	18 (50.0)	
Lower	29 (25.4)	19 (41.3)	10 (14.7)		14 (38.9)	13 (36.1)	
Neoadjuvant therapy				0.539			1.000
None	73 (64.0)	31 (67.4)	42 (61.8)		23 (63.9)	23 (63.9)	
Chemotherapy	41 (36.0)	15 (32.6)	26 (38.2)		13 (36.1)	13 (36.1)	
Histology				0.085			1.000
SCC	104 (91.2)	39 (84.8)	65 (95.6)		33 (91.2)	33 (91.2)	
Adenocarcinoma	8 (7.0)	5 (10.9)	3 (4.4)		3 (8.8)	3 (8.8)	
Other	2 (1.8)	2 (4.3)	0 (0.0)		0 (0.0)	0 (0.0)	
cT				0.555			0.667
T1	43 (37.7)	14 (30.4)	29 (42.6)		11 (30.6)	13 (36.1)	
T2	27 (23.7)	11 (23.9)	16 (23.5)		8 (22.2)	11 (30.6)	
T3	42 (36.8)	20 (43.5)	22 (32.4)		16 (44.4)	11 (30.6)	
T4	2 (1.8)	1 (2.2)	1 (1.5)		1 (2.8)	1 (2.8)	
cN				0.22			0.767
N0	64 (56.1)	21 (45.7)	43 (63.2)		17 (47.2)	18 (50.0)	
N1	19 (16.7)	10 (21.7)	9 (13.2)		8 (22.2)	7 (19.4)	
N2	26 (22.8)	14 (30.4)	12 (17.6)		11 (30.6)	10 (27.8)	
N3	5 (4.4)	1 (2.2)	4 (5.9)		0 (0.0)	1 (2.8)	
cStage				0.165			0.893
I	39 (34.2)	14 (30.4)	25 (36.8)		11 (30.6)	12 (33.3)	
II	36 (31.6)	11 (23.9)	25 (36.8)		8 (22.2)	9 (25.0)	
III	38 (33.3)	21 (45.7)	17 (25.0)		17 (47.2)	15 (41.7)	
IV	1 (0.9)	0 (0.0)	1 (1.5)		0 (0.0)	0 (0.0)	

Data are presented as mean ± standard deviation or number (percentage) of patients. ASA PS, American Society of Anesthesiologists physical status; BMI, body mass index; cN, clinical lymph node metastasis; cStage, clinical stage; cT, clinical depth of tumor invasion; PSM, propensity score matching; RAMIE, robot-assisted minimally invasive esophagectomy; SCC, squamous cell carcinoma; VATS-E, video-assisted thoracoscopic esophagectomy.

Table 2. Perioperative outcomes of patients with esophageal cancer after thoracoscopic esophagectomy

		Before PSM			After PSM		
	All	RAMIE	VATS-E		RAMIE	VATS-E	
	(n = 114)	(n = 46)	(n = 68)	P value	(n = 36)	(n = 36)	P value
Total operation time, min	617 ± 62	626 ± 58	610 ± 64	0.097	618 ± 57	600 ± 54	0.136
Thoracic operation time, min	306 ± 44	317 ± 40	299 ± 45	0.016	313 ± 40	295 ± 35	0.048
Bleeding, mL	114 ± 105	113 ± 86	115 ± 115	0.273	113 ± 79	111 ± 103	0.382
Lymphadenectomy				0.059			0.800
Two-field	38 (33.3)	20 (43.5)	18 (26.5)		12 (33.3)	11 (30.6)	
Three-field	76 (66.7)	26 (56.5)	50 (73.5)		24 (66.7)	25 (69.4)	
Abdominal procedure				< 0.001			< 0.001
Open	23 (20.2)	1 (2.2)	22 (32.4)		1 (2.8)	12 (33.3)	
Laparoscopic	91 (79.8)	45 (97.8)	46 (67.6)		35 (97.2)	24 (66.7)	
Number of harvested lymph nodes							
106recR	3.6 ± 2.5	4.2 ± 2.5	3.3 ± 2.4	0.037	4.2 ± 2.7	2.9 ± 1.9	0.039
106recL	2.9 ± 2.6	3.0 ± 2.3	2.8 ± 2.8	0.491	3.3 ± 2.4	2.4 ± 2.1	0.122
Radicality of surgery				0.438			0.314
R0	108 (94.7)	45 (97.8)	64 (94.1)		36 (100)	35 (97.2)	
R1/2	5 (5.3)	1 (2.2)	4 (5.9)		0 (0.0)	1 (2.8)	
Postoperative hospital stay, days	31.1 ± 28.3	22.4 ± 11.7	37.2 ± 34.3	< 0.001	23.2 ± 12.8	30.4 ± 18.6	0.018

Data are presented as mean ± standard deviation or number (percentage) of patients. PSM, propensity score matching; RAMIE, robot-assisted minimally invasive esophagectomy; VATS-E, video-assisted thoracoscopic esophagectomy; 106recL, left recurrent laryngeal nerve lymph node station; 106recR, right recurrent laryngeal nerve lymph node station.

Table 3. Complications in patients with esophageal cancer after thoracoscopic esophagectomy

		Before PSM			After PSM		
	All	RAMIE	VATS-E		RAMIE	VATS-E	
	(n = 114)	(n = 46)	(n = 68)	P value	(n = 36)	(n = 36)	P value
Recurrent laryngeal nerve paralysis				0.393			0.722
Present	19 (16.7)	6 (13.0)	13 (19.1)		4 (11.1)	5 (13.9)	
Absent	95 (83.3)	40 (87.0)	55 (80.9)		32 (88.9)	31 (86.1)	
Pneumonia				0.154			1.000
Present	25 (21.9)	7 (15.2)	18 (26.5)		5 (13.9)	5 (13.9)	
Absent	89 (78.1)	39 (84.8)	50 (73.5)		31 (86.1)	31 (86.1)	
Anastomotic leakage				0.005			0.089
Present	28 (24.6)	5 (10.9)	23 (33.8)		5 (13.9)	11 (30.6)	
Absent	86 (75.4)	41 (89.1)	45 (66.2)		31 (86.1)	25 (69.4)	
30-day mortality	0 (0.0)	0 (0.0)	0 (0.0)	1.000	0 (0.0)	0 (0.0)	1.000
90-day mortality	1 (0.9)	0 (0.0)	1 (1.5)	0.409	0 (0.0)	0 (0.0)	1.000

Data are presented as number (percentage) of patients. PSM, propensity score matching; RAMIE, robot-assisted minimally invasive esophagectomy; VATS-E, video-assisted thoracoscopic esophagectomy.

laryngeal nerve palsy was lower in the RAMIE than VATS-E group, although there was no statistically significant reduction in recurrent laryngeal nerve palsy before and after PSM. The importance of lymph node dissection around the bilateral recurrent laryngeal nerve in esophagectomy has also been noted, and the present study examined the number of right and left recurrent laryngeal nerve lymph nodes dissected. The number of lymph nodes dissected around the right recurrent laryngeal nerve was significantly higher in the RAMIE group than in the VATS-E group both before and after PSM. The number of nodes dissected around the left recurrent laryngeal nerve tended to be higher in the RAMIE group than in the VATS-E group, although the difference was not significant. These results suggest that RAMIE may be useful in increasing the number of lymph nodes dissected while preserving the function of the recurrent laryngeal nerve through precise surgical techniques. A trend toward an increased frequency of pneumonia has been noted in patients with recurrent laryngeal nerve palsy; in the present study, however, the frequency of pneumonia in the RAMIE group was lower than that in the VATS-E group (although this difference was not statistically significant).

A disadvantage of RAMIE is the long operation time. Our result of a long thoracic operation time in the RAMIE group is the same as in a previous report by Tsunoda et al.[19] They performed PSM of 165 patients with esophageal cancer who underwent RAMIE or minimally invasive surgery and found significantly longer thoracic operative times in the RAMIE group than in the minimally invasive surgery group both before and after PSM.[19] Morimoto et al.[20] retrospectively analyzed 87 patients who underwent minimally invasive esophagectomy and found that the median operative time of the thoracic approach was significantly longer in the RAMIE group than in the minimally invasive surgery group. Factors that may have contributed to this longer operation time may have been the roll-in/roll-out and docking process unique to robotic surgery as well as the learning curve to operate the robot itself.[21, 22] By contrast, some high-volume centers have reported that RAMIE has rather shorter operative times.[12] Future proficiency with the RAMIE technique may lead to shorter operation times and further reduce complications.

In the present study, we found a significantly lower incidence of anastomotic leakage in the RAMIE group than in the VATS-E group. This result may not be due to the influence of robotic surgery but rather to standardization of the anastomotic technique. As we previously reported, the incidence of anastomotic leakage was historically high in our institution because the anastomotic technique was not standardized and indocyanine green was not used.[18] Therefore, we standardized the anastomotic technique in July 2018, and the frequency of anastomotic leakage improved thereafter. Since RAMIE was started in 2020, the low frequency of anastomotic leakage was due to the standardization of the anastomotic technique, and the significant reduction in the postoperative hospital stay in the RAMIE group may have been due to the lower incidence of anastomotic leakage.

This study had two main limitations. First, this was a retrospective study from a single institution and involved a small number of patients. PSM was used to balance the two groups, but the results must be interpreted carefully because unknown confounding factors might have still affected the results. Second, because of the small number of patients with esophageal cancer at our institution, relatively old cases from 2013 were included in this study.

In conclusion, although RAMIE for esophageal cancer requires a longer thoracic surgery time, it might be a feasible and safe alternative to VATS-E for treating esophageal cancer. Further analysis is needed to clarify the advantages of RAMIE over VATS-E, especially in terms of long-term surgical outcomes.

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The authors declare no conflict of interest.

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