

Robot-assisted minimally invasive esophagectomy versus video-assisted minimally invasive esophagectomy: a systematic review and meta-analysis

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Background: Robot-assisted minimally invasive esophagectomy (RAMIE) has been demonstrated to offer realistic three-dimensional visual clarity, flexible movement and so on. The high cost is the main reason hampering universal application. The aim of this study was to compare the short-term outcomes of RAMIE versus video-assisted minimally invasive esophagectomy (VAMIE).

Methods: The PubMed, EMBASE and Web of Science databases were systematically searched up to June 1, 2021, for studies comparing RAMIE and VAMIE.

Results: Nineteen studies were enrolled, which consisted of a total of 4,714 patients, including 2,306 patients in the RAMIE group and 2,408 patients in the VAMIE group. In RAMIE patients, higher numbers of total lymph nodes (MD =0.171, 95% CI: 0.086–0.255, P<0.001) and lymph nodes along the left recurrent laryngeal nerve (RLN) (MD =0.219, 95% CI: 0.097–0.340, P<0.001) were removed. In RAMIE patients in the McKown group, higher numbers of total lymph nodes (MD =0.173, 95% CI: 0.080–0.265, P<0.001) and lymph nodes along the left RLN (MD =0.220, 95% CI: 0.090–0.350, P=0.001) were removed, while in those in the ESCC group, higher numbers of total lymph nodes (MD =0.249, 95% CI: 0.091–0.407, P=0.002) and lymph nodes along the left RLN (MD =0.239, 95% CI: 0.102–0.377, P=0.001) were removed.

Discussion: This study indicated that the main advantage of RAMIE was a greater number of harvested lymph nodes, which may be beneficial to diagnosis and local control. RCTs with larger sample sizes and studies reporting long-term outcomes are needed to evaluate the advantages and disadvantages of RAMIE and VAMIE.

Keywords: Robot-assisted minimally invasive esophagectomy (RAMIE); video-assisted minimally invasive esophagectomy (VAMIE); meta-analysis; short-term outcomes

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Introduction

Esophageal cancer is a gastrointestinal tumor that ranks seventh in terms of incidence and sixth in mortality (1). Although chemotherapy, radiotherapy and immunotherapy have been widely used in clinical practice, esophagectomy is still the primary treatment for patients with esophageal cancer. Video-assisted minimally invasive esophagectomy (VAMIE) has become increasingly prevalent due to the lower incidence of postoperative complications and shorter hospital stay compared with conventional open esophagectomy (2). However, VAMIE still has some limitations. Recently, the Da Vinci surgical system has been introduced, with advantages including realistic threedimensional visual clarity, flexible movement and so on. This system can filter out tremors and synchronize with surgeons' movements to a certain extent. Nevertheless, the high costs and the lack of haptic feedback are the main disadvantages impeding universal application. The safety and feasibility of robot-assisted minimally invasive esophagectomy (RAMIE) have been confirmed (3). Although RAMIE has been demonstrated to offer better visualization and enable meticulous dissection of the mediastinum structure and lymph nodes, the actual superiorities of RAMIE over VAMIE have not been verified. To date, two meta-analyses (4,5) are available for reporting the comparison between RAMIE and VAMIE. They reached an agreement with a lower incidence of vocal cord palsy in RAMIE and were inconsistent in other aspects. More high-quality studies have been published, and we investigated the actual advantages of RAMIE over VAMIE according to short-term outcomes. We present the following article in accordance with the PRISMA reporting checklist (available at https://dx.doi. org/10.21037/tcr-21-1482).

Methods

Literature search

The PubMed, EMBASE and Web of Science databases were searched from 1980 to June 1, 2021. The following search terms were used: ((((Esophageal Neoplasms) OR (Esophageal Neoplasm)) OR (Neoplasm, Esophageal)) OR (Esophagus Neoplasm)) OR ((Esophagectomy) OR (Esophagectomies))) AND ((((Robotic Surgical Procedures) OR (Procedure, Robotic Surgical)) OR (Procedures, Robotic Surgical)) OR (Robotic Surgical Procedure))) AND (((((Thoracoscopy) OR (Thoracoscopies Pleural Endoscopy)) OR (Pleuroscopy)) OR (Pleuroscopies)) OR (((((Thoracic Surgery, Video-Assisted) OR (Surgeries, Video-Assisted Thoracic)) OR (Surgery, Video-Assisted Thoracic)) OR (Thoracic Surgeries, Video-Assisted))).

Study selection

This meta-analysis enrolled randomized controlled trials (RCTs) and retrospective cohort studies (RCSs) comparing RAMIE and VAMIE in terms of short-term clinical outcomes. The following studies were excluded: case reports or reviews, studies on other topics such as the feasibility of RAMIE and articles with overlapping patients.

Outcomes of interest

The outcomes of interest consisted of the numbers of total lymph nodes, thoracic lymph nodes, and lymph nodes along the left recurrent laryngeal nerve (RLN) and right RLN, RLN paresis, anastomotic leakage, chylothorax, pneumonia, operative time (min), blood loss (mL), length of stay (LOS), 30-day mortality and 90-day mortality.

Quality assessment

The selected studies included 18 RCSs and 1 RCT, and the NOS and Cochrane Library were used for grading according to the types of studies. The risk of bias assessment was carried out by two reviewers (H Chen and Y Liu) independently. A third reviewer (H Peng) arbitrated disagreements.

Statistical analysis

The meta-analysis was performed using Stata 12.0. Continuous variables are presented as the standard mean difference (SMD) with a 95% confidence interval (CI). Dichotomous variables were pooled using risk ratios (RRs) with 95% CIs. Heterogeneity was evaluated by the c^2 -based test and P values. If high heterogeneity was observed (I²>50%), the random-effect model was used; otherwise, the fixed-effect model was used. Forest plots were created to show the pooled estimates for the studies. Subgroup analysis and sensitivity analysis were used to investigate the source of heterogeneity. Publication bias was assessed using Begg's test. P values <0.05 were considered statistically significant.

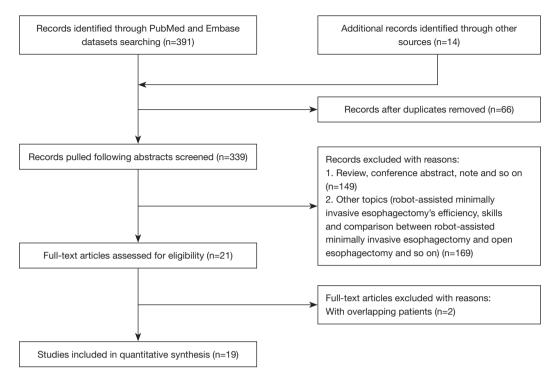


Figure 1 Flow chart of study selection.

Results

Basic characteristics

A total of 391 articles were found in PubMed and EMBASE (Figure 1). Another 14 articles were added after identification through other sources. After removing 66 duplicates, 339 articles remained. After reviewing the titles and abstracts, 318 articles were excluded because they did not fulfill the inclusion criteria. The remaining 21 articles were further assessed for eligibility by examining the full text. Finally, 19 relevant studies (6-24) were included in this meta-analysis. Two studies (25,26) were excluded due to data duplication. The treatment center published more than one article with overlapping patients. The final sample consisted of 4,714 patients, 2,306 of whom were subjected to RAMIE, while 2,408 were subjected to VAMIE. The basic characteristics of the included studies are presented in Table 1. All the incidence rates and mean values in the included studies are shown in Table 2. The RCSs were of high quality based on the NOS. The methodological quality assessment scores are summarized in Figure 2. One study was an RCT, and the quality assessment was high based on Cochrane analysis.

Number of harvested lymph nodes

The number of total lymph nodes excised was described in 12 studies, the number of thoracic lymph nodes was described in 4 studies, and the number of lymph nodes along the left and right RLNs was described in 4 studies. The meta-analysis indicated that in RAMIE patients, higher numbers of total lymph nodes (MD =0.171, 95% CI: 0.086-0.255, P<0.001) and lymph nodes along the left RLN (MD =0.219, 95% CI: 0.097-0.340, P<0.001) were removed (*Figure 3*). Begg's test was conducted to assess publication bias, and no publication bias was found for the number of total lymph nodes (P=0.732) or the number of lymph nodes along the left RLN (P=0.308). The differences between RAMIE and VAMIE were not statistically significant for other aspects.

Postoperative complications

RLN paresis was reported in 14 studies, anastomotic leakage was reported in 15 studies, and chylothorax was reported in 13 studies. Pooled data analysis showed that the differences in RLN paresis, anastomotic leakage and

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Table 1 Characteristics of the selected studies included in the meta-analysis

Study	Year	Country	Group	Number	Gender (M/F)	Age, years	BMI, kg/m ²	Site (upper/mid/lower)	Pathology (ESCC/EAC)	Neoadjuvant therapy	Surgical procedures	Type of study	NOS
Suda	2012	Japan	RAMIE	16	15/1	65 (53 to 86)	21.3 (17.5 to 26.3)	2/7/7	16/0	6	NA	RCS	7
			VAMIE	20	15/5	64.5 (50 to 79)	20.4 (14.9 to 24.8)	2/12/6	20/0	17	NA		
Weksler	2012	America	RAMIE	11	8/3	58.7±8.5	27.1	NA	0/10	4	Ivor-Lewis	RCS	7
			VAMIE	26	20/6	64.3±11.3	27.9	NA	3/23	10	Ivor-Lewis		
Park	2016	South Korea	RAMIE	62	57/5	64.3±8.0	23.5±2.8	8/15/39	62/0	8	Both	RCS	8
			VAMIE	43	40/3	66.2±7.4	23.3±3.1	7/9/27	43/0	4	Both		
Yerokun	2016	America	RAMIE	170	142/28	56/64/70	NA	156/14/0	NA	120	NA	RCS	7
			VAMIE	170	143/27	56/63/69	NA	160/10/0	NA	120	NA		
Weksler	2017	America	RAMIE	569	471/98	62.9±9.6	NA	NA	NA/447	405	NA	RCS	8
			VAMIE	569	489/80	62.8±9.3	NA	NA	NA/468	401	NA		
He	2018	China	RAMIE	27	20/7	61.0±8.0	21.5±2.7	1/18/8	23/NA	0	McKown	RCS	8
			VAMIE	27	20/7	61.6±9.8	21.9±2.8	3/15/9	25/NA	0	McKown		
Deng	2018	China	RAMIE	52	40/12	61.0±7.2	NA	10/33/9	52/0	NA	McKown	RCS	8
			VAMIE	52	39/13	60.9±9.2	NA	7/30/14	52/0	NA	McKown		
Grimminger	2018	Germany	RAMIE	25	22/3	61.1±11.1	25.6±4.3	0/2/23	7/18	9	Ivor-Lewis	RCS	7
-			VAMIE	25	19/6	63±8.7	25.5±4.5	0/5/20	9/16	7	Ivor-Lewis		
Chen	2019	China	RAMIE	54	41/13	61.8±9.4	22.7±2.9	NA	54/0	14	McKown	RCS	8
			VAMIE	54	43/11	61.8±8.3	23.0±2.7	NA	54/0	17	McKown		
Espinoza-Mercado	2019	America	RAMIE	406	NA	NA	NA	NA	NA	NA	NA	RCS	8
			VAMIE	406	NA	NA	NA	NA	NA	NA	NA		
Motoyama	2019	Japan	RAMIE	21	19/2	63 (44–76)	NA	6/7/8	21/0	0	NA	RCS	7
			VAMIE	38	32/6	66 (49–75)	NA	9/16/13	38/0	1	NA		
Washington	2019	America	RAMIE	18	17/1	61.9 (42–76)	27.6 (20.7–38.2)	NA	NA/14	18	McKown	RCS	8
i ao ingron	20.0	7 11101104	VAMIE	18	16/2	58.9 (40–70)	27.5 (19.2–39.4)	NA	NA/15	15	McKown		•
Zhang	2019	China	RAMIE	66	50/16	62.3±7.8	22.9±3.1	0/29/37	64/0	NA	Ivor-Lewis	RCS	8
	20.0	011110	VAMIE	66	50/16	62.0±7.8	23.1±4.5	0/26/40	65/0	NA	Ivor-Lewis		•
Chao	2020	America	RAMIE	39	35/4	57.41±8.59	22.35±2.76	12/16/11	38/1	39	McKown	RCS	8
	2020	7 11101104	VAMIE	67	65/2	54.55±7.93	22.34±3.25	12/35/20	65/2	67	McKown		•
Gong	2020	China	RAMIE	91	78/13	60.04	NA	7/31/53	86/NA	20	McKown	RCS	8
aong	2020	onina	VAMIE	144	130/14	60.22	NA	4/72/68	134/NA	28	McKown	1100	0
Xu	2020	China	RAMIE	292	220/72	64.34±8.25	22.96±2.95	20/214/58	292/0	NA	McKown	RCS	8
Au .	2020	Offina	VAMIE		216/76	64.91±7.99	23.21±3.19	24/214/54	292/0		McKown	105	0
Vang	2020	China	RAMIE	292 271	210/70	63.4±7.1	23.21±3.19 23.2±3.0	38/169/64	292/0	NA 29	McKown	RCS	8
Yang	2020	Griffia								29		6UN	0
	0000	China	VAMIE	271	221/50	63.5±7.4	23.2±2.9	31/171/69	270/0	28	McKown	DOT	
Не	2020	China	RAMIE	94	72/22	61.3±8.2	22.7±2.8	9/64/21	94/0	0	McKown	RCT	
			VAMIE	98	72/76	62.4±9.1	22.8±3.0	7/68/23	98/0	0	McKown		-
Balasubramanian	2021	England	RAMIE	22	14/8	60.91±9.31	19.07±2.08	0/6/6	17/5	17	Both	RCS	8

NA, not available, the enrolled studies did not show the result; RAMIE, robot-assisted minimally invasive esophagectomy; ESCC, esophageal squamous cell carcinoma; EAC, esophageal adenocarcinoma; RCS, retrospective cohort study; RCT, randomized controlled trial; BMI, body mass index; NOS, Newcastle-Ottawa Scale.

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Table 2 Incidence rates and mean values in the included studies

Study	Group	Ν	Total lymph nodes dissected	Thoracic lymph nodes dissected	Lymph nodes dissected along left RLN	Lymph nodes dissected along right RLN	RLN paresis	Anastomotic leak	Chylothorax	Pneumonia	Operative time	Blood loss	LOS	30-day mortality	90-day mortality
Suda	RAMIE	16	37.5 (23 to 63)	18.5 (11 to 39)	5.5 (0 to 13)	NA	9	6	0	1	NA	NA	22 (7 to 67)	0	0
	VAMIE	20	39 (24 to 63)	22.5 (13 to 41)	6.5 (0 to 14)	NA	17	2	2	4	NA	NA	35.5 (20 to 135)	0	0
Weksler	RAMIE	11	23±10	NA	NA	NA	1	1	NA	1	NA	NA	8.7±3.4	NA	NA
	VAMIE	26	23±10	NA	NA	NA	1	4	NA	4	NA	NA	10.0±7.7	NA	NA
Park	RAMIE	62	37.3±17.1	NA	NA	NA	8	5	NA	NA	490.3±84.0	462.9±493.9	NA	1	NA
	VAMIE	43	28.7±11.8	NA	NA	NA	10	1	NA	NA	458.4±111.9	466.8±333.0	NA	0	NA
Yerokun	RAMIE	170	11/16/21	NA	NA	NA	NA	NA	NA	NA	NA	NA	8/10/14	10	NA
	VAMIE	170	11/16/22	NA	NA	NA	NA	NA	NA	NA	NA	NA	8/10/13	15	NA
Weksler	RAMIE	569	16.0 (10.0 to 23.0)	NA	NA	NA	NA	NA	NA	NA	349±45	119±72	NA	32	46
	VAMIE	569	16.0 (10.0 to 23.0)	NA	NA	NA	NA	NA	NA	NA	285±66	158±82	NA	56	39
Не	RAMIE	27	20±7	NA	NA	NA	4	3	0	5	NA	NA	13.8±2.0	NA	0
	VAMIE	27	19±5	NA	NA	NA	3	1	1	2	NA	NA	12.8±2.7	NA	1
Deng	RAMIE	52	21.5±8.4	11.8±5.1	1.0±1.8	2.4±1.9	7	3	0	5	353.0±71.8	NA	14.3±6.9	NA	2
	VAMIE	52	17.3±6.5	10.1±4.3	0.4±0.8	1.9±2.2	4	2	1	4	274.2±51.7	NA	12.7±7.7	NA	2
Grimminger	RAMIE	25	24.5±11.4	NA	NA	NA	NA	3	1	2	410.2±75.1	NA	21.8±18.1	0	1
	VAMIE	25	25.0±9.4	NA	NA	NA	NA	4	0	3	338.8±52.1	NA	17.2±11.9	0	0
Chen	RAMIE	54	25.4±7.5	NA	NA	NA	7	5	1	8	187.2±34.0	NA	17.1±10.1	0	NA
	VAMIE	54	24.7±11.2	NA	NA	NA	17	2	2	13	193.4±27.1	NA	15.2±9.8	0	NA
Espinoza-Mercado	RAMIE	406	17 (11 to 24)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	16	31
	VAMIE	406	16 (10 to 22)	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA	13	25
Motoyama	RAMIE	21	52 (36 to 104)	23 (11 to 41)	6 (0 to 15)	NA	7	1	1	0	634 (529 to 699)	NA	NA	NA	NA
	VAMIE	38	59 (35 to 97)	20 (7 to 68)	4 (0 to 12)	NA	30	3	1	0	598.5 (475 to 761)	NA	NA	NA	NA
Washington	RAMIE	18	14.28 (4 to 30)	NA	NA	NA	NA	1	NA	NA	168 (127 to 212)	NA	9.9 (7 to 20)	NA	NA
	VAMIE	18	13.9 (2 to 28)	NA	NA	NA	NA	1	NA	NA	164 (135 to 25 to 228)	NA	9.8 (7 to 27)	NA	NA
Zhang	RAMIE	66	19.2±9.2	10.3±5.8	1.3±1.9	1.4±1.6	4	5	0	4	NA	200.0 (100.0 to 262.5)	9.0 (8.0 to 12.3)	0	1
	VAMIE	66	19.3±9.5	11.9±8.3	0.9±1.9	1.6±2.8	3	3	1	5	NA	200.0 (150.0 to 245.0)	9.0 (8.0 to 11.3)	0	1
Chao	RAMIE	39	29 (26 to 33)	14 (10 to 17)	3 (1 to 5)	1 (1 to 2)	4	NA	0	1	NA	NA	NA	0	0
	VAMIE	67	28 (21 to 35)	14 (10 to 17)	1 (0 to 4)	2 (1 to 3)	19	NA	2	11	NA	NA	NA	0	3
Gong	RAMIE	91	22.84±8.37	NA	2.35±3.00	2.74±2.03	20	4	1	9	318.02±53.90	215.49±125.40	16.57±8.00	NA	0
	VAMIE	144	23.07±10.18	NA	1.95±2.67	2.57±2.08	34	10	1	15	321.13±57.21	200.49±59.54	18.73±13.29	NA	0
Xu	RAMIE	292	21.83±7.73	12.60±4.22	2.27±0.90	3.06±1.05	24	21	3	25	NA	NA	NA	NA	4
	VAMIE	292	20.85±4.73	11.83±3.12	2.09±0.79	2.97±1.08	27	24	4	29	NA	NA	NA	NA	4
Yang	RAMIE	271	20.3±9.9	12.4±7.0	NA	NA	79	32	4	24	244.5±60.4	210.7±86.8	11 (6 to 54)	NA	0
	VAMIE	271	19.2±9.6	12.4±6.5	NA	NA	41	39	2	34	276.0±59.4	209.6±107.4	11 (4 to 94)	NA	2
He	RAMIE	94	29.2±12.5	NA	NA	NA	6	7	2	6	304.2±82.5	202.5±73.4	12 (5 to 78)	2	NA
	VAMIE	98	22.8±13.3	NA	NA	NA	9	9	2	9	315.5±35.7	216.8±44.6	13 (8 to 125)	1	NA
Balasubramanian	RAMIE	22	23.95±8.23	NA	NA	NA	3	0	1	3	513.18±91.23	138.86±31.2	12.18±6.35	NA	NA
	VAMIE	22	22.73±11.63	NA	NA	NA	1	1	1	4	444.77±64.91	133.18±34.8	12.73±7.83	NA	NA

NA, not available, the enrolled studies did not show the result; RLN, recurrent laryngeal nerve; LOS, length of stay; RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.

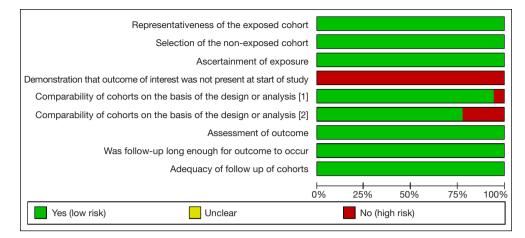


Figure 2 The Newcastle-Ottawa scale.

chylothorax were not statistically significant (*Figure 4*). Pneumonia was reported in 14 studies. One study did not divide patients into RAMIE and VAMIE groups and was therefore excluded. In 2 studies, RAMIE patients developed pneumonia more frequently than VAMIE patients. Moreover, VAMIE patients had a higher pneumonia incidence in 11 studies. Pooled data analysis showed that RAMIE was associated with a lower incidence of pneumonia (RR =0.842, 95% CI: 0.716–0.989, P=0.036).

Operative time, blood loss and LOS

A total of 9 studies reported the operative time. In 5 studies, RAMIE patients had longer operative times than VAMIE patients, while VAMIE patients had longer operative times in 4 studies. The meta-analysis showed no significant difference between RAMIE and VAMIE (P=0.161). Blood loss was reported in 6 studies, and LOS was reported in 7 studies. No significant differences in blood loss and LOS were found between these two techniques (*Figure 5*).

Mortality after the operation

The 30-day mortality rate was reported in 5 studies, and the 90-day mortality rate was reported in 9 studies. As shown in *Figure 6*, pooled data analysis showed that differences were not statistically significant for 30-day mortality (RR =0.826, 95% CI: 0.680-1.003, P=0.053) or 90-day mortality (RR =1.059, 95% CI: 0.911-1.231,

P=0.457).

Subgroup analysis

Summary of the meta-analysis results are shown in Table 3. According to surgical methods, patients were assigned to the McKown group in 9 studies and to the Ivor-Lewis group in 3 studies. In the McKown group, higher numbers of total lymph nodes (MD =0.173, 95% CI: 0.080-0.265, P<0.001) and lymph nodes along the left RLN (MD =0.220, 95% CI: 0.090-0.350, P=0.001) were removed in RAMIE patients than in VAMIE patients. No significant difference was found between RAMIE and VAMIE in the Ivor-Lewis group. Based on pathology, patients were diagnosed with esophageal squamous cell carcinoma (ESCC) in 9 studies, while esophageal adenocarcinoma (EAC) was not diagnosed in any studies. In the ESCC group, higher numbers of total lymph nodes (MD =0.249, 95% CI: 0.091–0.407, P=0.002) and lymph nodes along the left RLN (MD =0.239, 95% CI: 0.102–0.377, P=0.001) were removed in the RAMIE patients (Figure 7).

Discussion

Esophageal cancer causes a serious global health burden, and esophagectomy is considered the primary treatment. Traditional open esophagectomy has been gradually replaced by VAMIE. Some RCTs (27-29) have shown that VAMIE is associated with a lower incidence of postoperative complications and a better prognosis than open esophagectomy. Over the past decade, the Da Vinci

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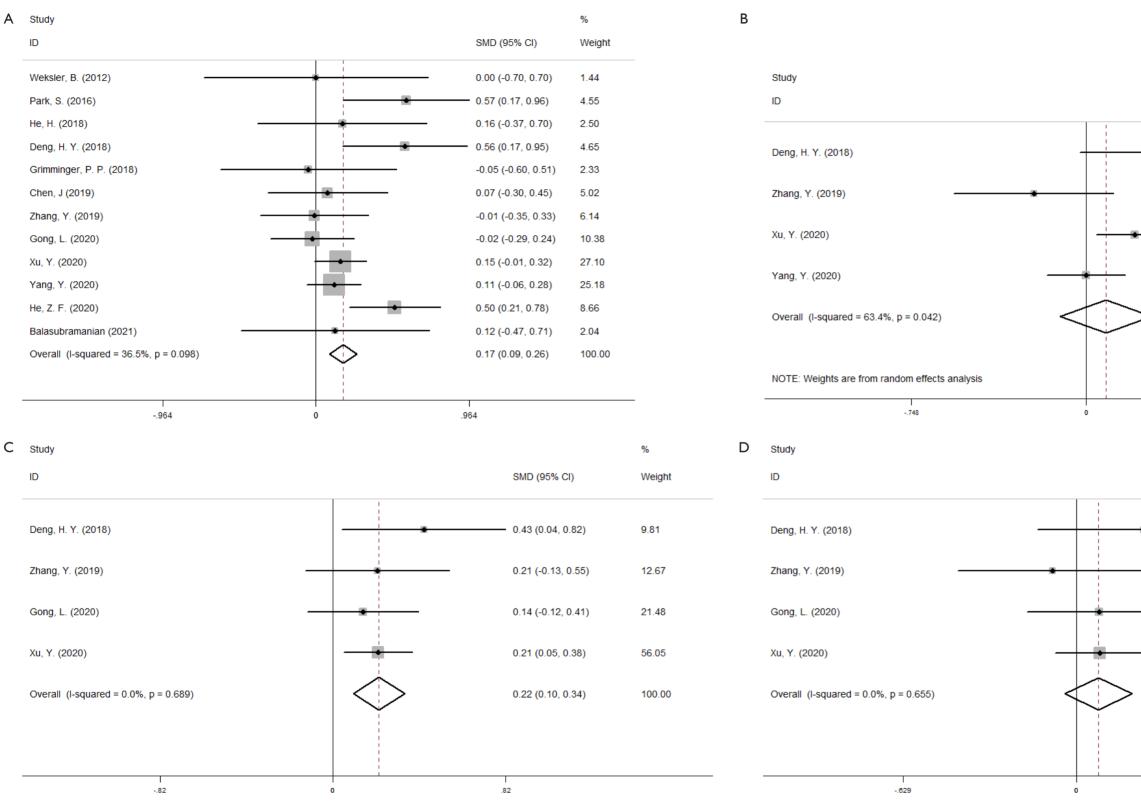


Figure 3 Comparison of the numbers of total lymph nodes (A), thoracic lymph nodes (B), lymph nodes along the left RLN (C) and right RLN (D) between RAMIE and VAMIE. RLN, recurrent laryngeal nerve; RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.

		%
	SMD (95% CI)	Weight
*	0.36 (-0.03, 0.75)	16.07
	-0.22 (-0.57, 0.12)	18.61
<u> </u>	0.21 (0.04, 0.37)	32.92
	0.00 (-0.17, 0.17)	32.40
>	0.08 (-0.11, 0.28)	100.00

	Γ
7	48

		%
	SMD (95% CI)	Weight
*	0.24 (-0.14, 0.63)	9.91
_	-0.09 (-0.43, 0.25)	12.66
	0.08 (-0.18, 0.35)	21.40
-	0.08 (-0.08, 0.25)	56.03
	0.08 (-0.04, 0.20)	100.00

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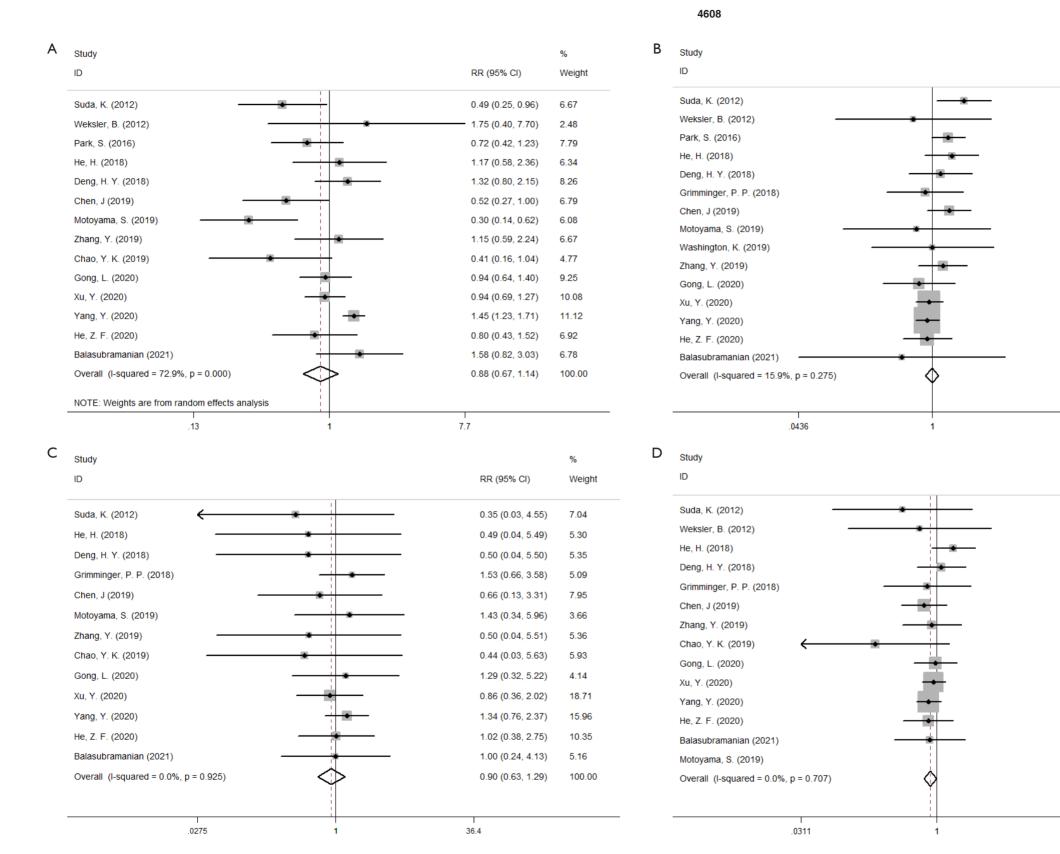


Figure 4 Comparison of RLN paresis (A), anastomotic leakage (B), chylothorax (C) and pneumonia (D) between RAMIE. RLN, recurrent laryngeal nerve; RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.

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	%
RR (95% CI)	Weight
2.10 (1.11, 3.97)	2.50
0.64 (0.10, 3.98)	1.52
1.45 (0.97, 2.15)	3.67
1.56 (0.83, 2.95)	2.00
1.21 (0.58, 2.55)	2.65
0.84 (0.34, 2.07)	3.47
1.47 (0.88, 2.45)	3.58
0.69 (0.12, 3.89)	1.53
1.00 (0.24, 4.16)	1.06
1.27 (0.72, 2.24)	4.16
0.73 (0.31, 1.69)	5.84
0.93 (0.67, 1.28)	23.51
0.89 (0.68, 1.17)	35.25
0.89 (0.50, 1.57)	8.16
0.49 (0.04, 5.49)	1.10
0.99 (0.85, 1.15)	100.00

23

	%
RR (95% CI)	Weight
0.41 (0.07, 2.48)	2.09
0.64 (0.10, 3.98)	1.36
1.53 (0.87, 2.67)	2.87
1.12 (0.60, 2.08)	4.09
0.78 (0.26, 2.38)	2.31
0.72 (0.40, 1.29)	8.99
0.88 (0.42, 1.87)	4.25
0.21 (0.03, 1.37)	4.32
0.96 (0.56, 1.66)	8.41
0.92 (0.68, 1.24)	24.81
0.81 (0.59, 1.11)	26.56
0.80 (0.43, 1.52)	6.91
0.83 (0.34, 2.08)	3.04
(Excluded)	0.00
0.84 (0.72, 0.99)	100.00

32.2

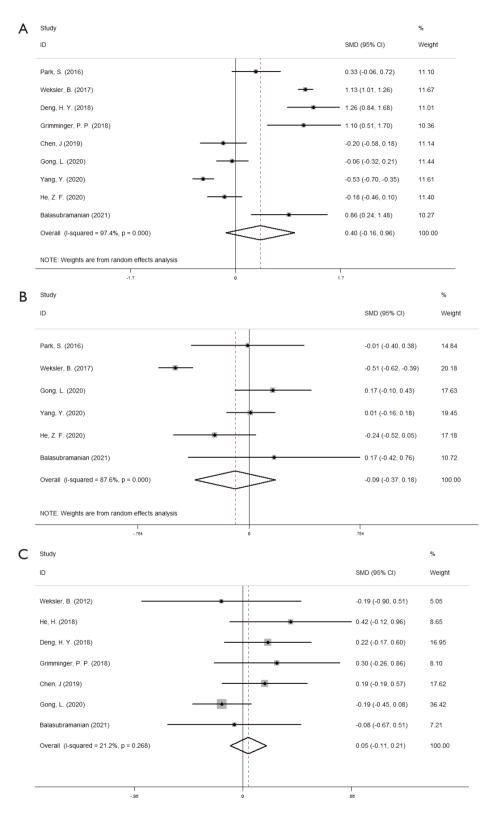


Figure 5 Comparison of operative time (A), blood loss (B) and LOS (C) between RAMIE and VAMIE. LOS, length of stay; RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.

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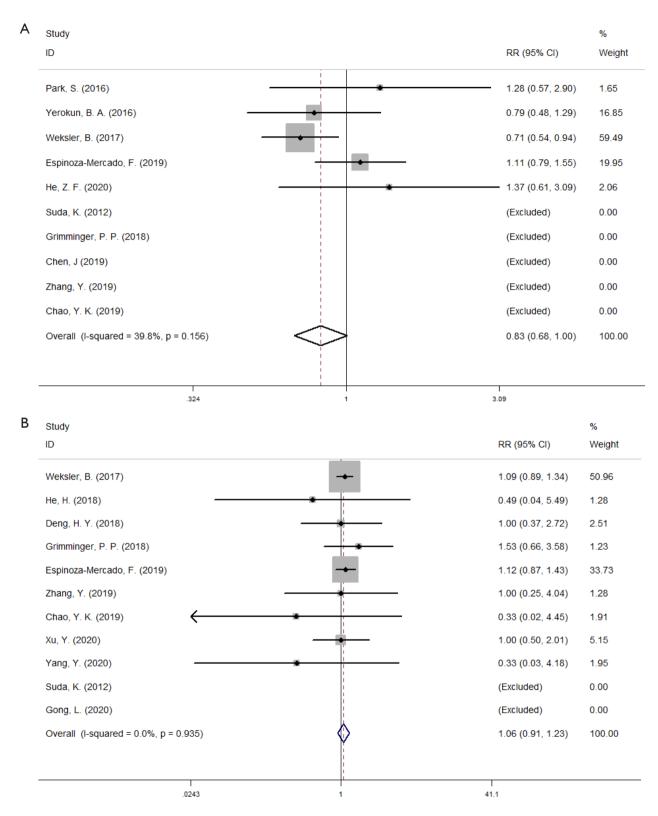


Figure 6 Comparison of 30-day mortality (A) and 90-day mortality (B) between RAMIE and VAMIE. RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.

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Table 3 Summary of the meta-analysis results

Outcomes of interest	Number	Inference	Fixed-effects mod	el	Random-effects mo	odel	Heterogeneity	
Jucomes of interest	Number	Interence	SMD/RR (95% CI)	Р	RR (95% CI)	Р	²	Р
otal								
Total lymph nodes	12	7, 8, 11, 12, 13, 14, 17, 20, 21, 22, 23, 24	0.171 (0.086, 0.255)	0.000	0.185 (0.066, 0.304)	0.002	36.50%	0.09
Thoracic lymph nodes	4	12, 18, 21, 22	0.094 (-0.012, 0.201)	0.082	0.085 (-0.112, 0.282)	0.400	63.40%	0.04
Lymph nodes along the left RLN	4	12, 18, 20, 21	0.219 (0.097, 0.340)	0.000	0.219 (0.097, 0.340)	0.000	0.00%	0.6
Lymph nodes along the right RLN	4	12, 18, 20, 21	0.078 (-0.043, 0.199)	0.208	0.078 (-0.043, 0.199)	0.208	0.00%	0.6
RLN paresis	14	6, 7, 8, 11, 12, 14, 16, 18, 19, 20, 21, 22, 23, 24	0.988 (0.880, 1.110)	0.844	0.876 (0.673, 1.140)	0.324	72.90%	0.0
Anastomotic leak	15	6, 7, 8, 11, 12, 13, 14, 16, 17, 18, 20, 21, 22, 23, 24	0.986 (0.848, 1.146)	0.852	1.110 (0.940, 1.312)	0.219	15.90%	0.27
Chylothorax	13	6, 11, 12, 13, 14, 16, 18, 19, 20, 21, 22, 23, 24	0.897 (0.625, 1.288)	0.558	1.086 (0.786, 1.502)	0.617	0.00%	0.92
Pneumonia	13	6, 7, 11, 12, 13, 14, 18, 19, 20, 21, 22, 23, 24	0.842 (0.716, 0.989)	0.036	0.895 (0.765, 1.048)	0.167	0.00%	0.70
Operative time	9	8, 10, 12, 13, 14, 20, 22, 23, 24	0.432 (0.350, 0.514)	0.000	0.400 (-0.159, 0.960)	0.161	97.40%	0.00
Blood loss	6	8, 10, 20, 22, 23, 24	-0.251 (-0.335, -0.168)	0.000	-0.094 (-0.372, 0.183)	0.506	87.60%	0.00
LOS	7	7, 11, 12, 13, 14, 20, 24	0.048 (-0.111, 0.207)	0.553	0.072 (-0.116, 0.260)	0.453	21.20%	0.26
30-day mortality	5	8, 9, 10, 15, 23	0.826 (0.680, 1.003)	0.053	0.923 (0.706, 1.209)	0.562	39.80%	0.15
90-day mortality	9	10, 11, 12, 13, 15, 18, 19, 21, 22	1.059 (0.911, 1.231)	0.457	1.091 (0.941, 1.265)	0.248	0.00%	0.93
1cKown								
Total lymph nodes	7	11, 12, 14, 20, 21, 22, 23	0.173 (0.080, 0.265)	0.000	0.195 (0.053, 0.338)	0.007	48.10%	0.07
Thoracic lymph nodes	3	12, 21, 22	0.128 (0.016, 0.240)	0.025	0.148 (-0.038, 0.333)	0.118	55.70%	0.10
Lymph nodes along the left RLN	3	12, 20, 21	0.220 (0.090, 0.350)	0.001	0.220 (0.090, 0.350)	0.001	0.00%	0.00
Lymph nodes along the right RLN	3	12, 20, 21	0.102 (-0.028, 0.232)	0.124	0.102 (-0.028, 0.232)	0.124	0.00%	0.74
RLN paresis	8	11, 12, 14, 19, 20, 21, 22, 23	1.068 (0.940, 1.213)	0.315	0.956 (0.717, 1.275)	0.760	71.10%	0.00
Anastomotic leak	8	11, 12, 14, 19, 20, 21, 22, 23	0.942 (0.793, 1.118)	0.492	0.995 (0.842, 1.175)	0.950	0.00%	0.48
Chylothorax	8	11, 12, 14, 19, 20, 21, 22, 23	0.902 (0.594, 1.369)	0.627	1.046 (0.713, 1.533)	0.819	0.00%	0.8
Pneumonia	8	11, 12, 14, 19, 20, 21, 22, 23	0.855 (0.721, 1.014)	0.072	0.912 (0.758, 1.098)	0.332	11.80%	0.33
Operative time	5	12, 14, 20, 22, 23	-0.207 (-0.324, -0.091)	0.000	0.038 (-0.452, 0.528)	0.879	93.50%	0.00
Blood loss	3	20, 22, 23	-0.002 (-0.129, 0.124)	0.971	-0.011 (-0.207, 0.185)	0.916	52.40%	0.12
LOS	4	11, 12, 19, 20	0.049 (-0.129, 0.227)	0.590	0.109 (-0.161, 0.379)	0.430	51.70%	0.10
30-day mortality	1	23	1.370 (0.607, 3.089)	0.449	_	-	-	-
90-day mortality	5	11, 12, 19, 21, 22	0.747 (0.421, 1.325)	0.318	0.878 (0.516, 1.496)	0.633	0.00%	0.75
SCC								
Total lymph nodes	7	8, 12, 14, 18, 21, 22, 23	0.206 (0.112, 0.300)	0.000	0.249 (0.091, 0.407)	0.002	56.60%	0.03
Thoracic lymph nodes	4	12, 18, 21, 22	0.094 (-0.012, 0.201)	0.082	0.085 (-0.112, 0.282)	0.400	63.40%	0.04
Lymph nodes along the left RLN	3	12, 18, 21	0.239 (0.102, 0.377)	0.001	0.239 (0.102, 0.377)	0.001	0.00%	0.58
Lymph nodes along the right RLN	3	12, 18, 21	0.077 (-0.060, 0.214)	0.272	0.077 (-0.060, 0.214)	0.272	0.00%	0.44
RLN paresis	9	6, 8, 12, 14, 16, 18, 21, 22, 23	1.016 (0.896, 1.151)	0.806	0.812 (0.578, 1.140)	0.229	80.10%	0.00
Anastomotic leak	9	6, 8, 12, 14, 16, 18, 21, 22, 23	1.009 (0.860, 1.182)	0.917	1.148 (0.932, 1.413)	0.195	37.20%	0.1
Chylothorax	8	6, 12, 14, 16, 18, 21, 22, 23	0.890 (0.585, 1.354)	0.587	1.047 (0.714, 1.536)	0.814	0.00%	0.8
Pneumonia	7	6, 12, 14, 16, 18, 21, 22	0.844 (0.705, 1.011)	0.065	0.860 (0.718, 1.028)	0.098	0.00%	0.9
Operative time	5	8, 12, 14, 22, 23	-0.188 (-0.311, -0.064)	0.003	0.119 (-0.439, 0.677)	0.675	94.00%	0.0
Blood loss	3	8, 22, 23	-0.048 (-0.184, 0.088)	0.490	-0.053 (-0.202, 0.095)	0.481	9.50%	0.3
LOS	2	12, 14	0.205 (-0.065, 0.475)	0.137	0.205 (-0.065, 0.475)	0.137	0.00%	0.9
30-day mortality	2	8, 23	1.330 (0.744, 2.377)	0.336	1.324 (0.744, 2.356)	0.339	0.00%	0.9
90-day mortality	4	12, 18, 21, 22	0.880 (0.513, 1.511)	0.644	0.955 (0.569, 1.603)	0.861	0.00%	0.8

RLN, recurrent laryngeal nerve; LOS, length of stay; ESCC, esophageal squamous cell carcinoma; SMD, STD mean difference; RR, relative risk; CI, confidence Interval.

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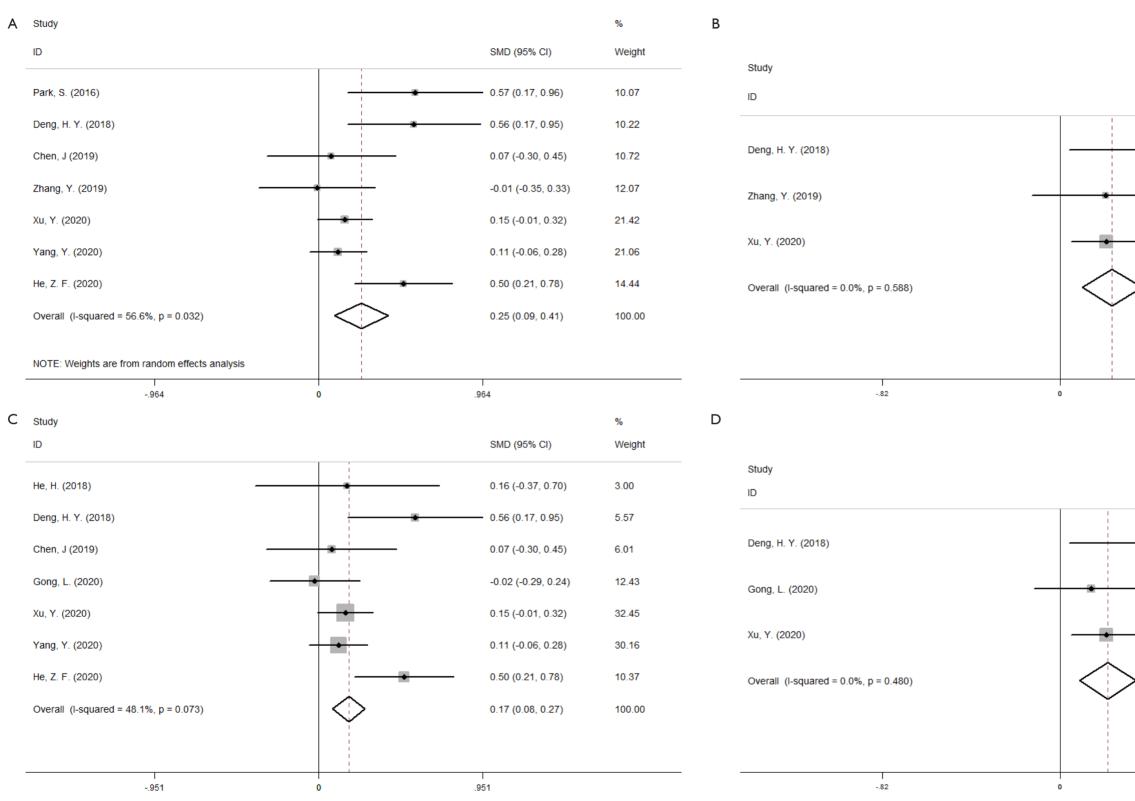


Figure 7 Comparison of the numbers of total lymph nodes (A) and lymph nodes along the left RLN (B) in the ESCC group and the numbers of total lymph nodes (C) and lymph nodes along the left RLN (D) in the McKown group between RAMIE and VAMIE. RLN, recurrent laryngeal nerve; ESCC, esophageal squamous cell carcinoma; RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.

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		%
	SMD (95% CI)	Weight
•	0.43 (0.04, 0.82)	12.49
	0.21 (-0.13, 0.55)	16.13
-	0.21 (0.05, 0.38)	71.38
>	0.24 (0.10, 0.38)	100.00

.82

		%
	SMD (95% CI)	Weight
*	0.43 (0.04, 0.82)	11.23
_	0.14 (-0.12, 0.41)	24.59
-	0.21 (0.05, 0.38)	64.18
>	0.22 (0.09, 0.35)	100.00

.82

surgical system has been applied to esophagectomy in an increasing number of hospitals. Although a large number of studies have reported the safety and efficiency of RAMIE, the high cost prevents its extensive application. Whether RAMIE can achieve better benefits than VAMIE is particularly important. To our knowledge, this is the third meta-analysis comparing outcomes between RAMIE and VAMIE. Jin et al. (4) reported the first meta-analysis and showed that RAMIE was associated with less estimated blood loss and a lower rate of RLN paresis. Zheng et al. (5) was the second to explore the difference through a meta-analysis and found that RAMIE was associated with a longer operative time and a lower incidence of pneumonia. More high-quality studies have subsequently been published. This meta-analysis enrolled 18 RCSs and 1 random control trial, which was published recently. We found that RAMIE was associated with higher numbers of total lymph nodes harvested and lymph nodes harvested along the left RLN and a lower incidence of pneumonia. No statistically significant difference between the two techniques was observed regarding the numbers of thoracic lymph nodes and lymph nodes along the right RLN, RLN paresis, anastomotic leakage, chylothorax, operative time, blood loss, length of stay (LOS), 30-day mortality or 90-day mortality. Vocal cord palsy is related to the extent of lymph node excision along the RLN.

The Da Vinci surgical system has more technical advantages. Its monitor and equipment are oriented in the same direction, which is beneficial to natural handeye coordination. The surgeon can adjust the camera lens to obtain a suitable surgical field without the aid of an assistant. The three-dimensional self-controlled magnified view allows better visualization of the upper mediastinum. Special equipment with 7 degrees of freedom provides surgical assistance in a limited anatomical space. The system can filter out tremors and synchronize with surgeons' movements to a certain extent, which can ensure stable and meticulous operation. Surgeons can be more focused without standing for a long time. However, a lack of haptic feedback complicates distinction of different organs based on hardness. The surgeon leading the team performs the operation using a console that is not located on the operating table and must address emergencies after meeting sterile requirements.

Lymphadenectomy is an important part of esophagectomy. Lymph node excision, especially along the bilateral RLNs, is crucial for both accurate staging and local control and can be expected to improve clinical outcomes in both ESCC and esophageal adenocarcinoma (30). Skeletonization of the RLN is facilitated by robotics given the articulated and non-tremulous arms. However, careful avoidance of thermal damage and transient traction to the RLN is required to prevent RLN paresis (31). This meta-analysis showed that RAMIE was associated with higher numbers of total lymph nodes harvested and lymph nodes harvested along the left RLN. This result persisted after subgroup analyses based on surgical methods and pathology.

Jin found that RAMIE was associated with a lower incidence of vocal cord palsy based on the finding that the difference in the number of lymph nodes harvested was not statistically significant. Zheng found a similar result when comparing the number of harvested lymph nodes. This meta-analysis indicated that in RAMIE patients, a higher number of lymph nodes along the left RLN were removed. However, no difference in the incidence of vocal cord palsy was found between RAMIE and VAMIE, which we speculated was because surgeons previously emphasized reducing the incidence of complications, but surgeons currently focus on removing a higher number of lymph nodes along the left RLN to improve prognosis.

Zheng *et al.* found that the operative time for RAMIE was significantly longer than that for VAMIE. The potential reasons may be as follows: (I) an assistant must reposition the robotic cart twice during each operation, and (II) surgeons were unfamiliar with RAMIE. Our results confirmed that the operative time would be shorter according to the learning curve with the development of robotic techniques and proficiency. No significant difference in blood loss or LOS was noted.

This meta-analysis found that RAMIE was associated with a lower incidence of pneumonia than VAMIE. However, we could not reach this conclusion in the McKown group and ESCC group. No differences in RLN paresis, anastomotic leakage or chylothorax were found between the two techniques. The 30-day mortality and 90day mortality showed no significant difference.

Two studies (25,26) were excluded due to data duplication. The treatment center published more than one article with overlapping patients. Motoyama (32) found that RAMIE could reduce the incidence of recurrence at the surgical site. Long-term outcomes, such as overall survival (OS) and disease-free survival (DFS), must be compared between RAMIE and VAMIE. Some complications, such as necrosis and TEF, should be considered. However, these complications have rarely been compared between RAMIE and VAMIE due to their low incidence rates. As more patients receive RAMIE, the incidence rates of necrosis and TEF must be evaluated in the future. More large-scale clinical studies, such as the study by Yang *et al.* (33) are urgently needed to compare these two techniques.

Conclusions

This study indicated that RAMIE and VAMIE had similar effects and safety. The main advantage of RAMIE is a greater number of harvested lymph nodes, which may be beneficial to diagnosis and local control. RCTs with larger sample sizes and studies reporting long-term outcomes are needed to evaluate the advantages and disadvantages of RAMIE and VAMIE.

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Footnote

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Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at https://dx.doi.org/10.21037/tcr-21-1482). 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.

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