



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

Hao Chen<sup>1#^</sup>, Yiyang Liu<sup>1#</sup>, Hao Peng<sup>2</sup>, Rongchun Wang<sup>2</sup>, Kang Wang<sup>1</sup>, Demin Li<sup>1</sup>

<sup>1</sup>Department of Cardiothoracic Surgery, Jinling Hospital, Jinling School of Clinical Medicine, Nanjing Medical University, Nanjing, China;

<sup>2</sup>Department of Cardiothoracic Surgery, Affiliated Jinling Hospital, Medical School of Nanjing University, Nanjing, China

*Contributions:* (I) Conception and design: H Chen, Y Liu, D Li; (II) Administrative support: D Li, K Wang; (III) Provision of study materials or patients: H Chen, R Wang; (IV) Collection and assembly of data: H Chen, Y Liu; (V) Data analysis and interpretation: H Chen, H Peng; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.

<sup>#</sup>These authors contributed equally to this work.

*Correspondence to:* Demin Li, MD, PhD; Kang Wang, MD. Department of Cardiothoracic Surgery, Jinling Hospital, Jinling School of Clinical Medicine, Nanjing Medical University, 305 East Zhongshan Road, Xuanwu District, Nanjing 210002, China. Email: dr.demin@126.com; lw37413@sina.com.

**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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<sup>^</sup> ORCID: 0000-0001-9683-8278.

## 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 three-dimensional 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

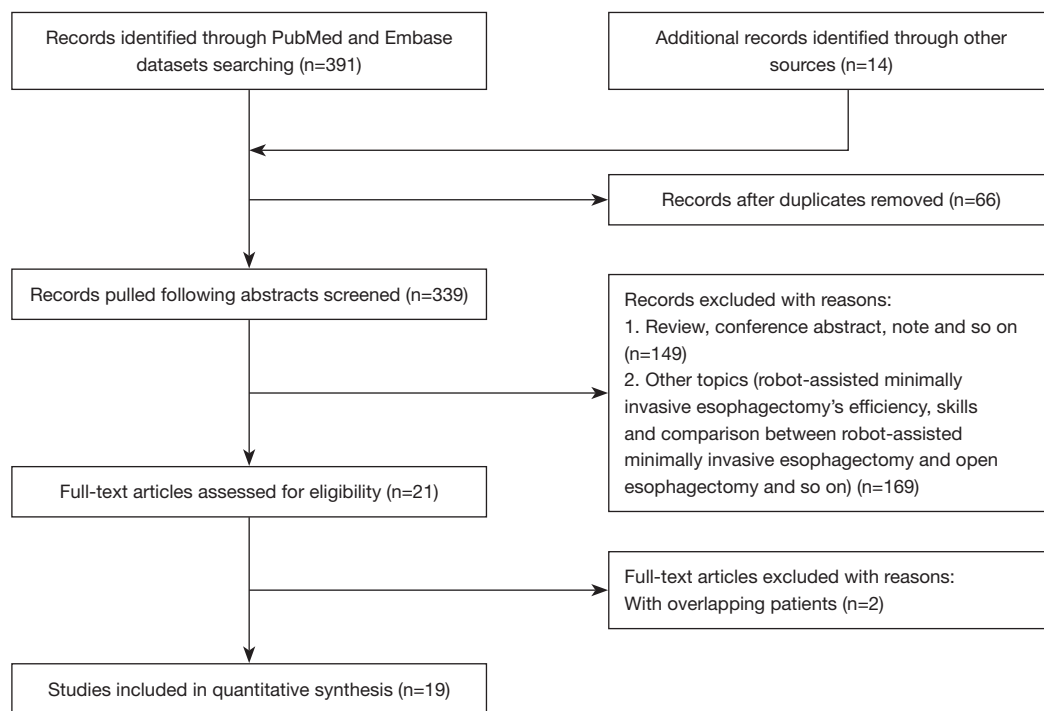
The outcomes of interest consisted of the numbers of total lymph nodes, thoracic lymph nodes, and lymph nodes along the left recurrent laryngeal nerve (RLN) and right RLN, RLN paresis, anastomotic leakage, chylothorax, pneumonia, operative time (min), blood loss (mL), length of stay (LOS), 30-day mortality 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 ( $I^2 > 50\%$ ), 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

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

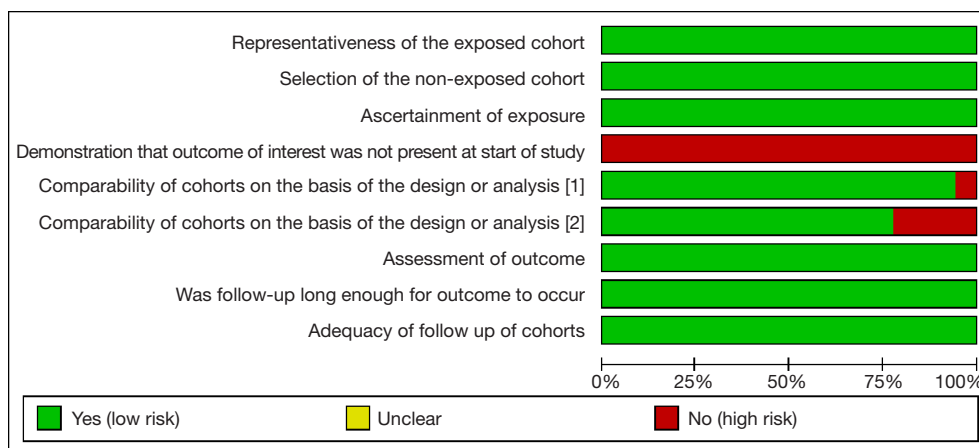
Study	Year	Country	Group	Number	Gender (M/F)	Age, years	BMI, kg/m <sup>2</sup>	Site (upper/mid/lower)	Pathology (ESCC/EAC)	Neoadjuvant therapy	Surgical procedures	Type of study	NOS
Suda	2012	Japan	RAMIE	16	15/1	65 (53 to 86)	21.3 (17.5 to 26.3)	2/7/7	16/0	6	NA	RCS	7
			VAMIE	20	15/5	64.5 (50 to 79)	20.4 (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	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
			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
			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
			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
			VAMIE	144	130/14	60.22	NA	4/72/68	134/NA	28	McKown		
Xu	2020	China	RAMIE	292	220/72	64.34±8.25	22.96±2.95	20/214/58	292/0	NA	McKown	RCS	8
			VAMIE	292	216/76	64.91±7.99	23.21±3.19	24/214/54	292/0	NA	McKown		
Yang	2020	China	RAMIE	271	222/49	63.4±7.1	23.2±3.0	38/169/64	271/0	29	McKown	RCS	8
			VAMIE	271	221/50	63.5±7.4	23.2±2.9	31/171/69	270/0	28	McKown		
He	2020	China	RAMIE	94	72/22	61.3±8.2	22.7±2.8	9/64/21	94/0	0	McKown	RCT	
			VAMIE	98	72/26	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
			VAMIE	22	12/10	59.27±11.60	18.91±2.07	1/5/4	17/5	19	Both		

NA, not available, the enrolled studies did not show the result; RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-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.

Table 2 Incidence rates and mean values in the included studies

Study	Group	N	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
He	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,

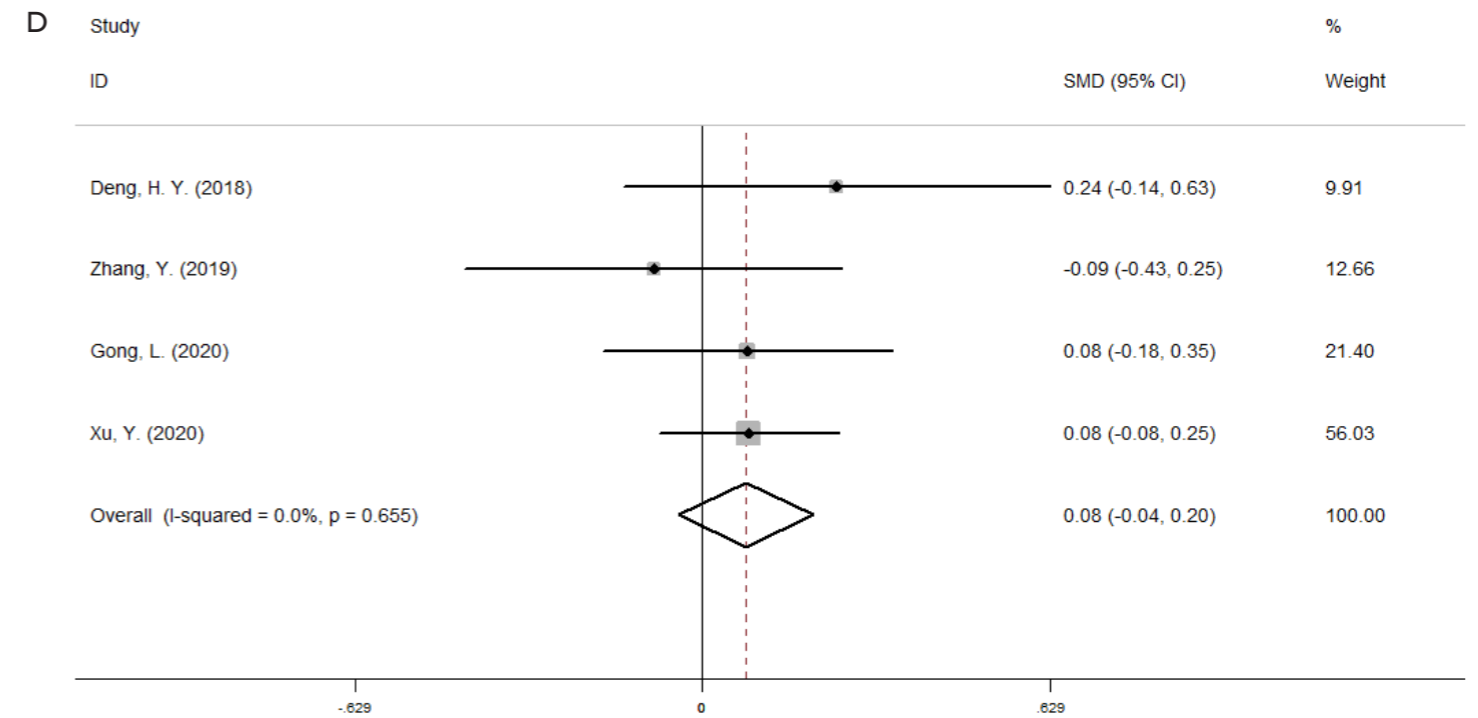
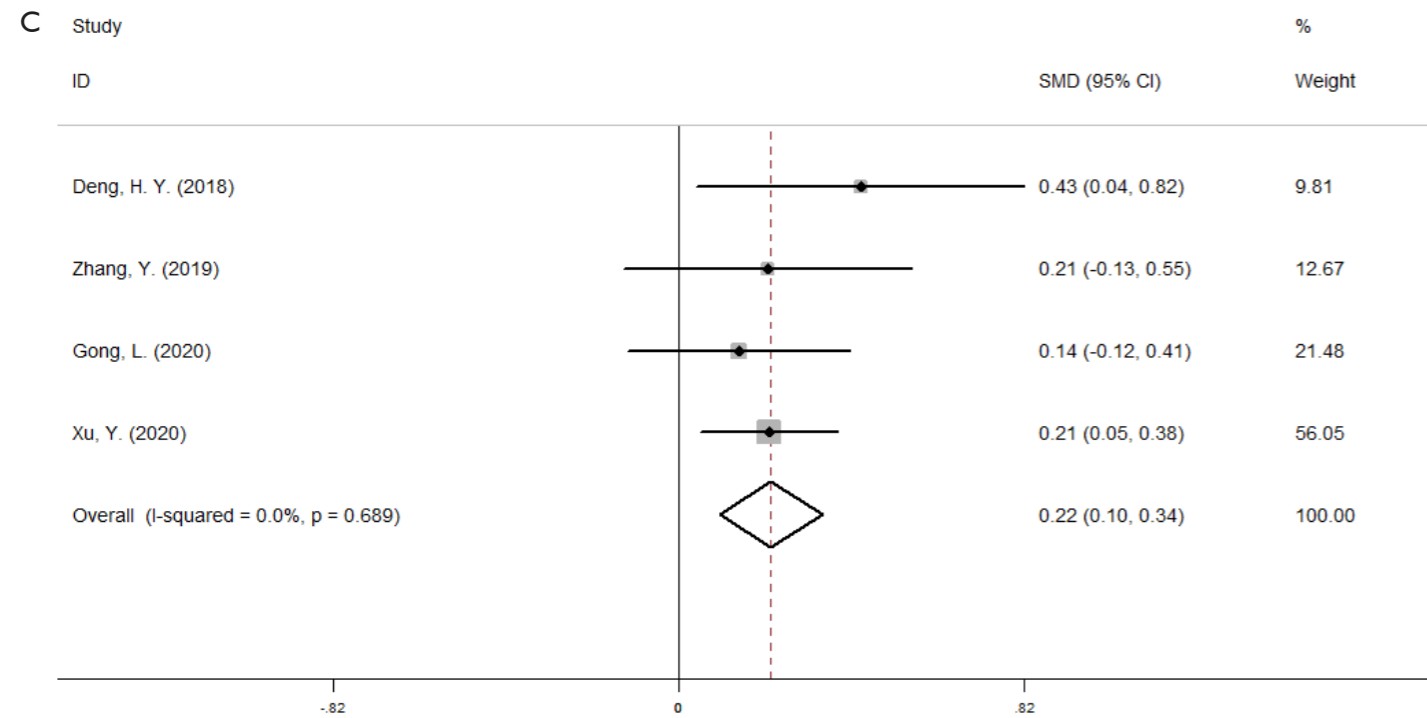
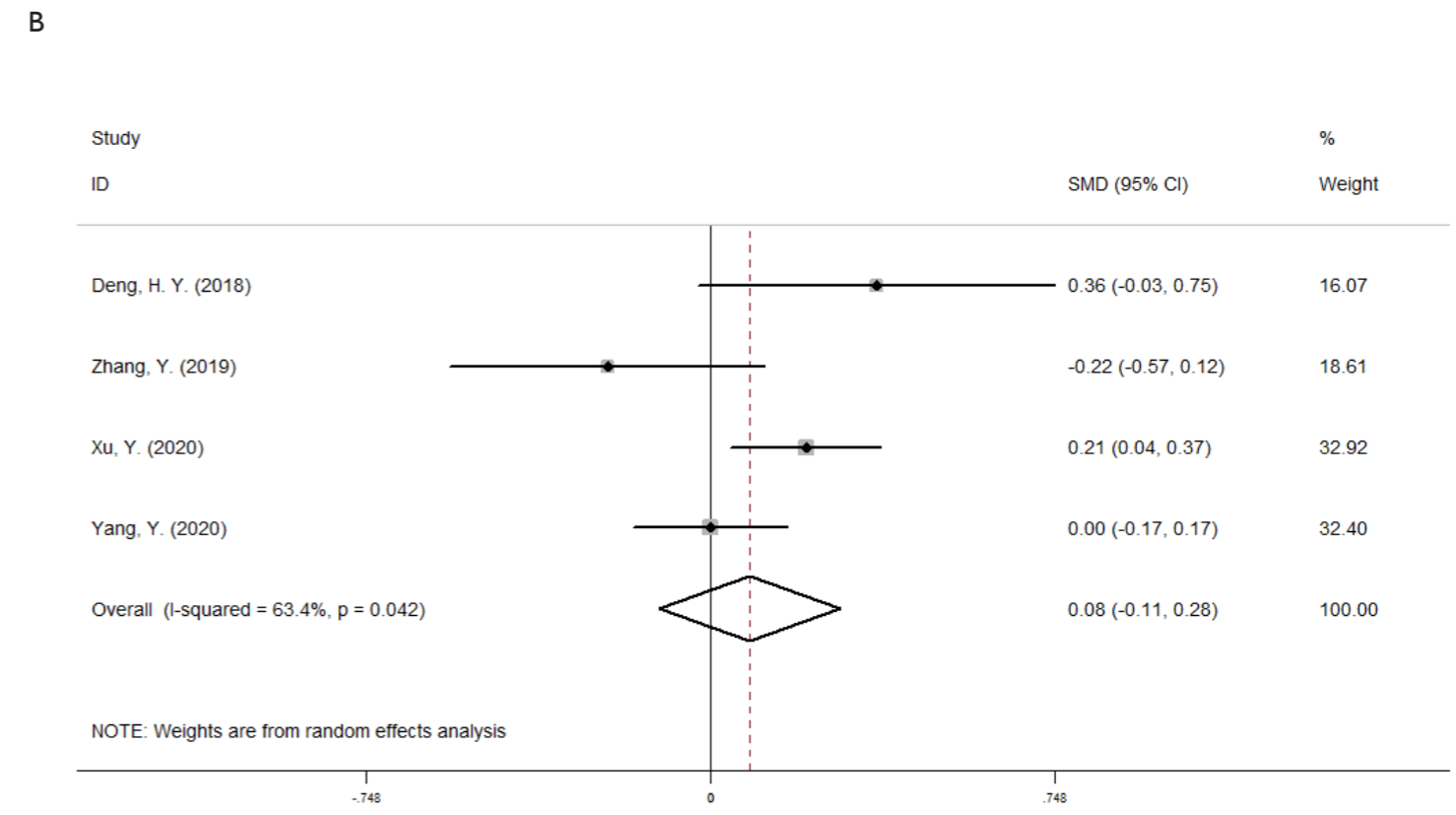
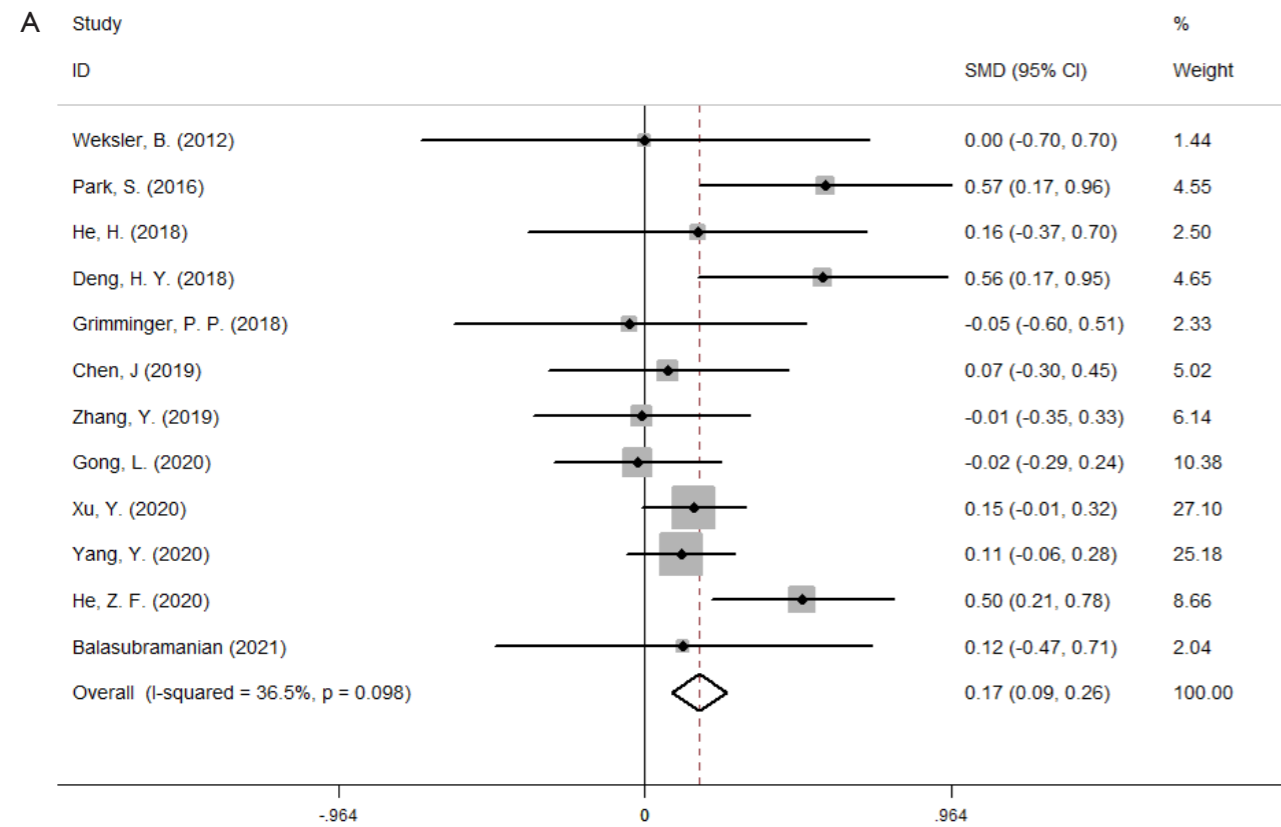
P=0.457).

### **Subgroup analysis**

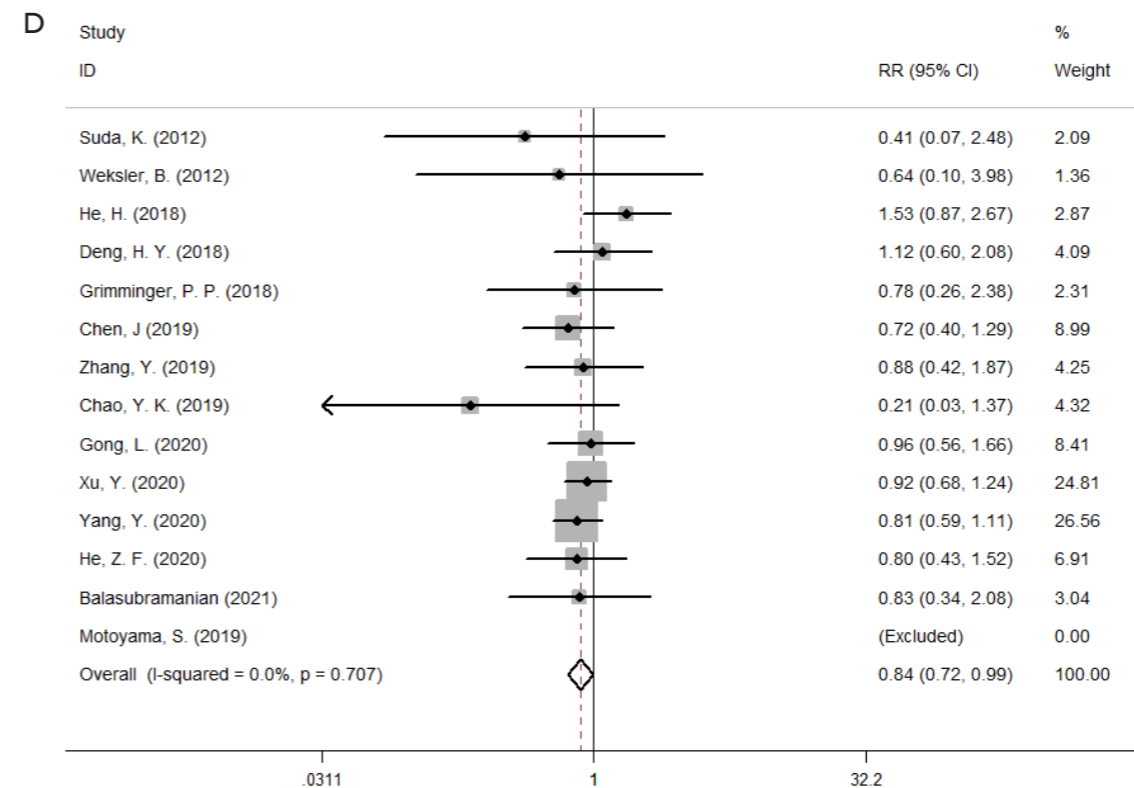
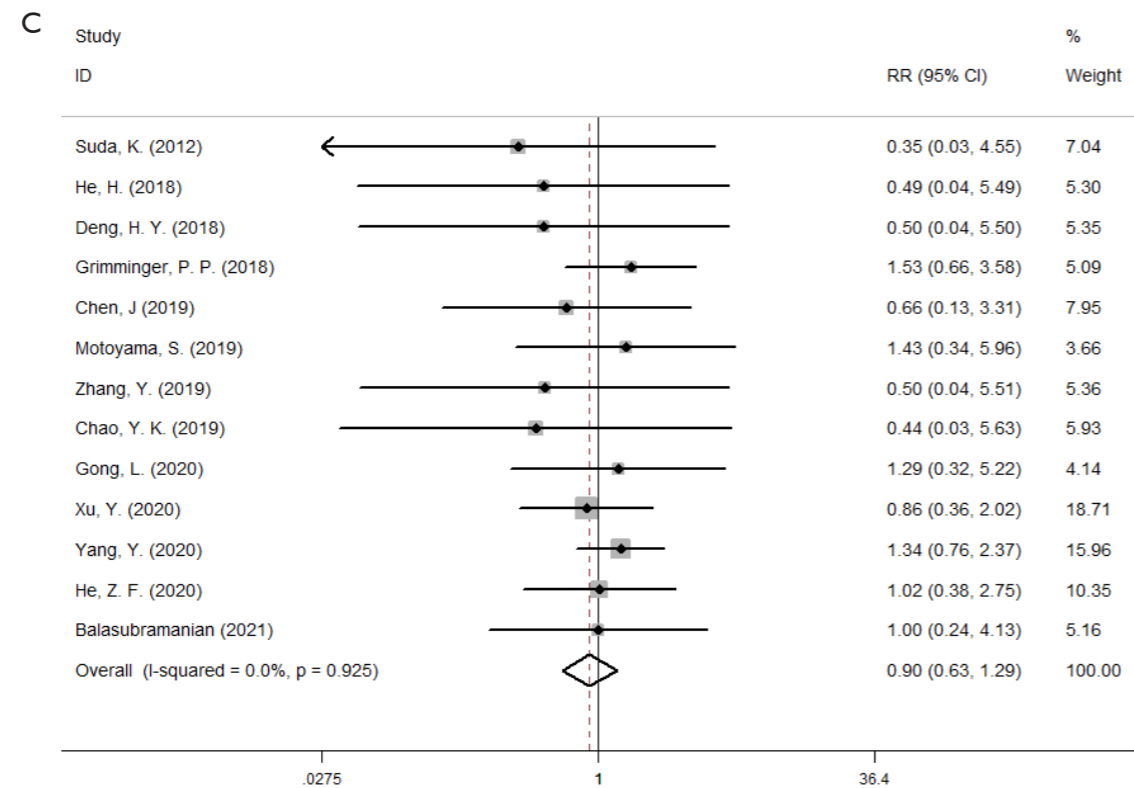
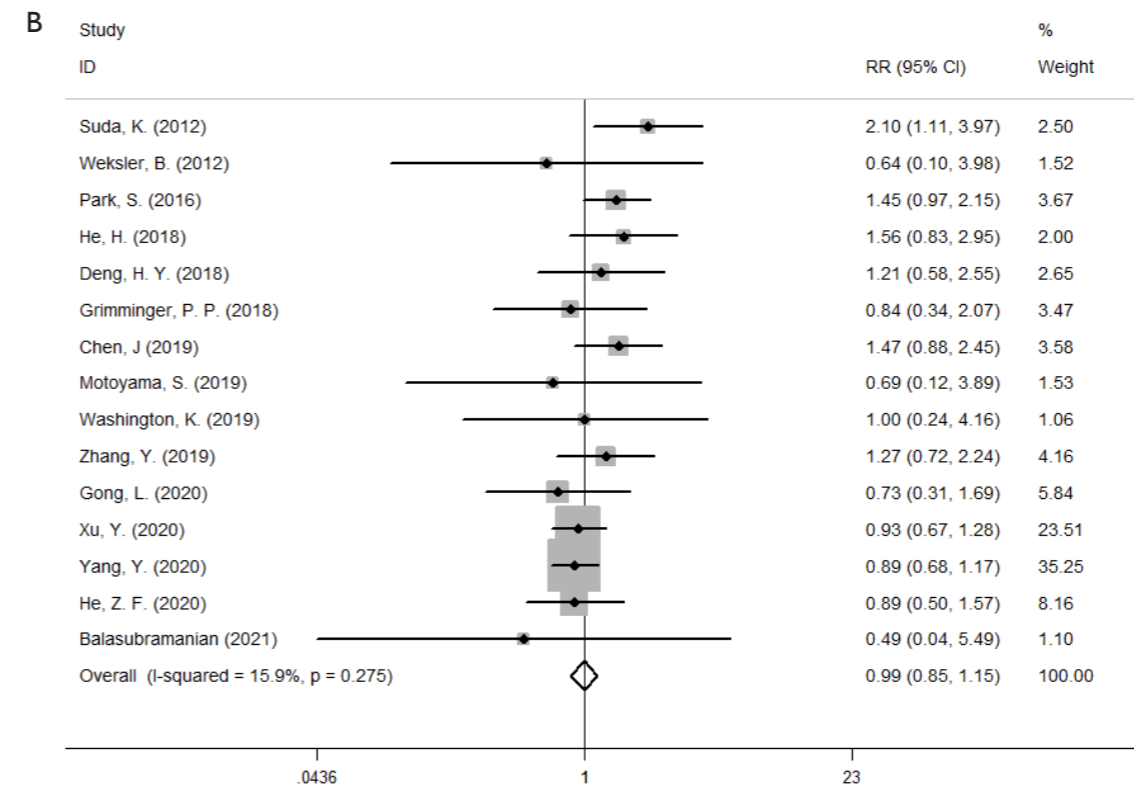
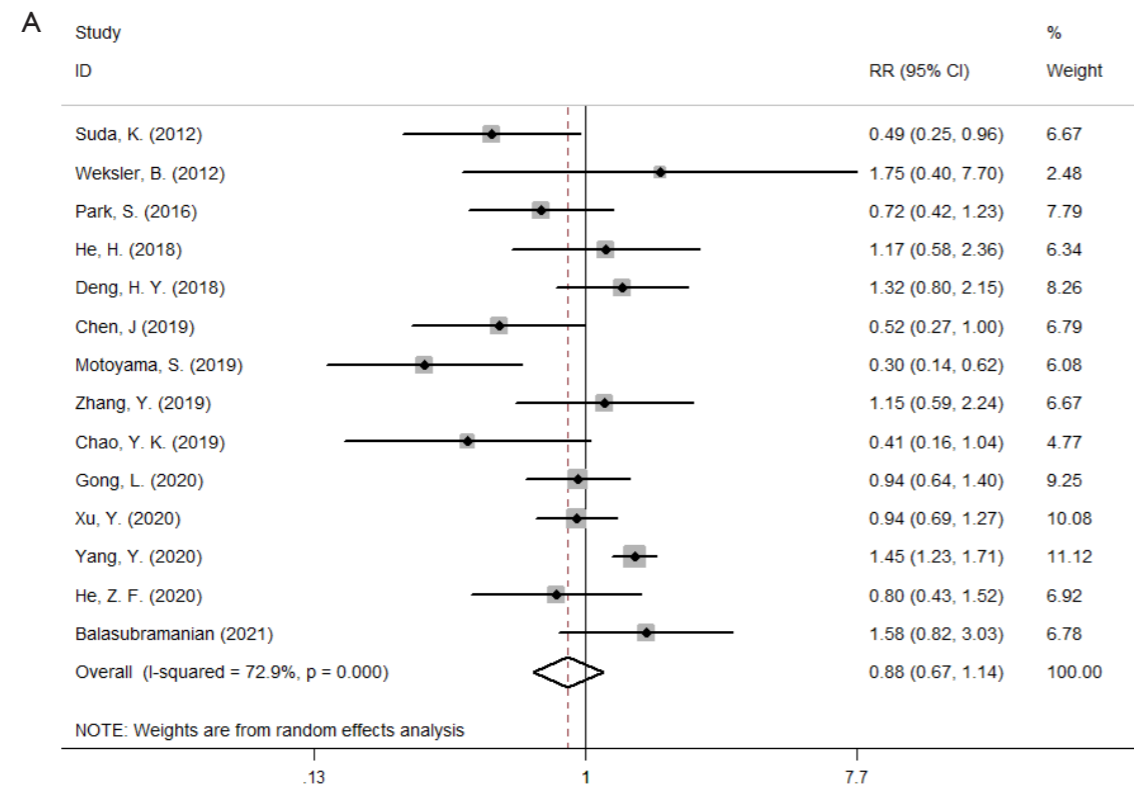
Summary of the meta-analysis results are shown in *Table 3*. According to surgical methods, patients were assigned to the McKown group in 9 studies and to the Ivor-Lewis group in 3 studies. In the McKown group, higher numbers of total lymph nodes (MD =0.173, 95% CI: 0.080–0.265, P<0.001) and lymph nodes 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

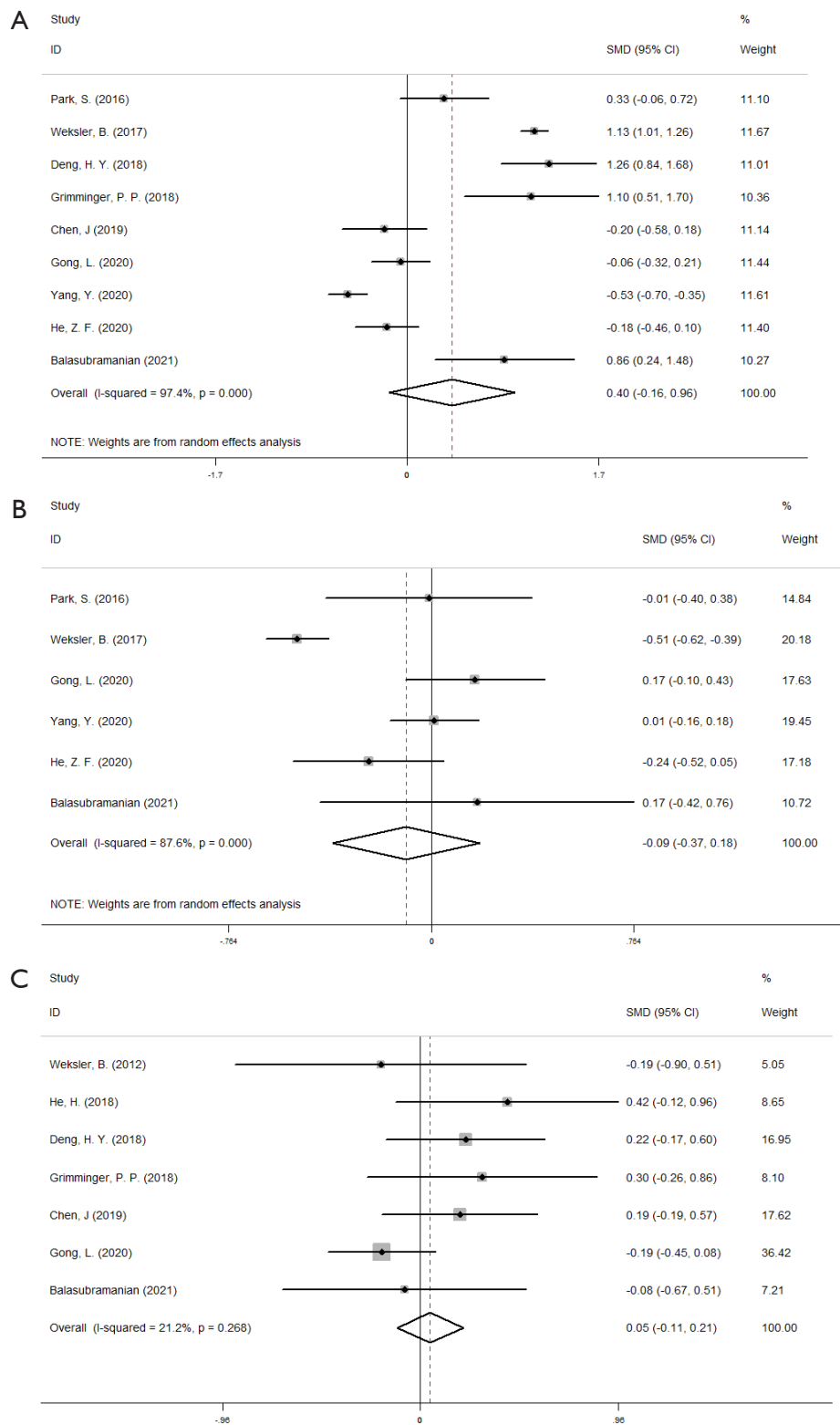


**Figure 3** Comparison of the numbers of total lymph nodes (A), thoracic lymph nodes (B), lymph nodes along the left RLN (C) and right RLN (D) between RAMIE and VAMIE. RLN, recurrent laryngeal nerve; RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.

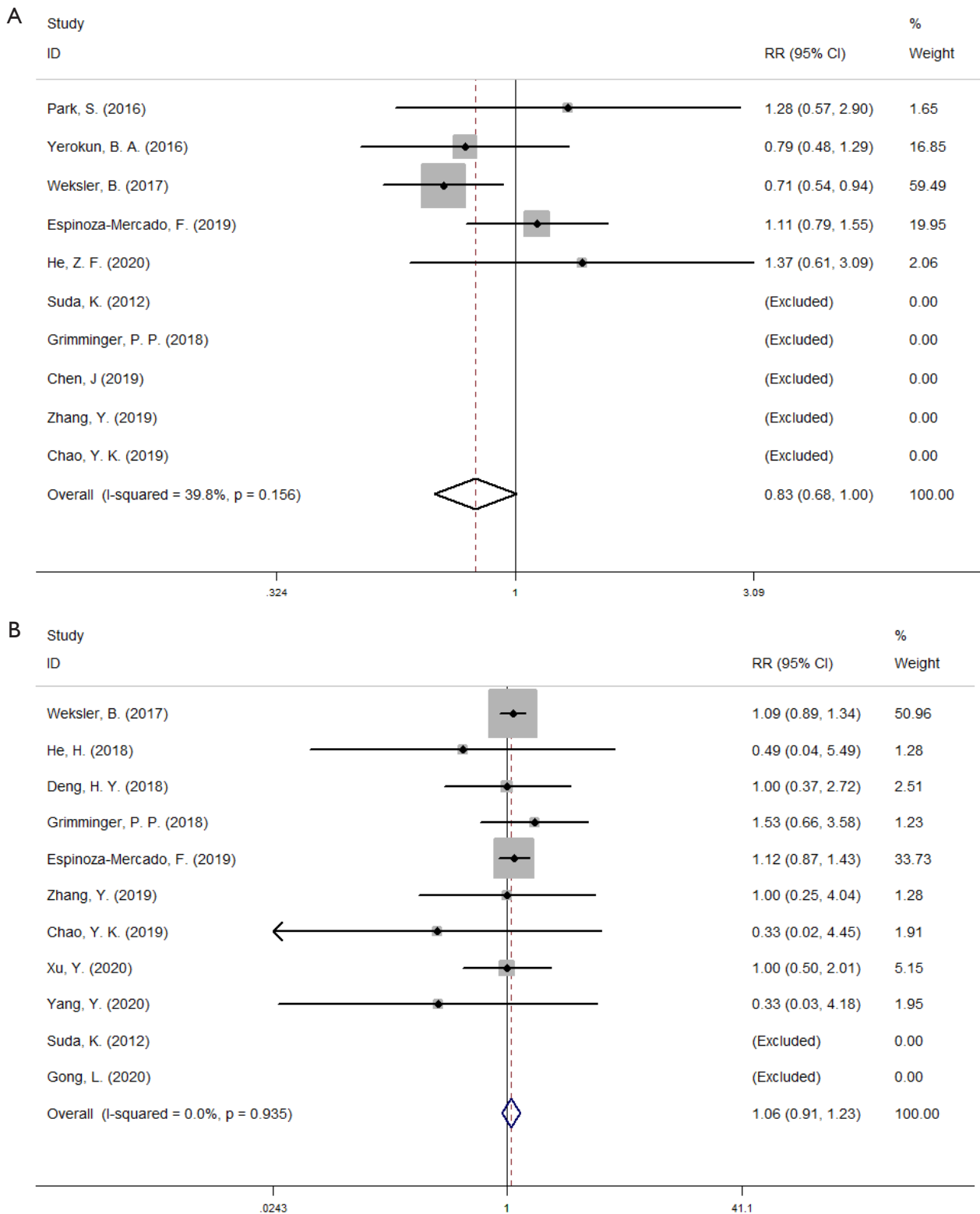


**Figure 4** Comparison of RLN paresis (A), anastomotic leakage (B), chylothorax (C) and pneumonia (D) between RAMIE and VAMIE. RLN, recurrent laryngeal nerve; RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.





**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.

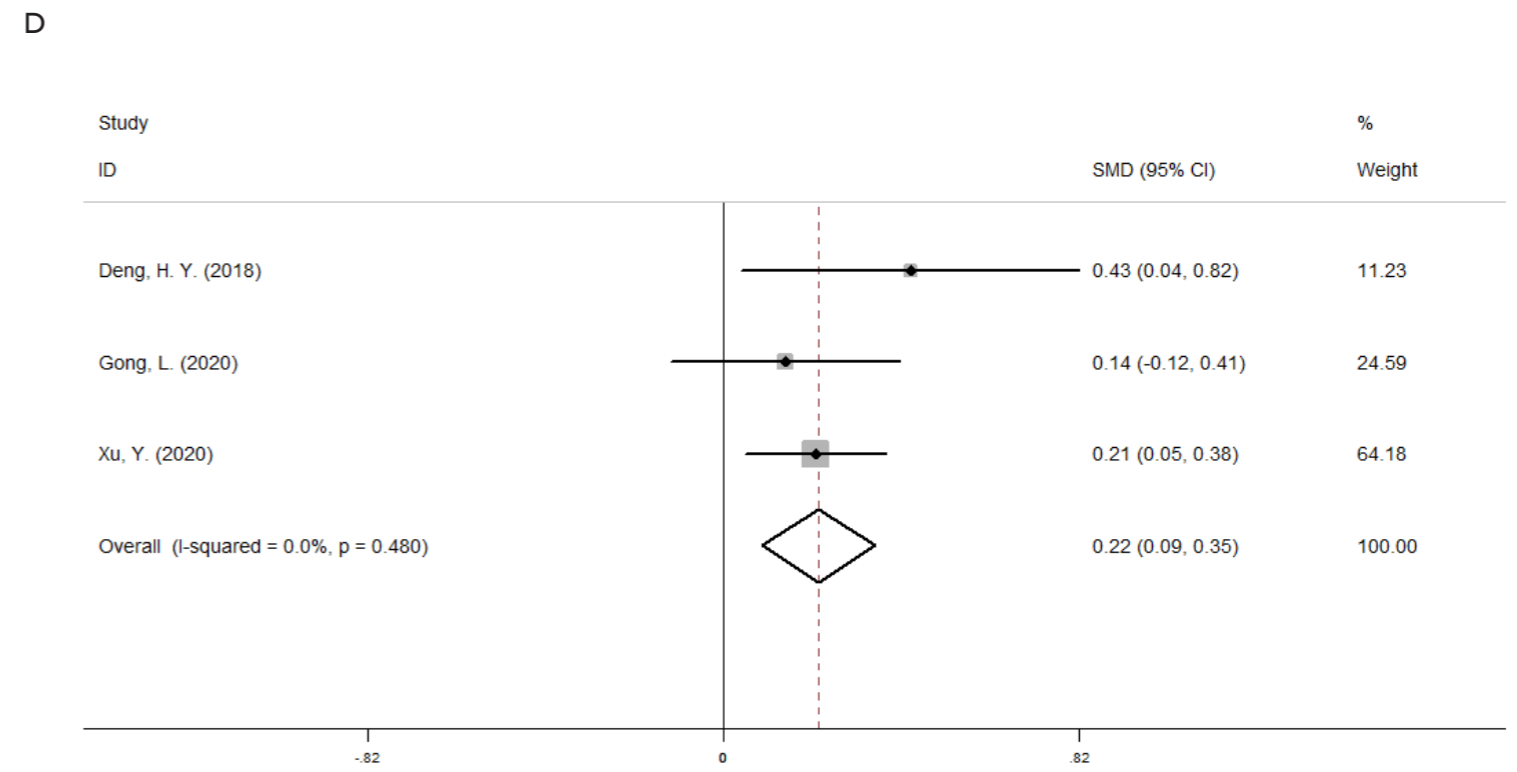
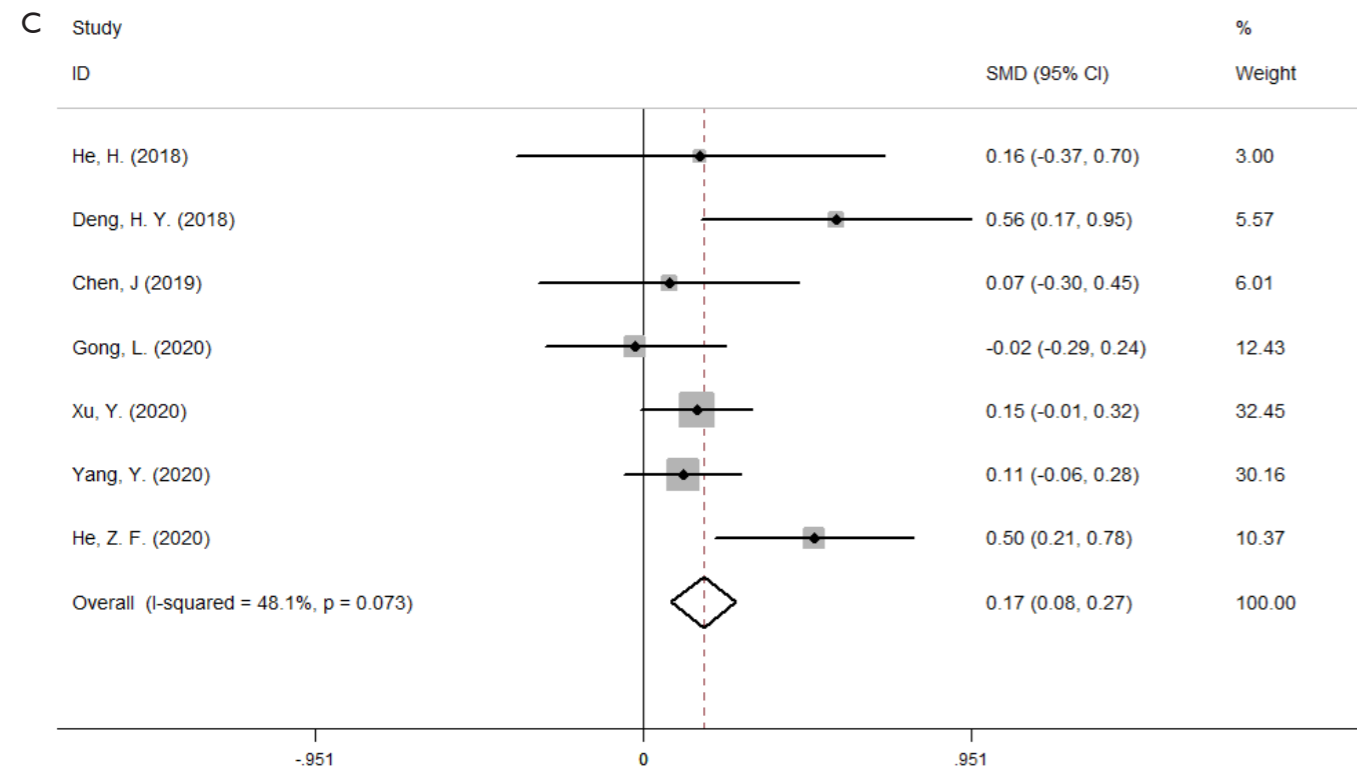
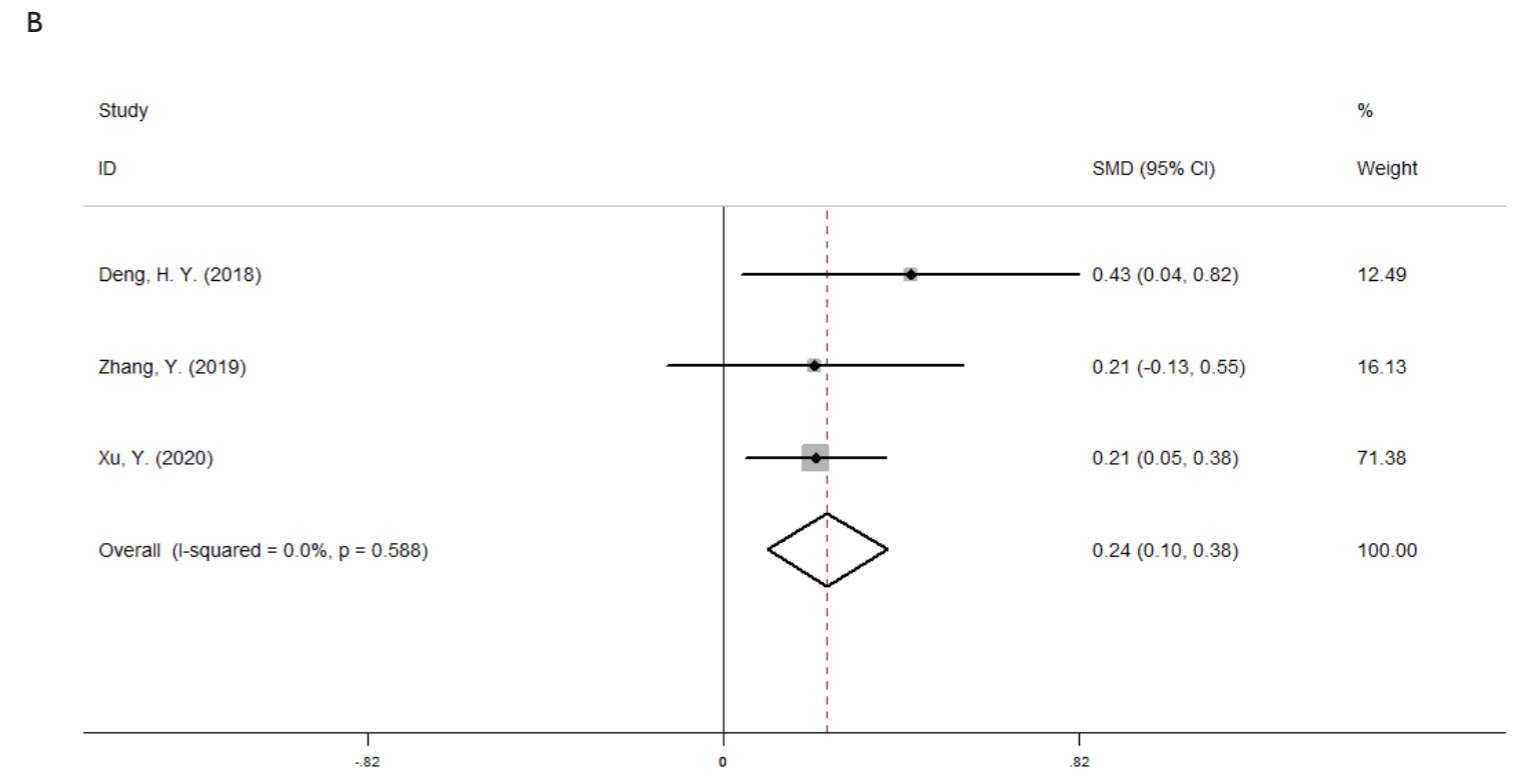
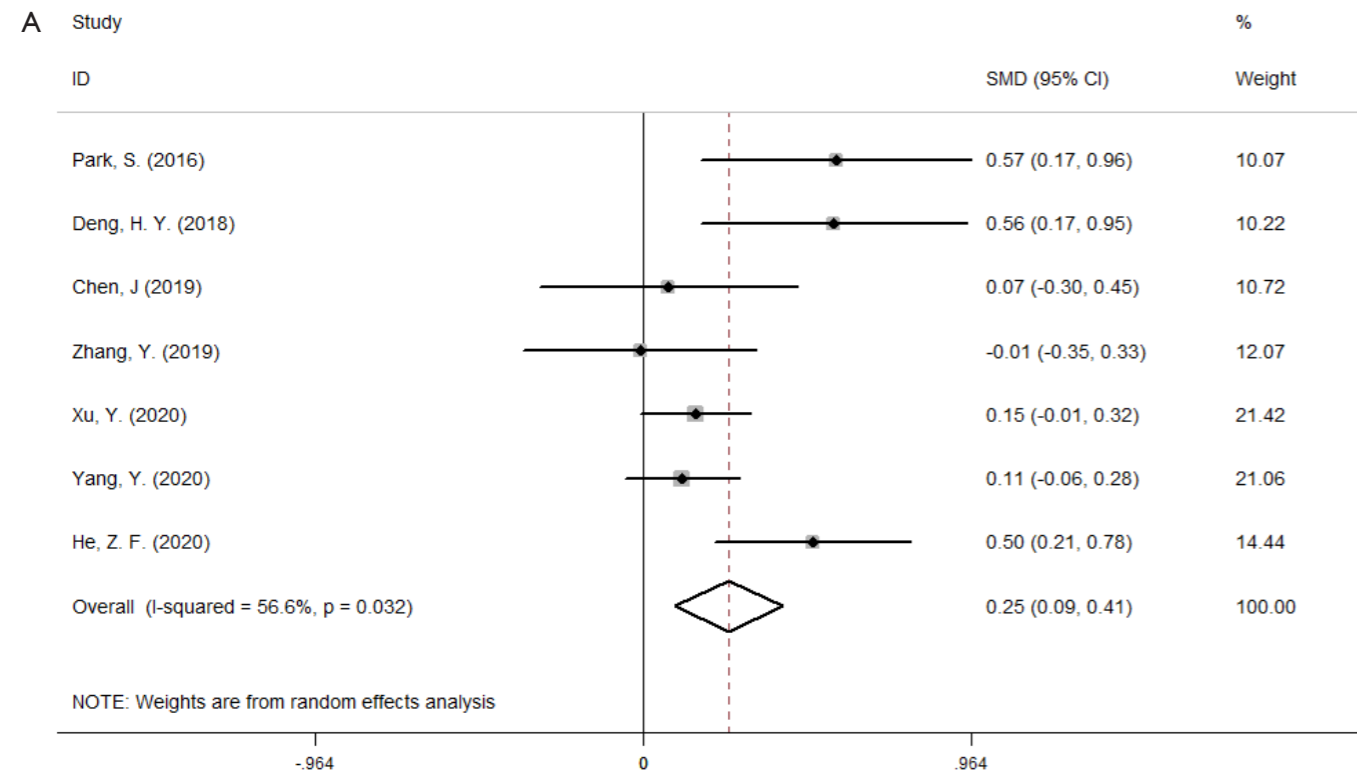


**Figure 6** Comparison of 30-day mortality (A) and 90-day mortality (B) between RAMIE and VAMIE. RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.

Table 3 Summary of the meta-analysis results

Outcomes of interest	Number	Inference	Fixed-effects model		Random-effects model		Heterogeneity	
			SMD/RR (95% CI)	P	RR (95% CI)	P	I <sup>2</sup>	P
<b>Total</b>								
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%	0.098
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%	0.042
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%	0.689
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%	0.655
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%	0.000
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%	0.275
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%	0.925
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%	0.707
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%	0.000
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%	0.000
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%	0.268
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%	0.156
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%	0.935
<b>McKown</b>								
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%	0.073
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%	0.104
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%	0.001
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%	0.748
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%	0.001
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%	0.489
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%	0.877
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%	0.339
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%	0.000
Blood loss	3	20, 22, 23	-0.002 (-0.129, 0.124)	0.971	-0.011 (-0.207, 0.185)	0.916	52.40%	0.123
LOS	4	11, 12, 19, 20	0.049 (-0.129, 0.227)	0.590	0.109 (-0.161, 0.379)	0.430	51.70%	0.102
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%	0.756
<b>ESCC</b>								
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%	0.032
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%	0.042
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%	0.588
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%	0.446
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%	0.000
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%	0.121
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%	0.831
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%	0.908
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%	0.000
Blood loss	3	8, 22, 23	-0.048 (-0.184, 0.088)	0.490	-0.053 (-0.202, 0.095)	0.481	9.50%	0.331
LOS	2	12, 14	0.205 (-0.065, 0.475)	0.137	0.205 (-0.065, 0.475)	0.137	0.00%	0.919
30-day mortality	2	8, 23	1.330 (0.744, 2.377)	0.336	1.324 (0.744, 2.356)	0.339	0.00%	0.908
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%	0.851

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



**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.

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 hand-eye 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 90-day 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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*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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## References

1. Bray F, Ferlay J, Soerjomataram I, et al. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2018;68:394-424.
2. Guo W, Ma X, Yang S, et al. Combined thoracoscopic-laparoscopic esophagectomy versus open esophagectomy: a meta-analysis of outcomes. *Surg Endosc* 2016;30:3873-81.
3. Yang Y, Li B, Hua R, et al. Assessment of Quality Outcomes and Learning Curve for Robot-Assisted Minimally Invasive McKeown Esophagectomy. *Ann Surg Oncol* 2021;28:676-84.
4. Jin D, Yao L, Yu J, et al. Robotic-assisted minimally invasive esophagectomy versus the conventional minimally invasive one: A meta-analysis and systematic review. *Int J Med Robot* 2019;15:e1988.
5. Zheng C, Li XK, Zhang C, et al. Comparison of short-term clinical outcomes between robot-assisted minimally invasive esophagectomy and video-assisted minimally invasive esophagectomy: a systematic review and meta-analysis. *J Thorac Dis* 2021;13:708-19.
6. Suda K, Ishida Y, Kawamura Y, et al. Robot-assisted thoracoscopic lymphadenectomy along the left recurrent laryngeal nerve for esophageal squamous cell carcinoma in the prone position: technical report and short-term outcomes. *World J Surg* 2012;36:1608-16.
7. Weksler B, Sharma P, Moudgill N, et al. Robot-assisted minimally invasive esophagectomy is equivalent to thoracoscopic minimally invasive esophagectomy. *Dis Esophagus* 2012;25:403-9.
8. Park S, Hwang Y, Lee HJ, et al. Comparison of robot-assisted esophagectomy and thoracoscopic esophagectomy in esophageal squamous cell carcinoma. *J Thorac Dis* 2016;8:2853-61.
9. Yerokun BA, Sun Z, Yang CJ, et al. Minimally Invasive Versus Open Esophagectomy for Esophageal Cancer: A Population-Based Analysis. *Ann Thorac Surg* 2016;102:416-23.
10. Weksler B, Sullivan JL. Survival After Esophagectomy: A Propensity-Matched Study of Different Surgical Approaches. *Ann Thorac Surg* 2017;104:1138-46.
11. 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.
12. Grimmer PP, Tagkalos E, Hadzijušević E, et al. Change from Hybrid to Fully Minimally Invasive and Robotic Esophagectomy is Possible without Compromises. *Thorac Cardiovasc Surg* 2019;67:589-96.
  13. 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.
  14. Chen J, Liu Q, Zhang X, et al. Comparisons of short-term outcomes between robot-assisted and thoraco-laparoscopic esophagectomy with extended two-field lymph node dissection for resectable thoracic esophageal squamous cell carcinoma. *J Thorac Dis* 2019;11:3874-80.
  15. Espinoza-Mercado F, Imai TA, Borgella JD, et al. Does the Approach Matter? Comparing Survival in Robotic, Minimally Invasive, and Open Esophagectomies. *Ann Thorac Surg* 2019;107:378-85.
  16. Motoyama S, Sato Y, Wakita A, et al. Extensive Lymph Node Dissection Around the Left Laryngeal Nerve Achieved With Robot-assisted Thoracoscopic Esophagectomy. *Anticancer Res* 2019;39:1337-42.
  17. Washington K, Watkins JR, Jay J, et al. Oncologic Resection in Laparoscopic Versus Robotic Transhiatal Esophagectomy. *JSLs* 2019;23:e2019.
  18. 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.
  19. Chao YK, Wen YW, Chuang WY, et al. Transition from video-assisted thoracoscopic to robotic esophagectomy: a single surgeon's experience. *Dis Esophagus* 2020;33:doz033.
  20. Gong L, Jiang H, Yue J, et al. Comparison of the short-term outcomes of robot-assisted minimally invasive, video-assisted minimally invasive, and open esophagectomy. *J Thorac Dis* 2020;12:916-24.
  21. He ZF, Zheng TL, Liu DL, et al. Comparison of short-term and long-term efficacy between robot-assisted and thoracoscopy-laparoscopy-assisted radical esophageal cancer surgery. *Zhonghua Wei Chang Wai Ke Za Zhi* 2020;23:390-5.
  22. Xu Y, Li XK, Cong ZZ, et al. Long-term outcomes of robotic-assisted versus thoraco-laparoscopic McKeown esophagectomy for esophageal cancer: a propensity score-matched study. *Dis Esophagus* 2021;34:doaa114.
  23. Yang Y, Zhang X, Li B, et al. Short- and mid-term outcomes of robotic versus thoraco-laparoscopic McKeown esophagectomy for squamous cell esophageal cancer: a propensity score-matched study. *Dis Esophagus* 2020;33:doz080.
  24. Balasubramanian S, Chittawadagi B, Misra S, et al. Propensity matched analysis of short term oncological and perioperative outcomes following robotic and thoracoscopic esophagectomy for carcinoma esophagus- the first Indian experience. *J Robot Surg* 2021. [Epub ahead of print].
  25. Chao YK, Hsieh MJ, Liu YH, et al. 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.
  26. Deng HY, Huang WX, Li G, et al. Comparison of short-term outcomes between robot-assisted minimally invasive esophagectomy and video-assisted minimally invasive esophagectomy in treating middle thoracic esophageal cancer. *Dis Esophagus* 2018.
  27. Yun JK, Chong BK, Kim HJ, et al. Comparative outcomes of robot-assisted minimally invasive versus open esophagectomy in patients with esophageal squamous cell carcinoma: a propensity score-weighted analysis. *Dis Esophagus* 2020;33:doz071.
  28. Mehdorn AS, Möller T, Franke F, et al. Long-Term, Health-Related Quality of Life after Open and Robot-Assisted Ivor-Lewis Procedures-A Propensity Score-Matched Study. *J Clin Med* 2020;9:3513.
  29. Halpern AL, Friedman C, Torphy RJ, et al. Conversion to open surgery during minimally invasive esophagectomy portends worse short-term outcomes: an analysis of the National Cancer Database. *Surg Endosc* 2020;34:3470-8.
  30. Oshikiri T, Takiguchi G, Urakawa N, et al. Novel "Modified Bascule Method" for Lymphadenectomy Along the Left Recurrent Laryngeal Nerve During Robot-Assisted Minimally Invasive Esophagectomy. *Ann Surg Oncol* 2021;28:4918-27.
  31. Hosoda K, Niihara M, Ushiku H, et al. Prevention of intra-thoracic recurrent laryngeal nerve injury with robot-assisted esophagectomy. *Langenbecks Arch Surg* 2020;405:533-40.
  32. Motoyama S, Sato Y, Wakita A, et al. Lower local recurrence rate after robot-assisted thoracoscopic esophagectomy than conventional thoracoscopic surgery

- for esophageal cancer. *Sci Rep* 2021;11:6774.
33. Yang Y, Zhang X, Li B, et al. Robot-assisted esophagectomy (RAE) versus conventional minimally invasive esophagectomy (MIE) for resectable esophageal

squamous cell carcinoma: protocol for a multicenter prospective randomized controlled trial (RAMIE trial, robot-assisted minimally invasive Esophagectomy). *BMC Cancer* 2019;19:608.

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