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Original Article

Comparison of short-term outcomes between robot-assisted minimally invasive esophagectomy and video-assisted minimally invasive esophagectomy in treating middle thoracic esophageal cancer

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SUMMARY. **Whether the robot-assisted minimally invasive esophagectomy (RAMIE) has any advantages over the video-assisted minimally invasive esophagectomy (VAMIE) remains controversial. In this study, we tried to compare the short-term outcomes of RAMIE with that of VAMIE in treating middle thoracic esophageal cancer from a single medical center. Consecutive patients undergoing RAMIE or VAMIE for middle thoracic esophageal cancer from April 2016 to April 2017 were prospectively included for analysis. Baseline data and pathological findings as well as short-term outcomes of these two group (RAMIE group and VAMIE group) patients were collected and compared. A total of 84 patients (RAMIE group: 42 patients; VAMIE group: 42 patients) were included for analysis. The baseline characteristics between the two groups were comparable. RAMIE yielded significantly larger numbers of total dissected lymph nodes (21.9 and 17.8, respectively; $P = 0.042$) and the right recurrent laryngeal nerve (RLN) lymph nodes (2.1 and 1.2, respectively; $P = 0.033$) as well as abdominal lymph nodes (10.8 and 7.7, respectively; $P = 0.041$) than VAMIE. Even though RAMIE may consume more overall operation time, it could significantly decrease total blood loss compared to VAMIE (97 and 161 mL, respectively; $P = 0.015$). Postoperatively, no difference of the risk of major complications or hospital stay was observed between the two groups. In conclusion, RAMIE had significant advantage of lymphadenectomy especially for dissecting RLN lymph nodes over VAMIE with a comparable rate of postoperative complications. Further randomized controlled trials are badly needed to confirm and update our conclusions.**

KEY WORDS: **esophageal cancer, minimally invasive esophagectomy (MIE), robot assisted, video assisted.**

INTRODUCTION

Worldwide, esophageal cancer remains to be the ninth most common cancer and the sixth most common cause of death from cancer.[1] For non-advanced esophageal cancer, surgical resection still remains to be an important therapeutic modality. Traditionally, radical esophagectomy with lymphadenectomy via open thoracotomy was widely adopted. However, due to its substantial morbidity and mortality, video-assisted thoracoscopic minimally invasive esophagectomy (VAMIE) was introduced to avoid open thoracotomy,[2,3] which has been proved to be feasible and comparable to open esophagectomy, at least in short term, with improved postoperative recovery.[4,5] More recently, robot-assisted minimally invasive esophagectomy (RAMIE) has been introduced with the advantages of increased magnification, dexterity, and three-dimensional visual clarity.[6] Although RAMIE is believed to offer more excellent visualization and enable meticulous dissection of the mediastinum structures facilitating the complex thoracoscopic procedures,[7] the actual advantages of RAMIE over VAMIE have not been well established. Only several studies have found that RAMIE was equivalent or even superior to VAMIE in radical lymphadenectomy.[8,9] However, these evidence was scarce, and more evidence is badly needed. Therefore, in this study, we tried to compare short-term outcomes

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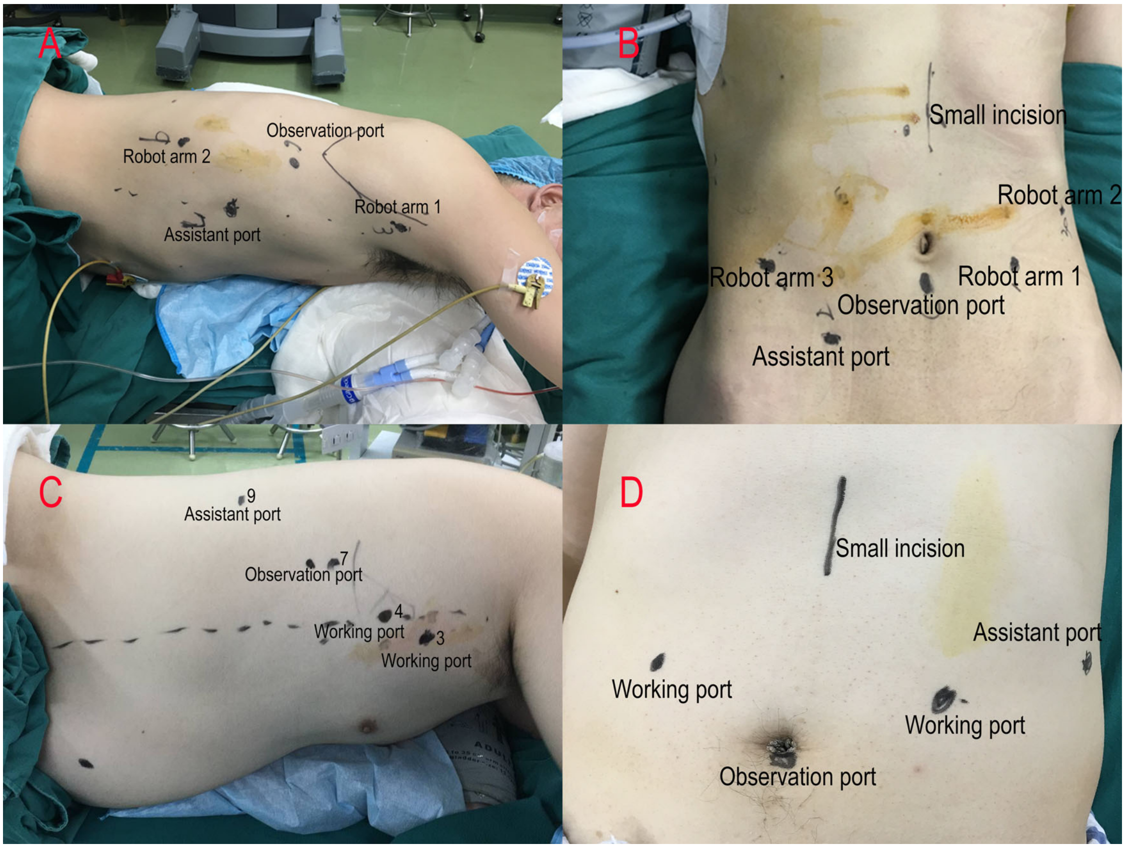

Fig. 1 Ports design for robot-assisted minimally invasive esophagectomy: (A) thoracic part; (B) abdominal part and for video-assisted minimally invasive esophgactomy: (C) thoracic part; (D) abdominal part.

of RAMIE and VAMIE in treating middle thoracic esophageal cancer for the first time from a major Chinese medical center and hoped to add evidence into the data pool comparing RAMIE and VAMIE. To our knowledge, this is one of the largest cohorts focusing on current topic worldwide.

METHODS AND MATERIALS

Patients

We retrospectively collected perioperative data of patients undergoing RAMIE or VAMIE consecutively for middle thoracic esophageal cancer without any previous neoadjuvant therapy by the same two surgical teams (Dr. Lin and Dr. Wang, who performed both RAMIE and VAMIE at the indicated period) in our department from April 2016 to April 2017. Preoperatively, all those patients underwent endoscopy, endoscopic ultrasound, chest CT, abdominal CT, cervical ultrasonography, and pulmonary function and blood testing routinely, and were evaluated as resectable middle thoracic esophageal cancer preoperatively (cT1-3N0-2). Because we offered two choices of minimally invasive esophegctomy (RAMIE and VAMIE) to those patients, they chose either RAMIE or VAMIE at their own wills. Posteriorly, all patients were stage according to the eighth edition of TNM staging for esophageal cancer.[10] This study was approved by the Ethics Committee of West China Hospital, Sichuan University (No.20170730). Because this study was a retrospective cohort analysis and analyzed anonymously, the ethics committee waived the need for informed consents from those patients.

Surgical procedures of RAMIE and VAMIE

All consecutive patients received the robot-assisted or video-assisted McKeown minimally invasive esophagectomy with two-field lymphadenectomy. RAMIE was carried out with robotic system (da Vinci Si System, Intuitive Surgical Inc., Sunnyvale, CA). All patients in both RAMIE and VAMIE were intubated with left-side double-lumen tube under general anesthesia. Our ports designed for thoracic part of RAMIE were as followed: with patient in the left semiprone position, one observation port was placed at the sixth intercostal space (ICS) along posterior axillary line, and one working port (robot arm 1) was placed at the third ICS along the mid-axillary line and another working port (robot arm 2) was placed at the ninth ICS along the posterior axillary line, and finally an assistant port was placed at the seventh ICS along the anterior axillary line (Fig. 1A). Our ports designed for abdominal part

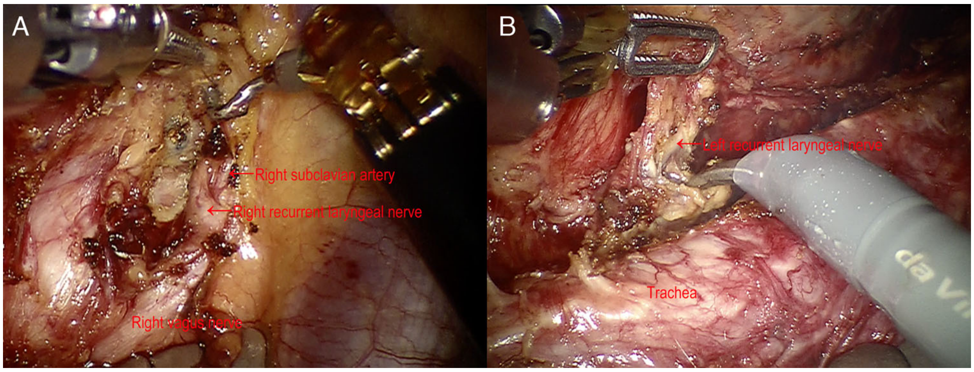

Fig. 2 Intraoperative imagines of robot-assisted minimally invasive esophagectomy in dissecting lymph nodes along recurrent laryngeal nerve (RLN): (A) Right RLN lymph nodes; (B) Left RLN lymph nodes.

of RAMIE were shown in Figure 1B. Our ports for thoracic part of VAMIE were as followed: one observation port was placed at the seventh ICS along posterior axillary line, and one 10-mm working port was placed at the third ICS along the anterior axillary line and another 5-mm working port was placed at the fourth ICS along the midaxillary line, and finally a 5-mm assistant was placed at the ninth ICS scapular line (Fig. 1C). Moreover, our ports for abdominal part of VAMIE were shown in Figure 1D. For both RAMIE and VAMIE, artificial pneumothorax by 8 mmHg CO_2 insufflation was established, and mediastinal and abdominal lymph nodes dissection as well as dissection of lymph nodes along bilateral recurrent laryngeal nerves (RLN) were carefully achieved (lymph node dissection in RAMIE was shown in Fig. 2). Selective en masse ligation of the thoracic duct as previously described[11] was performed to prevent postoperative chylothorax. A 4-cm-wide gastric tube was created with preservation of the right gastroepiploic artery along the greater curvature by the aid of a linear stapling device (Johnson & Johnson) after the stomach was pulled out through an additional small upper mid-abdominal incision. Finally, a layered hand-sewing esophagogastric anastomosis in the left neck was performed as we previously described.[11]

Data for analysis

The baseline data including demographic data and comorbidities of those included patients (including hypertension, coronary artery disease, diabetes, and chronic obstructive pulmonary disease) were collected. Pathological outcomes including pathology type, TNM stage, and lymph nodes yields were collected and analyzed. Lymph nodes yields included total number of lymph nodes dissected and positive lymph nodes. Here, we divided these lymph nodes into mediastinal lymph node group (right and left RLN lymph nodes, 7#, 8#, 9#, 15#) and abdominal lymph node group (#16, #17, #18, #19, #20). Perioperative data concerning operation time, blood loss, postoperative hospital stay, major complications (including severe pneumonia, anastomotic leakage, RLN paralysis, postoperative chylothorax), and 30-day mortality were also reviewed and analyzed. All of those major complications were evaluated according to the Society of Thoracic Surgeons and the European Society of Thoracic Surgeons joint definitions,[12] and severe pneumonia was defined as grade 3 (tracheostomy or intubation with mechanical ventilation) and higher by using the Clavien–Dindo classification.[13]

Statistical analysis

Statistical analysis was performed using the IBM SPSS software (version 22.0; IBM Corp., Armonk, NY, USA). Data were represented as the mean ± standard deviation for continuous variables or number (%) for categorical data. For continuous variables, Student's test or Mann-Whitney U test was applied, depending on normality of distribution; while for categorical data, chi-square or Fisher's exact test was applied. Statistical significance was set as a two-sided P value < 0.05.

RESULTS

Patient baseline characteristics

A total of 84 patients were retrieved. All of them suffered with middle thoracic esophageal cancer. Forty-two patients underwent RAMIE and the other 42 patients received VAMIE. The baseline clinical characteristics between RAMIE group and VAMIE group were shown in Table 1. The demographic data between the two groups were similar. The comorbidity rate in the two groups was comparable (31.0% and 31.0%, respectively; $P = 1.00$), and the detailed comorbidity conditions were also comparable between the two groups. Moreover, the clinical TNM stage of these patients in RAMIE group

Table 1 Comparison of baseline characteristics of patients in RAMIE and VAMIE

Characteristics	RAMIE ($N = 42$)	VAMIE ($N = 42$)	P value
Age (mean ± SD)	60.7 ± 6.9	61.8 ± 9.5	0.581*
Gender (male/female)	35/7	33/9	0.578
Height (mean ± SD)	164.6 ± 5.6	164.3 ± 6.1	0.810
Weight (mean ± SD)	62.2 ± 9.6	59.3 ± 9.2	0.160
Major comorbidity (N, %)	13 (28.6%)	13 (28.6%)	1.00
Hypertension	10 (23.8%)	7 (16.7%)	0.415
Coronary artery disease	1 (2.4%)	3 (7.1%)	0.616**
Diabetes	2 (4.8%)	2 (4.8%)	1.00**
COPD	2 (4.8%)	3 (7.1%)	1.00**
Clinical TNM stage (N, %)			0.498
I	9 (21.4%)	7 (16.7%)	
II	22 (52.4%)	19 (45.2%)	
III	11 (26.2%)	16 (38.1%)	

*Mann–Whitney U test; **Fisher's exact test.
COPD, chronic obstructive pulmonary disease; RAMIE, robot-assisted minimally invasive esophagectomy; SD, standard deviation; VAMIE, video-assisted minimally invasive esophagectomy.

and VAMIE group was also similar ($P = 0.498$). None of these patients received neoadjuvant therapy because they were evaluated as resectable disease, and all patients achieved R0 resection. None of them experienced conversion.

Pathological finds and lymph node yields

All those patients had squamous cell carcinoma. There was no significant difference between RAMIE group and VAMIE group regarding pT stage ($P = 0.293$), pN stage ($P = 0.122$), differentiation grade ($P = 0.090$), and pTNM stage ($P = 0.165$) (Table 2).

The mean total number of lymph nodes (mediastinum and abdomen) dissected in the RAMIE group was significantly larger than that in the VAMIE group (21.9 and 17.8, respectively; $P = 0.042$), and the mean number of positive lymph nodes tended to be larger in the RAMIE group (1.3 and 0.88, respectively; $P = 0.334$). Even though RAMIE yielded similar number of mediastinal lymph nodes to VAMIE (11.1 and 10.0, respectively; $P = 0.401$), it yielded significantly more number of abdominal lymph nodes than VAMIE (10.8 and 7.7, respectively; $P = 0.041$). And for bilateral RLN lymph nodes, RAMIE yielded significantly more right RLN lymph nodes than VAMIE (2.1 and 1.2, respectively; $P = 0.033$) and a comparable number of left RLN lymph nodes to VAMIE (0.69 and 0.86, respectively; $P = 0.619$) (Table 2).

Perioperative outcomes

RAMIE took significantly longer total operation time than VATMIE (354 and 284 minutes, respectively; $P < 0.001$). However, the total blood loss volume in RAMIE group was significantly less than that in VAMIE group (97 and 161 mL, respectively; $P = 0.015$). Patients in RAMIE group also had similar postoperative hospital stay to patients in the VAMIE group (14.1 and 12.1 days,

Table 2 Comparison of pathological outcomes between RAMIE and VAMIE in middle thoracic esophageal cancer

Pathological outcomes	RAMIE ($N = 42$)	VAMIE ($N = 42$)	P value
pT stage (N, %)			0.294
T1	12 (28.6%)	8 (19.0%)	
T2	8 (19.0%)	5 (11.9%)	
T3	22 (52.4%)	29 (69.0%)	
pN stage (N, %)			0.122
N0	24 (57.1%)	20 (47.6%)	
N1	12 (28.6%)	14 (33.3%)	
N2	3 (7.1%)	8 (19.0%)	
N3	3 (7.1%)	0 (0%)	
Grade (N, %)			0.090
1	2 (4.8%)	1 (2.4%)	
2	18 (42.9%)	28 (66.7%)	
3	22 (52.4%)	13 (31.0%)	
pTNM (N, %)			0.165
I	8 (19.0%)	6 (14.3%)	
II	20 (47.6%)	13 (31.0%)	
III	11 (26.2%)	21 (50.0%)	
IVa	3 (7.1%)	2 (4.8%)	
Number of LN dissected (mean ± SD)	21.9 ± 9.9	17.8 ± 8.3	0.042
Number of positive LN (mean ± SD)	1.3 ± 3.0	0.88 ± 1.2	0.384*
Number of mediastinal LN dissected (mean ± SD)	11.1 ± 5.8	10.0 ± 5.9	0.401
Number of abdominal LN dissected (mean ± SD)	10.8 ± 8.1	7.7 ± 4.8	0.041*
Number of right RLNLN dissected (mean ± SD)	2.1 ± 2.0	1.2 ± 1.5	0.033
Number of left RLNLN dissected (mean ± SD)	0.69 ± 1.6	0.86 ± 1.4	0.619

*Mann–Whitney U test.
LN, lymph node; RAMIE, robot-assisted minimally invasive esophagectomy; SD, standard deviation; VAMIE, video-assisted minimally invasive esophagectomy.

Table 3 Comparison of short-term outcomes between RAMIE and VAMIE

Perioperative outcomes	RAMIE	VAMIE	*P* value
Mean of total operation time (minutes)	354 ± 65	284 ± 57	<0.001
Mean of total blood loss (mL)	97 ± 62	161 ± 153	0.016*
Mean postoperative hospital stay (day)	14.1 ± 6.8	12.1 ± 5.7	0.153
Total Major complications (N, %)	8 (19.0%)	10 (23.8%)	0.595
Detailed complications (N, %)			
Severe pneumonia	3 (7.1%)	2 (4.8%)	1.00**
Anastomotic leakage	2 (4.8%)	1 (2.4%)	1.00**
RLN paralysis	4 (9.5%)	6 (14.3%)	0.500
Postoperative chylothorax	1 (2.4%)	1 (2.4%)	1.00**
30-day mortality (N, %)	0 (0%)	1 (2.4%)	1.00**

*Mann–Whitney U test; **Fisher's exact test.
RAMIE, robot-assisted minimally invasive esophagectomy; VAMIE, video-assisted minimally invasive esophagectomy.

respectively; $P = 0.153$). The rate of major complications between the two groups was comparable (19.0% and 23.8%, respectively; $P = 0.595$), and the rates in detailed major complications such as severe pneumonia ($P = 1.00$), anastomotic leakage ($P = 1.00$), RLN paralysis ($P = 0.500$), and postoperative chylothorax ($P = 1.00$) were all comparable. Within 30 days after surgery, one patient in VAMIE group died of esophagobronchial fistula, while no patient died in RAMIE group ($P = 1.00$) (Table 3).

DISCUSSION

Middle thoracic esophageal cancer accounts for the highest percentage of esophageal cancer in Chinese patients,[14] and is more likely to have both RLN and mediastinal lymph nodes metastasis.[15] We intended to select middle thoracic esophageal cancer operated only by two attendings who do both RAMIE and VAMIE during the same period to reduce the heterogeneity of this cohort study. We compared the short-term outcomes of RAMIE with that of VAMIE in treating middle thoracic esophageal cancer. We found that RAMIE yielded significantly more lymph nodes than VAMIE especially in dissecting right RLN lymph nodes and abdominal lymph nodes. Mainly because of needing docking twice in one operation, RAMIE took longer operation time, but was associated with less blood loss than VAMIE without any increased risk of perioperative major complications. To our knowledge, this is one of largest cohort studies comparing RAMIE with VAMIE and the first such study from a single major Chinese medical center.

RAMIE was first introduced in 2004 by Kernstine *et al.*,[6] and it was believed to possess excellent maneuverability and great visualization compared with traditional VAMIE.[16] Previous studies have demonstrated the safety and feasibility of applying RAMIE in treating esophageal cancer.[17–20] However, whether RAMIE is superior to VAMIE remains unclear and the actual advantages of RAMIE over VAMIE are far from well established. Affected by the limited operation volume and heterogeneities among those studies, previous studies have drawn controversial conclusions. Lymphadenectomy remains to be an important part of esophagectomy, and whether RAMIE has any advantages of lymphadenectomy over VAMIE remains unclear. Weksler *et al.*[8] included 11 patients with RAMIE and 26 VAMIE patients, and compared the short-term outcomes of these two groups. They found that the number of dissected lymph nodes (mean number: 23 and 23, respectively; $P = 0.950$) was comparable between the two groups. Yerokun *et al*[21] included 170 RAMIE patients and 170 VAMIE patients, and also found RAMIE was equivalent to VAMIE without any clear advantages of lymphadenectomy (Median number of harvested lymph nodes: 16 and 16, respectively; $P = 0.954$). Suda *et al.*[22] included 16 RAMIE patients and 20 VAMIE patients, and found that lymph nodes yields was comparable between RAMIE and VAMIE (total number of dissected lymph nodes: 37.5 and 39, respectively; $P = 0.485$), too. However, recently, Park *et al.*[9] conducted similar comparative study by including 62 RAMIE patients and 43 VAMIE patients. They found that the RAMIE group had significantly larger total number of dissected lymph nodes (37.3 vs. 28.7; $P = 0.003$) and numbers of lymph nodes dissected from upper mediastinum (10.7 vs. 6.3; $P = 0.032$), and abdomen (12.2 vs. 7.8; $P = 0.007$) compared to the VAMIE group. Chao *et al.*[23] included 34 pairs of RAMIE and VAMIE patients, and also found that RAMIE yielded significantly more left RLN lymph nodes than VAMIE (mean number: 5.3 and 3.4, respectively; $P = 0.007$) even though they found no significant difference of total dissected lymph nodes (mean number: 37.2 and 36.2, respectively; $P = 0.807$) between the two groups. This study found that RAMIE yielded significantly more total dissected lymph nodes (mean number: 21.9 and 17.8, respectively; $P = 0.042$) as well as abdominal lymph nodes (mean number: 10.8 and 7.7, respectively; $P = 0.04$) than VAMIE, adding to the evidence that RAMIE had advantage in lymphadenectomy over VAMIE. Previously, Kim *et al*.[24] have demonstrated the feasibility of RAMIE in lymphadenectomy along bilateral RLNs. This study showed that RAMIE could yield more right RLN lymph nodes (mean number: 2.1 and 1.2, respectively; $P = 0.033$) than VAMIE without increasing rate of RLN paralysis, proving that RAMIE had the advantage of lymphadenectomy for RLN lymph nodes over VAMIE with a relatively large sample size. As for intraoperative blood loss, nearly most of previous study found that no significant difference of blood loss volume between RAMIE and VAMIE. However, we found that RAMIE had significantly less blood loss than VAMIE, which we believe was owning greatly to the meticulous dissection under excellent visualization of robot, indicating the less invasiveness of RAMIE. Moreover, for postoperative complications, only Suda *et al*.[22] found that RAMIE significantly reduced the incidence of vocal cord palsy ($P = 0.018$) and hoarseness ($P = 0.015$) compared to VAMIE. However, other previous studies[8,9,23] together with this study showed no significant difference of the rate of postoperative complications between RAMIE and VAMIE, demonstrating that RAMIE was safe and feasible. There are several technical characteristics of RAMIE contributing to its advantages of lymphadenectomy over VAMIE without increasing any risk of postoperative complications: First, robotic surgery offers significant better visualization by providing 3-demensional magnified views with superior imaging quality, which could significantly facilitate identifying various structures in mediastinum as well as abdomen. Second, robotic surgery provides with freely articulated movement of the robotic arms, which enables more meticulous dissection greatly avoiding nerve injury during lymphadenectomy.

The reported average operation time for RAMIE was about 439–490 minutes,[8,9] which was similar to our report. However, previous studies showed no significant difference of operation time between RAMIE and VAMIE.[8,9] However, we found that RAMIE consumed significantly longer operation time than VAMIE. The possible reasons are: RAMIE needs docking twice in each operation, and the robotic carts need to be repositioned when thoracic phase was over and abdominal phase began. Surgeons and their teams were more familiar with VAMIE considering that we just began with RAMIE in April 2016, and have performed VAMIE for over years.

This study had several limitations. First, this study is a nonrandomized comparative analysis, which could limit the validity of our results. Second, this study still suffered from the limitation of relatively small sample size. Finally, comparisons of long-term outcomes between RAMIE and VAMIE are badly needed in the future.

CONCLUSIONS

In this nonrandomized study, we compared the short-term outcomes of RAMIE with that of VAMIE. We found that RAMIE had significant advantages of lymphadenectomy especially for dissecting RLN lymph nodes over VAMIE without increasing any risk of postoperative complications. Even though RAMIE may take longer operation time, considering it needs redocking time, it showed less minimal invasiveness than VAMIE regarding the significantly decreased total blood loss. Further studies and randomized controlled trials, however, are needed to confirm our conclusions.

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Conflict of interests: None declared.

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