



International consensus statement on robot-assisted minimally invasive esophagectomy (RAMIE)

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Introduction

The technique of minimally invasive esophagectomy (MIE) is constantly evolving. According to an international survey, the proportion of surgeons performing MIE has increased from only 14% in 2009 to more than 50% in 2014 (1,2). MIE has been proven to improve perioperative results

by MORO and TIME trials (3-6), and with comparable disease-free survival (DFS) and overall survival (OS) to open surgery. However, thoracoscopic-assisted MIE requires a long learning curve and accumulation of a large number of cases. Both large Asian medical centers and a national database review in the United States indicated

that the reoperation rate of MIE was significantly higher than that of open surgery during the same period (7,8). In the process of developing thoracoscopic procedure, it is possible to sacrifice the principles of oncology, especially in the learning stage.

The emergence of robotic technology may overcome some of the shortcomings of traditional MIE, enabling junior esophageal and open surgeons to quickly complete minimally invasive transformation. Robot-assisted minimally invasive esophagectomy (RAMIE) was first performed by Dr. Santi Horgan in August 2002 using a transhiatal approach. RAMIE-McKeown appeared in 2002 (9), and a series of case reports was formed in 2006 (10). Since then, centers in Europe, North America and Asia have reported their own experiences of RAMIE. Based on the literature to date, the feasibility and safety of RAMIE appears to be similar to MIE and open esophagectomy (11-14). The ROBOT trial is presently the only randomized controlled trial (RCT) to compare RAMIE and open esophagectomy. Results of the ROBOT trial have indicated better perioperative recovery with RAMIE and comparable oncological outcomes (15). However, no previous RCT study demonstrated the superiority of RAMIE to traditional thoracoscopy, with the exception of two ongoing studies of *REVATE* and *RAMIE* (16,17). Retrospective studies suggest improved lymphadenectomy, decreased intraoperative blood loss, and potentially shorter intensive care unit stays (18).

At present, the RAMIE technique is only routinely carried out in a few large centers. As a new technology, consensus statements can shorten the learning curve for practitioners and provide specific guidance for quickly mastering the technology. The Upper GI International Robotic Association has focused on similar work before, as *The Da Vinci Ivor Lewis Esophagectomy Procedure Guide* was described in detail in their consensus. However, the limitation of this consensus is that it does not fully consider the surgical principle and technical habits of robotic surgery for esophageal squamous cell carcinoma (ESCC), especially Asian ESCC, such as radical dissection of upper mediastinal lymph nodes and the three-incision surgical approach (19). This portion of patients accounts for more than half of the world's esophageal cancer patients.

To summarize technical experience with RAMIE on a larger scale, shorten the learning curve for the beginners, improve the safety of surgery, and judge the feasibility of RAMIE technology through the participation of more surgeons, we invited representative international experts to participate in the development of this consensus. In

addition, we searched online databases for published articles related to RAMIE; for evidence-based methods, all evidences were graded using the GRADE system and upgraded or downgraded after integrating experts' opinions until a final consensus statement was reached. We present the following article in accordance with the AGREE reporting checklist (available at <http://dx.doi.org/10.21037/jtd-20-1945>).

Methods

We referred to the *World Health Organization Handbook for Guideline Development* and established the Consensus Development Group (CDG). We identified potential experts by performing a literature review using the PubMed/Medline database with the keywords "robot" and "esophagectomy". Experts who agreed to participate were also requested to invite respective regional experts in robotic esophagectomy. An initial working group identified representative international esophageal surgical centers and individual surgeons. Experts were defined as having performed more than 50 cases of robotic esophagectomy, as we previously demonstrated a significant reduction of operating time after 40 cases (18). A total of 23 international experts were initially identified, of which 21 agreed to participate in the consensus statements, with the following missions:

- (I) Define the scope of the consensus and draft key questions relevant to the current status of RAMIE;
- (II) Administer questionnaires to experts and tabulate the results;
- (III) Grade the quality of the evidence;
- (IV) Draft preliminary recommendations;
- (V) Write the draft consensus;
- (VI) Publish and promote consensus statements.

Experts in the CDG voted on the recommendations according to the quality of evidences and surgeons' preferences. The GRADE Grid method and Delphi vote were used to formulate the recommendations. The GRADE grid allows experts on the consensus panel to record their views about the balance between advantages and disadvantages of a specific procedure, based on their opinion of the available evidence. To guide the use of GRADE grid, all participants received instructions describing factors that influence the strength of a recommendation and the implications of strong and weak recommendations.

We defined the way of assigning levels of evidences and statements as follows.

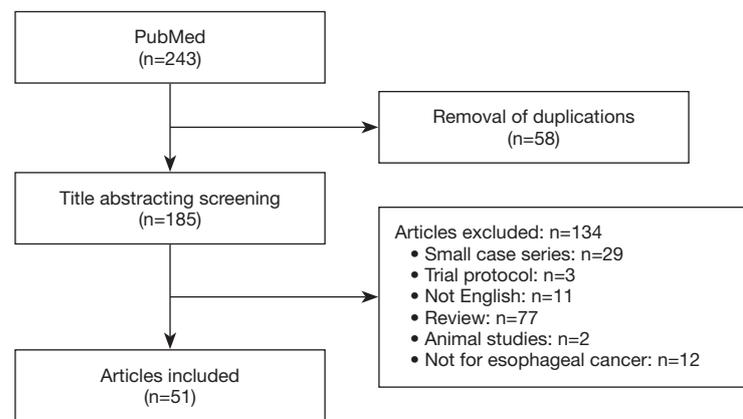


Figure 1 Flow chart of literature review.

(I) Factors that influence the strength of a recommendation

- Balance between desirable and undesirable effects—the larger the difference between desirable and undesirable effects, the more likely a strong recommendation is warranted. The narrower the gradient, the more likely a weak recommendation is warranted.
- Quality of evidence—the higher the quality of evidence, the more likely a strong recommendation is warranted.
- Values and preferences—the more variability in values and preferences, or more uncertainty in values and preferences, the more likely a weak recommendation is warranted.

(II) Implications of strong and weak recommendations

- Strong recommendation

Most patients in this situation would benefit from the recommended course of action, while only a small proportion would not. Most surgeons should agree with the consensus statement.
- Weak recommendation

Most patients in this situation would not benefit from the course of action, which may even be harmful to health. Most surgeons would not agree with the consensus statement.
- No specific recommendation

If the advantages and disadvantages of the referred consensus statement are equivalent, or there is not sufficient evidence to support the recommendation.

In May 2019, all experts were invited by e-mail to

participate in the consensus statement and received a personal Excel file to fill out the survey. Two rounds of voting were conducted. It was decided by the group that when 66.7% of the experts approved the recommendation, a consensus had been reached and the statement could be made. To provide methodological support, the Consensus Secretary Group (CSG) performed a systematic review of the literature and investigation of surgeons' preferences, along with the Chinese GRADE Center. All members of the CDG and CSG were required to disclose potential conflicts of interest, which were reviewed by the group chairs.

For literature review (*Figure 1*), the PubMed database was searched for: “robot” AND “esophagectomy”, and their synonyms or abbreviations. No additional search software or special features were used. The search was limited to papers describing original patient data for a series of more than 10 patients in the English language. The investigators (BL and YY) independently performed screening and article selection procedures. All articles that fulfilled the eligibility criteria were included in our systematic review. Duplicate publications with derivative patients were excluded. Search results and the selection process were summarized in a flowchart. Each article was screened for first author, year of publication, number of subjects, study population characteristics, and study design. Furthermore, postoperative complications, and oncologic results were assessed.

Results

Twenty-three international surgeons who are experts in the field of robotic esophagectomy were invited to participate in the consensus statement. As mentioned above, two

rounds of electronic surveys were carried out. A total of 8 topics and 91 questions were reviewed and voted on by 21 experts (two experts did not provide responses in the first round). After applying the selection criteria to all searched abstracts, 51 articles remained available for analysis. Finally, 27 statements were recommended based on the experts' opinions and systematic literature review. The main topics of the statements fall under the following areas: surgical approach, anesthesia, patient position, trocar arrangement, surgical technique, learning curve, complications, and survival outcomes.

Surgical approach

- ❖ RAMIE is always the preferred approach when the robot machine is available, regardless of clinical stage or whether neoadjuvant therapy has been received.

GRADE of evidence: low; strength of recommendation: weak.

Consensus reached: 78% agreement.

- ❖ The transthoracic esophagectomy (TTE) is the preferred approach in RAMIE, especially for squamous cell carcinoma.

GRADE of evidence: low; strength of recommendation: strong.

Consensus reached: 67% agreement.

- ❖ Transhiatal esophagectomy (THE) is safe and feasible for adenocarcinoma.

GRADE of evidence: low; strength of recommendation: weak.

Consensus reached: 78% agreement.

RAMIE can be performed by two main approaches: transhiatal and transthoracic. The choice of surgical approach for RAMIE is based on the surgeon's experience and characteristics of the tumor. We analyzed data from 27 centers that had performed RAMIE for more than 10 cases. Among them, the transhiatal approach was adopted in 4 centers (14.8%), the Ivor Lewis procedure in 5 centers (18.5%), and the McKeown procedure in 13 centers (48.1%); both Ivor Lewis and McKeown procedures were performed in the remaining 5 centers (18.5%) (*Table 1*).

TTE

In Asia, most surgeons prefer the RAMIE McKeown procedure (three incisions). This is due in large part to the greater prevalence of squamous cell carcinoma in the patient population and, accordingly, an increased need to manage

the biology of squamous cell cancer (20,21). RAMIE-Ivor Lewis appears to be the preference for middle and lower esophageal cancer (22-24). Again, this procedure addresses the biology of the disease and appears to have a lower rate of anastomotic leak. Based on concerns about anastomotic leakage, an increasing number of European and American experts have turned to Ivor Lewis technology. According to our analysis (*Table 1*), the Ivor Lewis procedure was applied in 10 (43.5%) of the 23 centers, of which 3 centers (30%) were in Asia; whereas, the McKeown procedure was performed in 18 centers (78.3%), of which 11 centers (61.1%) were in Asia. Emphasis on the McKeown technique in Asia stems from deep attention to upper mediastinum and cervical lymph node dissection, as well as a high incidence of middle and upper thoracic squamous cell carcinomas. In addition, the incidence of cervical anastomotic leakage in Asian patients has always remained within an acceptable range.

THE

THE, which is thought to preserve pulmonary function and potentially enhance postoperative recovery (25,26), is frequently applied for the treatment of adenocarcinoma of the lower esophagus or early squamous cell esophageal cancer (27,28). THE was the first robotic-assisted esophagectomy performed, mainly because robotic surgery at the time had only been carried out on the abdomen, and so it started with this hybrid approach (29). At present, robotic dissection can reach freely up to the lower pulmonary vein through the hiatus, but cannot easily reach the carina. Moreover, whether THE allows radical mediastinal lymphadenectomy remains a concern, which is the key difference from a transthoracic procedure. Increased likelihood of mediastinal bleeding and airway damage also remain important issues for THE. To further improve the efficiency of lymphadenectomy during THE, Mori *et al.* (30) developed a non-transthoracic esophagectomy procedure combining RATHE and a video-assisted cervical approach. The authors believed that this procedure could achieve the same lymph node dissection result as the transthoracic approach while significantly reducing postoperative pulmonary complications. These techniques provide a new direction for RATHE; however, studies with larger sample sizes are still required to verify their safety and feasibility. In the future, robots may also be used in transhiatal esophageal surgery. One key technique that still needs to be addressed is a flexible, single-arm, multi-operation tunnel technology, such as the SP system. A Japanese surgeon has also

Table 1 Surgical approaches and short-term perioperative outcomes in the literature on robot-assisted esophagectomy

Authors	Year	Case	Approach	Nodes removed	Surgical time	Intraoperative bleeding	Hospital stay	Pulmonary complications (%)	Anastomotic leak (%)	RLN palsy (%)
Galvani <i>et al.</i>	2008	18	TH	14	267	54	10	11	33	5
Coker <i>et al.</i>	2014	23	TH	15	231	100	9	13	9	NA
Mori <i>et al.</i>	2016	22	TH	30 mediastinal	524	385	18	0	18	4.5
Dunn <i>et al.</i>	2017	100	TH	17	264	75	8	11	16	33
Hodari <i>et al.</i>	2015	54	Ivor Lewis	16.2	362	74.4	12.9	11.1	6.8	NA
Wee <i>et al.</i>	2016	20	Ivor Lewis	23.2	455.5	275	8	5	0	NA
Cerfolio <i>et al.</i>	2016	85	Ivor Lewis	22	360	35	11	7.1	4.3	NA
Meredith <i>et al.</i>	2018	147	Ivor Lewis	20.4	415	150	9	10.9	2.7	NA
Zhang <i>et al.</i>	2018	61	Ivor Lewis	19.3	315.6	189.3	10	6.6	9.8	8.2
Wang <i>et al.</i>	2019	31	Ivor Lewis	17.1	387.4	110	12	6.5	6.5	NA
Sarkaria <i>et al.</i>	2013	21	Mc 4/IL 7	20	556	307	10	23.8	38	NA
Park <i>et al.</i>	2016	62	Mc 56/IL 6	37.3	490.3	462.9	NA	14.5	8.1	12.9
Okusanya <i>et al.</i>	2017	25	Mc 2/IL 23	26	661	250	8	20	4	NA
Guerra <i>et al.</i>	2018	38	Mc 14/IL 24	33	550	80	10	8	16	2.6
Kernstine <i>et al.</i>	2007	14	McKeown	18	NA	NA	NA	NA	14	NA
Boone <i>et al.</i>	2009	47	McKeown	29	450	625	18	44.7	21.3	19.1
Weksler <i>et al.</i>	2012	11	McKeown	23	439	200	8.7	18.2	9.1	
van der Sluis <i>et al.</i>	2015	108	McKeown	26	381	340	16	33	19	9
Puntambekar <i>et al.</i>	2015	83	McKeown	18.4	204.9	86.6	10.4	1.2	3.6	2.4
Yi <i>et al.</i>	2015	79	McKeown	20.6	245	75	10.2	6.3	7.6	2.5
Park <i>et al.</i>	2016	114	McKeown	43.5	419.6	208.7	16	9.6	14.9	26.3
Chiu <i>et al.</i>	2017	20	McKeown	18.2	499.5	355.7	13	5	15	25
Somashekhar <i>et al.</i>	2017	35	McKeown	32	352	380	8	2.9	0	2.9
Chao <i>et al.</i>	2018	37	McKeown	37	NA	94.1	17.5	8.1	2.7	21.6
He <i>et al.</i>	2018	27	McKeown	20	349	118	13.8	18.5	11.1	14.8
Deng <i>et al.</i>	2019	79	McKeown	20.6	356.7	103.9	14.4	7.6	7.6	10.1
Chen <i>et al.</i>	2019	68	McKeown	24.7	187.5	115.7	16.7	17.6	8.8	14.7
Yang <i>et al.</i>	2019	271	McKeown	20.3	244.5	210.7	11	8.9	11.8	29.2

TH, transhiatal; Mc, McKeown; IL, Ivor Lewis; NA, not available.

developed a non-transthoracic esophagectomy procedure comprising RATHE and a video-assisted cervical approach, but it is still far from a full robotic non-transthoracic esophagectomy (30,31).

Anesthesia and patient's position

- ❖ CO₂ insufflation is routinely applied during the thoracic phase of RAMIE-McKeown.
GRADE of evidence: low; strength of recommendation: strong.
Consensus reached: 89% agreement.
- ❖ Proper trocar placement and the patient's position are crucial for RAMIE.
GRADE of evidence: low; strength of recommendation: strong.
Consensus reached: 100% agreement.
- ❖ A third robotic arm helps to achieve better surgical exposure.
GRADE of evidence: low; strength of recommendation: weak.
Consensus reached: 78% agreement.

Anesthesia management and patient positioning during RAMIE are very similar to those of MIE. Single-lumen endotracheal intubation with a right bronchial blocker and CO₂ insufflation assistance is the most common procedure for thoracic exposure in Asia. CO₂ insufflation can expand the mediastinum and maximize exposure of the intrathoracic esophagus by means of depressing the diaphragm caudally and pushing the lung anteriorly (32). Single-lumen tracheal intubation can facilitate lymph node dissection at the carina and upper mediastinum, especially 106recL nodes along the left of the recurrent laryngeal nerve (RLN). Double-lumen tracheal intubation is preferred by European and American doctors, either for Ivor Lewis or McKeown approaches, and is reliable to provide a safe surgical environment.

Semi-prone position (30–45 degree) is used for the thoracic phase of RAMIE by both Asian and Europe surgeons for McKeown esophagectomy, while the left lateral decubitus position is commonly used for Ivor Lewis (33–37). Trugeda *et al.* (38) reported utilization of the prone position for the RAMIE-Ivor Lewis procedure because they believed that this position allowed for better exposure of the esophagus and less injury to the lungs and hilar structures. However, this method is rarely adopted by other surgeons (39). Reverse Trendelenburg position is the basic position for upper gastrointestinal dissection, as well as the abdominal phase of RAMIE.

Trocar arrangement depends on the surgeon's preference. Proper trocar placement is strongly recommended in the consensus statement, but we have not given a recommended uniform method. As every doctor has their own preferences and tendencies, trocar placement will be different. Even so, proper trocar placement is the basic requirement for a successful RAMIE, which has been agreed upon by all experts. According to the surgeon's previous experience, three or four robotic arms are commonly applied for RAMIE. For RAMIE-Ivor Lewis, the four-arm mode is recommended because it helps to complete the thoracic anastomosis (40). For RAMIE-McKeown, use of the three-arm mode with the help of an assistant can effectively complete dissection of the thoracic esophagus and mediastinal lymph nodes (41). Use of the third robot arm (controlled by the operator) allows excellent operating exposure to be achieved through the application of stable and self-controllable tractions and counteractions on the esophagus and trachea. With the help of a third robotic arm, the surgeon can perform left RLN LND while maintaining full use of the primary "working" arms, ultimately ensuring a safer and easier approach to nodal dissection (20).

En bloc resection, total mesoesophagus excision (TME), and thoracic duct resection

- ❖ TME is recommended in RAMIE because it may result in better local control of tumor recurrence.
GRADE of evidence: low; strength of recommendation: weak.
Consensus reached: 67% agreement.
- ❖ En bloc resection of tumors and lymph nodes is mandatory; however, the thoracic duct is not routinely resected.
GRADE of evidence: low; strength of recommendation: weak.
Consensus reached: 78% agreement.
- ❖ Prophylactic ligation of the thoracic duct cannot prevent postoperative chylothorax.
GRADE of evidence: low; strength of recommendation: weak.
Consensus reached: 78% agreement.

The concept of TME comes from radical surgery for rectal cancer (42) and has been carried forward by Japanese surgeons for esophageal cancer resection. The essence of TME for the treatment of esophageal cancer is to use the anatomical space between the esophagus and its adjacent structures to maximally excise the esophagus and nerves,

blood vessels, and lymphatic adipose tissues around it, which emphasizes the importance of *en bloc* excision of the mesoesophagus. However, some studies indicated that there was no difference between TME and non-TME with regard to the number of lymph nodes harvested. Nevertheless, Akiyama *et al.* (43) showed that the overall recurrence rate was significantly lower in the TME group (23.0% *vs.* 43.4%; $P=0.011$). Specifically, TME resulted in a decreased rate of mediastinal lymph node recurrence (2.3% *vs.* 11.3%; $P=0.026$). Thus, TME may have an advantage for local control of tumor recurrence. But this is a purely Asian concept, and it is very difficult to accurately identify the mesoesophagus, especially in patients who have undergone neoadjuvant radiotherapy. But with the assistance of robotic technology, TME can more easily be performed.

As it has been shown that the thoracic duct can contain metastatic tumor cells (44,45), it is recommended to remove the thoracic duct and its surrounding tissue upon the completion of TME (43,46). Schurink *et al.* (44) also demonstrated the presence of thoracic duct lymph nodes in 86% of cadaveric specimens, implying the possibility of node metastasis. However, thoracic duct resection may involve many physiological changes, such as the risk of postoperative chylothorax, changes in long-term immune status, possible hemodynamic effects, and absorption of nutrients from abdominal lymphatic drainage (47). Indeed, some studies demonstrated that thoracic duct resection is associated with poor prognosis and regional lymph node relapse in ESCC (48,49). Therefore, routine use of thoracic duct resection remains controversial (43,46). In terms of surgical techniques, RAMIE can more easily complete thoracic duct resection (47,50).

Anastomosis

- ❖ The mechanical stapler technique is recommended for anastomosis in RAMIE.

GRADE of evidence: low; strength of recommendation: weak.

Consensus reached: 78% agreement.

- ❖ Intrathoracic anastomosis should be made as high as possible, and may be more accessible in RAMIE compared with MIE.

GRADE of evidence: low; strength of recommendation: weak.

Consensus reached: 67% agreement.

- ❖ Reinforcement of the staple line of the gastric conduit is not routinely advised due to a lack of high-level

evidence.

GRADE of evidence: low; strength of recommendation: weak.

Consensus reached: 67% agreement.

It is well known that a higher position of intrathoracic anastomosis can ensure a better resection margin and reduce the symptoms of reflux, especially for ESCC patients in Asia. The technical specifications for anastomosis were listed as follows: (I) anastomotic configuration: end-to-end, end-to-side, side-to-end, or side-to-side; (II) technique: robotic hand-sewn, circular stapling, or linear stapling; (III) suture technique: single layer, double layer, continuous, or interrupted; (IV) reinforcement of the anastomosis with omentum or pleura. Conventional thoracoscopic anastomosis techniques can be performed better using the robotic technology.

Hand-sewn intrathoracic anastomosis can reduce the incidence of postoperative anastomotic stenosis; however, due to its high technical demands, few surgeons attempt this technique under conventional thoracoscopy. Robotic assistance makes this technology a reality with a minimally invasive approach. The “T” shape or over-flap anastomosis with linear stapling technique has been used by many surgeons for anastomosis orifices with a wide diameter. The circular stapler remains the most reliable instrument to assist with an anastomosis, although it carries the disadvantage of complications associated with stricture (51). To reduce the likelihood for anastomotic leak, an omentum flap can be performed to reinforce Ivor Lewis anastomosis.

Several meta-analyses have compared stapled and hand-sewn anastomotic techniques. These studies have included both randomized and non-randomized trials, and have found no significant differences in anastomotic leak rates between the two anastomotic techniques (52-54). A network meta-analysis conducted by Kamarajah (55) demonstrated that stapled anastomosis, including circular- and linear-stapled, are associated with lower anastomotic leak rates compared with hand-sewn anastomosis following esophagectomy. Moreover, linear-stapled anastomosis is associated with a lower rate of anastomotic stricture compared with hand-sewn anastomosis. In the future, large high-quality randomized trial data are needed to provide evidence to compare the three anastomosis techniques.

Lymph node dissection

- ❖ RAMIE should be superior to MIE in terms of upper mediastinal lymph node dissection.

GRADE of evidence: moderate; strength of recommendation: strong.

Consensus reached: 89% agreement.

- ❖ Lymph node dissection along the bilateral RLNs is recommended; however, skeletonization of RLNs is not widely performed.

GRADE of evidence: moderate; strength of recommendation: weak.

Consensus reached: 67% agreement.

- ❖ Skeletonization of the celiac axis is recommended to achieve radical node dissection.

GRADE of evidence: low; strength of recommendation: weak.

Consensus reached: 67% agreement.

- ❖ Cervical para-esophageal lymph nodes (No. 101) can be partially dissected during the thoracic phase of RAMIE.

GRADE of evidence: low; strength of recommendation: weak.

Consensus reached: 67% agreement.

- ❖ Subcarinal lymph nodes must be routinely dissected.

GRADE of evidence: low; strength of recommendation: strong.

Consensus reached: 100% agreement.

Lymphadenectomy is a critical component of radical esophagectomy for the treatment of esophageal cancer. Therefore, the majority of studies concerning the application of RAMIE have focused on better lymphadenectomy, especially for mediastinal lymph node dissection. However, the conclusions derived from previous studies are not consistent. Retrospective studies of Ivor Lewis and McKeown procedures by Park *et al.* (22) and Deng *et al.* (56) found that RAMIE yielded more dissected lymph nodes than conventional MIE. However, several other studies have demonstrated that the number of total dissected lymph nodes was comparable between the two surgical techniques (57,58). van Rijswijk and colleagues (59) conducted an international survey to identify differences in esophageal cancer surgery in terms of surgical approach and extent of lymphadenectomy. In their survey, the extent of lymphadenectomy showed great variation among all experts. Users of the Japanese Society of Esophageal Diseases (JSED) classification (used by 100% of Asian respondents) performed a more extended cervical lymphadenectomy, as opposed to users of the American Joint Committee on Cancer classification (used by 79% of European respondents) (60). Therefore, it is difficult for us to infer which surgery is more conducive to lymph node

dissection by means of comparing the results of different regions. Thus, clinical research with RCTs should be used to answer this question.

Based on their rich experience of RAMIE and MIE, 89% of experts in this consensus agreed on the comment “RAMIE should be superior to MIE in terms of extensive mediastinal lymphadenectomy”. The advantage of robotic surgery lies in its fine operation in a narrow space, which has been proven by its utilization for the dissection of upper mediastinal lymph nodes of ESCC. In Asia, RAMIE has been found to be more consistently thorough for mediastinal lymphadenectomy compared with MIE. The mediastinum, especially along both RLNs, is a common site for early metastasis and spread of upper and middle ESCC (61,62). Kim *et al.* (63) demonstrated that the skeletonization of RLNs results in an increased number of mediastinal lymph nodes harvested (30.3 *vs.* 19.6) and lymph nodes along RLN chains (13.5 *vs.* 4.8). Although RLN palsy was more common in patients with skeletonization of RLNs (31.8 *vs.* 5.6), all of these patients recovered within 1 year after surgery. In another propensity-matched study, Chao *et al.* (20) reported that skeletonization of RLNs did not increase the efficacy of lymph node dissection, as well as a similar incidence of RLN palsy. Lymph nodes at stations 16a1 and 16a2 of the para-aortic, truncus coeliacus, posterior surface of the pancreatic head, and arteria hepatica communis were the primary sites for abdominal metastasis after radical surgery for esophageal cancer (64). During the abdominal phase, skeletonization of the celiac axis is always recommended to achieve radical lymph node dissection, either for adenocarcinoma or squamous cell carcinoma.

Perioperative outcomes

- ❖ RAMIE does not increase the incidence of intraoperative adverse events compared with open or thoracoscopic approaches.

GRADE of evidence: moderate; strength of recommendation: strong.

Consensus reached: 83% agreement.

- ❖ Intraoperative airway injury can be repaired with robotic assistance.

GRADE of evidence: low; strength of recommendation: strong.

Consensus reached: 100% agreement.

- ❖ The overall rate of postoperative complications in RAMIE is comparable with MIE, while the incidence of RLN injury is lower than MIE.

GRADE of evidence: moderate; strength of recommendation: weak.

Consensus reached: 67% agreement.

- ❖ RAMIE can decrease the incidence of postoperative pulmonary complications compared with open esophagectomy.

GRADE of evidence: moderate; strength of recommendation: strong.

Consensus reached: 89% agreement.

Unplanned events of RAMIE include but are not limited to the following: thoracic or abdominal adhesions, trocar puncture-related iatrogenic injury, RLN injury, airway injury, intraoperative hemorrhage, intraoperative ventricular arrhythmia, and R2 resection. The occurrence of intraoperative unplanned events may increase the incidence of postoperative complications and compromise the quality of tumor resection. If an unexpected event occurs during the operation, RAMIE is better equipped to fix it compared with traditional thoracoscopy, such as adhesion dissection, airway injury repair, and R0 resection of the invading tumor.

Incidence of postoperative complications after RAMIE differs among different centers, depending on the histologic type, surgical procedure, reconstruction approach, and lymph node dissection (Table 1). Generally, RAMIE did not change the 90-day mortality rate compared with MIE. For the McKeown procedure, the incidence of postoperative pulmonary complications was 7.6–18.5%, the incidence of anastomotic leakage was 2.7–14.9%, the incidence of vocal cord paralysis (VCP) was 10.1–26.3%, the length of postoperative hospital stay was 8–17 days, and the postoperative 90-day mortality rate was 0–2.7% (65,66). However, results reported in the literature are primarily from single-center retrospective studies, which do not reflect real-world postoperative complications after RAMIE. The ROBOT trial demonstrated the minimally invasive effect of RAMIE, as well as better perioperative recovery and comparable oncological outcomes compared with open esophagectomy for the treatment of esophageal cancer (15).

With regard to quality of life (QOL) after RAMIE, several groups have reported outcomes. Both van der Sluis *et al.* (15) and Sarkaria *et al.* (67) demonstrated that RAMIE is safe and results in reduced perioperative morbidity, improved early QOL, and equivalent oncological outcomes compared with open esophagectomy.

Thus far, no related study has focused on anastomotic stricture after RAMIE. Anastomotic stricture with dysphagia has a negative effect on the patient's QOL and

considerably worsens the patient's postoperative nutritional status. Most strictures develop within the first 2–3 months after operation, and up to 50% are minimal, as assessed by endoscopy (68). Improvement of anastomotic techniques and application of the circular stapler have effectively reduced leak rates following esophagogastrotomy, but stricture formation has become more frequent because of stapler size limitations and anastomotic scar formation (69). Chen and co-workers reported that semi-mechanical esophagogastric anastomosis could prevent stricture formation more effectively than hand-sewn or circular stapler esophagogastrotomy, without increasing gastroesophageal reflux (70). According to the literature, the main potential risk factors associated with postoperative benign anastomotic stricture include anastomotic technique, limited circular stapler diameter, poor vascular supply, and anastomotic leak, which significantly impair long-term QOL (71,72).

Learning curve

- ❖ Operative time is an essential index of the learning curve for RAMIE.

GRADE of evidence: moderate; strength of recommendation: weak.

Consensus reached: 78% agreement.

- ❖ The efficacy of lymphadenectomy is an essential index of the learning curve for RAMIE.

GRADE of evidence: moderate; strength of recommendation: strong.

Consensus reached: 94% agreement.

- ❖ The learning curve of RAMIE is shorter than MIE in the thoracic phase.

GRADE of evidence: low; strength of recommendation: weak.

Consensus reached: 78% agreement.

Few reports describe the learning curve for RAMIE. Central evaluation indicators for the learning curve include docking time, operative time, efficacy of lymphadenectomy, postoperative complications, and postoperative stay. Regarding the operation time, there was no agreement in our questionnaire. In previous studies comparing RAMIE and MIE, the operation time was also inconsistent (58,73). In our opinion, use of robots should improve the efficiency of esophagectomy in RAMIE after achieving proficient docking and undocking. However, future RCT including the RAMIE trial (18) will give us the answers. Several previous studies reported that the learning curve

for surgeons with experience in RAMIE is about 20 to 40 cases, which is significantly shorter than for MIE, especially for the thoracic phase (74,75). Park *et al.* (76) indicated that a minimum of 20 cases is required before a surgeon is experienced enough to perform safe dissection of bilateral RLN nodes. In another retrospective study (73), the authors reported that the most accurate evaluation indicators of the learning curve for RAMIE were operative time, lymph node dissection, complications, and length of hospital stay. van der Sluis *et al.* (77) demonstrated that a structured proctoring program could shorten the learning curve for young surgeons. Zhang *et al.* (78) found that surgeons with extensive experience in open and laparoscopic surgeries for esophageal cancer could reach proficiency in the RAMIE McKeown procedure after 26 cases. This was also the first study to describe the learning curve of assistants involved in RAMIE, especially for docking and undocking time. Evaluation of the learning curve for RAMIE in newly introduced surgeons should be divided into two levels: first, the surgical completion rate is evaluated according to the average operative time; second, the quality of surgery is evaluated according to the learning curve judgment indicators. Lymphadenectomy, which is a critical component of radical esophagectomy in the treatment of esophageal cancer, should be considered an essential index to assess the learning curve for RAMIE.

Survival outcomes

- ❖ RAMIE can achieve better local control of tumor recurrence compared with MIE.
GRADE of evidence: low; strength of recommendation: weak.
Consensus reached: 67% agreement.
- ❖ Long-term survival outcomes of RAMIE compared with MIE and open esophagectomy still need further evidence.
GRADE of evidence: moderate; strength of recommendation: strong.
Consensus reached: 100% agreement.
- ❖ Improvement in long-term survival will promote the development of RAMIE.
GRADE of evidence: low; strength of recommendation: weak.
Consensus reached: 72% agreement.

As a relatively recent technology, data regarding the oncologic efficacy and long-term survival of RAMIE are limited. As such, ongoing and further RCTs are called

for to show improved outcomes of RAMIE. We believe that improvement in long-term survival will promote the development of RAMIE.

For ESCC treatment, RAMIE should be superior to MIE in terms of extensive mediastinal lymphadenectomy. Although no high-quality literature supports this statement at present, several previous retrospective studies demonstrated that RAMIE can achieve better local control of tumor recurrence compared with MIE. Retrospective studies by Park *et al.* (22) and Deng *et al.* (56) reported that RAMIE yielded more dissected lymph nodes than conventional MIE. Chao *et al.* (20) also showed that compared with MIE, RAMIE resulted in a higher lymph node yield along the left RLN without increasing morbidity. Park *et al.* demonstrated that RAMIE is associated with better total mediastinal lymphadenectomy, including dissection of the RLN nodes, especially for upper or middle ESCC (79). The rate of locoregional tumor recurrence could be decreased after RAMIE. van der Sluis *et al.* (80) reported the long-term results of 108 patients who underwent RAMIE. The 5-year OS rate was 42.0%, the median DFS was 21 months, and the median OS was 29 months. Tumor recurrence occurred in 51 patients (49.5%) and was locoregional only in 6 patients (6.0%), systemic only in 31 patients (30.0%), and combined in 14 patients (14.0%). According to their results, RAMIE was oncologically effective and provided excellent local control with a low percentage of local recurrence at long-term follow-up. Weksler *et al.* (81) reported that there were no differences in the long-term survival of patients with esophageal cancer undergoing RAMIE, MIE, and open esophagectomy. Notably, they considered that the surgeon's experience and ability might be more critical than the surgical approach for esophageal cancer. Park *et al.* (22) demonstrated that 5-year OS and recurrence-free survival (RFS) rates were similar between patients undergoing RAMIE and MIE. Yerokun *et al.* (82) analyzed 4,266 patients in the National Cancer Database who underwent RAMIE (231 cases), MIE (1,077 cases), or open esophagectomy (2,958 cases) for esophageal cancer. Comparison of survival based on surgical procedures showed that: the 3-year OS was not different between RAMIE and MIE for adenocarcinoma, but the 3-year OS for RAMIE was significantly higher than MIE for squamous cell carcinoma (84% vs. 56%, $P=0.034$). In 2018, Espinoza-Mercado *et al.* (83) demonstrated that RAMIE and MIE had similar 30- and 90-day mortality rates, as

well as long-term survival rates comparable with open esophagectomy, and no significant differences in median OS estimates according to the National Cancer Database.

Summary

In these consensus statements, we can find many details of technique in robot-assisted esophagectomy. We hope they will provide a reference for the beginners and reduce their learning curve. Compared with both traditional open and thoracoscopic surgery, we have yet to see the advantages of RAMIE for oncological outcomes. What are the benefits of RAMIE? We believe that it offers improved surgical efficiency, facilitates a more comfortable surgical experience, and promotes more sophisticated complex surgical techniques, such as precision anastomosis technology. If all of these things are done well, improvements in the quality of treatment received by the entire esophageal cancer population may be achieved.

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