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Comparing Surgical Outcomes between Conventional Thoracoscopic Esophagectomy *vs*. Robotic Esophagectomy: A Review

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Abstract

Background: With a dismal 5-year survival rate and a place among the worst malignancies, esophageal cancer is a global health crisis. Invasive therapies such as esophagectomy are frequently used today. Although Robotic-Assisted Minimally Invasive Esophagectomy (RAMIE) is a potential remedy, further investigation is needed to see how it compares to conventional thoracoscopic Minimally Invasive Esophagectomy (MIE).

Objective: The most recent studies (2017-2023) on Robotic-Assisted Minimally Invasive Esophagectomy (RAMIE) and Minimally Invasive Esophagectomy (MIE) for the treatment of esophageal cancer are covered in this review. In terms of clinical metrics, we compared the long-term results of RAMIE with those of the more conventional thoracoscopic esophagectomy (IVOR-LEWIS and McKeown). We address issues related to surgery, technique advantages and disadvantages, and the demand for more research.

Method: We conducted an extensive literature review, analyzing recent studies and clinical trials centered on RAMIE and MIE to identify trends in surgical outcomes and patient experiences.

Key Findings: RAMIE has the potential to produce better postoperative outcomes, including shorter hospital stays and better cosmetics. Learning curves and differences in surgical expertise become limitations. Patient satisfaction and long-term oncologic results are still understudied.

Conclusion: RAMIE offers possibilities for treatment for esophageal cancer, with potential long-term benefits. To evaluate long-term effects and thoroughly compare RAMIE *vs*. MIE, additional research is needed. Esophageal cancer surgery will be shaped by ongoing clinical studies, which will provide information on patient outcomes and survival rates for these novel strategies.

Keywords: Minimally Invasive Esophagectomy (MIE); Robot Assisted Minimally Invasive Esophagectomy (RAMIE); Esophageal cancer

Introduction

Esophageal cancer, which is classified as an upper gastrointestinal tract malignancy, is caused by a cellular growth erratum along the esophageal tube; and is a leading cause of cancer-related death [1]. The 5-year survival rate for esophageal cancer is currently believed to be between 15% to 25%, making it the eighth most frequent cancer worldwide and the sixth most common cause of cancer mortality [2,3]. In China, cancer is a significant burden according to GLOBOCAN 2020's data, which projects approximately 19,292,789 cases [4]. With over 346,633 instances, esophageal cancer appears to be a major issue in this country, as it highlights its significant impact on the total prevalence of cancer in the nation [5].

In addition to the conventional methods used for complex procedures, such as esophagectomies, there has been an introduction of Minimally Invasive Esophagectomy (MIE) along with Robotic-Assisted Minimally Invasive Surgery (RAMIE) [6]. The methods of esophagectomy to treat esophageal cancer are currently debated, as it is still widely regarded to have a poor outcome [7].

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Recent studies have revealed significant favorable outcomes with the inclusion of neoadjuvant treatment along with esophagectomy methods, allowing patients to be evaluated for a meticulous preoperative staging and ameliorated postoperative care [6]. There have been significant findings, revealing an improved survival rate of patients in the past 30 years, reflecting a survival rate of 50% [8]. The modification of esophagectomy techniques is ever growing for data reveals an increase to 40% from a 10% survival rate over a 5-year period when esophageal cancer patients elect for these curative surgeries [9].

Challenges often hinder the esophagectomy procedure before the surgery can be performed on a patient. Esophageal cancers are often situated proximal to vital structures such as the trachea, bronchi, pericardium, azygos vein, aorta, complex lymphatic networks and diaphragm [6]. Factors that should be considered prior to proceeding with esophagectomy are the level of malignancy that has invaded the vital structures and lymph node metastasis [6]. Current esophagectomy procedures are decided heavily by the surgeon's skills where the ideal goal has been resections with the intent of removing the primary tumor [6,10]. MIE was first introduced in 1992 where it combined thoracoscopic techniques with laparoscopy, with the goal of decreasing the rate of respiratory complications associated with thoracotomy while simultaneously aiming to reduce morbidity of the patient [11]. RAMIE is a favorable fascination in one of the surgical approaches for esophageal cancer where it takes advantage of advanced manipulation of robotic precision with in-depth surgical perspectives playing around with the precise maneuver of limited surgical space [12]. Both these approaches are the most modern approach to esophagectomy as a perspective toward better outcomes.

Esophagectomy is one of the most invasive procedures, and since postoperative morbidity and mortality are still a challenge, there is a critical need for more studies to find answers that would minimize this issue [13]. The purpose of our review objectively assesses the surgical outcomes comparing between robotic esophagectomy and conventional thoracoscopic esophagectomy, for patients with esophageal cancer over a defined period based on several literature reviews. The main goal of our study is to understand which procedures had a better outcome post-operatively with current literature. Our resultant purpose would also analyze any procedure related complications, mortality rates within hospitals, and rate of readmissions upon interventional treatments. This article compares the surgical outcomes of robotic esophagectomy and conventional thoracoscopic esophagectomy, focusing on Ivor-Lewis and McKeown.

Method

Quality control and literature search

Databases such as Google Scholar, PubMed, Online Library Wiley and Science Direct, were searched for: "RAMIE," "Robotic-Assisted Minimally Invasive," "MIE," "Minimally Invasive Esophagectomy," "Esophagectomy," "Ivor-Lewis", "McKeown" and their synonyms. There was no additional search software or special features that were use as part of our literature searches. The search sensitivity was cross referenced to include relevant articles and reviews using the PubMed feature, dating from 2017 to 2023. The search was limited to papers published in English and contained original patient data, where samples of patients were more than 20 individuals, and included patients from age groups 18 to 75 years of age. Inclusion criteria included literature reviews, meta-analysis, systematic reviews, prospective studies, retrospective studies, case studies and trend analysis. Articles were not limited by region and included those from China, Japan, Germany, USA, France, and UK.

Exclusion criteria were papers published in a foreign language and required translation, those that used animal models and cohort sample of less than 20 patient samples. The final review articles included in our paper for comparison and analytical determination was 31 review articles. Additionally, the first authors of this paper independently evaluated the included studies, and disagreements were resolved through discussion.

Statistical analysis

Our review paper utilizes analysis based on comparing existing literatures relevant to our topic, where we summarize the key findings from various studies based on the surgical outcomes. We highlighted the consistencies and discrepancies found when comparing the literature reviews included in our analysis. The goal of our analytical method was to provide an easier understanding for readers to discern the surgical outcomes when comparing RAMIE with MIE.

Body of the Review

Esophageal cancer

The genomic profiles which lead to esophageal cancer has been identified as having the origins from Squamous Cell Cancers (SCC), which tend to occur in the upper to mid-level of the esophagus; and Adenocarcinomas (AC), which tend to occur in the lower esophagus and gastroesophageal junction [14]. Hence, the discernment in the origin of cell types will influence the formation of the esophageal cancer. In China, esophageal cancer has a high incidence with several risk factors such as tobacco, alcohol consumption, poor diet, obesity, genetics and lack of exercise contributing to the causation of the disease [4,14]. With a global incidence rate of 79.7% and a predicted increase in incidence of 2 to 3 times, esophageal cancer is a serious issue, especially in Asian countries [4]. In order to determine if a patient is suitable for one of the interventions, there are factors that need to be contemplated. Amongst them include clinicopathologic staging, lymphovascular invasion and proximal invasion to vital organs near the esophagus [6,15]. The review by Espinoza-Mercado selected discrete demographic pools which were selected from patients in high-volume hospitals. The patient demographic was selected from 2004 to 2015 which studied adult patients who were subjected to esophagectomy interventions for SCC and AC of the esophagus [15]. In addition, Herron's evaluation chose its patient demographics based on preoperative staging following the use of neoadjuvant therapies; using instruments like PET Computed Tomography (CT) and endoscopic ultrasonography to assess whether the patient is fit for the intervention. The esophagectomy interventions, involving MIE and RAMIE were endorsed by esophageal surgeons for it was found to decrease morbidity rates and reduce Postoperative Morbidity (POM) [16].

Conventional thoracoscopic esophagectomy

MIE approaches have gradually become a standard in esophagectomies to overcome the complexity and challenges surrounding the procedure. The IVOR-Lewis or McKeown conventional thoracoscopic esophagectomy is a widely used treatment for esophageal cancer [17]. The execution of IVOR-Lewis of McKeown is subjected to the locality of the cancer lesion, surgeon's preference, and skills; as well as the surgeon's experience [17]. The MIE approach combines abdominal and transthoracic perspectives by using a tube-shaped stomach conduit, pulled up as a replacement

Table 1: Postoperative complication article analysis.

Panel A: Postoperative Complication Analysis Comparing RAMIE and MIE								
Reference	**Study Type**	**Anastomotic Leakage**	**Pulmonary Complications**	**Chyle leak**	**Recurrent Laryngeal Nerve Injury (RLNI)**	**Estimated Blood Loss**	**Pain Control**	**Lymph Node (LN) Harvest**
[30]	Propensity-Matched Analysis	RAMIE: 12% MIE: 18%	Pneumonia RAMIE: 12% MIE: 18%	N/A	N/A	N/A	N/A	RAMIE: 27 MIE: 23
[31]	Meta-analysis and Systematic Review	Same incidence in RAMIE and MIE	Same incidence in RAMIE and MIE	N/A	MIE had higher incidence	RAMIE had lower incidence	N/A	No statistic difference
[32]	Retrospective analysis	Same incidence in RAMIE and MIE	Same incidence in RAMIE and MIE	N/A	N/A	N/A	N/A	No statistic difference
[33]	Single-center retrospective cohort study	N/A	N/A	RAMIE: Higher incidence	RAMIE: Lower incidence	RAMIE: Lower incidence	N/A	RAMIE: Higher resection rates
[34]	Randomized Controlled Trial	N/A	N/A	N/A	RAMIE: Lower incidence	N/A	N/A	RAMIE: Higher resection rates
[35]	Systematic Review and Meta-Analysis	RAMIE: Higher incidence	RAMIE: Lower incidence	N/A	RAMIE: Lower incidence	RAMIE: Lower incidence	RAMIE: Lower incidence	N/A
[36]	Propensity score matched short-term outcome analysis	RAMIE: Lower incidence (4.3%)	N/A	N/A	N/A	N/A	RAMIE: Lower incidence	No statistic difference
[37]	Single high-volume academic center Literature Review	No statistic difference	No statistic difference	No statistic difference	No statistic difference	No statistic difference	No statistic difference	RAMIE: Higher resection rates
[16]	Systematic Literature and Meta-Analysis	MIE: Lower incidence	N/A	N/A	N/A	N/A	N/A	N/A
[10]	Randomized Control Trials, Meta-Analyses, Retrospective study	MIE: Lower incidence	No significant difference	N/A	N/A	RAMIE: 120ml-330ml MIE:100ml- 350 ml	N/A	RAMIE: Higher resection rates
[38]	Multicenter phase III trial RAMIE	N/A	N/A	N/A	N/A	N/A	N/A	N/A
[39]	Literature Review Article	N/A	RAMIE: Lower incidence	N/A	N/A	N/A	N/A	RAMIE: Higher resection rates
[40]	Randomized Controlled Trial	RAMIE: 12.2% MIE: 11.3%	RAMIE: 13.8% MIE: 14.7%	N/A	RAMIE: 32.6% MIE: 27.1%	No statistic difference	N/A	RAMIE: Higher resection rates (67.6%)
[19]	Systematic Literature + Meta-Analysis	N/A	MIE: 10%	MIE: 3%	N/A	N/A	N/A	N/A
[20]	Retrospective cohort study	N/A	No statistic difference	N/A	N/A	N/A	N/A	RAMIE: Higher resection rates
[11]	Meta-Analyses	MIE: O% incidence when compared to OE	MIE: Decrease to 29%	N/A	MIE: Ranges between 3.6-7%	MIE: 200 mL	N/A	N/A
[15]	Multicentre Meta-Analysis, Prospective study	N/A	N/A	N/A	N/A	N/A	N/A	RAMIE: Higher resection rates
[8]	Single-Center, Comparative cohort, Prospective Analysis	No statistic difference	MIE: Increase from 54% to 65%	N/A	N/A	N/A	N/A	N/A
[29]	Single centre, retrospective study	No statistic difference	RAMIE: 38.8% MIE: 38%	N/A	N/A	N/A	N/A	RAMIE: Higher resection rates
[17]	Single-centre, retrospective study	N/A	N/A	N/A	N/A	MIE: Higher incidence	N/A	N/A

[24]	Literature Review	RAMIE: Influenced by surgeon's skills	MIE: Lower incidence	N/A	RAMIE: Lower incidence	N/A	N/A	RAMIE: Higher resection rates
[41]	Trend Analysis	RAMIE: Higher incidence	RAMIE: higher incidence	N/A	N/A	N/A	N/A	N/A
[9]	Multicentre, Randomized controlled trial	N/A	MIE: 18% incidence	N/A	N/A	N/A	N/A	N/A
[26]	Systematic Review	MIE: 4-38%	MIE: 6-48%	N/A	MIE: 4-35%	N/A	N/A	N/A
[28]	Prospective Trial of RAMIE, non-randomized trial	RAMIE: 3%	RAMIE: Lower in complications by 14%	N/A	N/A	RAMIE: 250ml	N/A	RAMIE: Higher resection rates
[12]	Narrative Literature Review, Includes Randomized control trials and large population-based cohort studies	MIE: 21.4%	MIE: Higher incidence	N/A	RAMIE: Lower incidence	N/A	MIE: Lower incidence	RAMIE: Higher resection rates
[23]	Literature Review	RAMIE: Higher incidence	MIE: Lower Incidence	N/A	RAMIE: Higher incidence	MIE: Lower incidence	N/A	N/A
[42]	Single-center study	N/A	RAMIE: 21% MIE: 28%	N/A	N/A	N/A	N/A	RAMIE: Higher resection rates
[27]	Single center, Randomized control trial	RAMIE: 59%	RAMIE: 59%	N/A	N/A	RAMIE: Lower incidence	N/A	N/A
[43]	Meta-Analysis	No statistic difference	RAMIE: Lower incidence (19.6%)	RAMIE: 9.2%	MIE: Lower incidence	RAMIE: Lower incidence	N/A	RAMIE: Higher resection rates
[44]	Meta-Analysis and Systematic Review	No statistic difference	MIE: Lower incidence	RAMIE: Lower incidence	MIE: Higher incidence	RAMIE: Lower incidence	N/A	RAMIE: Higher resection rates

for the resected esophagus [17]. There are variations to the underlying concept of MIE, where the approach could be either transhiatal, transthoracic or three-field (abdominal-thoracic-cervical) [17]. McKeown requires a three-field approach, where incisions are made in the chest, abdomen and neck. In contrast, the IVOR-Lewis only requires a two-field approach, having incisions made in the chest and abdomen. The IVOR-Lewis and McKeown techniques are most chosen as the MIE intervention, where both procedures require a specific en bloc resection of the esophagus, along with radical mediastinal lymph node removal [18].

MIE was introduced to overcome the transthoracic esophagectomy that was equated with the high rates of morbidity [19]. Casas's systematic and meta-analysis review studied the overall morbidity, pulmonary postoperative complications, anastomotic leak, chyle leak and mortality. Amongst the 39 studies which Casa's team had analyzed, the data yielded 39% in overall morbidity rate, a 10% occurrence in postoperative pneumonia, 12% reported arrhythmias, an anastomotic leak rate of 8%, chyle leak rate of 3%, reoperation rate of 11% and a 30-day mortality rate of 2% [19]. Casas's team identified that MIE IVOR-Lewis was a challenging procedure with high morbidity rates, but it had an improved postoperative benchmark when compared to transthoracic esophagectomy procedures [19].

A retrospective cohort study by Chigozirim analyzed the Overall Survival (OS) and disease-free survival after patients received either MIE or RAMIE interventions [20]. It was deduced from their data, that there were some comparable results between RAMIE and MIE when they looked into the pulmonary post-operation complications, ICU re-admissions, infectious complications and mortality rates. A total cohort sample of 246 patients were studied in their study where their data yielded no difference in overall survival (p=0.69) or disease-free survival (p=0.70) [20]. Their postoperative complication data revealed no significant differences in rates of major morbidity with pneumonia (p=0.34), chylothorax (p=0.95), recurrent laryngeal nerve injury (p=1.00), anastomotic leak (p=0.49), intraoperative complications (p=0.73) and complete resection rates (p=0.68) [20]. Chigozirim also stated their analysis on a 90-day mortality (p=0.73) and increase hospital stay (p=0.89). Chigozirim's team advocated that RAMIE over the MIE technique was superior in terms of benefiting the overall outcome, where we will discuss the RAMIE benefits with supporting literature in the next subsection.

Robotic esophagectomy

The introduction of RAMIE in 2003 demonstrated a novel approach in performing esophagectomies for resectable esophageal cancers [21,22]. As stated above, the surgical approaches to esophageal cancer have been challenging for its locality spans both the thoracic and abdominal compartment, where it's positioning makes the approach difficult, due to its proximity to vital structures that are not readily resectable [23]. The goal in pioneering RAMIE in this field is to therefore perform esophagectomy procedures with less invasive methods, where it ideally reduces morbidity correlated with thoracotomy [23].

RAMIE is an innovative approach, extended from MIE, by providing three-dimensional visualization, improved instrument articulation, tremor filtration with high-caliber ergonomics; allowing for greater technical precision [24]. RAMIE has been put forth as a favorable esophagectomy technique for it is a procedure which requires smaller incisions, has better postoperative benefits including reduced lengths of hospital stay and improved cosmesis [24]. RAMIE trials

Table 2: Clinical metrics and surgical performance article analysis.

Panel B: Clinical Metrics and Surgical Performance Analysis Comparison of RAMIE and MIE								
Reference	**Study Type**	**LOS**	**ICU Stay**	**Mortality Rate**	**Morbidity Rate**	**Operation Time**	**Surgeon Experience**	**Cost-effectiveness**
[30]	Propensity-Matched Analysis	RAMIE: 12 days MIE: 19 days	RAMIE: 1 to 43 days MIE: 1 to 17 days	No statistic difference	N/A	RAMIE: 383 minutes MIE: 321 minutes	N/A	N/A
[31]	Meta-analysis and Systematic Review	Same between RAMIE and MIE	N/A	No statistic difference	No statistic difference	N/A	N/A	RAMIE: More expensive
[32]	Retrospective Analysis	RAMIE: Shorter duration	N/A	No statistic difference	No statistic difference	RAMIE: 444.6 minutes MIE: 417.9 minutes	N/A	RAMIE: More expensive
[33]	Single-center retrospective cohort study	RAMIE: Shorter duration	N/A	N/A	N/A	N/A	RAMIE: Surgeon's expertise is critical	N/A
[34]	Randomized Controlled Trial	N/A	N/A	N/A	N/A	N/A	RAMIE: Surgeon's expertise is critical	N/A
[35]	Systematic Review and Meta-Analysis	No statistic difference	No statistic difference	No statistic difference	No statistic difference	RAMIE: longer operative time	RAMIE: Surgeon's expertise is critical	N/A
[36]	Propensity score matched short-term outcome analysis	RAMIE: Shorter stay	RAMIE: Shorter stay	N/A	No statistic difference	N/A	N/A	N/A
[37]	Single high-volume academic center Literature Review	RAMIE: Shorter stay	No statistic difference	No statistic difference	No statistic difference	No significant difference	N/A	N/A
[16]	Systematic Literature and Meta-Analysis	MIE: 11.9 days	N/A	MIE: 37% Mortality rate	N/A	N/A	N/A	N/A
[10]	Randomized Control Trials, Meta-Analyses, Retrospective study	No statistic difference	N/A	RAMIE: 0-9%	N/A	RAMIE: Shorter operative time	RAMIE: Surgeon's expertise is critical	N/A
[38]	Multicenter phase III trial RAMIE	N/A	N/A	N/A	N/A	N/A	N/A	N/A
[39]	Literature Review Article	N/A	N/A	N/A	N/A	RAMIE: Surgeon's expertise is critical	RAMIE: Surgeon's expertise is critical	N/A
[40]	Randomized control Trial	N/A	N/A	RAMIE and MIE: 0.6% in both groups	N/A	RAMIE: 203.8 minutes MIE: 244.9 minutes	N/A	N/A
[19]	Systematic Literature + Meta-Analysis	MIE: 11.2 days	MIE: 2 days	MIE: 2%	MIE: Major morbidity: 20%	N/A	N/A	N/A
[20]	Retrospective cohort study	No statistic difference	N/A	No statistic difference	No statistic difference	N/A	N/A	N/A
[11]	Meta-Analyses	MIE: 3 days less	N/A	MIE: 68%	N/A	MIE: 329 minutes	N/A	N/A
[15]	Multicentre Meta-Analysis, Prospective study	MIE: 9 days RAMIE: 9 days	No statistic difference	N/A	N/A	N/A	N/A	N/A
[8]	Single-Center, Comparative cohort, Prospective Analysis	MIE: Decrease to 2%	N/A	MIE: Improve 2% to 5%	MIE: Morbidity increase from 54% to 68%	N/A	N/A	N/A
[29]	Single-Centre, Retrospective study	N/A	N/A	N/A	N/A	RAMIE: only 254 minutes	N/A	N/A
[17]	Single-centre Retrospective Study	N/A	N/A	N/A	N/A	N/A	Surgeon's expertise is critical	N/A

[24]	Literature Review	N/A	N/A	No statistic difference	No statistic difference	N/A	Surgeon's expertise is critical	N/A
[41]	Trend Analysis	N/A	N/A	No statistic difference	N/A	N/A	N/A	N/A
[9]	Multicentre, Randomized controlled trial	N/A	N/A	MIE: 77% lower risk	N/A	N/A	N/A	N/A
[26]	Systematic Review	N/A	N/A	MIE: Lower incidence	MIE: lower incidence	N/A	Surgeon's expertise is critical	RAMIE: More expensive
[28]	Prospective Trial of RAMIE, non-randomized trial	RAMIE: 9 days	RAMI: 8% cases admission	RAMIE: 2%	N/A	N/A	N/A	N/A
[12]	Narrative Literature Review, Includes Randomized control trials and large population-based cohort studies	No statistic difference	N/A	MIE: Lower rates	No statistic difference	RAMIE: Shorter operative time	Surgeon's expertise is critical	N/A
[23]	Literature Review	MIE: Shorter stay	N/A	N/A	N/A	N/A	Surgeon's expertise is critical	N/A
[42]	Single-center study	RAMIE: 12 days MIE: 13 days	N/A	N/A	N/A	N/A	N/A	N/A
[27]	Single center study	N/A	N/A	N/A	N/A	N/A	N/A	N/A
[43]	Meta-Analysis Review	N/A	N/A	RAMIE: 4.0%	N/A	MIE: Shorter operative time	Surgeon's expertise is critical	N/A
[44]	Met-analysis and Systematic Review	RAMIE shorter stay	N/A	No statistic difference	No statistic difference	RAMIE: Shorter operative time	N/A	N/A

in the past 17 years, had shown exceptional perioperative morbidity and improved quality of life when it was compared with traditional open esophagectomies for esophageal cancer [23]. The improved outcomes had been attributed to the steep learning curve associated with introduction of new technology for complex procedures such as esophagectomy as well as adopted structured protocols aimed to improve the surgeon's proficiency [24,25]. Khaitan's paper analyzed the ROBOT trial which reported data in 2019 on a randomized controlled trial from a single institution, where the findings determined an overall lesser surgical-related complication following the RAMIE procedure (p=0.02), fewer pulmonary complications (p=0.005) and a lower case of arrhythmias (p=0.01) [24].

RAMIE, being an expansion of MIE, is essentially a modified and improved means of laparoscopic transhiatal approach, being mainly developed for there were concerns in regards to thoracoscopic safety in the longer term for esophageal cancer patients [23]. The RAMIE procedure differs amongst centers around the world, primarily reliant on the approaches utilized by the surgeons in their center, according to multiple literature assessments. This makes the interpretation and comparisons between known cases challenging. A systematic review performed by Ruurda et al. in 2015, studied 16 cases which showed initial feasibility and safety with RAMIE, when compared with MIE and open esophagectomy, in terms of short-term oncology outcomes [23,26]. The same research team employed a single center with more than 600 RAMIE cases in a 2015 randomized controlled trial to compare open esophagectomy to RAMIE. In their trial, the surgical outcome of RAMIE reveals a lower percentage of overall surgery-related and cardiopulmonary complication, lower postoperative pain, better quality of life, and improved postoperative functional recovery time [27].

A published comparative study by Sarkaria and their team, revealed that short term quality of life for patients who had elected for RAMIE was much better, where pulmonary complications postoperatively was also significantly reduced [28]. The study by Sarkaria also revealed there was a reduction in infective complications, a decline in ICU re-admissions as well as a surge in lymph node yield in patients who had chosen RAMIE as their form of intervention [23,28]. Their comparative study studied 170 patients, where RAMIE patients had reported reduced length of hospital stay (p<0.001), and hospital readmission rate (p=0.38) [28]. The most significant postoperative complication data revealed anastomotic leakage in RAMIE patients (p=0.38) [28].

A more recent retrospective single-institution study published by Haoyao et al., compared perioperative and a 2-year outcome of RAMIE with MIE, where the results yielded that RAMIE has a shorter operation time where it is correlated with surpassing surgical efficiency with possible low mortality rate and reoccurrence [29]. The overall outcome of these reviews has determined that RAMIE is a safe procedure which yields promising outcomes in reducing perioperative morbidity, improved quality of life with better oncology results. Haoyao's study used a total of 251 cases with the incidence of overall complication (p=0.911); where the rate of anastomotic leakage (p=0.08) and incidence of vocal cord paralysis (p=0.483) [29].

Discussion

We established that RAMIE was essentially an expansion of MIE, to improve safety, reduce postoperative pulmonary complications, and reduce re-admissions to hospitalizations and to decrease the chances of anastomotic leakage. In our findings, we separated our verdict into Table 1, 2, where we looked into postoperative complication surgical outcomes as well as clinical metrics which

includes surgical performance.

Key findings: Postoperative complication surgical outcomes.

Anastomotic leakage: Anastomotic leakage, one of the most serious post-esophagectomy consequences, is linked to higher postoperative morbidity and mortality where one of the most dreaded side effects of esophagectomy is an anastomotic leak, which increases postoperative mortality, lengthens hospital stays, and adds to hospital and patient expenses [45,46]. Several papers such as those reported by Zheng, Khaitan and van Boxel, have reported MIE with having lesser leak incidence [23,35,41]. This could be attributed to several risk factors which include neoadjuvant chemotherapy, history of Chronic Obstructive Pulmonary Disease (COPD), history of tobacco smoking, history of artery calcification, diabetes, obesity and arrhythmias [47]. A retrospective single-center study had claimed that preoperative FEV1< 2.18 was also one of the contributing factors that can increase the incidence of anastomotic leakage [47]. Other studies have previously reported that anastomotic leakage was prone to occur if there was anastomotic tissue hypoperfusion where the lack of insufficient oxygen supply to the site of surgery can ultimately cause the leak [47]. A discrepancy found was that, RAMIE had reported 25.3% worse in anastomotic leak [10].

Pulmonary complications: Our overall findings indicated that RAMIE had reported lesser incidences of pulmonary complications [28,30,35,39,40,42,43]. We can see these in several literature reviews we had analyzed such as Tagkalos, Zheng and Yang [30,35,40]. The common complaints of pulmonary complications include inadequate ventilation, pleural effusion, atelectasis and pneumonia; where this complication can be considered one of the most serious complications associated with esophagectomies [43]. The factors that make a patient more predispose to this issue is if they have a history of diabetes, history of lung disease, a <65% FEV1 predictor, history of tobacco smoking and if they have a higher staging of the disease [48]. Additionally, the positioning of patients for RAMIE procedure has allowed esophagectomies to be performed without selective bronchial intubation, which reduces the prevalence of pulmonary complications [49]. A meta-analysis review by Hosoda also had shown that with RAMIE, there have been relatively lower reported incidences of postoperative pneumonia [43].

Chyle leak: Chyle leak, despite being a relatively rare complication, can happen after surgery in the thorax, abdomen, and neck, is a condition where there is persistent lymphatic fluid leaking [50]. Chylothorax is a well-known complication that can occur after esophagectomy, where the incidence is most often attributed to extensive lymph node dissection or en bloc resections of thoracic ducts [50]. Due to its seriousness as a postoperative complication that can be fatal, several studies have stated it causes malnutrition, fluid imbalance, and immune system damage [50,51]. Based on our analysis, we determined that MIE performed better than RAMIE when it comes to the rate of incidence for Chyle leak [33,43]. It was reported that with RAMIE, there was incidences of disruption in the thoracic duct and lymphatic fluids of the interstitial region into the pleural space [33]. As such, it can significantly lead to some adverse outcomes, which include hypovolemia, metabolic and nutritional depletion, infection and even to an extent, mortality [50,52,53]. The analysis of chyle leak incidence points to the possibility that a surgeon's skill and method may have an impact on the incidence, where thoracic duct ligation showed lower chylothorax incidence [54]. The study by Tetsuya et al. revealed that MIE performed significantly better than RAMIE in incidences of chyle leak, however it had failed to mention the type of ligation used in their methods, but instead attributed chyle leak to use of early enteral feeding [33].

Recurrent Laryngeal Nerve Injury (RLNI): One of the most prevalent postoperative implications following esophagectomy was identified as RLNI [55]. Recurrent Laryngeal Nerve innervates the cricopharyngeal muscle which forms the upper esophageal sphincter, playing a pivotal role in swallowing [56]. Commonly, patients with RLNI reports of hoarseness, dyspnea, difficulty in coughing and there have been reported incidences where it is a risk factor in increasing morbidity [34,57,58]. Since RLNI is one of the most prevalent postoperative problems following esophagectomy, it is critical that we examine it as a severe post-operative complication [59]. It was also found that cases of RLNI leads to pulmonary complications which ultimately leads to an increase incidence of ICU stay [30,56]. RAMIE was concluded to have reduced incidences in cases of RLNI based on our selected pool of literature review. This was determined because RAMIE offered better visualization in their procedures compared to MIE, thus the occurrence of RLNI was reported to be significantly lesser [44]. Despite this, there are relative sparse studies that have reported long-term prognosis after RLNI, and even lesser studies regarding RLNI after RAMIE procedure. A study in 2017 however, have stated that the known causes that result in RLNI had been identified as thermal injury, stretching, compression or vascular compromise to the recurrent laryngeal nerve itself [57]. However, this was identified to be the cause for esophagectomies following MIE procedures. A recent study also found that excessive lymph node harvest in the para-recurrent laryngeal nerve area may lead to significant incidences of RLNI [40]. However, as of right now, there hasn't been enough research on this postoperative complication to pinpoint what causes RLNI differently in RAMIE and MIE procedures over a period of time.

Estimated blood loss: Major intraoperative blood loss will lead to unfavorable survival outcomes following post-esophagectomy, where a higher amount of blood loss is associated with higher mortality and morbidity rates [60-62]. Our analysis identified that RAMIE produced lower estimated blood loss in occurrences where the estimated blood loss varied from 120 ml to 330 ml [10]. In comparison to MIE, where the average blood loss has been reported to be approximately 400 ml [31]. The identifiable factors that contributed significantly to amount of blood lost during the procedures were duration of surgery, surgeon's skills and if azygos arch division was performed [60]. Interestingly, there was also some correlations if a patient had obesity, where it was revealed that BMI can influence the amount of blood loss during the procedure [60,63]. Despite identifying BMI to be an associated risk factor that may influence blood loss, there has been no agreeable consensus to its role for studies regarding this element is limited [64]. The data we gathered on RAMIE had showed a positive trend in reducing intraoperative bleed and in some incidences where the procedure successfully preserves the azygos arch; which shows a reduction in estimated blood loss. Contrarily, one paper by van Boxel and his team, had contradicted this outcome and suggested MIE had a lesser estimated blood loss [23].

Pain control: Engagement of effective pain management after post-esophagectomy shows there is a correlation in lesser complications, earlier patient recovery and leads to higher patient satisfaction [65]. Pain management is crucial in post-esophagectomy procedures for the procedure itself makes muscles and intercostal nerves prone to injury, which leaves patient feeling discomfort and

having higher risk of pulmonary postoperative pulmonary problems, such as Chronic Post-Surgical Pain (CPSP) [66-68]. It has been established that the gold standard pain management therapeutics involve either Thoracic Epidural Analgesia (TEA) or intravenous Patient-Controlled Analgesia (PCA) or lumbar Paravertebral Nerve Block (PVNB) [65]. Despite this, research on this postoperative consequence is still comparatively limited; only one prospective study has recently revealed its results by contrasting the usage of TEA and PCR for postoperative pain treatment in patients having RAMIE [65]. Rosner's team revealed that TEA was associated with lower median pain scores, and remains the gold standard of perioperative analgesia for esophagectomy procedures [65,69,70]. According to our selected reviews, patients were given a pain scoring tool of Numeric Rating Scale (NRS) to assess their pain scores, and it was shown that RAMIE was superior to MIE in terms of pain control [35,36]. This is highly suggestive that the pain treatment for minimizing pulmonary problems, postoperative discomfort, and to improve patient comfort was preferable with RAMIE [71]. However, a limitation noted in our selected reviews was, neither paper mentioned if TEA, PCA or PVNB were used alongside the RAMIE or MIE procedure, which can influence the decision outcome for either study. Contrarily, there was a known meta-analysis study which had investigated postoperative pain management where their data had determined there were no statistically significant differences reported between using TEA and PCA as a postoperative therapeutic [72]. This postoperative complication should be studied further with research explicitly looking into the type of analgesics used along with RAMIE or MIE to determine which analgesia yields a more favorable outcome.

Lymph Node (LN) harvest: The development of robotic-assisted surgery with high-resolution three-dimensional imaging, tremor filtering, and articulated instruments during operation is said to be superior in mediastinal LN dissection for better exposure of surgical field, obtaining more complete and accurate LN harvesting [26,73]. However, there has been a trend in the reported outcomes where despite RAMIE being efficient in LN harvesting, it is prone to significant injury to the recurrent laryngeal nerves [29,40,74]. According to our analysis, RAMIE yields to show an improve efficiency and accuracy, along with an increase in the number of lymph node harvesting [28,30]. Complete nodal harvest is essential during esophagectomies for accuracy in staging and to reduce the risk of recurrence. There had been several studies which has showed that higher lymph node resections are associated with improved overall survival [10,15,20,24,28-30,34,37-39]. It is therefore, not surprising that RAMIE, a more advanced accuracy tool for esophagectomies, was shown to be more accurate in lymph node harvesting. Interestingly, the paper by Hosoda had expressed that the extent and quality to harvesting lymph nodes is influenced by the histological type of esophageal cancers where if a patient is diagnosed with adenocarcinoma, lymph node dissection is the standard care for esophageal cancer [43]. It was also expressed that the efficiency of harvesting could also be influenced by varying procedures globally and may impact the reported data in Hosoda's review analysis.

Key Findings: Clinical metrics and surgical performance.

Length of Stay (LOS): The incidences of post-operative complications have a strong correlation to increased length of hospital stay [75,76]. An increased duration to hospital stay is an unfavorable outcome in esophagectomies for it is associated with poor overall survival and puts a strain on the patient's finances [77-79]. LOS is an important clinical metric to study in esophagectomy procedures, for it provides and important insight into the efficiency of different postoperative care pathways and hospital performances [80]. Postoperative LOS is an objective parameter which highly reflects the postoperative recovery and survival rate of a patient [79]. Generally, RAMIE has been attributed to lesser days in hospital with data revealing on average of 9 days of total hospitalization. This is because RAMIE has lesser postoperative complications that would require observation and monitoring in hospital [30,36]. This innovative surgical technique uses robotic precision through tiny incisions to lessen operative stress, blood loss, and tissue damage [30,36]. Common complications are less likely to occur with better visualization and dexterity; giving RAMIE the advantage in esophagectomy techniques. Thus, patients have a higher outcome in quicker recovery, reducing the need for extended hospitalization. In conclusion, RAMIE's minimally invasive design and better results leads to shorter hospital stays.

Intensive Care Unit (ICU) stay: The invasive nature of esophagectomies often times led patients to be routinely admitted to the ICU for one of the following reasons, such as hemodynamic support, pain management and respiratory support [81]. The paper by Tagkalos, their team had decided that in terms of postoperative ICU stays, RAMIE substantially surpasses MIE. Their research has repeatedly demonstrated that patients who receive RAMIE have shorter stays in the intensive care unit. Accordingly, RAMIE patients only spent one day on average in the ICU, compared to two days for MIE patients (P=0.029) [30]. Another study by Babic that reported a statistically significant reduction in ICU stays for RAMIE patients [p=0.0218] supported this pattern [36]. There were less postoperative complications in RAMIE patients than in MIE patients (27% *vs.* 47%; p=0.0225) [36]. As such, based on these results, it thoroughly supports RAMIE as a good option for minimizing postoperative ICU stays and enhancing patient outcomes. However, there are some studies which contradicts and have stated there has been no statistically significant differences, and could be attributed to the ICU admission policy per hospital, where the studies are conducted [15,31,35,37,81]. Another study had also stated that the hospital variation in length of ICU stay was not associated with ICU readmission, mortality and postoperative complications; but instead attributed this to the ICU duration policy of their hospital per severity of postoperative surgery [82].

Mortality and morbidity rate: Esophagectomy has historically been linked to a high postoperative morbidity and fatality rate; now, despite improvements in perioperative care and minimally invasive procedures, it is still linked to morbidity rates of over 50% and mortality rates of 6% to 9% [61,83-86]. A study in 2022 had claimed that the overall mortality rate decreased in patients that underwent RAMIE in comparison to those that elected for MIE, with the overall median survival rate being 42 months [87]. The study of mortality and morbidity rate as an important clinical metric allows surgeons to identify if a particular choice of operative approach can indeed minimize risk of postoperative complications, leading to reduction in morbidity and mortality rates. However, based on our analysis, majority of the papers we had chosen had determined that there was no significant difference in mortality and morbidity rate when compared with RAMIE and MIE. This could be attributed to improved patient selection across studies, surgical technique and advances in perioperative management [88]. Our analysis leans towards the deduction where enhanced surgical procedures are crucial factors that can influence the postoperative complications, mortality and morbidity rates.

Operation time: Prolonged operative times will have an adverse impact to postoperative morbidity, and does have a significant impact in postoperative complications [89]. RAMIE was determined to yield a better success in operation time for the procedure generally takes approximately 203 min to 444 min [29,35]. This provides an overall greater feasibility for the patient, for they will be required to be in surgery for a lesser duration which leads to lower incidences of post-operative complications. As such, it was concluded that quality of life of patients significantly improves with RAMIE procedures. However, operation time is also subjective to surgeon's experiences, methods used and skills [34]. The study by Valsangkar's et al. identified that using Ivor-Lewis in MIE correlated with longer operative times which led to an outcome of increased rates of pneumonia, duration of stay and mortality [89]. This suggests that methods use in esophagectomies have a role in influencing the duration of operation time, which can essentially influence the post-operative complications that comes after.

Surgeon experience: There is a learning curve associated with sophisticated minimally invasive methods like MIE and RAMIE, which could have an effect on postoperative outcomes such as morbidity rates [90]. Eleven out of the 31 literature reviews we have analyzed had claimed that a surgeon's experience, skills and learning curve play a major role in the surgery's outcome [10,12,17,23,26,33-35,39,41,43]. The quality of the surgery as well as postoperative complication incidences are greatly correlated to a surgeon's experience [30]. MIE and RAMIE both require technical and surgical skills, and thus, learning curves and how well adept a surgeon is to the procedure is vital in determining a favorable outcome. Given that RAMIE utilizes robotic advancement technology, the learning curves of how a surgeon quickly adapts and master is dependent on the frequency of their exposure [91]. The more exposure a surgeon is to the particular procedure, the surgical outcomes will lead to a better yield. The learning curves for surgeons have been expressed as the frequency of console times performing the particular procedure, where they are assessed according to 5 stages of skill acquisition [91]. The stages of acquisition had heavily been suggestive per the number of cases a surgeon has performed, where a surgeon is deemed competent when they have performed approximately 50 cases and expert level, when they have performed more than 100 cases [91].

Cost-effectiveness: RAMIE requires considerable expenses that may or may not be covered by health insurance companies globally. It is an expenditure that has been deemed to be costly and may not be affordable by low-earning to middle-earning income families. Despite showing outcomes that are beneficial to a patient with esophageal cancer, it is still debatable if the costs, truly outweighs the overall survival outcome. The treatment cost is a substantial factor in choosing the therapeutic interventions by patients [92]. As to date, not many studies have showed a cost-benefit profile that can argue for implementing the need for RAMIE over MIE in esophageal cancers, when both procedures yield almost similar postoperative survival outcomes. The cost-effectiveness analysis has widely considered the difference between the interventions by observing changes in outcomes and occurrence of complications in their own hospital perspectives [93]. As such, analyzing the cost-effectiveness between studies that look into this concern has disparities from each other, for one's hospital perspective may not necessarily abide to the same viewpoint as another. Cost-effectiveness is also subjective to treatment strategies based on the patient's esophageal cancer staging and level of invasiveness [92]. In addition, the satisfaction to pay for RAMIE procedures is attributed to different levels of willingness-to-pay values, and it correlates well with household income with obtainable favorable outcomes [93]. The general consensus by healthcare providers have also expressed their willingness to pay, if the postoperative complication costs significantly lesser than the treatment of complications itself [93]. Additionally, the current debate asks the possible reasons in having preference of RAMIE rather than MIE and this could be attributed to the inherent advantages of its robotic platform, technical innovation and precisions, a shorter learning curve and a long-term cost savvy investment for patients [94]. Hence, it is vital we look into cost-effectiveness for it can impact decision making and long-term health care management [95].

Overall analysis

Despite having a univariate analysis in major perioperative events for both RAMIE and MIE, as stated in Khaitan's literature review, it was found that MIE generally, had longer procedure times and this can be a potential strain to the patient [41]. It was established in Khaitan's univariate statistical analysis that RAMIE is more likely to have more complexity in anastomotic leakage, pulmonary emboli and chylothorax [41]. Additionally, it was found in the same investigation that there was no difference in operative mortality between RAMIE and MIE, proving that both techniques are effective [41].

In terms of one being used more favorably than the other is highly dependent on the clinicopathologic staging and invasion of the cancer to other vital structures [35]. RAMIE technique is much preferred for sentinel lymph node sampling and lymphadenectomy for it has a better precision with getting closer to the vital structures, without many presently known complications [23]. Additionally, RAMIE is also the favored technique when performing lymph node harvesting, as stated by Khaitan and van der Sluis's et al. [41,42]. However, both MIE and RAMIE methods for esophageal resection showed almost no drastic significance to each other, with both having equivalent long-term oncology outcomes, reducing perioperative morbidity and an improved quality of life [23]. The improved and favored outcomes with both RAMIE and MIE are highly dependent on the surgeon's skills and experience, and are one of the contributing factors that give the patient a better prognosis. Further data analysis comparing the long-term outcome of RAMIE and MIE are still in the process.

From the several literature reviews we have read, it is quite clear that there are sparse data available when comparing RAMIE to MIE. Most notably, there has been a recent open trial set to compare RAMIE to MIE in a controlled setting, where the study incorporates four centers in China, focusing on patients with SCC [40]. Their study had hypothesized that RAMIE will ideally have similar oncologic outcomes and long-term quality of life, with reduced operation time; however, this data has not yet been published. Across the board, the studies performed are not consistent with each other, where some were limited to single-institution and some were multi-centered; making the analysis of each data challenging to determine a feasible outcome. As each institution and study reported slightly different techniques for performing the procedures, we would also have to take into account the inconsistent nature of the data. This is because each surgeon has a unique set of skills and experience that may not be consistent across studies. Additionally, the surgical approaches were not randomly assigned to patients, and it was pre-determined according to clinicopathologic staging set by the institutions, which may influence data biasness as a result. Longer follow-ups have to be further performed in regards to analyzing the outcome of RAMIE

and MIE, as current data only deduces the consequences of a 5-year timeline. However, for future prospects in this research field, there are ongoing clinical trials that are currently recruiting (NCT03094351 and NCT04306458), where it specifically gathers data comparing RAMIE and MIE over a primary outcome of 5-year overall survival rate.

Conclusion

Our review of recent studies on RAMIE and MIE for the treatment of esophageal cancer has yielded important insights. RAMIE, an expansion of MIE, has a number of benefits that lead to higher levels of technical precision, including three-dimensional visualization, enhanced instrument articulation, tremor filtration, and high-caliber ergonomics. When compared to conventional open esophagectomies, RAMIE operations had better postoperative results, including shorter hospital stays and enhanced cosmesis. The steep learning curve that comes with introducing new technologies and implementing organized protocols to improve surgeon competency can be blamed for the better results of RAMIE.

Notably, the several completed and ongoing trial analysis showed that RAMIE and MIE had different rates of arrhythmias, pulmonary problems, and complications connected to surgery. These results demonstrate RAMIE's potential as a beneficial esophagectomy approach for enhancing postoperative morbidity and quality of life in esophageal cancer patients.

Future study should concentrate on long-term effects and additional contrasts of RAMIE and MIE approaches, taking into account elements like oncologic outcomes, quality of life, and patient satisfaction. Current clinical trials will provide important information to better comprehend the benefits and efficacy of RAMIE in the treatment of esophageal cancer.

In conclusion, the comparison of RAMIE with MIE has shown that RAMIE has the potential to be a cutting-edge surgical strategy for the treatment of esophageal cancer. It's potential to improve patient outcomes and quality of life is indicated by its technical advantages, improved surgical results, and decreased complications. However, more investigation is required to examine its long-term impacts and carry out thorough evaluations of its advantages and effectiveness in comparison to MIE. The knowledge gathered from ongoing clinical trials will be an invaluable asset in determining the direction of esophageal cancer surgery in the future.

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