Robot-assisted Surgery for Esophageal Cancer: Analysis of Short- and Long-term Outcomes

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PREFACE

The VA Evidence Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The program is comprised of three ESP Centers across the US and a Coordinating Center located in Portland, Oregon. Center Directors are VA clinicians and recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Center Program and Cochrane Collaboration. The Coordinating Center was created to manage program operations, ensure methodological consistency and quality of products, and interface with stakeholders. To ensure responsiveness to the needs of decision-makers, the program is governed by a Steering Committee comprised of health system leadership and researchers. The program solicits nominations for review topics several times a year via the program website.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, Deputy Director, ESP Coordinating Center at Nicole.Floyd@va.gov.

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This report is based on research conducted by the Evidence Synthesis Program (ESP) Center located at the **West Los Angeles VA Medical Center, Los Angeles, CA**, funded by the Department of Veterans Affairs, Veterans Health Administration, Health Services Research and Development. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (*e.g.*, employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.

ACKNOWLEDGMENTS

This topic was developed in response to a nomination by Mark Wilson, MD, PhD and William Gunnar, MD, JD, FACHE for the purpose of understanding the potential benefits and costs for robot-assisted surgery. The scope was further developed with input from the topic nominators (*ie*, Operational Partners), the ESP Coordinating Center, the review team, and the technical expert panel (TEP).

In designing the study questions and methodology at the outset of this report, the ESP consulted several technical and content experts. Broad expertise and perspectives were sought. Divergent and conflicting opinions are common and perceived as healthy scientific discourse that results in a thoughtful, relevant systematic review. Therefore, in the end, study questions, design, methodologic approaches, and/or conclusions do not necessarily represent the views of individual technical and content experts.

The authors gratefully acknowledge Sachi Yagyu and Zhaoping Li for their contributions to this project.

Operational Partners

Operational partners are system-level stakeholders who have requested the report to inform decision-making. They recommend Technical Expert Panel (TEP) participants; assure VA relevance; help develop and approve final project scope and timeframe for completion; provide feedback on draft report; and provide consultation on strategies for dissemination of the report to field and relevant groups.

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Technical Expert Panel (TEP)

To ensure robust, scientifically relevant work, the TEP guides topic refinement; provides input on key questions and eligibility criteria, advising on substantive issues or possibly overlooked areas of research; assures VA relevance; and provides feedback on work in progress. TEP members are listed below:

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Peer Reviewers

The Coordinating Center sought input from external peer reviewers to review the draft report and provide feedback on the objectives, scope, methods used, perception of bias, and omitted evidence. Peer reviewers must disclose any relevant financial or non-financial conflicts of interest. Because of their unique clinical or content expertise, individuals with potential conflicts may be retained. The Coordinating Center and the ESP Center work to balance, manage, or mitigate any potential nonfinancial conflicts of interest identified.

TABLE OF CONTENTS

FIGURES

TABLES

EXECUTIVE SUMMARY

INTRODUCTION

Worldwide adoption of robot-assisted surgery continues to increase and has been applied to esophagectomy for esophageal cancer. Since 2009, there has been a more than 9-fold increase in robot-assisted minimally invasive esophagectomy (RAMIE) operations performed. Despite the rapid adoption of RAMIE, several questions about its utility compared to open esophagectomy and other video-assisted minimally invasive esophagectomy (VAMIE) approaches remain, especially with regard to long-term oncologic outcomes. Another important consideration is the economics of the robotic platform, which requires an upfront investment and costs for annual maintenance, instruments, staff and training, and infrastructure upgrade. We conducted a systematic review to help clinicians, patients, and policymakers weigh these approaches in patients undergoing esophagectomy for cancer.

METHODS

This topic was developed in response to a nomination by Dr. Mark Wilson, National Director of Surgery, and Dr. William Gunnar, Director, National Center for Patient Safety, Veterans Health Administration. Key questions were then developed with input from the topic nominator, the ESP coordinating center, the review team, and the technical expert panel (TEP).

The Key Questions were:

KQ1: What is the clinical effectiveness of robot-assisted esophagectomy compared to thoracoscopic/laparoscopic or open esophagectomy for cancer?

KQ2: What is the cost-effectiveness of robot-assisted esophagectomy compared to thoracoscopic/laparoscopic or open esophagectomy for cancer?

Data Sources and Searches

We conducted broad searches using terms relating to “robotic surgery” or “esophagectomy” or “cancer.” We searched PubMed (1/1/13-5/5/20), Cochrane (1/1/13-5/11/20), Ovid Medline (1/1/13-5/5/20), and Embase (1/1/13-5/6/20).

Study Selection

Studies were included if they were randomized clinical trials (RCTs) or observational studies comparing robot-assisted surgery with either thoracoscopic/laparoscopic and/or open surgical approaches for esophagectomy for cancer. We also included publications of cost-effectiveness models that compared robot-assisted surgery with thoracoscopic/laparoscopic or open surgical approaches. We included all RCTs regardless of outcomes and sample size. Observational studies were subjected to additional selection criteria. Observational studies with fewer than 10 subjects in either arm of the study were excluded. Additionally, observational studies from the same data source, either large databases or single institutional databases, were considered to have a large overlap if >50% of the same subjects were potentially included in multiple studies or if there was >50% overlap in the enrollment period. In this instance, the publication with the most recent data and the most outcomes of interest was included. For clarity, we elected to refer to

robot study arms as RAMIE. We refer to all non-robotic video-assisted arms as VAMIE, which includes the different varieties of thoracoscopic/laparoscopic approaches.

Data Abstraction and Quality Assessment

We abstracted data on the following: study design, patient characteristics, sample size, intra-operative outcomes (operating room [OR] time, lymph nodes [LN] harvested, estimated blood loss [EBL]), short-term post-operative outcomes (anastomotic leak, recurrent laryngeal nerve [RLN] palsy, pulmonary complications, length of stay [LOS], total complications, and mortality), long-term oncologic outcomes (recurrence and cancer-free survival), and data needed for the Cochrane Risk of Bias tool or Cochrane Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I).

Data Synthesis and Analysis

Because only 2 RCTs were identified, each comparing RAMIE to a different approach (one compared to VAMIE and the other to open esophagectomy), we did not conduct a meta-analysis of trials. The observational studies were too clinically heterogeneous to support a meta-analysis; hence, our synthesis is narrative. We used the criteria of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group to assess the certainty of evidence across studies.

RESULTS

Results of Literature Search

We identified 390 potentially relevant citations, of which 146 were included at the abstract screening level. From these, a total of 23 abstracts were excluded. Twenty-two publications were identified at full-text review as meeting initial inclusion criteria: 20 publications with clinical outcomes, 1 publication with both clinical and cost outcomes (therefore 21 in total had clinical outcomes), and 1 publication with only cost outcomes. See Figure 1 for literature flow.

Summary of Results for Key Questions

KQ1: What is the clinical effectiveness of robot-assisted esophagectomy compared to thoracoscopic/laparoscopic or open esophagectomy for cancer?

In general, OR time for RAMIE was longer than VAMIE and open esophagectomy. Although the RCT comparing RAMIE and VAMIE demonstrated near-equivalent OR times between study arms, several propensity-matched observational and unmatched observational studies concluded OR times were longer for RAMIE. The majority of studies demonstrated a signal of greater LN harvest with RAMIE compared with VAMIE and open esophagectomy. RAMIE consistently had less blood loss than VAMIE, but in no study was this difference statistically significant. Alternatively, RAMIE was associated with less blood loss compared to open esophagectomy across the majority of studies.

Regarding short-term post-operative outcomes, there was no evidence of a difference in anastomotic leak or RLN palsy rates between RAMIE compared with either VAMIE or with open esophagectomy. RAMIE may be associated with slightly fewer pulmonary complications

compared with VAMIE based on consistent findings across the majority of studies. The benefit of RAMIE on the rate of pulmonary complications was more apparent compared with open esophagectomy. It is unclear if LOS in the US was shorter with RAMIE compared with VAMIE. There were few studies that had mixed results. In contrast, RAMIE was likely associated with decreased LOS compared with open esophagectomy based on 2 of 3 studies, including 1 RCT. RAMIE had similar rates of total complications compared with VAMIE but was associated with decreased total complications when compared with open esophagectomy. Short-term mortality (within 90 days) was similar between RAMIE and VAMIE. However, short-term mortality between RAMIE and open esophagectomy was less clear due to differences between studies, but RAMIE likely did not have worse mortality.

With regard to oncologic outcomes, 1 RCT found statistically significantly longer cancer-free survival in patients treated with RAMIE as compared to those treated with VAMIE. There was no difference between RAMIE and VAMIE for recurrence rate. There was no difference in recurrence rate and cancer-free survival between RAMIE and open esophagectomy.

KQ2: What is the cost-effectiveness of robot-assisted esophagectomy compared to thoracoscopic/laparoscopic or open esophagectomy for cancer?

The total expenses or cost of RAMIE compared with open esophagectomy in the RCT found no difference between study arms, while the observational study comparing RAMIE with VAMIE found the robot-assisted approach was more expensive. There were serious limitations to both of these studies. Neither study included any description of how costs were derived; there is no mention of the time horizon, the financial "perspective" (costs vs charges vs payments), or the methods used to obtain estimates. In particular, with respect to the cost of the robot, it is unclear whether or not these studies included relevant costs such as instrument, maintenance, or depreciation expenses. It is also unclear how to compare cost estimates from China to the Netherlands or how these might compare to costs in the US.

Given the paucity of evidence and significant limitations of the available evidence, we are unable to draw strong conclusions about the cost-effectiveness of RAMIE compared to VAMIE or open esophagectomy.

DISCUSSION

Key Findings and Certainty of Evidence

RAMIE is associated with longer OR times compared with VAMIE and open esophagectomy. The certainty of evidence was low for the comparison of RAMIE and VAMIE and high for RAMIE compared with open esophagectomy based on consistency. There was greater lymph node harvest with RAMIE compared with VAMIE and open esophagectomy with low and moderate strength of evidence, respectively. There was moderate certainty of evidence that there were no differences in EBL between RAMIE and VAMIE. Conversely, there was high certainty of evidence that RAMIE was associated with less EBL compared with open esophagectomy. There was moderate certainty of evidence that the rate of anastomotic leak or RLN palsy were not different between RAMIE and VAMIE. The certainty of evidence was low for the slightly fewer pulmonary complications with RAMIE compared with VAMIE. There was moderate certainty of evidence that this benefit was more apparent comparing RAMIE with open

esophagectomy. There was moderate certainty of evidence that there were no differences with LOS or total complications between RAMIE and VAMIE. There was very low certainty of evidence that RAMIE was associated with a shorter LOS compared with open esophagectomy, due to limited data. On the other hand, there was moderate certainty of evidence that RAMIE had fewer total complications compared with open esophagectomy. There was moderate and very low certainty of evidence that there were no differences in short-term mortality (within 90 days) for RAMIE compared with VAMIE or open esophagectomy, respectively. Regarding long-term outcomes, there was very low certainty of evidence that cancer recurrence is not different between RAMIE and VAMIE or open esophagectomy due to a paucity of studies evaluating this outcome. Cancer-free survival is similar between RAMIE and open esophagectomy but improved when compared with VAMIE. The certainty of evidence is again very low due to limited studies assessing this outcome.

Formal cost-effectiveness studies comparing RAMIE with other approaches were not identified. The total expenses or cost of RAMIE compared with open esophagectomy based on 1 RCT from the Netherlands suggests there is no difference between study arms. Alternatively, RAMIE was more expensive than VAMIE based on a single observational study from China. Definitive conclusions regarding the balance between the benefits, risks, and cost cannot be made based on these 2 studies due to several methodologic differences, paucity of additional studies addressing some measure of cost, and the lack of a formal cost-effective analysis.

Applicability

No studies were specific to VA populations. The applicability of these results to VA populations may depend on both the similarity of the patients studied to VA patients and the experience of the surgical teams using the robot to the VA surgical team experience. However, the benefits for the robot-assisted approach may still be realized despite patient-level differences (VA patient population has greater burden of comorbidities than the general population), which will need to be confirmed in future studies. Robot-assisted operations are becoming prominent in thoracic surgery, so the experience will likely translate well into the VA setting. Our group, in conjunction with another VA research team, is in the early stages of utilizing VA NSQIP data to assess the frequency and trends of robot-assisted surgery for esophagectomy in Veterans as well as analyze its association to clinical outcomes.

Research Gaps/Future Research

Several research gaps are apparent. First, numerous techniques are used to perform an esophagectomy: combinations of robot-assisted, open, or minimally invasive approaches. We focused on comparing robot-assisted surgery for the thoracic portion of the procedure; however, outcomes like anastomotic leak might not be comparable depending on the tumor location and location of the anastomosis. Several other outcomes related to esophagectomy correlate with pre-operative variables, such as receipt of neoadjuvant therapy, tumor stage, and comorbid status. Although several studies in this review match for these characteristics, there are inconsistencies with reporting these variables across studies. It is difficult to determine the influence of the robot-assisted approach when there are few RCTs or well-designed, matched studies.

Second, regional variations of surgical practice and esophageal cancer epidemiology exist. The predominant histologic type of esophageal cancer in East Asian countries is squamous cell

carcinoma, while adenocarcinoma predominates in the US. Risk factors differ and underscore important clinical variation in patient populations. Further, East Asian countries have a higher incidence of esophageal cancer and thus higher surgical volume.

Third, the surgeon's physical experience using robot-assisted techniques is important to assess. The robotic platform has demonstrated improved ergonomics and less musculoskeletal complaints from surgeons compared to open and other minimally invasive surgical techniques, but this has not been universally observed. Research is needed to assess quality of life, chronic physical injuries, and longevity across approaches.

Fourth, the learning curve likely has an impact on certain outcomes like OR time, blood loss, and intra-operative complications. This learning curve is typically present with most evolving surgical technology; however, its influence should lessen with time and experience. Therefore, the learning curve may be considered as a potential factor in our findings.

Fifth, there is a lack of high-quality evidence on long-term and oncologic benefits, or risks, of RAMIE. Most studies comparing RAMIE focus on intra-operative and post-operative outcomes. Several observational studies that assessed long-term oncologic outcomes were small and had large attrition. To that end, RAMIE is gaining popularity and more cases are being performed each year, so within several years larger studies with adequate follow-up may be available.

Sixth, there is a paucity of studies directly comparing cost between RAMIE and other comparable approaches. There is a need for standardized methods to assess cost (*ie*, analytics, consistent definitions of cost, how upfront capital was accounted for, how to adjust for training staff, *etc*). Formal cost-effectiveness studies are needed.

Further, there has been evidence in other cancer types, mainly in gynecologic oncology that *worse* survival may occur with minimally invasive surgery. This finding supports the ongoing need for rigorous investigation into the comparative benefits and risks of robotic surgery across specialties and cancer types.

CONCLUSIONS

In summary, esophagectomy is a complex procedure with a high rate of morbidity, and while the robot-assisted approach has the potential to improve several important patient outcomes, current data are too limited to provide definitive conclusions. Future research should include RCTs or well-designed prospective matched studies with adequate power and follow-up to assess long-term as well as oncologic outcomes in patients undergoing robot-assisted surgery for esophageal cancer, including the determination of risks as well. Additional work should weigh the financial differences of the robot-assisted esophagectomy relative to the clinical advantages and disadvantages.

ABBREVIATIONS TABLE

ASA	American Society of Anesthesiologists
BMI	Body Mass Index
CCI	Charlson Comorbidity Index
CFS	Cancer-Free Survival
EBL	Estimated Blood Loss
GRADE	Grading of Recommendations Assessment, Development and Evaluation
LN	Lymph Node
LOS	Length of Stay
LR	Local Recurrence
MIE	Minimally Invasive Esophagectomy
NACT	Neoadjuvant Chemotherapy
NIS	National Inpatient Samples
NSQIP	National Surgical Quality Improvement Program
OE	Open Esophagectomy
OR	Operating Room
OS	Overall Survival
RLN	Recurrent Laryngeal Nerve
QALY	Quality-Adjusted Life Year
QOL	Quality of Life
RAMIE	Robot-Assisted Minimally Invasive Esophagectomy
RCT	Randomized Clinical Trial
ROBINS-I	Risk of Bias in Non-Randomized Studies-of Interventions
VAMIE	Video-Assisted Minimally Invasive Esophagectomy

EVIDENCE REPORT

INTRODUCTION

Worldwide adoption of robot-assisted surgery continues to increase, particularly for cancer and thoracic operations. Esophageal cancer is the seventh most common cancer diagnosis globally each year, with an estimated 572,000 new cases in 2018.[1] Esophagectomy is an important component of esophageal cancer treatment and is performed using open, conventional minimally invasive techniques (thoracoscopic and laparoscopic), or robot-assisted approaches. In 2016, there were over 1,800 robotic esophagectomies performed worldwide, a 9-fold increase from those performed in 2009.[2]

Historically, open esophagectomy (OE) is the standard surgical approach for esophageal cancer and is often combined with perioperative chemotherapy or chemoradiation for more advanced disease.[3,4] However, OE is a technically difficult operation with an associated morbidity and mortality of nearly 50% and 5%, respectively.[5] Minimally invasive approaches have been adopted, combining laparoscopic and thoracoscopic techniques with a handful of trials demonstrating fewer post-operative complications and similar oncologic outcomes.[6-8]

Robot-assisted minimally invasive esophagectomy (RAMIE) offers additional benefits to standard minimally invasive approaches due to the 540 degrees of wrist articulation, three-dimensional perspective, and greater magnification which may allow for a more meticulous dissection.[9,10] Despite the rapid adoption of RAMIE, several questions remain about its utility compared to OE and other minimally invasive approaches, especially with regard to long-term oncologic outcomes. Another important consideration is the economics of the robotic platform, which requires an upfront investment and costs for annual maintenance, instruments, staff and training, and infrastructure upgrade.

Individual studies and systematic reviews comparing RAMIE to MIE or OE have methodological variations and inconsistent reporting of oncologic and surgery-related outcomes. This is complicated further by the multiple approaches for esophagectomy (Ivor-Lewis, McKeown, and transhiatal) as well as determining if the benefit of the robot lies in the abdominal or thoracic phase of a multi-field esophagectomy.

Robot-assisted surgery for esophageal cancer is being increasingly used, and it is imperative to examine how it compares to open and other minimally invasive approaches, with an emphasis on long-term oncologic outcomes. We have conducted a systematic review to help clinicians, patients, and policymakers weigh these approaches in patients undergoing esophagectomy for cancer.

TOPIC DEVELOPMENT

This topic was developed in response to a nomination by Dr. Mark Wilson, National Director of Surgery, and Dr. William Gunnar, Director, National Center for Patient Safety, Veterans Health Administration. Key questions were then developed with input from the topic nominator, the ESP coordinating center, the review team, and the technical expert panel (TEP).

The Key Questions were:

KQ1: What is the clinical effectiveness of robot-assisted esophagectomy compared to thoracoscopic/laparoscopic or open esophagectomy for cancer?

KQ2: What is the cost-effectiveness of robot-assisted esophagectomy compared to thoracoscopic/laparoscopic or open esophagectomy for cancer?

The review was registered in PROSPERO: CRD42020198907.

SEARCH STRATEGY

We conducted broad searches using terms relating to "robotic surgery" or "esophagectomy" or "cancer." We searched PubMed (1/1/13-5/5/20), Cochrane (1/1/13-5/11/20), Ovid Medline (1/1/13-5/5/20), and Embase (1/1/13-5/6/20). Prior to 2013, robot-assisted procedures for esophagectomy were not widely being performed and many surgeons were still in the early so-called "learning curve". As such, our technical expert panel considered evidence from studies published prior to the year 2013 to be insufficiently relevant to modern practice. See Appendix A for complete search strategy.

STUDY SELECTION

Three team members working in pairs (MM/MG and MM/RS) independently screened the titles of retrieved citations. For titles deemed relevant by at least 1 person, abstracts were then screened independently in duplicate by 5 team members working in pairs (MM/MG; MM/MMG; MM/PT; and MM/RS). All disagreements were reconciled through group discussion. Full-text review was conducted in duplicate by 2 independent team members (MM and MD) with any disagreements resolved through discussion.

Studies were included at either the abstract or the full-text level if they were randomized clinical trials (RCTs) or observational studies comparing robot-assisted surgery with either thoracoscopic/laparoscopic or open surgical approaches for the included surgical procedure. The approach in the robotic arm (*eg*, Ivor-Lewis, McKeown, transthoracic, transhiatal) needed to be similar to the comparison arm to be included. We included all RCTs regardless of outcomes studied or sample size. Observational studies were subjected to additional selection criteria. Observational studies with less than 10 subjects in either arm of the study were excluded. Additionally, observational studies from the same data source, either large databases or single institutional databases, were considered to have a large overlap if >50% of the same subjects were included in multiple studies or if there was >50% overlap in the enrollment period. In this instance, the publication with the most recent data and the most outcomes of interest was included. We also included publications of cost-effectiveness models that compared robot-assisted surgery with thoracoscopic/laparoscopic or open surgical approaches.

DATA ABSTRACTION

Data extraction was completed in duplicate (MM/MD; MM/MMG; and MM/MG). Data from a non-English study was extracted by 1 member of the research team (MMG) with assistance from an English-speaking physician with extensive experience in systematic reviews whose native

language is the non-English language of interest. All discrepancies were resolved with full group discussion. We abstracted data on study design and pre-operative patient and tumor characteristics, intra-operative outcomes, short-term outcomes, long-term clinical/oncologic outcomes, and data needed for the Cochrane Risk of Bias tool or Cochrane Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I).

Intra-operative outcomes of interest included the duration of the operation (OR time), estimated blood loss (EBL), and number of lymph nodes (LN) harvested. The short-term outcomes of interest included anastomotic leak, recurrent laryngeal nerve (RLN) palsy and/or hoarseness, pulmonary complications (*ie*, pneumonia, pleural effusion), duration of hospitalization (length of stay [LOS]), total post-operative complications, and mortality within 90 days. Long-term oncologic outcomes of interest were cancer recurrence and cancer-free survival. Of note, we used total OR time when reported. For LOS, since non-US studies have notably longer LOS (more than a week typically), we decided to only plot US-based studies in our analysis figures. For total post-operative complications, we reported this outcome if it was specifically provided or, if not, we reported major complications if available. Continuous outcomes were analyzed using the mean or median along with a measure of dispersion (standard deviation, inter-quartile range) to calculate the difference and 95% confidence interval between arms. For binary outcomes, the number of subjects with the outcome was collected and a risk difference was derived with its 95% confidence interval.

QUALITY ASSESSMENT

RCTs were assessed for quality (risk of bias) with the Cochrane Risk of Bias tool.[11] This tool requires an assessment of whether a study is at high or low (or unknown) risk of bias in 7 domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting, and other (See Appendix C for tool; Appendix E for table). We used the Risk of Bias In Non-randomized Studies – of Interventions (ROBINS-I) for observational studies.[12] This tool requires an assessment of whether a study is at critical, serious, moderate, or low risk of bias (or no information) in 7 domains: confounding, selection bias, bias in measurement classification of interventions, bias due to deviations from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported result (see Appendix D for tool; Appendix F for table). Since observational studies are not required to have published an *a priori* protocol, we operationalized the last domain (bias in selection of the reported result) as requiring that studies report the most common variables.

DATA SYNTHESIS

Because there was a paucity of RCTs, we did not conduct a meta-analysis of trials. The observational studies were too clinically heterogeneous to support meta-analysis; hence, our synthesis is narrative.

RATING THE BODY OF EVIDENCE

We used the criteria of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group.[13] GRADE assesses the certainty of the evidence based on

the assessment of the following domains: risk of bias, imprecision, inconsistency, indirectness, and publication bias. This results in categories as follows:

High: We are very confident that the true effect lies close to that of the estimate of the effect.

Moderate: We are moderately confident in the effect estimate. The true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different.

Low: Our confidence in the effect estimate is limited. The true effect may be substantially different from the estimate of the effect.

Very low/Insufficient: We have very little confidence in the effect estimate. The true effect is likely to be substantially different from the estimate of effect.

PEER REVIEW

A draft version of the report was reviewed by technical experts and clinical leadership. Reviewer comments and our responses are documented in Appendix B.

RESULTS

We identified 390 potentially relevant citations, of which 146 were included at the abstract screening level. From these, a total of 101 abstracts were excluded: Wrong comparison (n=66), wrong intervention (n=1), review/editorial (n=19), systematic review (n=7), and protocol (n=8). This left 45 publications for full-text review, of which 23 publications were excluded for the following reasons: wrong intervention (n=6), wrong comparison (n=3), small sample size (n=1), not original research (n=1), duplicate or studies with a large overlap of patients from the same data source (n=11), and unavailable (n=1). A full list of excluded studies from the full-text review is included in Appendix I. A total of 22 publications were identified at full-text review as meeting initial inclusion criteria: 20 publications with clinical outcomes, 1 publication with both clinical and cost outcomes, and 1 publication with only cost outcomes. See Figure 1 for literature flow. Descriptions of included publications are available in the Evidence Table (Appendix G).

DESCRIPTION OF EVIDENCE

We identified 22 publications that met the inclusion criteria, of which 1 only reported cost data. As such, 21 studies reported clinical outcomes. Of these, 2 were RCTs,[14,15] and the remaining were observational studies. One RCT from the Netherlands randomized 109 patients with esophageal cancer to RAMIE (robot-assisted thoracic portion and laparotomy) or open esophagectomy (thoracotomy and laparotomy).[14] The other RCT from China randomized 192 patients with esophageal squamous cell carcinoma to RAMIE (robot-assisted thoracic and abdominal portions) or total thoracolaparoscopic MIE.[15] Both RCTs reported intra-operative, short-term, and long-term, cancer-specific outcomes.

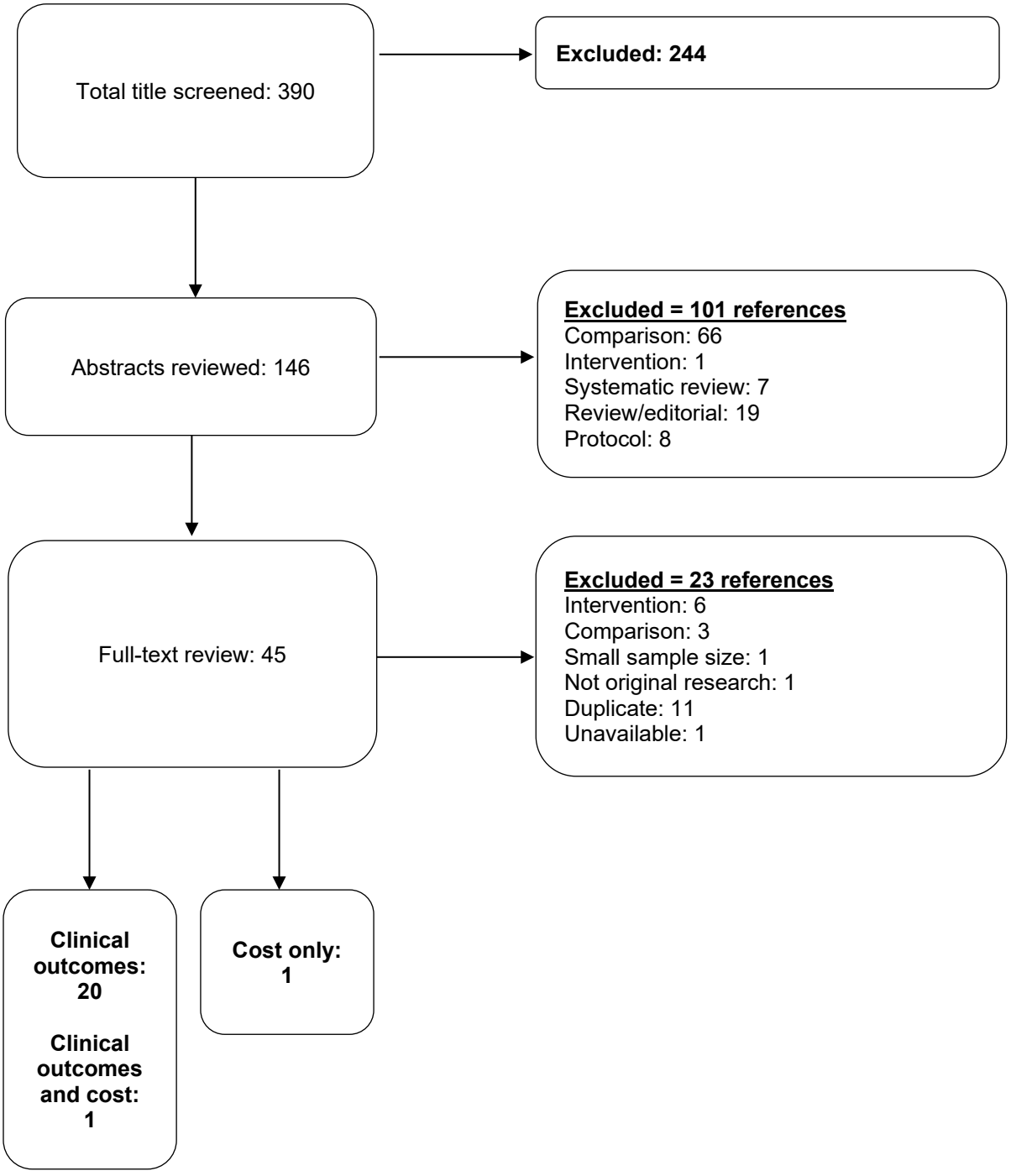
Of the 19 observational studies, 11 were propensity matched for patient characteristics and pre-operative factors, such as age, sex, BMI, certain comorbidities, receipt of neoadjuvant treatment, and clinical cancer staging.[16-26] The majority of the observational studies were from East Asia, with only 5 studies coming from the US. [19,22,27-29] The robot and non-robot cohorts of each study had comparable surgical approaches and varied in size from 36 to 5,553 patients. Ten observational studies compared transthoracic RAMIE with MIE.[16-18,20,22-24,26,30,31] Four studies compared transthoracic RAMIE with open esophagectomy.[21,25,28,32] One study utilized the robot for the abdominal portion only.[33] Three studies compared MIE, RAMIE, and open esophagectomy,[19,27,34] and 1 study compared transhiatal MIE with transhiatal RAMIE.[29] Two studies were from large national databases.[19,22] The study from the National Surgical Quality Improvement Program (NSQIP) database compared open esophagectomy with all minimally invasive esophagectomies (RAMIE and MIE combined) for the primary analysis but performed a secondary analysis comparing MIE and RAMIE with 2:1 propensity matching.[22] Only data from the secondary analysis was abstracted for this review. The other database study analyzed patients from the National Cancer Database and compared RAMIE, MIE, and open esophagectomy.[19]

All observational studies reported intra-operative and short-term outcomes, but only one-third reported long-term, cancer-specific outcomes. The majority of studies described tumor location and histologic type of cancer. Due to epidemiologic differences in esophageal cancer subtype, patients in the studies from East Asia primarily had squamous cell carcinoma, and the patients in the US studies predominantly had adenocarcinoma. Certain pre-operative factors, such as tumor location, stage, receipt of neoadjuvant therapy, and location of the anastomosis are known to

correlate with perioperative outcomes and are shown for each study in Appendix G. The surgical approach (*eg*, McKeown, Ivor-Lewis), operative technique for the thoracic and abdominal portions, and location and method of creating the anastomosis are provided in more detail in Appendix H (Operative Techniques of Included Studies).

For clarity, we elected to refer to robot-assisted study arms as robot-assisted minimally invasive esophagectomy (RAMIE) for the remainder of our report. Likewise, we refer to all video-assisted arms as video-assisted minimally invasive esophagectomy (VAMIE), which includes the different varieties and combinations of thoracoscopic/laparoscopic approaches.

Figure 1. Literature Flow Chart



KEY QUESTION 1 – What is the clinical effectiveness of robot-assisted esophagectomy compared to thoracoscopic/laparoscopic or open esophagectomy for cancer?

Intra-operative Outcomes

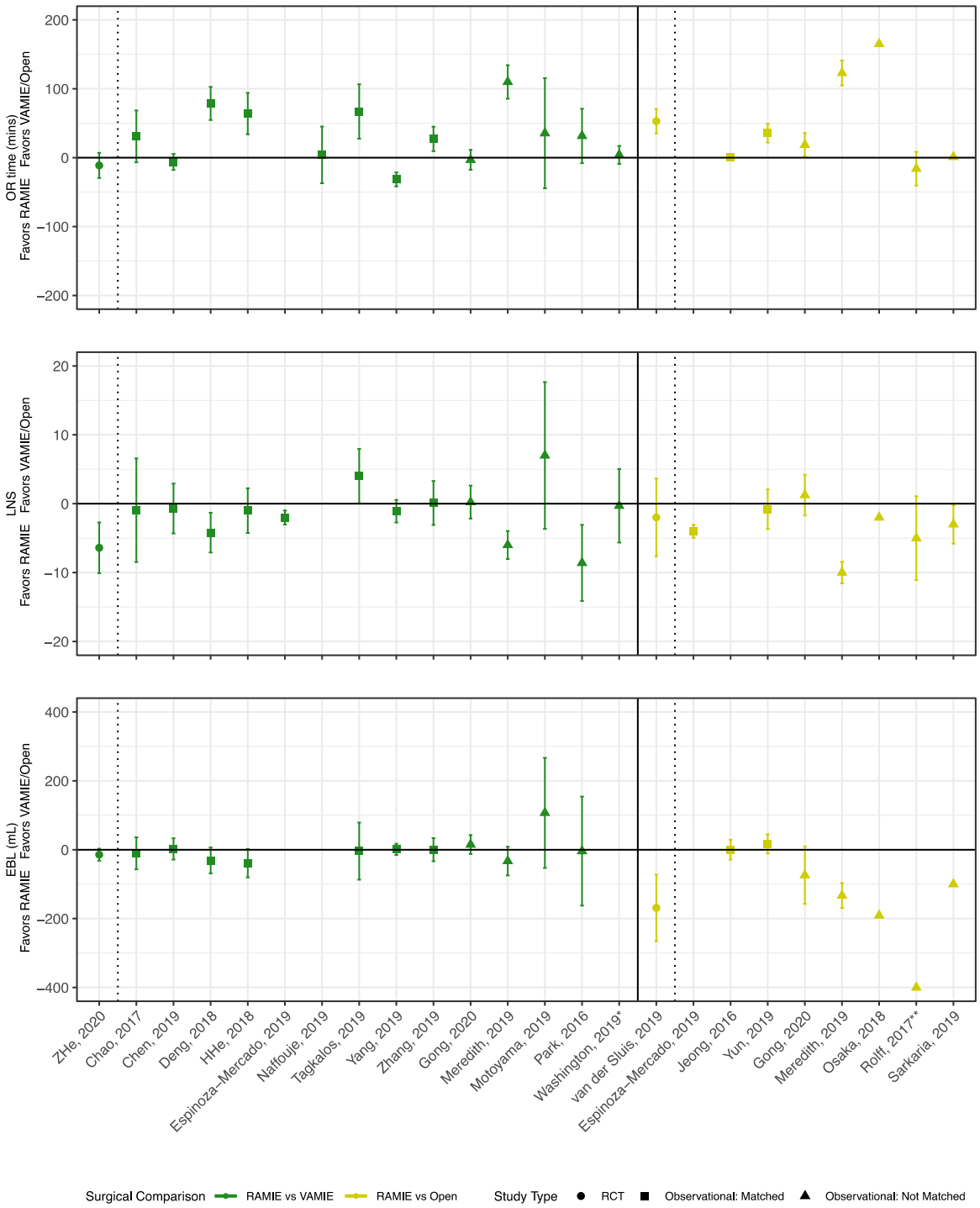
Intra-operative: RAMIE compared with VAMIE

Figure 2 presents 3 intra-operative outcomes: OR time, LN harvest, and EBL. For the RCT,[15] OR time was not longer for RAMIE as compared to VAMIE. The number of LNs harvested was greater for RAMIE, and EBL was not different. For the observational studies, OR time was reported as longer for RAMIE in 4 of the matched studies[18,20,23,26] and as no difference in 3 of the other matched studies.[16,17,22] One matched study reported shorter OR time[24] for RAMIE. For the unmatched observational studies, 1 reported longer OR time with RAMIE[27] and 4 reported no difference.[29-31,34] Two of the matched studies reported a greater number of LNs harvested for RAMIE,[18,19] whereas 6 reported no difference.[16,17,20,23,24,26] For unmatched observational studies, 2 reported greater number of LNs harvested with RAMIE,[27,31] and 3 reported no difference.[29,30,34] None of the matched or unmatched observational studies reported differences in EBL for RAMIE as compared to VAMIE.[16-18,20,23,24,26,27,30,31,34]

Intra-operative: RAMIE compared with Open Esophagectomy

For the RCT,[14] OR time was significantly longer for RAMIE compared to the open approach. The number of lymph nodes harvested was not different in the RAMIE arm. EBL was less for RAMIE. For the observational studies, there was a signal of longer OR time for RAMIE (4 reported significantly longer;[25,27,32,34] 3 no difference[21,28,33]). Seven studies reported on the number of LNs harvested and of these, 3 reported higher numbers removed by the RAMIE approach.[19,27,32] More than half of the observational studies reported less EBL with RAMIE[27,28,32,33] whereas 3 reported no difference.[21,25,34]

Figure 2. Intra-operative Outcomes



RAMIE=robot−assisted minimally invasive esophagectomy, VAMIE=video−assisted minimally invasive esophagectomy
*=robotic transhiatal vs laparoscopic transhiatal
**robot abdomen + thoracotomy vs open

[1]Dotted line separates RCT from the observational studies
[2]Solid line separates the studies comparing RAMIE with VAMIE or RAMIE with open esophagectomy

Short-term Post-operative Outcomes

Figure 3 presents 6 short-term post-operative outcomes: anastomotic leak, recurrent laryngeal nerve palsy/hoarseness, pulmonary complications, duration of hospitalization, total complications, and mortality. Twelve studies compared RAMIE vs VAMIE,[15-18,20,22-24,26,29-31] 6 studies compared RAMIE with open esophagectomy,[14,21,25,28,32,33] and 3 studies compared RAMIE with both VAMIE and open esophagectomy.[19,27,34]

Short-Term: RAMIE compared with VAMIE

Of the studies comparing RAMIE with VAMIE, 14 assessed anastomotic leak, and there was no significant difference between study arms or trend favoring RAMIE or VAMIE in either the RCT or the 8 matched and 5 unmatched observational studies.[15-18,20,22-24,26,27,29-31,34] Cervical anastomoses were used in 9 studies, including 8 studies primarily or exclusively utilizing the McKeown approach[15-18,20,24,31,34] and 1 utilizing a transhiatal approach.[29] Three studies directly compared intrathoracic anastomoses with an Ivor-Lewis approach in both study arms.[22,23,26] One study was from a large database and compared robot-assisted Ivor-Lewis with an unspecified "transthoracic" MIE, suggesting at least 1 study arm had an intrathoracic anastomosis.[27] Another study reported a transthoracic approach for both study arms but did not specify whether an intrathoracic or cervical anastomosis was performed.[30] There was no clear difference favoring RAMIE or VAMIE when evaluating studies with a cervical or intrathoracic anastomosis separately.

The RCT found no difference in recurrent laryngeal nerve (RLN) palsy between study arms.[15] Of the 6 matched observational studies assessing RLN injury, 1 reported lower RLN palsy with RAMIE,[17] 1 reported lower RLN palsy with VAMIE,[24] and 4 reported no difference.[16,19,20,26] For the 3 unmatched studies, 1 reported lower rate of RLN palsy as compared to RAMIE,[30] and 2 reported no difference.[31,34]

The RCT[15] did not report a difference in pulmonary complications for RAMIE as compared to VAMIE. One propensity matched study reported fewer pulmonary complications[24]; however, the other 7 studies did not.[16-18,20,22,23,26] None of the 4 unmatched observational studies reported a difference between RAMIE and VAMIE approaches.[27,30,31,34] Most of the studies had a point estimate of effect falling within the 95% confidence interval of the RCT, which may suggest a possible signal that there may be fewer pulmonary complications in RAMIE compared with VAMIE.

None of the 4 US observational studies assessing LOS found a significant difference between RAMIE as compared to VAMIE; 2 were matched and 2 were unmatched studies.[19,22,27,29] One of these studies compared robot-assisted and laparoscopic transhiatal esophagectomy, which had no difference in LOS.[29] Nine non-US studies evaluated LOS, of which none demonstrated differences between RAMIE and VAMIE (see Appendix G. Evidence table).[15-18,20,23,24,26,34] All but 1 of the 9 non-US studies had a LOS with a central tendency (mean or median) greater than 10 days in both study arms,[26] whereas all US studies had a measure of central tendency of 10 days or less.

Ten studies assessed outcomes for total complications.[15,18,20,22,24,26,27,29,31,34] One study compared robot-assisted transhiatal and laparoscopic transhiatal esophagectomy.[29] The remaining studies

compared a robot-assisted transthoracic approach to a thoracoscopic approach. Neither the RCT nor the matched and unmatched observational studies found a difference in complications.

Mortality was assessed in 14 studies.[15-20,22-24,26,27,29,31,34] Mortality was not different in the RCT or the matched and unmatched observational studies. In general, mortality rate was low across all studies.

Short-Term: RAMIE compared with Open Esophagectomy

Eight studies comparing RAMIE and open esophagectomy assessed anastomotic leak rate.[14,21,25,27,28,32-34] The RCT, 2 matched observational studies, and 5 unmatched observational studies reported no difference in leak rate. One observational study utilized the robot for the abdominal portion combined with thoracotomy, which did not demonstrate a difference in anastomotic leak rates, as the technique for creating the anastomosis was the same in both arms of the study.[33]

Of the 2 matched[21,25] and 3 unmatched observational studies[28,32,34] assessing RLN palsy, none found a difference between RAMIE and open esophagectomy.

Eight studies assessed pulmonary complications.[14,21,25,27,28,32-34] The rate of pulmonary complications was lower for RAMIE and open esophagectomy in the RCT.[14] One matched observation study and 2 unmatched observational studies also reported a lower rate for RAMIE.[25,27,28] The largest difference was seen in the RCT[14] but significance was also achieved in the 1 matched observational study[25] and 2 unmatched observational studies.[27,28] One matched observational study and 3 unmatched observational studies did not report a difference in pulmonary complications.[21,32-34]

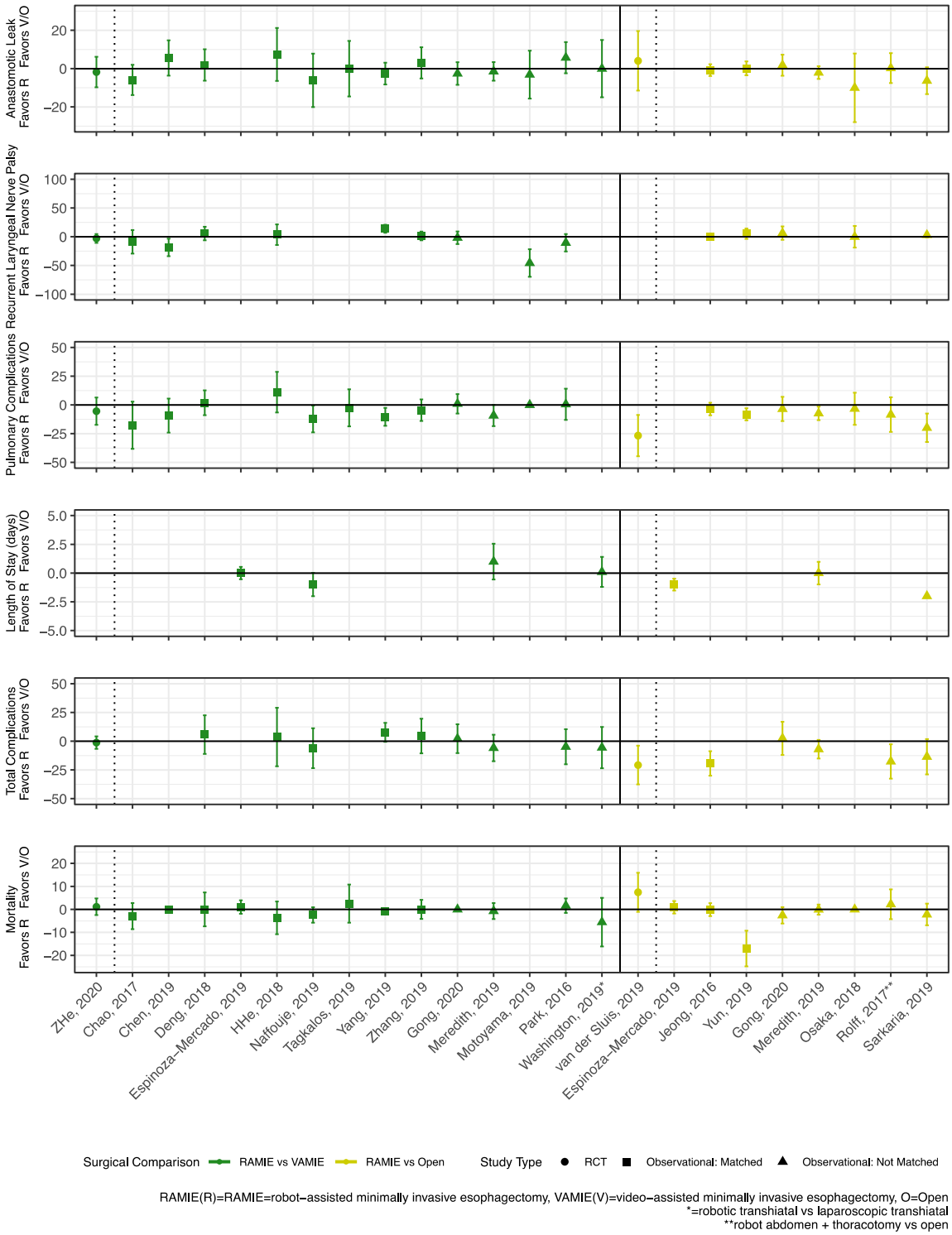
Three US studies evaluated LOS.[19,27,28] One matched observational study[19] and an unmatched observational study[28] demonstrated a shorter time to discharge with RAMIE. The third study (unmatched observational) did not find any differences in LOS between the study arms.[27] Of the 6 non-US studies that assessed LOS,[14,21,25,32-34] 2 demonstrated a shorter hospital stay for RAMIE compared with open esophagectomy (see Appendix G. Evidence Table).[32,33] The central tendency for LOS was greater than 10 days in both arms of the non-US studies except for one.[33] One out of the 3 US studies had LOS with a central tendency greater than 10 days.[28]

Six studies assessed total complication rate.[14,21,27,28,33,34] The RCT demonstrated a lower total complication rate with RAMIE.[14] Additionally, 1 matched observational study[21] and 1 unmatched study[33] showed reduced rates of total complications with RAMIE. Of note, the unmatched study compared the utilization of the robot for the abdominal portion with laparotomy (thoracic portion was performed via thoracotomy in both study arms). Three additional unmatched studies reported no difference total complications with RAMIE as compared to open esophagectomy.[27,28,34]

Mortality was assessed in 9 studies.[14,19,21,25,27,28,32-34] The RCT reported no different in mortality for RAMIE compared with open esophagectomy.[14] One matched observational study found that

RAMIE was associated with a lower mortality compared with open esophagectomy.[25] The remaining studies did not show a difference in mortality between study arms.

Figure 3. Short-term Post-operative Outcomes



RAMIE(R)=RAMIE=robot−assisted minimally invasive esophagectomy, VAMIE(V)=video−assisted minimally invasive esophagectomy, O=Open
*=robotic transhiatal vs laparoscopic transhiatal
**robot abdomen + thoracotomy vs open

[1]Dotted line separates RCT from the observational studies
[2]Solid line separates the studies comparing RAMIE with VAMIE or RAMIE with open esophagectomy

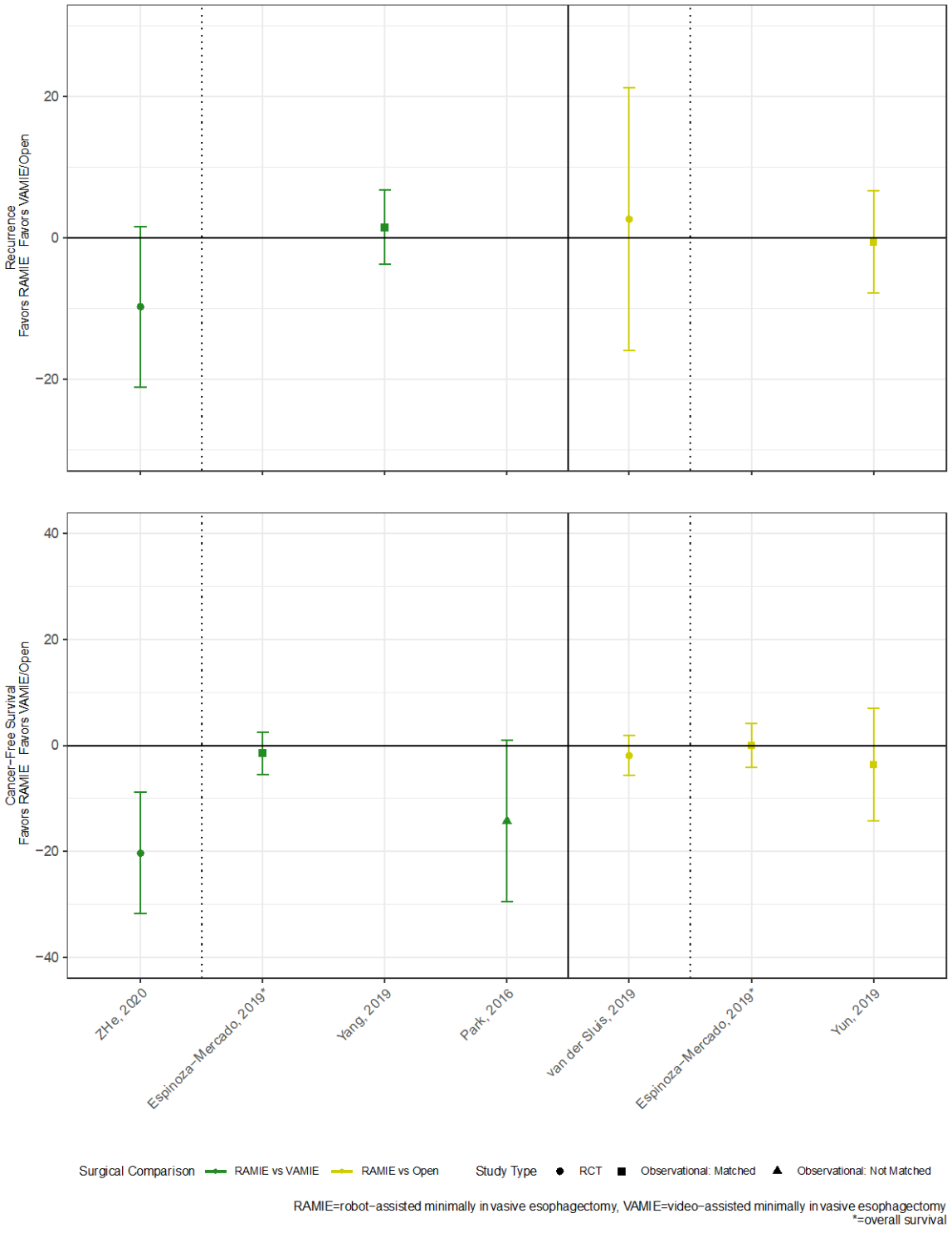
Long-term Outcomes

Long-term: RAMIE compared with VAMIE or Open Esophagectomy

Figure 4 presents graphically the results of long-term outcomes for recurrence and cancer-free survival. These outcomes were less frequently reported than the intra-operative and short-term post-operative outcomes. These were evaluated in 2 RCTs[14,15] and 3 observational studies.[24,25,31] One study reported overall survival instead of cancer-free survival.[19]

The RCT reported no difference in recurrence rate for RAMIE as compared to VAMIE, but a better cancer-free survival.[15] Recurrence rate was not different in the 1 matched observational study that reported on RAMIE as compared to VAMIE.[24] For the matched observational study that only reported overall survival, there was no difference between RAMIE and VAMIE.[19] Cancer-free survival was not different between RAMIE and VAMIE for 1 unmatched observational study.[31] The one RCT and 2 matched observational studies comparing RAMIE to open esophagectomy did not report differences in either of these long-term outcomes.[14,19,25]

Figure 4. Long-term Outcomes



[1]Dotted line separates RCT from the observational studies
[2]Solid line separates the studies comparing RAMIE with VAMIE or RAMIE with open esophagectomy

Summary of Findings

In general, OR time for RAMIE was longer than VAMIE and open esophagectomy. Although the RCT comparing RAMIE and VAMIE demonstrated OR times that were not different between study arms, several propensity-matched observational and unmatched observational studies concluded OR times were longer for RAMIE. The majority of studies demonstrated a signal of greater LN harvest with RAMIE compared with VAMIE and open esophagectomy. RAMIE may be associated with less EBL compared with VAMIE, but none of the findings reached statistical significance. Alternatively, RAMIE was associated with less EBL compared with open esophagectomy across the majority of studies.

Regarding short-term post-operative outcomes, the rate of anastomotic leak and RLN palsy did not appear to be different between RAMIE compared with either VAMIE or with open esophagectomy approaches. A difference in outcomes for different approaches (*ie*, McKeown and Ivor-Lewis esophagectomy) was not identified, and none of the studies reached statistical significance. RAMIE may be associated with slightly fewer pulmonary complications compared with VAMIE based on consistent findings across the majority of studies. The benefit of RAMIE on the rate of pulmonary complications was more apparent compared with open esophagectomy. It is unclear if LOS in the US was shorter with RAMIE compared with VAMIE, as there were too few studies with mixed results to draw a conclusion. In contrast, RAMIE was likely associated with decreased LOS compared with open esophagectomy based on 2 studies,[14,28] including 1 RCT. RAMIE had similar rates of total complications compared with VAMIE but was associated with decreased total complications when compared with open esophagectomy. Short-term mortality (within 90 days) was similar between RAMIE and VAMIE. Short-term mortality between RAMIE and open esophagectomy was less clear due to differences between studies, but RAMIE likely did not have worse mortality.

With regard to oncologic outcomes, RAMIE may be associated with better cancer-free survival compared with VAMIE. However, this conclusion was based primarily on 1 RCT.[15] There was no difference between RAMIE and VAMIE for recurrence rate. There was no difference in recurrence rate and disease-free survival between RAMIE and open esophagectomy.

Certainty of Evidence for Key Question 1

RAMIE compared with VAMIE

We judged the certainty of evidence for the outcome of longer OR time and improved lymph node harvest for RAMIE compared with VAMIE as low due to inconsistency and imprecision. We judged the certainty of evidence that there are no differences in EBL and anastomotic leak between RAMIE and VAMIE as moderate due to inconsistency. RLN palsy was determined to be not different with low certainty of evidence based on inconsistency. The certainty of evidence for the outcome of fewer pulmonary complications in RAMIE compared with VAMIE was deemed low due to inconsistency and relatively small estimated effect. The certainty of evidence that there are no differences in LOS or total complications between RAMIE and VAMIE is moderate due to some inconsistency and imprecision due to limited data. We judged the certainty of evidence that there is no difference in mortality between RAMIE and VAMIE as moderate due to some imprecision. Regarding long-term outcomes, we deemed the certainty of evidence

that recurrence is not different between RAMIE and VAMIE as very low due to inconsistency, imprecision due to a paucity of studies, and serious study limitations due to large attrition rates in 1 study.[24] The certainty of evidence that cancer-free survival is longer for RAMIE compared with VAMIE is very low for the same reasons.

RAMIE compared with Open Esophagectomy

We judged the certainty of evidence for the outcome of longer OR time for RAMIE compared with open esophagectomy as high. The certainty of evidence of improved lymph node harvest favoring RAMIE was judged to be moderate due to imprecision. We judged the certainty of evidence that EBL is less for RAMIE as high. The certainty of evidence that anastomotic leak is not different between RAMIE and open esophagectomy is moderate due to imprecision. We deemed the certainty of evidence that RLN palsy is not different between RAMIE and open esophagectomy as moderate due to study limitations. The certainty of evidence that RAMIE is associated with a lower rate of pulmonary complications compared with open esophagectomy is deemed to be moderate due to imprecision. We judged the certainty of evidence that LOS is shorter for RAMIE compared with open esophagectomy as very low due to inconsistency and imprecision due to sparsity of data. The certainty of evidence that there are fewer total complications with RAMIE compared with open esophagectomy is moderate due to some imprecision. The certainty of evidence that short-term mortality is not different between RAMIE and open esophagectomy is deemed to be very low due to inconsistency and imprecision. The certainty of evidence that recurrence and cancer-free survival are similar for RAMIE compared with open esophagectomy is very low due to imprecision, paucity of studies, and study limitations.

Table 1. Certainty of Evidence for Key Question 1

Outcome	Study Limitations	Consistency	Directness	Precision	Certainty of Evidence
Intra-operative					
Operating Room Time RAMIE > VAMIE RAMIE > Open	RCT: Low Matched observational studies: Moderate Unmatched observational studies: High	Inconsistent Consistent	Direct Direct	Imprecise Precise	Low High
Lymph Node Harvest RAMIE >VAMIE RAMIE > Open	RCT: Low Matched observational studies: Moderate Unmatched observational studies: High	Inconsistent Consistent	Direct Direct	Imprecise Imprecise	Low Moderate
Estimated Blood Loss RAMIE = VAMIE RAMIE < Open	RCT: Low Matched observational studies: Moderate Unmatched observational studies: High	Inconsistent Inconsistent	Direct Direct	Precise Precise	Moderate High
Short-term Post-operative					
Anastomotic Leak RAMIE = VAMIE RAMIE = Open	RCT: Low Matched observational studies: Moderate Unmatched observational studies: High	Inconsistent Consistent	Direct Direct	Precise Imprecise	Moderate Moderate
Recurrent Laryngeal Nerve Palsy RAMIE = VAMIE RAMIE = Open	RCT: Low Matched observational studies: Low Unmatched observational studies: Moderate	Inconsistent Consistent	Direct Direct	Precise Precise	Low Moderate
Pulmonary Complications RAMIE < VAMIE RAMIE < Open	RCT: Low Matched observational studies: Moderate Unmatched observational studies: High	Inconsistent Consistent	Direct Direct	Precise Imprecise	Low Moderate
LOS RAMIE = VAMIE RAMIE < Open	 Matched observational studies: Moderate 	 Inconsistent Inconsistent	 Direct Direct	 Imprecise Imprecise	 Moderate Very Low

Outcome	Study Limitations	Consistency	Directness	Precision	Certainty of Evidence
	Unmatched observational studies: High				
Total Complications RAMIE = VAMIE	RCT: Low Matched observational studies: Moderate	Inconsistent	Direct	Imprecise	Moderate
RAMIE < Open	Unmatched observational studies: High	Consistent	Direct	Imprecise	Moderate
Mortality RAMIE = VAMIE	RCT: Low Matched observational studies: Moderate	Consistent	Direct	Imprecise	Moderate
RAMIE = Open	Unmatched observational studies: High	Inconsistent	Direct	Imprecise	Very Low
Long-term/Oncologic					
Recurrence RAMIE < VAMIE	RCT: Low Matched observational studies: Moderate	Inconsistent	Direct	Imprecise	Very Low
RAMIE = Open	Unmatched observational studies: High	Inconsistent	Direct	Imprecise	Very Low
Cancer-Free Survival RAMIE > VAMIE	RCT: Low Matched observational studies: High	Inconsistent	Direct	Imprecise	Very Low
RAMIE = Open	Unmatched observational studies: High	Consistent	Direct	Imprecise	Very Low

KEY QUESTION 2 – What is the cost-effectiveness of robot-assisted esophagectomy compared to thoracoscopic/ laparoscopic or open esophagectomy for cancer?

No studies evaluated the cost-effectiveness of robot-assisted surgery compared with open or thoracoscopic/laparoscopic surgery for esophagectomy for cancer. Two publications included in their analysis some measure of cost (see Table 2).[17,35] One was a retrospective cohort study from a single institution in China comparing transthoracic RAMIE with transthoracic VAMIE. The second was an RCT from a single institution in the Netherlands comparing transthoracic RAMIE with open thoracotomy. The RCT was an abstract[35] published ahead of the full manuscript.[14] The abstract contains cost data that was not included in the final publication. Both were small studies including approximately 50 patients in the robotic arm.

Table 2. Evidence Table for Cost Studies

Author Year	Study Design, Number of Institutions, Country	Comparison(s)	Number of surgeons	Sample size	Source of cost data	Cost data	Misc Outcomes
Chen, 2019[17]	Retrospective cohort (propensity matched) Single institution China	Robot-assisted McKeown esophagectomy vs thoracolaparoscopic McKeown	Single surgical team	**Matched** Robot: 54 Lap: 54	Not stated	**Matched** **Total expenses (USD):** Robot: $25,300±9,000 Lap: $20,800±9,000 (p = 0.009) **Expenses/day (USD):** RAMIE: $1,700±700 TLMIE: $1,500±400 (p = 0.028)	**Matched** Duration: 187 min (robot) vs 193 min (lap), p=0.30 ICU stay 4.0 days (robot) vs 2.5 days (lap), p=0.14 Total LOS 17.1 days (robot) vs 15.2 days (lap), p=0.33
Van der Sluis, 2018[35]	RCT Single institution Netherlands	Robot-assisted thoracolaparoscopic esophagectomy vs open transthoracic esophagectomy	Two surgeons	Robot: 54 Open: 55	Not stated	**Mean costs:** Robot: €34,892 Open: €39,463 (p = 0.07)	Total OR time 349 min (robot) vs 296 min (open), p<0.001 ICU stay 1 day (robot) vs 1 day (open), p=0.45 Total LOS 14 days (robot) vs 16 days (open), p=0.33

Summary of Findings

The RCT found no statistical difference in total expenses or cost, while the observational study found the robot-assisted approach was more expensive. There are serious limitations to both of these studies. Neither study included any description of how costs were derived; there is no mention of the time horizon, the financial "perspective" (costs vs charges vs payments), or the methods used to obtain estimates. In particular, with respect to the cost of the robot, it is unclear whether or not these studies included relevant costs such as instrument, maintenance, or depreciation expenses. It is unclear how to compare cost estimates from China to the Netherlands or how these might compare to costs in the US.

Given the paucity of evidence and significant limitations of the available evidence, we are unable to draw any conclusion about the cost-effectiveness of RAMIE compared with VAMIE or open esophagectomy.

LIMITATIONS

Publication Bias

We were not able to test for publication bias and can make no conclusions about its possible existence. However, we feel it is extremely unlikely that there exists a high-quality randomized trial of robot-assisted surgery versus other surgical approaches that we did not identify and has similarly escaped detection by all other experts in this field. There is probably a plentitude of observational experiences about robot-assisted therapies from individual institutions that have never been published, and the available literature likely represents only a small fraction of what could be known using observational studies.

Study Quality

The RCTs were judged to have low risk of bias for short-term outcomes, such as intra-operative and short-term post-operative outcomes, and long-term oncologic outcomes. The observational studies were judged to have moderate risk of bias due to their non-random assignment of treatments for short-term outcomes and high risk of bias for longer-term outcomes. Many of the observational studies did not state how robotic esophagectomy was decided or offered for each patient, causing a risk of selection bias. However, of these studies, 11 were propensity matched, which mitigates the risk of selection bias, reducing the risk from serious to moderate. In terms of long-term outcomes, the high risk of bias is due to the fact that most of the studies calculated survival despite a high attrition rate, with some studies with an attrition rate over 50%.

Heterogeneity

The 2 general comparisons of the studies were RAMIE compared with VAMIE and RAMIE compared with open esophagectomy. We evaluated these 2 comparison groups separately to account for methodologic heterogeneity. Despite this, there was still significant heterogeneity between the studies. For example, the majority of studies compared transthoracic robot-assisted surgery to open or other minimally invasive approaches, but there are several transthoracic methods (*eg*, Ivor-Lewis and McKeown esophagectomies) and several hybrid combinations, such as utilizing the robot for the transthoracic portion combined with laparotomy or laparoscopy for the abdominal portion. Further, there are differences between studies with regard to certain

techniques, such as creation of the anastomosis, patient positioning, and port placement, that may have an impact on outcomes.

In addition to the variety of procedures performed, certain outcomes were also measured differently across studies. For example, with regard to lymph node harvest, some studies performed a 2-field or 3-field lymphadenectomy. Similarly, some studies reported lymph nodes harvested from specific sites (*eg*, right and left RLN lymph nodes). RAMIE may have some benefit in terms of lymph node harvest in these particular areas, but it was not reported consistently across studies. Another outcome that was heterogeneous across studies is total complications. While many studies used validated tools such as the Clavien-Dindo classification to define severity of complications, many did not. There was even variability within studies that used the Clavien-Dindo classification because select studies reported grade ≥3 complications while others reported complications that were ≥2. Moreover, many studies classified the post-operative complications into categories and listed the specific complications and frequencies within these categories; however, a handful of studies grouped all complications into one measurement without defining which complications were included. Furthermore, studies did not give specifics, in general, on how complications were treated, like how anastomotic leaks were managed for the different approaches.

Applicability of Findings to the VA Population

None of the included studies were specific to VA populations. The applicability of these results to VA populations may depend on both the similarity of the patients studied to VA patients and the experience of the surgical teams using the robot to VA surgical team experience. However, the benefits for the robot-assisted approach may still be realized despite patient-level differences (VA patient population has greater burden of comorbidities than the general population), which will need to be confirmed in future studies. Robot-assisted procedures are gaining popularity in thoracic surgery, and the adoption of this platform for esophagectomy will likely translate well into the VA setting. Our group, in conjunction with another VA research team, is in the early stages of utilizing VA NSQIP data to assess the frequency and trends of robot-assisted surgery for esophagectomy in Veterans as well as analyze its association to clinical outcomes.

Research Gaps/Future Research

Several research gaps are apparent. First, there are numerous surgical techniques for performing an esophagectomy (*ie*, Ivor-Lewis, McKeown, transhiatal, thoracoabdominal); any combination of robot-assisted, open, or minimally invasive approaches can be utilized. Often, tumor characteristics, such as size and location (upper, mid-, or lower esophagus), dictate which approach or combination is used. We focused on comparing robot-assisted surgery for the thoracic portion of the procedure. However, even when grouping studies that performed a transthoracic esophagectomy, certain outcomes like anastomotic leak might not be generalizable depending on where the anastomosis was located (*eg*, intrathoracic anastomosis for Ivor-Lewis esophagectomy or cervical anastomosis for McKeown esophagectomy). Therefore, determining the influence of the robot-assisted approach in comparison to other techniques is difficult to disentangle when RCTs or well-designed, matched studies are few.

Additionally, the robotic platform can be used in various stages of an esophagectomy (thoracic or abdominal portions). Na et al,[36] which was not included in our review, performed a propensity-matched analysis comparing hybrid RAMIE (robot for the thoracic portion combined

with laparotomy) with total RAMIE (*ie*, thoracic and abdominal portions performed with robot). There were no differences in clinical outcomes between approaches; however, the small sample size limited the comparisons. Ideally, studies like this, but with a larger number of patients, could help elucidate differences between specific robotic uses within techniques, such as the abdominal portion in this example. In fact, the Society of Thoracic Surgeons (STS) National Database has worked to expand patient follow-up to 5 years and to include specifics on the various types of approaches, which will allow for more detailed comparisons in the future.

Second, regional variations of surgical practice and esophageal cancer epidemiology exist. The predominant histologic type of esophageal cancer in East Asian countries is squamous cell carcinoma while adenocarcinoma predominates in the US.[37-39] The 5-year survival is less than 25% between the 2 subtypes, but the risk factors differ and underscore important clinical variation in patient populations.[38,39] For example, gastroesophageal reflux disease and obesity are risk factors for adenocarcinoma, while smoking, alcohol consumption, and nutritional deficiencies are risk factors for squamous cell carcinoma.[37-39] Further, East Asian countries in general have a higher incidence of esophageal cancer and thus higher surgical volume.[37-39]

Third, in addition to understanding the relationship of clinical outcomes for patients, the surgeon's physical experience is relevant. The robotic platform has demonstrated improved ergonomics and less musculoskeletal complaints from surgeons compared with open and other minimally invasive surgical techniques, but this has not been universally observed.[40] There is evidence that a prolonged time sitting at the robot-assisted console may add physical challenges. The physical impact of minimally invasive versus open surgery on the surgeon is still debated. Physical discomfort and symptoms of poor posture have been reported with minimally invasive surgery as compared to open surgery.[41,42] However, objective intraoperative measurement of surgeon posture suggests open surgery is more demanding for the neck and trunk.[43] Research is needed to assess detailed quality of life, assessment of chronic physical injuries, and longevity of operating compared across these approaches.

Fourth, the learning curve likely has an impact on certain outcomes like OR time, blood loss, and intra-operative complications. Its influence on reported outcomes in the literature is hard to discern, as the majority of studies fail to comment on the previous robotic experience or if a learning curve was specifically present. This learning curve is typically present with most evolving surgical technology;. However, the influence of the learning curve should lessen with time and experience.[44] Therefore, the learning curve may be a potential factor in our findings.

Fifth, there is a lack of high-quality evidence demonstrating the long-term and oncologic benefits, or risks, of RAMIE. The majority of studies comparing RAMIE focus on intra-operative and post-operative outcomes. Intra-operative events have a direct impact on short-term outcomes and potentially an indirect influence on long-term functional status and cancer control. However, new data suggests anastomotic leak does not compromise long-term outcomes or oncological control.[45] Two RCTs, 1 comparing RAMIE to VAMIE[15] and another comparing RAMIE to open esophagectomy,[14] evaluated recurrence and disease-free survival with adequate follow-up. However, these were relatively small studies (n=192 and n=99, respectively). Several observational studies that assessed long-term oncologic outcomes were small and had large attrition. To that end, RAMIE is gaining popularity and more cases are being performed each year, so within several years there may be large studies with adequate follow-up that become available.

Sixth, there is a paucity of studies directly comparing cost between RAMIE and other comparable approaches. Only 2 studies had some measure of cost, but both came from different countries and practice settings and do not generalize well to cost in the US. There is a need for standardized methods to assess cost – which applies to all robot-assisted operations, (*ie*, analytics, consistent definitions of cost, how upfront capital was accounted for, how to adjust for training staff, *etc*). Along these lines, formal cost-effectiveness studies that weigh the benefits and risks along with cost are needed.

Further, the recent Laparoscopic Approach to Cervical Cancer trial compared minimally invasive surgery, including laparoscopic and robotic, to open surgery in early-stage cervical cancer and found *worse* survival in the minimally invasive group.[46] In response, the FDA issued a warning: "The relative benefits and risks of surgery using robotically-assisted surgical devices compared with conventional surgical approaches in cancer treatment have not been established." The FDA encouraged research on robotic surgery, emphasizing impact on long-term clinical and oncologic outcomes. Careful analysis is warranted.

CONCLUSIONS

In summary, esophagectomy is a complex procedure with a high rate of morbidity, and while the robot-assisted approach has the potential to provide beneficial outcomes, current data is too limited to provide definitive conclusions. Future research should include RCTs or well-designed prospective matched studies with adequate power and follow-up to assess long-term as well as oncologic outcomes in patients undergoing robot-assisted surgery for esophageal cancer, including determination of risks. Additional work should also weigh the financial differences of the robot-assisted esophagectomy relative to the clinical advantages and disadvantages.

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APPENDIX A. SEARCH STRATEGIES

DATABASE SEARCHED & TIME PERIOD COVERED:
PUBMED – 2013-2020
362 results

(Randomized) OR ("control")) OR (randomly)) OR (trial)) OR (comparative)) OR (prospective))

AND

(Esophageal neoplasms[MESH terms]) OR ("Esophageal neoplasm")) OR ("Esophageal cancer")) OR ("Esophagus neoplasm")) OR ("Oesophageal neoplasm")) OR ("Oesophageal cancer")) OR ("Esophageal squamous cell carcinoma")) OR (Esophageal squamous cell carcinoma[MESH terms])) OR (Esophageal adenocarcinoma)) OR ("Esophagus cancer")))

AND

("minimally invasive") OR (Minimally invasive)) OR (Laparoscopic)) OR (Thoracoscopic)) OR (Thoracolaparoscop*)) OR (Laparothoracoscop*)) OR (Video-assisted)) OR (video assisted)) OR (Video-assisted thoracic surgery)) OR (VATS)) OR (Open)) OR (Thoracotomy)) OR (Laparotomy)) OR (Transhiatal)) OR (McKeown)) OR ("Three-hole")) OR (3-hole)) OR (Ivor-Lewis)) OR (Esophagectomy)) OR (Oesophagectomy)) OR (Esophagectomies)) OR (Oesophagectomies)) OR (Esophageal resection)) OR (Oesophageal resection)) OR (Trans-hiatal)))

AND

"thoracic surgical procedures"[MESH Terms]) OR (Robotic Surgical Procedures [MeSH terms])) OR (Robotics)) OR (Robot-assisted)) OR (Robot))

Filters: from 2013 – 2020

DATABASE SEARCHED & TIME PERIOD COVERED:
OVID MEDLINE & Epub Ahead of Print, In-Process & Other Non-Indexed Citations and Daily – 2013-2020
1 result

(randomized or "control" or randomly or trial or comparative or prospective).af.

AND

exp Esophageal Neoplasms/ OR exp esophageal Squamous Cell Carcinoma/ OR ("esophageal neoplasm" or "esophageal cancer" or "esophagus neoplasm" or "oesophageal neoplasm" or "oesophageal cancer" or "esophageal squamous cell carcinoma" or "esophageal adenocarcinoma" or "esophagus cancer").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

AND

("minimally invasive" or "minimally invasive" or laparoscopic or thoracoscopic or thoracolaparoscop* or laparothoracoscop* or "video-assisted" or "video assisted" or "video-assisted thoracic surgery" or "VATS" or open or thoracotomy or laparotomy or transhiatal or McKeown or "three-hole" or "3-hole" or "Ivor-Lewis" or esphagectomy or oesophagectomy or esophagectomies or oesophagectomies or "esophageal resection" or "oesophageal resection" or "trans-hiatal").mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

AND

exp Thoracic Surgical Procedures/ OR exp/Robotic Surgical Procedures/ OR (robotics or "robot-assisted" or robot).mp. [mp=title, abstract, original title, name of substance word, subject heading word, floating sub-heading word, keyword heading word, organism supplementary concept word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

AND

Publication years 2013-2020

DATABASE SEARCHED & TIME PERIOD COVERED:
EMBASE – 2013-2020
15 results

randomized:ti,ab,kw OR control:ti,ab,kw OR randomly:ti,ab,kw OR trial:ti,ab,kw OR comparative:ti,ab,kw OR prospective:ti,ab,kw

AND

'esophageal neoplasms'/exp OR 'esophageal neoplasm':ti,ab,kw OR 'esophageal cancer':ti,ab,kw OR 'esophagus neoplasm':ti,ab,kw OR 'oesophageal neoplasm':ti,ab,kw OR 'oesophageal cancer':ti,ab,kw OR 'esophageal squamous cell carcinoma':ti,ab,kw OR 'esophageal squamous cell carcinoma'/exp OR 'esophageal adenocarcinoma':ti,ab,kw OR 'esophagus cancer':ti,ab,kw

AND

'minimally invasive':ti,ab,kw OR 'minimally invasive':ti,ab,kw OR laparoscopic:ti,ab,kw OR thoracoscopic:ti,ab,kw OR thoracolaparoscop*:ti,ab,kw OR laparothoracoscop*:ti,ab,kw OR 'video-assisted':ti,ab,kw OR 'video assisted':ti,ab,kw OR 'video-assisted thoracic surgery':ti,ab,kw OR vats:ti,ab,kw OR open:ti,ab,kw OR thoracotomy:ti,ab,kw OR laparotomy:ti,ab,kw OR transhiatal:ti,ab,kw OR mckeown:ti,ab,kw OR 'three hole':ti,ab,kw OR '3-hole':ti,ab,kw OR 'ivor-lewis':ti,ab,kw OR esophagectomy:ti,ab,kw OR

oesophagectomy:ti,ab,kw OR esophagectomies:ti,ab,kw OR oesophagectomies:ti,ab,kw OR 'esophageal resection':ti,ab,kw OR 'oesophageal resection':ti,ab,kw OR 'trans-hiatal':ti,ab,kw

AND

'thoracic surgicial procedures' OR 'robotic surgerical procedures' OR robotics:ti,ab,kw OR 'robot-assisted':ti,ab,kw OR robot:ti,ab,kw

AND

Publication years 2013-2020

DATABASE SEARCHED & TIME PERIOD COVERED:
COCHRANE Reviews – 2013- 2020
12 results

ID Search Hits
#1 MeSH descriptor: [Esophageal Neoplasms] explode all trees
#2 MeSH descriptor: [Esophageal Squamous Cell Carcinoma] explode all trees
#3 (Randomized OR control OR randomly OR trial OR comparative OR prospective):ti,ab,kw
#4 ("Esophageal neoplasm" OR "Esophageal cancer" OR "Esophagus neoplasm" OR "Oesophageal neoplasm" OR "Oesophageal cancer" OR "Esophageal squamous cell carcinoma" OR "Esophageal adenocarcinoma" OR "Esophagus cancer"):ti,ab,kw
#5 #1 OR #2 OR #4
#6 ("minimally invasive" OR "Minimally invasive" OR Laparoscopic OR Thoracoscopic OR Thoracolaparoscop* OR Laparothoracoscop* OR "Video-assisted" OR "video assisted" OR "Video-assisted thoracic surgery" OR VATS OR Open OR Thoracotomy OR Laparotomy OR Transhiatal OR McKeown OR "Three-hole" OR "3-hole" OR "Ivor-Lewis" OR Esophagectomy OR Oesophagectomy OR Esophagectomies OR Oesophagectomies OR "Esophageal resection" OR "Oesophageal resection" OR "Trans-hiatal"):ti,ab,kw
#7 MeSH descriptor: [Thoracic Surgical Procedures] explode all trees
#8 MeSH descriptor: [Robotic Surgical Procedures] explode all trees
#9 (robotics OR "robot-assisted" OR robot):ti,ab,kw (Word variations have been searched)
#10 #7 OR #8 OR #9
#11 #3 AND #5 AND #6 AND #10

AND

Publication years Jan 2013- Dec2020

APPRENDIX B. PEER REVIEWER COMMENTS AND AUTHOR RESPONSES

Reviewer comments	Authors Responses
Yes - Yang L, Wang T, Weidner TK, Madura JA 2nd, Morrow MM, Hallbeck MS. Intraoperative musculoskeletal discomfort and risk for surgeons during open and laparoscopic surgery. Surg Endosc. 2020 Oct 20. doi: 10.1007/s00464-020-08085-3. Epub ahead of print. PMID: 33083930.	Thank you for this reference. We have included it in our discussion. This study highlights the physical burdens of open surgery and the potential benefit of laparoscopic and robotic surgery.
Outcomes of esophagectomy are known to correlate with certain preoperative variables including tumor location, stage, neoadjuvant therapy and with intraoperative technique such as MIS and/or robot used for thoracic, abdominal, both, and anastomotic location/technique. Appendix G provides insightful summaries of matching strategies used in included studies. Would clearer reference to matching of critical factors and citation of Appendix G in the Discussion (or Methods) section be advisable?	Thank you for your suggestion. We included a reference to Appendix G in the discussion. We agree that these are important variables to consider. Many of the studies corrected for these factors with propensity matching. Also, the majority of studies included in this review utilized the same approach (McKeown or Ivor-Lewis) in the study arms but utilized a different technique (robot vs open or MIE). Of note, we used inclusion criteria to identify studies where the robotic approach was the within study comparison.
This paper appears to be well written and researched. It has included the review of major literature in the adaption of the robotic platform to the esophagectomy. Especially for use in the VA, many centers already have the Da Vinci Robot, so it makes sense to try to utilize it for Esophagectomy without a huge cost burden. However, there are some issues that may arise especially with esophageal cancer volume and robotics in various centers. I Regarding study selection, only studies with greater than 10 patients per arm were included when it comes to observational studies. Why not include studies with less than 10?	Case series with less than 10 subjects in each study arm were deemed too high risk for potential biases because of the differences in patient level factors and tumor factors. Differences (or the lack of) between study groups in these smaller studies would be more potentially underpowered and may lead to incorrect conclusions. Also, only one study (including at the abstract and full text review) was identified with a study arm with less than 10 patients (N=4) in the abstract and full text screening phases.
Next, I had a question regarding anastomotic leak when comparing RAMIE with VAMIE or open. It states here at there were three studies with anastomotic leak difference between Open and RAMIE. Did this make a difference in outcomes? Were the leaks managed differently? And were the leaks with RAMIE less morbid and managed differently than the Open patients? Also, did this change adjuvant systemic therapy at all?	The draft had a typo regarding this. No studies comparing OE with RAMIE found a difference in anastomotic leak rate. This has been corrected. These are great questions, but unfortunately the published studies do not go into that level of detail. This was added to our limitations paragraph.
Page 8/line 11: why is the US specifically referenced for LOS in RAMIE vs VAMIE? is there an LOS difference outside of the US?	There are international variations in length of stay with many non-US studies allowing very prolonged hospital stays based on a variety of factors (cultural, health care system, *etc*). As such, the association of the procedure approach (robot) would differ based on the origin of the study. Thus, for this one outcome we elected to restrict the analysis to USA-only

	studies, as we judged these would be more relevant to the VA population and system.
9/15: "there are no differences LOS...", consider inserting the word WITH before LOS.	Thank you noticing this error. It has been corrected.
13/21: abbreviation for open esophagectomy needed (OE)	The requested edit was made.
13/25: i feel this paragraph implies that minimally invasive approaches may be less technically demanding than OE, which is untrue. minimally invasive approaches are much more technically demanding but have fewer postoperative complications. Possibly removing the wording that "OE is a technically difficult operation", or just that esophagectomy is a technically difficult operation whether done open or by minimally invasive approaches.	We agree. Thank you for making this important point. Esophagectomy is a technically challenging operation and minimally invasive techniques require additional expertise to be proficient. We have corrected this to convey that esophagectomy, regardless of approach or technique, is technically difficult.
23/18: when it is described that the studies reported a difference in leak rate, it is not obvious which had lower leak rates (RAMIE or OE). Because in the summary it is stated that there is no difference, possibly it is meant to state "...observational studies reported NO difference in leak rate."?	Thank you noticing this discrepancy. We have corrected it in the manuscript.
36/5: "...which was not an include in our review...", possibly change to "which was not INCLUDED in our review".	Thank you for careful review. We have made the requested change.
36/33: I find it odd that there is a reference that shows increased physical discomfort and symptoms or poor posture with laparoscopy when compared with open surgery, my understanding is the opposite. Possibly more references need to be included or the statement can be deemed as an ongoing controversy with unclear understanding. One such is below. Yang L, Wang T, Weidner TK, Madura JA 2nd, Morrow MM, Hallbeck MS. Intraoperative musculoskeletal discomfort and risk for surgeons during open and laparoscopic surgery. Surg Endosc. 2020 Oct 20. doi: 10.1007/s00464-020-08085-3. Epub ahead of print. PMID: 33083930.	Thank you for your comments and your understanding of the existing controversy. We agree with you that typically laparoscopy should help to prevent musculoskeletal problems for surgeons. However, several questionnaire studies (which we referenced in our report) consistently found higher rates of physical discomfort with minimally invasive surgery compared to open. In contrast, the study you shared has objective data regarding surgeon posture and is an important aspect for this ongoing debate. We appreciate your insight in this matter and certainly it is unclear what role laparoscopy plays in minimizing surgeon discomfort.
This is an incredibly detailed and thoughtful review of the many potential clinical and economic benefits and risks of robotic esophagectomy compared to non-robotic approaches. There is clearly limited data from which the authors had to draw conclusions with only 2 RCTs and a total of 20 publications out of 390 potential papers that met inclusion criteria. Unfortunately, there is also tremendous diversity in terms of cancer epidemiology and with regards to surgical approach and technique. This heterogeneity is dizzying and makes it near impossible to draw conclusions from any comparisons across studies. This is well stated by the authors who comment that it is “difficult to disentangle” the impact of the robot from the various other techniques. That said, the authors	Thank you for those encouraging comments. We agree that the heterogeneity among the studies and paucity of RCTs were limitations and are hopeful that more data will soon emerge so that we can make definitive conclusions with a high level of certainty

<table>
<tr><td>should be commended for the rigorousness of their methodology. Frustratingly, their ability to draw meaningful conclusions is quite limited by the quality of publications, inconsistency, imprecision, bias, and heterogeneity. The section on research gaps and future research is the highlight of the paper.</td><td></td></tr>
<tr><td>While reading the text, I found myself asking, “Was the robot being used for the abdominal portion instead of laparoscopy or laparotomy? Was the robot used for the thoracic portion instead of thoracotomy or VATS? Was the anastomosis being done in the neck or in the chest? How was the anastomosis performed, hand sewn or stapled? Did the surgical approach include a pyloric relaxing procedure? Was a feeding tube placed at the time of esophagectomy?” Many of these technical differences have implications for OR time, pulmonary complications, etc. These variables may have an impact on measured outcomes that are independent of whether the robot was used. The answers to these questions can be found in Appendix G. I hesitate to make this suggestion given the herculean efforts involved in putting together this table, but it might be worth considering adding a few additional columns to simplify for the readers. Eg:

<table><tr><td></td><td></td><td>Abdomen</td><td>Chest</td><td>Neck</td><td>Anastomosis</td><td></td></tr><tr><td>Study A</td><td>VAMIE</td><td>Laparoscopy</td><td>VATS</td><td>NA</td><td>EEA</td><td></td></tr><tr><td></td><td>RAMIE</td><td>Laparoscopy</td><td>robotic</td><td>NA</td><td>EEA</td><td></td></tr><tr><td></td><td></td><td></td><td></td><td></td><td></td><td></td></tr></table></td><td>Thank you for this suggestion. We created an additional table to highlight the technical differences/surgical approaches between arms for each study. Specifically, we indicate the following when provided: the approach (McKeown, Ivor-Lewis, transhiatal), tool or technique used for the 2- or 3-stage operations (ie, robotic, thoracolaparoscopic, or open techniques for the abdomen and chest), and the anastomotic technique. Again, the main difference we were assessing was the within study comparison of the robotic portion of the operation.</td></tr>
<tr><td>I confess that I am often frustrated by the amount of effort that goes into general comparisons between robotic surgery and open surgery or robotic surgery and VATS/laparoscopy. The robot is a tool that is likely here to stay. With favorable ergonomics, excellent visualization, and an ever expanding pallet of graspers and energy at the surgeons disposal, adoption seems inevitable. New robotic platforms are coming to the market in the near future which are anticipated to decrease costs with new competition in the marketplace. I have argued with colleagues that a researchers time could be better spent contemplating more profound, substantive questions about the extent of resection, for example, or the intricacies of multimodal therapy, patient selection, etc. That said, I do find the authors reference to and the results of the Laparoscopic Approach to Cervical Cancer (LACC) trial intriguing. In the context of esophageal cancer, I would be surprised if we could ever detect a clear oncologic signal amidst the cacophonous noise of surgical esophagectomy research but this review, if nothing else, has prompted me to reconsider my indifference. I encourage the</td><td>Thank you for your comments. We feel that an updated systematic review will be warranted when robot-assisted esophagectomy becomes widely adopted, more long term outcomes are published, and additional robotic platforms on the market.</td></tr>
</table>

authors to continue with their future endeavors and would be glad to continue to participate in trial design and enrollment.	
I think that this is a very well designed and executed study of techniques for esophagectomy. The conclusions are limited due to the limitations in RCTs or other large patient population studies. The results are not surprising. Utilizing minimally invasive techniques in esophageal resection improves patent outcomes. Even when the surgical procedure is a hybrid of minimally invasive and open techniques patients do better as described in NEJM. The technique, MIS/open, versus the tool, RAMIE/VAMIE determines patient benefit. The tool (robot, LAPVATS) should be chosen based on Surgeon comfort and availability. Future studies will be impacted greatly by STS database including 5 year survival for cancer surgeries. This database is more clear in the definitions of open and MIS. Hybrid techniques will be identifiable. Hopefully this can help answer questions related to long term survival implications of open vs MIS abdominal approaches, open vs MIS chest approaches and cervical/chest anastomoses.	Thank you for your comments. Indeed the STS database may have additional granularity and better long-term data such that we can hopefully understand if the platform affects these outcomes. We added some of your points to our discussion.
Yes, the findings are presented in a way that is helpful for decision-making.	Thank you for the comment.
No recommendations; presentation format supports utilization decisions.	We appreciate your comments.
The report will be utilized in conjunction with the other ESP robotic-assisted surgery reports. The findings will inform policy and decisions by facilities/VISNs to purchase robotic technology.	Thank you for the comment.
Esophagectomy-specific outcome tracking	Thank you for the comment.
Recommend VA webinar/cyberseminar and presentation to the surgical community of practice to be coordinated by the National Surgery Office.	We are happy to participate.
I support plans for a national VHA webinar and will also assess for VISN Surgery Integrated Clinical Community presentation by ESP Center.	We are happy to participate.
Thoracic Surgeons, Oncologists, and GI providers	Anesthesiologists and surgical oncologists may be interested as well.
Very, excellent report.	Thank you for your comment.
Very satisfied. Report clearly assessed available literature and identified limitations/gaps and potential areas for future research. Conclusions were appropriate based upon available information and completed narrative analysis.	We appreciate your comments.

APPENDIX C. COCHRANE RISK OF BIAS TOOL

The Cochrane Collaboration's Tool for Assessing Risk of Bias*

Domain	Support for judgement	Review authors' judgement
Selection bias.		
Random sequence generation.	Describe the method used to generate the allocation sequence in sufficient detail to allow an assessment of whether it should produce comparable groups.	Selection bias (biased allocation to interventions) due to inadequate generation of a randomised sequence.
Allocation concealment.	Describe the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocations could have been foreseen in advance of, or during, enrolment.	Selection bias (biased allocation to interventions) due to inadequate concealment of allocations prior to assignment.
Performance bias.		
Blinding of participants and personnel *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Detection bias.		
Blinding of outcome assessment *Assessments should be made for each main outcome (or class of outcomes).*	Describe all measures used, if any, to blind outcome assessors from knowledge of which intervention a participant received. Provide any information relating to whether the intended blinding was effective.	Detection bias due to knowledge of the allocated interventions by outcome assessors.
Attrition bias.		
Incomplete outcome data *Assessments should be made for each main outcome (or class of outcomes).*	Describe the completeness of outcome data for each main outcome, including attrition and exclusions from the analysis. State whether attrition and exclusions were reported, the numbers in each intervention group (compared with total randomized participants), reasons for attrition/exclusions where reported, and any re-inclusions in analyses performed by the review authors.	Attrition bias due to amount, nature or handling of incomplete outcome data.
Reporting bias.		
Selective reporting.	State how the possibility of selective outcome reporting was examined by the review authors, and what was found.	Reporting bias due to selective outcome reporting.
Other bias.		
Other sources of bias.	State any important concerns about bias not addressed in the other domains in the tool. If particular questions/entries were pre-specified in the review's protocol,	Bias due to problems not covered elsewhere in the table.

	responses should be provided for each question/entry.	

* http://handbook.cochrane.org/ in Table 8.5.a

APPENDIX D. RISK OF BIAS IN NON-RANDOMISED STUDIES – OF INTERVENTIONS (ROBINS-I)

Bias Domains Included in ROBINS-I[12]

Pre-intervention	Risk of bias assessment is mainly distinct from assessments of randomised trials
Bias due to confounding	Baseline confounding occurs when one or more prognostic variables (factors that predict the outcome of interest) also predicts the intervention received at baseline ROBINS-I can also address time-varying confounding, which occurs when individuals switch between the interventions being compared and when post-baseline prognostic factors affect the intervention received after baseline
Bias in selection of participants into the study	When exclusion of some eligible participants, or the initial follow-up time of some participants, or some outcome events is related to both intervention and outcome, there will be an association between interventions and outcome even if the effects of the interventions are identical This form of selection bias is distinct from confounding—A specific example is bias due to the inclusion of prevalent users, rather than new users, of an intervention
At intervention	Risk of bias assessment is mainly distinct from assessments of randomised trials
Bias in classification of interventions	Bias introduced by either differential or non-differential misclassification of intervention status Non-differential misclassification is unrelated to the outcome and will usually bias the estimated effect of intervention towards the null Differential misclassification occurs when misclassification of intervention status is related to the outcome or the risk of the outcome, and is likely to lead to bias
Post-intervention	Risk of bias assessment has substantial overlap with assessments of randomised trials
Bias due to deviations from intended interventions	Bias that arises when there are systematic differences between experimental intervention and comparator groups in the care provided, which represent a deviation from the intended intervention(s) Assessment of bias in this domain will depend on the type of effect of interest (either the effect of assignment to intervention or the effect of starting and adhering to intervention).
Bias due to missing data	Bias that arises when later follow-up is missing for individuals initially included and followed (such as differential loss to follow-up that is affected by prognostic factors); bias due to exclusion of individuals with missing information about intervention status or other variables such as confounders
Bias in measurement of outcomes	Bias introduced by either differential or non-differential errors in measurement of outcome data. Such bias can arise when outcome assessors are aware of intervention status, if different methods are used to assess outcomes in different intervention groups, or if measurement errors are related to intervention status or effects
Bias in selection of the reported result	Selective reporting of results in a way that depends on the findings and prevents the estimate from being included in a meta-analysis (or other synthesis)

APPENDIX E. QUALITY ASSESSMENT FOR INCLUDED RCT STUDIES

Author, year	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias
He, 2020[15]	○	◒	◒	◒	Short-term: ○ Long-term: ○	○	○
van der Sluis, 2019[14]	○	○	○ *Patients blinded to intervention	● Trial coordinators recorded daily outcomes	Short-term: ○ Long-term: ○	○	○

○ = low risk of bias ● = risk of bias ◒ = unknown

* low risk of bias for primary outcomes (all-cause mortality and amputation-free survival, but high risk of bias for secondary outcome

APPENDIX F. QUALITY ASSESSMENT FOR INCLUDED OBSERVATIONAL STUDIES

Author, year	Confounding	Selection bias	Bias in measurement classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Other source of bias
Chao 2018[16]	**Low**	**Moderate** RAMIE offered to all patients after 2014, but it was only partially insured while MIE was fully covered	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**
Chen 2019[17]	**Low**	**Moderate** Unknown how intervention offered; propensity matched for pre-op factors	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**
Deng 2019[18]	**Low**	**Low** Offered RAMIE & VAMIE, patients chose on their own will	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**
Espinoza-Mercado 2019[19] NCDB	**Low**	**Moderate** Unknown how intervention offered; propensity matched for pre-op factors	**Moderate** Unable to differentiate the surgical approach – transhiatal, IL, McKeown	**Low**	**Low**	**Low**	**Low**	**n/a**
Gong 2020[34]	**Serious** Clinical stage and neoadjuvant treatment were different between treatment arms	**Serious** Unknown who was offered which technique	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**
He 2018[20]	**Low**	**Moderate** Unknown how intervention offered; propensity matched for pre-op factors	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**
Jeong 2016[47]	**Low**	**Moderate**	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**

Author, year	Confounding	Selection bias	Bias in measurement classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Other source of bias
		RAMIE recommended for specific indications (*eg*, low clinical stage); however, the propensity matched for most of these factors				Standardized tools were used to assess pain and delirium		
Meredith 2019[27]	**Serious** No p-values provided	**Serious** Unknown how intervention offered	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**
Motoyama 2019[30]	**Low**	**Serious** Unknown how intervention offered; between 2014 and 2018. RAMIE was not covered by insurance; so only those who could pay underwent robot during that time period	**Low**	**Low**	**Low**	**Low**	**Moderate** Do not report several outcomes	**n/a**
Naffouje 2019[22] NSQIP	**Low**	**Moderate** Unknown how intervention offered; propensity matched for pre-op factors	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**
Osaka 2018[32]	**Moderate** List very few patient characteristics	**Serious** Unknown who was offered RAMIE. Do not explicitly state what the "criteria for robot" are that they used to match open surgery	**Low**	**Low**	**Low**	**Low**	**Moderate** Do not report several outcomes that are given in similar studies	**n/a**
Park 2016[48]	**Low**	**Serious** Unknown who RAMIE was offered to	**Low**	**Low**	**Short-term outcomes: Low** **Long-term outcomes: Serious** (>50%	**Low**	**Serious** Several outcomes of high importance	**n/a**

Author, year	Confounding	Selection bias	Bias in measurement classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Other source of bias
					lost to follow up at 5-year outcomes)		not included (*ie*, LOS).	
Rolff 2017[33]	**Serious** Very few patient characteristics, no clinical oncologic data, *etc*	**Moderate** Intervention depended on date of operation and robot availability. However, large tumors and BMI >35 were initially precluded from robot. This changed early in the study and the restriction on BMI was relaxed	**Low**	**Low**	**Low**	**Low**	**Moderate** Few outcomes given	**n/a**
Sarkaria 2019[28]	**Low**	**Moderate** Receipt of RAMIE depended on which surgeon the patient was referred to	**Low**	**Low**	**Low**	**Moderate** Subjective data collected by research staff. Used validated tools/ questionnaires	**Low**	**n/a**
Tagkalos 2019[23]	**Low**	**Moderate** Unknown how intervention offered; propensity matched for pre-op factors	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**
Washington 2019[29]	**Serious** Very few patient characteristics listed	**Moderate** Receipt of RAMIE was dependent on robot availability and other factors. Transition was made to all robot, so it hints that most patients toward the end of the study were all offered RAMIE. No propensity matching.	**Low**	**Low**	**Low**	**Low**	**Serious** Missing some outcomes compared to similar studies	**n/a**

Author, year	Confounding	Selection bias	Bias in measurement classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Other source of bias
Yang 2019[24]	**Low**	**Low** Some patients were randomized as part of an ongoing trial, and others were given the choice and selected on their own will. Authors state there was no intended selection bias toward one option versus the other. Patients were also propensity matched.	**Low**	**Low**	**Short-term outcomes: Low** **Long-term outcomes: Serious** Relatively short follow-up time; authors point out that their follow up time was adequate for time to recurrence as opposed to overall survival analysis	**Low**	**Low**	**n/a**
Yun 2019[25]	**Low**	**Moderate** Patients were able to decide between open or robot, but bulky tumors or large metastatic lymph nodes were contraindications to RAMIE; cohorts were adjusted with propensity score inverse probabilities	**Low**	**Low**	**Short-term outcomes: Low** **Long-term outcomes: Serious** Large loss to follow up, particularly in the robot arm	**Low**	**Low**	**n/a**
Zhang 2019[26]	**Moderate** Even after PSM, TNM stage is worse for Robot cohort, but not significant	**Moderate** Patients were able to decide between open or robot, but between 2014 and 2015 – part of the enrollment period – RAMIE was not performed; propensity matching performed	**Low**	**Low**	**Low**	**Low**	**Low**	**n/a**

APPENDIX G. EVIDENCE TABLES

Patient Characteristics and Intra-operative Outcomes

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	Robot (RAMIE)	Other minimally invasive approach (VAMIE)	Open	Robot (RAMIE)	Other minimally invasive approach (VAMIE)
Chao 2018[16] N Retrospective Y Single institution N N	McKeown (transthoracic robot + laparoscopic) vs McKeown (VATS + laparoscopic). Stapled cervical anastomosis for both.		Matched N=34 Age: 56.76 (8.39) Male: 32 (94.1) BMI: NR ASA: NR Comorbidity index: 2.88 (1.27) Smoking: NR DM: NR Albumin: NR Tumor location: Upper: 10 (29.4) Mid: 15 (44.1) Lower: 9 (26.5) Stage: I/II: 16 (47.1) III: 18 (52.9) Neoadjuvant treatment: 17 (50) Squamous: 34 (100)	Matched N=34 Age: 53.47 (8.69) Male: 33 (97.1) BMI: NR ASA: NR Comorbidity index: 2.88 (1.27) Smoking: NR DM: NR Albumin: NR Tumor location: Upper: 10 (29.4 Mid: 19 (55.9) Lower: 5 (14.7) Stage: I/II: 16 (47.1) III: 18 (52.9) Neoadjuvant treatment: 17 (50) Squamous: 34 (100)		Matched Thoracic OR time: 231.15 (42.84) EBL: 92.06 (99) Transfusions: 3 (8.8) Conversions: 0 (0) LN harvest: 37.18 (18.25) Margins: R0: 34 (100)	Matched Thoracic OR time: 200.15 (103.48) EBL: 102.65 (96.67) Transfusions: 2 (5.9) Conversions: 0 (0) LN harvest: 36.24 (12.95) Margins: R): 33 (97.1)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
Chen 2019[17] N Retrospective Y Single institution/ 1 surgical team N N **COST**	Robotic McKeown vs MIE (laparoscopy & VATS) McKeown		Matched N: 54 Age: 61.8 (9.4) Male: 41 (75.9) BMI: 22.7 (2.9) ASA: NR Comorbidity index: NR Smoking: 25 (46.3) DM: 1 (1.9) Albumin: NR cT stage: 1: 14 (25.9) 2: 7 (13) 3: 33 (61.1) 4a: 0 cN stage: 0: 30 (55.6) 1: 11 (20.4) 2: 11 (20.4) 3: 2 (3.7) Neoadjuvant chemoradiation: 14 (25.9) Squamous cell carcinoma: 54 (100)	Matched N: 54 Age: 61.8 (8.3) Male: 43 (79.6) BMI: 23 (2.7) ASA: NR Comorbidity index: NR Smoking: 27 (50) DM: 1 (1.9) Albumin: NR cT stage: 1: 15 (27.8) 2: 7 (13) 3: 31 (57.4) 4a: 1 (1.9) cN stage: 0: 22 (40.7) 1: 14 (25.9) 2: 16 (29.6) 3: 2 (3.7) Neoadjuvant chemoradiation: 17 (31.5) Squamous cell carcinoma: 54 (100)		Matched OR time: 187.2 (34) EBL: 118.9 (77.4) Conversion: NR LN harvest: 25.4 (7.5) Negative margins: 54 (100)	Matched OR time: 193.4 (27.1) EBL: 116.5 (85.9) Conversion: NR LN harvest: 24.7 (11.2) Negative margins: 54 (100)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
Deng 2018[18] N Retrospective (prospective inclusion) Y Single institution/2 surgeons N N	Robot McKeown (abd and thoracic portions) vs thoraco-laparoscopic McKeown		Matched N: 52 Age: 61 (7.2) Male: 40 (76.9) Height: 163.4 (6.8) Weight: 58.7 (8) ASA: NR Major comorbidity: 12 (23.1) Smoking: NR DM: 3 (5.8) Albumin: NR Tumor location: Upper: 10 (19.2) Mid: 33 (63.5) Lower: 9 (17.3) Esophagogastric: 0 Clinical Stage: I: 12 (23.1) II: 36 (69.2) III: 4 (7.7) Squamous: 52 (100)	Matched N: 52 Age: 60.9 (9.2) Male: 39 (75) Height: 163.5 (5.5) Weight: 59.9 (8.5) ASA: NR Major comorbidity: 14 (26.9) Smoking: NR DM: 2 (3.8) Albumin: NR Tumor location: Upper: 7 (13.5) Mid: 30 (57.7) Lower: 14 (26.9) Esophagogastric: 1 (1.9) Clinical Stage: I: 9 (17.3) II: 35 (67.3) III: 8 (15.4) Squamous: 52 (100)		Matched OR time: 353 (71.8) Thoracic time: 130.6 (28.7) Abdominal time: 94.5 (21.6) EBL: 96.3 (53.4) LN harvest: 21.5 (8.4) Mediastinal LN harvest: 11.8 (5.1) Abdominal LN harvest: 9.7 (6.4) R RLN LN harvest: 2.4 (1.9) L RLN LN harvest: 1 (1.8)	Matched OR time: 274.2 (51.7) Thoracic time: 121.7 (24.6) Abdominal time: 87.5 (20.9) EBL: 127.5 (127.8) LN harvest: 17.3 (6.5) Mediastinal LN harvest: 10.1 (4.3) Abdominal LN harvest: 7.3 (5.1) R RLN LN harvest: 1.9 (2.2) L RLN LN harvest: 0.4 (0.8)
Espinoza-Mercado 2019[19] Y (NCDB 2010-2015)	Robot-assisted vs minimally invasive vs open	Unmatched N: 3,542 Age (med, IQR): 63 (56-69)	Unmatched N: 433 Age (med, IQR): 64 (57-70)	Unmatched N: 1,578 Age (med, IQR): 63 (57-69)	Margin: R0: 3,318 (94) LN harvest	Margin: R0: 408 (94.9) LN harvest	Margin: R0: 1,474 (94.1) LN harvest

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
Retrospective Y 1,500+ Y N		Male: 2,995 (84.6) White: 3,308 (93.4) CCI zero: 2,434 (68.7) CCI 1: 892 (25.2) CCI ≥2: 216 (6.1) Tumor location: Mid: 422 (11.9) Lower: 3,120 (88.1) cT Stage: T1: 719 (20.5) T2: 761 (21.7) T3: 1,895 (54.1) cN stage: N0: 1,785 (50.8) N1: 1,329 (37.8) N2: 33 (9.5) Grade: Well-differentiated: 222 (7.1) Moderately-differentiated:	Male: 371 (85.7) White: 398 (91.9) CCI zero: 311 (71.8) CCI 1: 95 (21.9) CCI ≥2: 24 (5.9) Tumor location: Mid: 53 (12.2) Lower: 380 (87.8) cT Stage: T1: 72 (16.7) T2: 79 (18.4) T3: 263 (61.2) cN stage: N0: 214 (49.4) N1: 171 (39.5) N2: 40 (9.2) Grade: Well-differentiated: 38 (9.7) Moderately-differentiated: 175 (44.6) Poorly-differentiated: 179 (45.7) pT stage: T1: 156 (37.9)	Male: 1,348 (85.4) White: 1,490 (94.4) CCI zero: 1,088 (68.9) CCI 1: 384 (24.3) CCI ≥2: 106 (6.8) Tumor location: Mid: 184 (11.7) Lower: 1,394 (88.3) cT Stage: T1: 346 (22.1) T2: 341 (21.8) T3: 826 (52.8) cN stage: N0: 821 (52.3) N1: 591 (37.6) N2: 133 (8.5) Grade: Well-differentiated: 145 (10.3) Moderately-differentiated: 593 (41.9) Poorly-differentiated: 676 (47.8) pT stage: T1: 569 (38.7) T2: 279 (19)	(med, IQR): 13 (8-20)	(med, IQR): 17 (11-24)	(med, IQR): 15 (9-22)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
		1,374 (43.9) Poorly-differentiated: 1,532 (49) pT stage: T1: 1,113 (35.8) T2: 633 (19.2) T3: 1,264 (40.6) pN stage: N0: 2,186 (64.4) N1: 734 (21.6) N2: 326 (9.6) p Stage: 0: 252 (7.1) 1: 1,140 (32.2) 2: 1,153 (32.6) 3: 997 (28.1) Neoadjuvant chemoradiation: 2,230 (63.6) Neoadjuvant chemotherapy: 215 (6.1) Adenocarcinoma: 3,022 (85.3) SCC: 520 (14.7)	T2: 83 (20.1) T3: 136 (33) pN stage: N0: 275 (64.9) N1: 99 (23.3) N2: 33 (7.8) p Stage: 0: 40 (10.1) 1: 143 (35.9) 2: 137 (34.4) 3: 78 (19.6) Neoadjuvant chemoradiation: 290 (67.1) Neoadjuvant chemotherapy: 21 (4.9) Adenocarcinoma: 363 (83.8) SCC: 70 (16.2)	T3: 511 (34.8) pN stage: N0: 987 (65.1) N1: 307 (20.3) N2: 163 (10.9) p Stage: 0: 123 (8.6) 1: 514 (36.1) 2: 475 (33.4) 3: 310 (21.8) Neoadjuvant chemoradiation: 981 (62.6) Neoadjuvant chemotherapy: 89 (5.7) Adenocarcinoma: 3,022 (85.3) SCC: 520 (14.7)			

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
Matched data for Espinoza-Mercado 2019[19]		Matched N: 406 Age (med, IQR): 64 (56-68) Male: 354 (87.2) White: 382 (94.1) CCI zero: 280 (69) Tumor location: Lower: 346 (85.2) Clinical Stage: 0: 4 (1) I: 113 (27.8) II: 120 (29.6) III: 169 (41.6) cT Stage: Tis: 4 (1) T1: 93 (22.9) T2: 87 (21.4) T3: 211 (52) T4: 8 (2) cN stage: N0: 201 (51) N1: 143 (35.2) N2: 47 (11.6)	Matched N: 406 Age: 64 (57-70) White: 374 (92.1) Male: 349 (86) CCI zero: 296 (72.9) Tumor location: Lower: 357 (87.9) Clinical Stage: 0: 6 (1.5) I: 89 (21.9) II: 138 (34) III: 173 (42.6) cT Stage: Tis: 5 (1.2) T1: 66 (16.3) T2: 74 (18.2) T3: 248 (61.1) T4: 10 (2.5) cN stage: N0: 207 (49.5) N1: 160 (39.4) N2: 38 (9.4) N3: 7 (1.7) Grade: Poorly-differentiated:	MIE vs RAMIE matched patient/pre-op characteristics not reported. The outcomes for matched are shown, however.	OR time: NR EBL: NR Conversion: NR Margin: R0: 374 (92.1) LN harvest(med, IQR): 13 (7-21)	OR time: NR EBL: NR Conversion: NR Margin: R0: 383 (95) LN harvest(med, IQR): 17 (11-24)	OR time: NR EBL: NR Conversion: NR Margin: R0: 388 (96.3) LN harvest(med, IQR): 16 (10-22)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
		N3: 6 (1.5) Grade: Poorly-differentiated: 173 (42.6) Neoadjuvant chemoradiation: 252 (62.1) Neoadjuvant chemotherapy: 18 (4.4) Adenocarcinoma : 341 (84)	172 (42.4) Neoadjuvant chemoradiation: 276 (68) Neoadjuvant chemotherapy: 17 (4.2) Adenocarcinoma: 344 (84.7)				
Gong 2020[34] N Retrospective N Single institution/ 4 surgeons (only 2 surgeons performed robot) N N	Open vs total robotic vs thoraco-laparoscopic McKeown	N: 77 Age: 59.77 Race: NR Male: 74 (96.1) BMI: NR CCI: 0: 5 (6.5) 1: 28 (36.4) 2: 33 (42.9) 3: 11 (14.3) 4: 0 Smoking: NR DM: NR	N: 91 Age: 60.04 Race: NR Male: 78 (85.71) BMI: NR CCI: 0: 8 (8.79) 1: 25 (27.47) 2: 40 (44) 3: 14 (15.38) 4: 4 (4.4) Smoking: NR DM: NR	N: 144 Age: 60.22 Race: NR Male: 130 (90.28) BMI: NR CCI: 0: 10 (6.94) 1: 44 (30.56) 2: 64 (4.44) 3: 22 (15.28) 4: 4 (2.78) Smoking: NR DM: NR	OR time: 299.38 (57.98) EBL: 289.61 (355) Total LN harvest: 24.09 (10.77) Cervical LN: 1.25 (4.3) Upper mediastinum LN: 4.33 (3.61) Middle	OR time: 318.02 (53.9) EBL: 215.49 (125.4) Total LN harvest: 22.84 (8.37) Cervical LN: 0.29 (1.99) Upper mediastinum LN: 6.22 (4.1) Middle	OR time: 321.13 (57.21) EBL: 200.49 (59.54) Total LN harvest: 23.07 (10.18) Cervical LN: 0.42 (1.7) Upper mediastinum LN: 5.63 (3.88) Middle mediastinum LN:

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
		Albumin: NR Tumor location: Upper: 8 (10.39) Mid: 37 (48.05) Lower: 32 (41.56) Clinical Stage: I: 2 (2.6) II: 21 (27.27) III: 47 (61.04) IVA: 7 (9.09) Neoadjuvant therapy: 40 (51.95) Squamous cell carcinoma: 74 (96.1) Adenocarcinoma: NR	Albumin: NR Tumor location: Upper: 7 (7.69) Mid: 31 (34.07) Lower: 53 (58.24) Clinical Stage: I: 15 (16.48) II: 38 (41.76) III: 34 (37.36) IVA: 4 (4.4) Neoadjuvant therapy: 20 (21.98) Squamous cell carcinoma: 86 (94.51) Adenocarcinoma: NR	Albumin: NR Tumor location: Upper: 4 (2.78) Mid: 72 (50) Lower: 68 (47.22) Clinical Stage: I: 20 (13.89) II: 59 (40.97) III: 47 (32.64) IVA: 18 (12.5) Neoadjuvant therapy: 28 (19.44) Squamous cell carcinoma: 134 (93.06) Adenocarcinoma: NR	mediastinum LN: 7.81 (4.89) Lower mediastinum: 1.77 (2.32) Abdominal LN: 8.94 (5.55) Right RLN LN: 2.14 (1.95) Left RLN LN: 29 (37.66) Margins positive: R0 resection: 75 (97.4)	mediastinum LN: 6.34 (3.74) Lower mediastinum: 1.9 (1.87) Abdominal LN: 8.13 (5.53) Right RLN LN: 2.74 (2.03) Left RLN LN: 2.35 (3.0) Margins positive: R0 resection: 91 (100)	7.2 (4.69) Lower mediastinum: 1.74 (2.18) Abdominal LN: 8.1 (4.77) Right RLN LN: 2.57 (2.08) Left RLN LN: 1.95 (2.67) Margins positive: R0 resection: 144 (100)
He 2018[20] N Retrospective Y Single institution	McKeown RAMIE (abdominal and thoracic portions) vs VAMIE (MIE for thoracic and		N: 27 Age: 61 (8) Male: 20 (74.1) BMI: 21.5 (2.7) FEVI%: 94.6 (13.8) CCI: 1: 1 (3.7)	N: 27 Age: 61.6 (9.8) Male: 20 (74.1) BMI: 21.9 (2.8) FEVI%: 92.9 (23) CCI: 1: 4 (14.8)		OR time: 349 (45) EBL: 119 (72) Lymph node harvest: 20 (7)	OR time: 285 (66) EBL: 158 (82) Lymph node harvest: 19 (5)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
N N	abdominal portions)		2: 10 (37) 3: 13 (48.1) 4: 3 (11.1) Tumor location: Upper: 1 (3.7) Mid: 18 (66.6) Lower: 8 (29.6) pT stage: T1: 4 (14.8) T2: 13 (48.1) T3: 10 (37) pN stage: N0: 13 (48.1) N1: 10 (37) N2: 3 (11.1) N3: 1 (3.7) Tumor grade: Well-differentiated: 2 (7.4) Moderately differentiated: 19 (70.4) Poorly differentiated: 6 (22.2) Squamous: 23 (85.2)	2: 8 (29.6) 3: 11 (40.7) 4: 4 (14.8) Tumor location: Upper: 3 (11.1) Mid: 15 (55.6) Lower: 9 (33.3) pT stage: T1: 1 (3.7) T2: 13 (48.1) T3: 13 (48.1) pN stage: N0: 18 (66.6) N1: 8 (29.6) N2: 1 (3.7) N3: 0 Tumor grade: Well-differentiated: 6 (22.2) Moderately differentiated: 17 (63) Poorly differentiated: 4 (14.8) Squamous: 25 (92.6)			
He 2020[15] N	Robot-assisted esophagectomy		N: 94 Age: 61.3 (8.2)	N: 98 Age: 62.4 (9.1)		Operating time: Thoracic	Operating time: Thoracic portion:

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
RCT N Single institution/ NR surgeons N N	and thoraco-laparoscopic esophagectomy		Race: NR Male: 72% BMI: 22.7 ASA: 1: 6 (6.4) 2: 82 (87.2) 3: 6 (6.4) Smoking: NR DM: 12 (12.8) Tumor location: intrathoracic Upper: 9 (9.6) Mid: 64 (68.1) Lower: 21 (22.3) Stage: 0-I: 51 (54) II: 29 (30.9) III: 14 (14.9) Neoadjuvant: NR Squamous: 94 (100) Adenocarcinoma: 0	Race: NR Male: 72% BMI: NR ASA: 22.8 1: 9 (9.2) 2: 80 (81.6) 3: 9 (9.2) Smoking: NR DM: 14 (14.3) Tumor location: intrathoracic Upper: 7 (7.1) Mid: 68 (69.4) Lower: 23 (23.5) Stage: 0-I: 49 (50.0) II: 34 (34.7) III: 15 (15.3) Neoadjuvant: NR Squamous: 98 (100) Adenocarcinoma: 0		portion: NR Abd + cervical: NR Total: 304.2 (82.5) Thoracic EBL: NS Total EBL: 202.5 (73.4) Transfusions: NR Conversions total: 1 Thoracic conversion (to lap transhiatal): NR Complications: NR LN harvest: 22.2 (12.5) Margins positive: R0: 88 (95.7)	NR Abd + cervical: NR Total: 315.5 (35.7) Thoracic EBL: NS Total EBL: 216.8 (44.6) Transfusions: NR Conversion total: 1 Thoracic conversion (to lap transhiatal): NR Complications: NR LN harvest: 20.1 (8.3) Margins positive: R0: 93 (96.9)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
Jeong 2016[21] N Retrospective Y Single institution N N	Robot: 3-hole or 3-field (laparotomy; only thoracic portion is robotic) Open: Ivor-Lewis, 3-hole, or 3-field	N: 159 Age >65 years: 50 (31%) Male: 149 (94) BMI: 22.7 (2.9) ASA >2: 1 (0.6) Smoking: 138 (87) DM: 18 (11) Albumin, med/IQR: 4.3 (4.1-4.5) Tumor location: NR Clinical stage: I: 101 (64) II: 46 (29) III: 10 (6) IV: 2 (1)	N: 88 Age >65 years: 25 (28%) Male: 80 (91) BMI: 22.6 (2.5) ASA >2: 2 (2) Smoking: 76 (86) DM: 9 (10) Albumin, med/IQR: 4.3 (4.2-4.6) Tumor location: NR Clinical stage: I: 59 (67) II: 23 (26) III: 5 (6) IV: 1 (1)		OR time (hours, median/IQR): 4.4 (3.8-5.1) EBL (med/IQR): 200 (150-300) Intraop transfusion: 4 (2.5) Intraop afib: 9 (6)	OR time (hours, median/IQR): 4.8 (3.9-5.6) EBL (med/IQR): 200 (100-250) Intraop transfusion: 0 Intraop afib: 7 (8)	
Meredith 2019[27] N Retrospective (prospectively maintained database) N	Six approaches compared. The only robotic approach is Ivor-Lewis. Comparable methods using	N: 475 Age: 64 (11) Male: 412 (86.7) BMI: 28 (6) ASA: I: 2 (0.5) II: 207 (54)	N: 144 Age: 66 (10) Male: 113 (78.5) BMI: 28 (9) ASA: I: 0 II: 50 (35.2)	N: 95 Age: 62 (9) Male: 81 (85.3) BMI: 27 (5) ASA: I: 1 (1.1) II: 53 (60.9)	OR time (min; mean/SD): 286 (69) EBL: 289 (354) Complications: 7 (1.5) LN harvest: 10	OR time (min; mean/SD): 409 (104) EBL: 156 (107) Complications: 2 (1.4) LN harvest: 20	OR time (min; mean/SD): 299 (87) EBL: 189 (188) Complications: 2 (2.1) LN harvest: 14

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
Unknown Y N	other approaches in this study are open Ivor-Lewis and MIE transthoracic.	III: 172 (44.9) IV: 2 (0.5) CCI: NR Smoking: NR DM: NR Albumin: NR Tumor location: NR Clinical Stage: I: 47 (12.6) II: 142 (38.2) III: 162 (43.5) IV: 13 (3.5) Neoadjuvant therapy: 274 (57.7)	III: 90 (63.4) IV: 2 (1.4) CCI: NR Smoking: NR DM: NR Albumin: NR Tumor location: NR Clinical Stage: I: 32 (23.5) II: 46 (33.8) III: 56 (41.2) IV: 1 (0.7) Neoadjuvant therapy: 112 (77.8)	III: 33 (37.9) IV: 0 CCI: NR Smoking: NR DM: NR Albumin: NR Tumor location: NR Clinical Stage: I: 12 (14.3) II: 24 (28.6) III: 42 (50) IV: 5 (6) Neoadjuvant therapy: 73 (76.8)	(6) Margins: R1: 18 (3.8) R2: 7 (1.5)	(9) Margins: R1: 0 R2: 0	(7) Margins: R1: 6 (6.5) R2: 0
Motoyama 2019[30] N Retrospective N Single institution N N	Robot: transthoracic (unclear how abdominal portion was performed) MIE: transthoracic (unclear how		N: 21 Age (med/range): 63 (44-76) Male: 19 (90) BMI: NR ASA: NR CCI: NR Smoking: NR DM: NR Albumin: NR	N: 38 Age (med/range): 66 (49-75) Male: 32 (84) BMI: NR ASA: NR CCI: NR Smoking: NR DM: NR Albumin: NR		OR time (min; med/range): 634 (529-699) OR time thoracic: 320 (242-401) EBL (med/range): 492 (195-1591) EBL thoracic:	OR time (min; med/range): 598.5 (475-761) OR time thoracic: 312.5 (152-417) EBL (med/range): 385 (177-3184) EBL thoracic:

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
	abdominal portion was performed)		Tumor location: Upper: 6 (29) Mid: 7 (33) Lower: 8 (38) Clinical T stage: T1b: 5 (24) T2: 5 (24) T3: 11 (52) Clinical N stage: N0: 8 (38) N1: 10 (48) N2: 3 (14) Clinical stage: IA: 4 (19) IB: 3 (14) IIA: 1 (5) IIB: 3 (14) IIIA: 7 (33) IIIB: 3 (14) Neoadjuvant Chemoradiation: 12 (57) Neoadjuvant chemo only: 0 Squamous cell carcinoma: 21 (100)	Tumor location: Upper: 9 (24) Mid: 16 (42) Lower: 13 (34) Clinical T stage: T1b: 16 (42) T2: 2 (5) T3: 20 (53) Clinical N stage: N0: 19 (50) N1: 13 (34) N2: 6 (15) Clinical stage: IA: 14 (37) IB: 2 (5) IIA: 3 (8) IIB: 2 (5) IIIA: 11 (29) IIIB: 6 (16) Neoadjuvant Chemoradiation: 19 (50) Neoadjuvant chemo only: 1 (3) Squamous cell carcinoma: 38 (100)		110 (15-375) LN harvest: 52 (36-104) LN harvest mediastinal: 23 (11-41)	165 (23-559) LN harvest: 59 (35-97) LN harvest mediastinal: 20 (7-68)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
Naffouje 2019[22] Y (NSQIP 2016-2017) Retrospective Y Many Y N	Open vs MIE (robot and all other MIE) Ivor-Lewis Secondary analysis compared laparoscopic vs robotic (2:1 propensity match)		Matched N: 41 Age: 62.76 (9.98) White: 39 (95.1) Black: 1 (2.4) Other race: 1 (2.4) Male: 36 (87.8) BMI: 27.8 (6.19) ASA: I: 0 II: 5 (12.2) III: 35 (85.4) IV: 1 (2.4) Smoking: 12 (29.3) DM: 6 (14.6) Albumin: 3.83 (0.61) cT stage: T1: 13 (31.7) T2: 12 (29.3) T3: 16 (39) T4: 0 Tx: 0 cN stage: 0: 28 (68.3) 1: 8 (19.5) 2: 4 (9.8)	Matched N: 82 Age: 63.27 (9.28) White: 75 (91.5) Black: 3 (3.7) Other race: 4 (4.8) Male: 72 (87.8) BMI: 27.98 (5.6) ASA: I: 0 II: 11 (13.4) III: 68 (82.9) IV: 3 (3.7) Smoking: 21 (25.6)) DM: 17 (20.7) Albumin: 3.86 (0.38) cT stage: T1: 32 (39) T2: 17 (20.7) T3: 31 (37.8) T4: 0 Tx: 2 (2.4) cN stage: 0: 52 (63.4) 1: 13 (15.9) 2: 14 (17.1)		OR time: 449 (116) Conversion to open: 1 (2.4) Negative margins: 35 (85.4)	OR time: 445 (96) Conversion to open: 7 (8.5) Negative margins: 74 (90.2)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
			3: 1 (2.4) Nx: 0 Neoadjuvant chemo: 30 (73.2) Neoadjuvant radiation: 30 (73.2) Adenocarcinoma: 37 (90.2) SCC: 4 (9.8) Other malignancy: 0	3: 0 Nx: 3 (3.7) Neoadjuvant chemo: 62 (75.6) Neoadjuvant radiation: 56 (68.3) Adenocarcinoma: 76 (92.7) SCC: 5 (6.1) Other malignancy: 1 (1.2)			
Osaka 2018[32] N Retrospective N Single institution N N	Robot (thoracic) with unknown method for abdomen vs thoracotomy and unknown for abdomen	N: 30 Age (med, range): 63 (46-77) Male: 27 (90) BMI: NR ASA: NR CCI: NR Smoking: NR DM: NR Albumin: NR Tumor location: Upper: 1 (3.3) Mid: 15 (50) Lower: 14 (46.7) Clinical Stage:	N: 30 Age (med, range): 62 (49-78) Male: 27 (90) BMI: NR ASA: NR CCI: NR Smoking: NR DM: NR Albumin: NR Tumor location: Upper: 1 (3.3) Mid: 15 (50) Lower: 14 (46.7) Clinical Stage: I: 14 (46.7)		OR time, minutes (med, range): 398 (329-498) EBL total (med, range): 388 (125-990) EBL thoracic (med, range): 135 (44-325) LN harvest (med, range): 23 (12-39)	OR time, minutes (med, range): 563 (476-713) EBL total (med, range): 197 (10-640) EBL thoracic (med, range): 21 (0-97) LN harvest (med, range): 25 (8-58)	

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
		I: 16 (53.3) II: 13 (43.3) III: 1 (3.3) Neoadjuvant chemo: 8 (26.7) Adenocarcinoma: NR Squamous cell carcinoma: NR	II: 10 (33.3) III: 6 (20) Neoadjuvant chemo: 13 (43.3) Adenocarcinoma: NR Squamous cell carcinoma: NR				
Park 2016[48] N Retrospective N Single Institution N N	Transthoracic robot vs transthoracic VATS. In the robot cohort, 90% were McKeown and 10% were Ivor-Lewis. Abdominal portion in the robotic cohort was done robotically in 58%. In the MIE cohort, abdominal		N: 62 Age: 64.3 (8) Male: 57 (91.9) BMI: 23.5 (2.8) ASA: I: 21 (33.9) II: 37 (59.7) III: 4 (6.5) Smoking: 49 (79) Never smoker: 13 (21) DM: 9 (14.5) Albumin: NR Tumor location: Upper: 8 (12.9) Mid: 15 (24.2) Lower: 39 (62.9) FEV1; pred%, SD:	N: 43 Age: 66.2 (7.4) Male: 40 (93) BMI: 23.3 (3.1) ASA: I: 11 (25.6) II: 32 (74.4) III: 0 Smoking: 35 (81.4) DM: 11 (25.6) Albumin: NR Tumor location: Upper: 7 (16.3) Mid: 9 (20.9) Lower: 27 (62.8) FEV1; pred%, SD: 106.7 (13.8)		OR time: Total: 490.3 (84) Thoracic: 185.2 (67.4) Abdominal: 305.1 (66.6) EBL: 462.9 (493.9) LN harvest: 37.3 (17.1)	OR time: Total: 458.4 (111.9) Thoracic: 120.1 (68.5) Abdominal: 338.4 (105.4) EBL: 466.8 (333) LN harvest: 28.7 (11.8)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
	portion was laparoscopic in 49%, 19% were Ivor-Lewis, and 81% were McKeown.		101.6 (17.1) Clinical stage: I: 23 (37.1) II: 28 (45.2) III: 11 (17.7) Clinical T stage: T1: 31 (50) T2: 21 (33.9) T3: 10 (16.1) Clinical N stage: N0: 42 (67.7) N+: 20 (32.3) Neoadjuvant chemoradiation: 8 (12.9) Squamous cell carcinoma: 62 (100)	Clinical stage: I: 21 (48.8) II: 15 (34.9) III: 7 (16.3) Clinical T stage: T1: 25 (58.1) T2: 13 (30.2) T3: 5 (11.6) Clinical N stage: N0: 27 (64.3) N+: 15 (35.7) Neoadjuvant chemoradiation: 4 (9.3) Squamous cell carcinoma: 43 (100)			
Rolff 2017[49] N Retrospective N Single institution N N	Open Ivor-Lewis vs Hybrid minimally invasive Ivor-Lewis (Robot in abdomen + thoracotomy)	N: 160 Age (med, range): 65 (22-88) Male: 125 (78) BMI (med, range): 26.6 (15.6-43.7) ASA:	N: 56 Age (med, range): 66 (39-86) Male: 50 (88) BMI (med, range): 25.8 (18.8-31.2) ASA: 1: 17 (30) 2: 28 (50)		OR time (med, range): 248 (100-420) EBL (med, range): 600 (100-4,400) LN harvest (med, range):	OR time (med, range): 232 (174-800) EBL (med, range): 200 (50-1,970) LN harvest (med, range):	

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
		1: 41 (26) 2: 80 (50) 3: 39 (24) 4: 0 CCI (med, range): 20.9 (0-100) Smoking: NR DM: NR Albumin: NR Tumor location: NR Stage: NR Neoadjuvant therapy: NR Adenocarcinoma: NR Squamous cell carcinoma: NR	3: 12 (21) 4: 1 (2) CCI (med, range): 12.2 (0-100) Smoking: NR DM: NR Albumin: NR Tumor location: NR Stage: NR Neoadjuvant therapy: NR Adenocarcinoma: NR Squamous cell carcinoma: NR		23 (11-60) Margins: NR	28 (15-61) Margins: NR	
Sarkaria 2019[28] N Non-randomized prospective trial N Single	Robotic Ivor-Lewis (62/64) and McKeown (2/64) vs open Ivor-Lewis (103/106) Thoracoabdomin	N: 106 Age (med, IQR): 63 (28-83) Male: 91 (85.8) BMI (med, IQR): 28.4 (16.9-49.5) ASA:	N: 64 Age (med, IQR): 61 (45-82) Male: 53 (82.8) BMI (med, IQR): 29.1 (15.6-47.8) ASA:		OR time (hours, median & range): 5.44 (3.5-10.3) EBL (med, range): 350 (100-2300)	OR time (hours, median & range): 6.4 (4.9-10.6) EBL (med, range): 250 (50-600)	

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
institution/8 surgeons (2 performed robotic) Y N	al (3/106) “All but 1 patient who underwent MIE did so via a total RAMIE approach.”	II: 15 (14.2) III: 84 (79.2) IV: 7 (6.6) # of comorbidities: 0: 31 (29.2) 1-2: 62 (58.5) >2: 13 (12.3) Smoking: NR DM: NR Albumin: NR Tumor location: GE junction: 104 (98.1) Distal: 2 (1.9) Stage: 0: 2 (1.9) I: 14 (13.2) II: 26 (24.5) III: 63 (59.4) IV: 1 (0.9) Neoadjuvant treatment: 87 (82.1) Squamous: 7 (6.6)	II: 9 (14.1) III: 51 (79.7) IV: 4 (6.3) # of comorbidities: 0: 23 (35.9) 1-2: 34 (53.1) >2: 7 (10.9) Smoking: NR DM: NR Albumin: NR Tumor location: GE junction: 60 (93.8) Distal: 4 (6.3) Stage: 0: 1 (1.6) I: 11 (17.5) II: 17 (27) III: 34 (54) IV: 0 (0) Neoadjuvant treatment: 48 (75) Squamous: 4 (6.3) Adenocarcinoma: 59 (93.7) Other pathology: 0 (0)		LN harvest (med, range): 22 (0-50) Margins positive (R1): 3 (2.8)	LN harvest (med, range): 25 (14-56) Margins positive (R1): 2 (3.1)	

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
		Adenocarcinoma: 98 (92.5) Other pathology: 1 (0.9)					
Tagkalos 2019[23] N Retrospective study of prospectively collected database Y Single institution/Single surgeon N N	Robot (thoracic and abdominal) Ivor-Lewis vs minimally invasive (VATS and laparoscopy) Ivor-Lewis		Matched: N: 40 Age: 62 BMI: 26.4 ASA: 1-2: 22 (55) 3-4: 18 (45) DM: 4 (10) Pulmonary comorbidities: 8 (20) CV comorbidities: 15 (37.5) Tumor location: Upper: 0 Mid: 8 (20) Lower: 32 (80) cT stage: 1-2: 7 (17.5) 3-4: 33 (82.5) cN stage: 0: 8 (20) 1: 32 (80)	Matched: N: 40 Age: 63 BMI: 25.6 ASA: 1-2: 19 (47.5) 3-4: 21 (52.5) DM: 5 (12.5) Pulmonary comorbidities: 6 (15) CV comorbidities: 16 (40) Tumor location: Upper: 2 (5) Mid: 6 (15) Lower: 32 (80) cT stage: 1-2: 10 (25) 3-4: 30 (75) cN stage: 0: 10 (25) 1: 30 (75) Chemoradiation: 21		Matched OR time (med, range): 388 (255-475) Abd time: 151 (80-250) Thoracic time: 223 (170-320) EBL: 339 (198) LN harvest (median, range): 27 (13-84) Negative margins: 38 (95)	Matched OR time (med, range): 321 (224-519) Abd time: 125 (66-325) Thoracic time: 201 (158-295) EBL: 343 (181) LN harvest (median, range): 23 (11-48) Negative margins: 39 (97.5)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Patient & Tumor Characteristics Preop N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			Intra-operative Outcomes OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
			Chemoradiation: 22 (55) Chemo only: 11 (27.5)	(52.5) Chemo only: 9 (22.5)			
van der Sluis 2019[14] N RCT N Single institution/2 surgeons N N	Open McKeown v Robot transthoracic with laparoscopic abdominal and open cervical portions	N: 55 Age: 65 (8.2) Male: 42 (76) BMI: 25.5 (4.7) ASA: 1: 11 (20) 2: 34 (62) 3: 10 (18) Comorbidity: 41 (75) Smoking: NR DM: NR Albumin: NR Tumor location: Upper: 0 (0) Mid: 8 (15) Lower: 29 (53) Clinical stage: IA: 4 (7) IIA: 3 (6) IIB: 18 (33) IIIA: 21 (38) IIIB: 6 (11)	N: 54 Age: 64 (8.9) Male: 46 (85) BMI: 26.1 (4.4) ASA: 1: 13 (24) 2: 37 (69) 3: 6 (11) Comorbidity: 43 (80) Smoking: NR DM: NR Albumin: NR Tumor location: Upper: 1 (2) Mid: 5 (9) Lower: 26 (48) Clinical stage: IA: 4 (7) IIA: 5 (9) IIB: 11 (20) IIIA: 13 (24) IIIB: 13 (24) IIIC: 8 (15)		Operating time: Thoracic portion: 135 (23.3) Abd + cervical: 161 (30.1) Total: 296 (33.9) Thoracic EBL: 200 (195-313) Total EBL: 568 (428-800) Complications: 9 (16.4) LN harvest: 25 (17-31) Margins positive: R1: 2 (4)	Operating time: Thoracic portion: 170 (34.6) Abd + cervical: 186 (38.7) Total: 349 (56.9) Thoracic EBL: 120 (78-200) Total EBL: 400 (258-581) Conversion total: 3 (5.6) Thoracic conversion (to lap transhiatal): 1 (1.9) Complications: 7 (13) LN harvest: 27 (17-33) Margins	

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
		IIIC: 3 (6) Neoadjuvant: 48 (87) Squamous: 12 (23) Adenocarcinoma: 43 (78)	Neoadjuvant: 48 (90) Squamous: 13 (24) Adenocarcinoma: 41 (76)			positive: R1: 2(4)	
Van Der Sluis 2018[35] N RCT N NR N N **Cost only**	Open transthoracic esophagectomy vs RAMIE						
Washington 2019[29] N Retrospective N Single institution/ Single surgeon	Robotic vs laparoscopic transhiatal esophagectomy		N: 18 Age: 61.9 (range 42-76) Male: 17 (94.4) BMI: 27.6 (range 20.7-38.2) ASA: NR CCI: NR Smoking: NR	N: 18 Age: 58.9 (range 40 to 70) Male: 16 (88.9) BMI: 27.5 (range 19.2-39.4) ASA: NR CCI: NR Smoking: NR		OR time: 168 (24) LN harvest: 14.28 (7.8) Margins positive (R1): 1 (5.6)	OR time: 164 (23.1) LN harvest: 13.9 (8.5) Margins positive (R1): 1 (5.6)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
Y N			DM: NR Albumin: NR Neoadjuvant treatment: 18 (100) cT stage: 1: 0 2: 4 (22.2) 3: 14 (77.8) cN stage: 0: 6 (33.3) 1: 12 (66.7) Squamous: 4 (22.2) Adenocarcinoma: 14 (77.8)	DM: NR Albumin: NR Neoadjuvant treatment: 15 (83.3) cT stage: 1: 3 (16.7) 2: 2 (11.1) 3: 12 (66.7) cN stage: 0: 6 (33.3) 1: 8 (44.4) Squamous: 3 (16.7) Adenocarcinoma: 15 (83.3)			
Yang 2019[24] N Retrospective Y Single institution/ Single surgeon N N	Robot McKeown (abd and thoracic portions) vs thoraco-laparoscopic McKeown		Matched N: 271 Age: 63.4 (7.1) Male: 222 (81.9) BMI: 23.2 (3) ASA: I: 4 (1.5) II: 243 (89.7) III: 24 (8.9) CCI: NR Smoking: NR DM: NR	Matched N: 271 Age: 63.5 (7.4) Male: 221 (81.5) BMI: 23.2 (2.9) ASA: I: 4 (1.5) II: 242 (89.3) III: 25 (9.2) CCI: NR Smoking: NR DM: NR		Matched OR time: 244.5 (60.4) Thoracic time: 85 (27.8) EBL: 210.7 (86.8) Thoracic conversion: 2 (0.7) Total LN harvest: 20.3	Matched OR time: 276 (59.4) Thoracic time: 102.9 (28.6) EBL: 209.6 (107.4) Thoracic conversion: 16 (5.9) Total LN harvest: 19.2 (9.6)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
			Albumin: NR Tumor location: Upper: 38 (14) Mid: 169 (62.4) Lower: 64 (23.6) Clinical stage: I: 70 (25.8) II: 97 (35.8) III: 79 (29.2) IV: 25 (9.2) Neoadjuvant therapy: 29 (10.7) Squamous cell: 271 (100)	Albumin: NR Tumor location: Upper: 31 (11.4) Mid: 171 (63.1) Lower: 69 (25.5) Clinical stage: I: 83 (30.6) II: 86 (31.7) III: 67 (24.7) IV: 35 (12.9) Neoadjuvant therapy: 28 (10.3) Squamous cell: 271 (100)		(9.9) Abdominal LN: 7.9 (4.8) Thoracic LN: 12.4 (7) RLN LN: 4.8 (3.3) Negative margins: 255 (94.1)	Abdominal LN: 6.8 (3.6) Thoracic LN: 12.4 (6.5) RLN LN: 4.1 (3) Negative margins: 254 (93.7)
Yun 2019[25] N Retrospective (prospective database) Y Single surgeon/Single institution N N	Open (Ivor-Lewis 54.4%; McKeown 45.6%) vs robot-assisted (Ivor-Lewis 57.1%; McKeown 42.9%) (abdominal portion was either robot-	Matched (Inverse probability of treatment weighting) N: 130* (table says 241, but it should be matched) Age: 63 (7.8) Male: 93% BMI: 23.4 (2.8)	Matched (Inverse probability of treatment weighting) N: 130 Age: 63 (8.6) Male: 92.6% BMI: 23.4 (3.3) ASA: NR CCI: NR Smoking: 81.9% DM: 14.4% Albumin: NR		Unadjusted OR time: 240 (48.9) EBL: 93.8 (140.9) LN harvest: 38.3 (12.9) Margins positive: 3.3% R0: 233 (96.7) R1: 7 (2.9) R2: 1 (0.4)	Unadjusted OR time: 275.6 (71.1) EBL: 110.8 (125.8) Conversion: 3 (2.3) LN harvest: 39.1 (13.8) Margins positive: 2.3% R0: 127 (97.7)	

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
	assisted or laparoscopic)	ASA: NR CCI: NR Smoking: 89.9% DM: 14.2% Albumin: NR Tumor location: Upper: 29.6% Mid: 48.3% Lower: 22.1% Clinical Stage: I: 60.6% II: 21.3% III: 18.1% Neoadjuvant treatment: 32.9% Squamous cell carcinoma: 100%	Tumor location: Upper: 27.5% Mid: 45.4% Lower: 27.1% Clinical Stage: I: 66.5% II: 18.1% III: 15.4% Neoadjuvant treatment: 25.5% Squamous cell carcinoma: 100%			R1: 3 (2.3) R2: 0	
Zhang 2019[26] N Retrospective Y Single institution/ Single surgeon N N	Robot-assisted Ivor-Lewis (abdomen and thorax robot) vs thoraco-laparoscopic Ivor-Lewis		Matched N: 66 Age: 62.3 (7.8) Male: 50 (75.8) BMI: 22.9 (3.1) ASA: 1: 30 (45.5) 2: 33 (50) 3: 3 (4.5)	Matched N: 66 Age: 62 (7.8) Male: 50 (75.8) BMI: 23.1 (4.5) ASA: 1: 26 (39.4) 2: 36 (54.5) 3: 4 (6.1)		Matched OR time: 302 (62.9) EBL: 200 (100-262.5) Conversion: 1 (1.5) LN harvest: 19.2 (9.2)	Matched OR time: 274.7 (38) EBL: 200 (150-245) Conversion: 0 LN harvest: 19.3 (9.5) Abd LN harvest:

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Patient & Tumor Characteristics Preop** N Age, mean yr (SD) Male, % Race/Ethnicity NH-White, % NH-Black, % NH-Asian, % Hispanic, % BMI, mean (SD) ASA class, mean (SD) Comorbidity index (CCI): Smoking current/former/unspecified DM Albumin Tumor Location (%) Stage Neoadjuvant therapy (%) Squamous (%) Adenocarcinoma (%)			**Intra-operative Outcomes** OR, time, min (SD) EBL, mL (SD) Transfusions (%) Conversion (%) Major Complications, N (%) Lymph node harvest, N (std dev/IQR) Margins positive (%)		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**
			Comorbidity: 28 (42.2) Smoking history: 33 (50) DM: NR Albumin: NR Tumor location: Mid: 29 (43.9) Lower: 37 (56.1) Neoadjuvant therapy: 0 Adenocarcinoma: 0 Squamous cell carcinoma: 64 (97)	Comorbidity: 32 (48.5) Smoking history: 42 (63.6) DM: NR Albumin: NR Tumor location: Mid: 26 (39.4) Lower: 40 (60.6) Neoadjuvant therapy: 0 Adenocarcinoma: 0 Squamous cell carcinoma: 65 (98.5)		Abd LN harvest: 8.9 (6.7) Thoracic LN harvest: 10.3 (5.8) R RLN LN harvest: 1.4 (1.6) L RLN LN harvest: 1.3 (1.9) Margins positive: 0	7.3 (5.9) Thoracic LN harvest: 11.9 (8.3) R RLN LN harvest: 1.6 (2.8) L RLN LN harvest: 0.9 (1.9) Margins positive: 0

Short- and Long-term Outcomes

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Short-term Outcomes** LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			**Long-term Outcomes** Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
Chao 2018[16] N Retrospective Y Single institution N N	McKeown (transthoracic robot + laparoscopic) vs McKeown (VATS + laparoscopic). Stapled cervical anastomosis for both.		Matched LOS: 16.36 (5.79) Readmissions: 5 (14.7) ICU stay (hours): 31.85 (18.22) Pneumonia: 2 (5.9) Pleural effusion: 4 (11.8) 30-day mortality: 0 (0) 90-day mortality: 0 (0) Anastomotic leak: 0 (0) Reoperations: NR RLN palsy: 7 (20.6)	Matched LOS: 17.82 (5.76) Readmissions: 4 (11.8) ICU stay (hours): 35.62 (47.33) Pneumonia: 6 (17.6) Pleural effusion: 6 (17.6) 30-day mortality: 0 (0) 90-day mortality: 1 (2.9) Anastomotic leak: 2 (5.9) Reoperations: NR RLN palsy: 10 (29.4)		NR	NR
Chen 2019[17] N Retrospective Y Single institution/1 surgical team N N **COST**	Robotic McKeown vs MIE (laparoscopy & VATS) McKeown		Matched LOS: 17.1 (10.1) Readmissions: NR ICU stay: 4 (6.3) Pneumonia: 8 (14.8) Chylothorax: 1 (1.9) MACE: 2 (3.7) Anastomotic leak: 5 (9.3) Hoarseness/RLN palsy: 7 (13) Mortality: 0	Matched LOS: 15.2 (9.8) Readmissions: NR ICU stay: 2.5 (3.7) Pneumonia: 13 (24.1) Chylothorax: 2 (3.7) MACE: 0 Anastomotic leak: 2 (3.7) Hoarseness/RLN palsy: 17 (31.5) Mortality: 0		NR	NR

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Short-term Outcomes** LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			**Long-term Outcomes** Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
			Total expense: $25,300 (9,000) Expenses/day: $1,700 (700)	Total expense: $20,800 (9,000) Expenses/day: $1,500 (400)			
Deng 2018[18] N Retrospective (prospective inclusion) Y Single institution/2 surgeons N N	Robot McKeown (abd and thoracic portions) vs thoraco-laparoscopic McKeown		Matched LOS: 14.3 (6.9) Total major complications: 15 (28.8) Grade 1-2 complications: 9 (17.3) Grade 3+ complications: 6 (11.5) Pneumonia: 5 (9.6) Chylothorax: 0 Anastomotic leak: 3 (5.8) RLN palsy: 7 (13.5) In-hospital mortality: 1 (1.9) 90-day mortality: 2 (3.8)	Matched LOS: 12.7 (7.7) Total major complications: 12 (23.1) Grade 1-2 complications: 6 (11.5) Grade 3+ complications: 6 (11.5) Pneumonia: 4 (7.7) Chylothorax: 1 (1.9) Anastomotic leak: 2 (3.8) RLN palsy: 4 (7.7) In-hospital mortality: 2 (3.8) 90-day mortality: 2 (3.8)		NR	NR
Espinoza-Mercado 2019[19] Y (NCDB 2010-2015) Retrospective Y	Robot-assisted vs minimally invasive vs open	Readmission: 239 (6.9) LOS (med, IQR): 10 (8-15) 30-day mortality: 130 (3.7)	Readmission: 26 (6.1) LOS (med, IQR): 9 (7-14) 30-day mortality: 18 (4.2)	Readmission: 96 (6.2) LOS (med, IQR): 9 (8-14) 30-day mortality: 50 (3.2) 90-day mortality: 114 (7.3)	Overall survival (med, months; 95% CI): 43.6 (40-46)	Overall survival (med, months; 95% CI): 58.8 (47-69)	Overall survival (med, months; 95% CI): 47.5 (42-52)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Short-term Outcomes** LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			**Long-term Outcomes** Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
1,500+ Y N		90-day mortality: 259 (7.4)	90-day mortality: 35 (8.2)				
Matched data for Espinoza-Mercado 2019[19]		LOS (med, IQR): 10 (8-16) Readmission: 25 (6.2) ICU stay: NR Complications: NR 30-day mortality: 20 (4.9) 90-day mortality: 32 (7.9)	LOS (med, IQR): 9 (7-14) Readmission: 24 (6.1) ICU stay: NR Complications: NR 30-day mortality: 16 (3.9) 90-day mortality: 31 (7.6)	LOS (med, IQR): 9 (8-15) Readmission: 20 (4.9) ICU stay: NR Complications: NR 30-day mortality: 13 (3.2) 90-day mortality: 25 (6.2)	Overall survival (med, months; 95% CI): 53.9 (42-85)	Overall survival (med, months; 95% CI): 58.8 (48-69)	Overall survival (med, months; 95% CI): 45.9 (33-58)
Gong 2020[34] N Retrospective N Single institution/4 surgeons (only 2 performed robot) N N	Open vs total robotic vs thoraco-laparoscopic McKeown	LOS: 16.66 (9.3) Reoperations: NR ICU stay: NR Total complications: 26 (33.77) Pneumonia: 10 (12.99) Atrial fibrillation: 10 (12.99) Anastomotic leak: 2 (2.6) Chylothorax: 3 (3.9) Bleeding: 0 RLN palsy: 12 (15.58) Wound infection: 2	LOS: 16.57 (8.0) Reoperations: NR ICU stay: NR Total complications: 33 (36.26) Pneumonia: 9 (9.89) Atrial fibrillation: 13 (14.29) Anastomotic leak: 4 (4.4) Chylothorax: 1 (1.1) Bleeding: 0 RLN palsy: 20 (21.98) Wound infection: 1 (1.67) ICU readmission: 6 (6.59)	LOS: 18.73 (13.29) Reoperations: NR ICU stay: NR Total complications: 49 (34.03) Pneumonia: 15 (10.42) Atrial fibrillation: 21 (14.58) Anastomotic leak: 10 (6.94) Chylothorax: 1 (0.7) Bleeding: 1 (0.7) RLN palsy: 34 (23.61) Wound infection: 0 ICU readmission: 12 (8.33)	NR	NR	NR

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	**Short-term Outcomes** LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			**Long-term Outcomes** Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
		(2.6) ICU readmission: 7 (9.09) Reoperations: NR Mortality (90-day): 2 (2.6)	Reoperations: NR Mortality (90-day): 0	Reoperations: NR Mortality (90-day): 0			
He 2018[20] N Retrospective Y Single institution N N	McKeown RAMIE (abdominal and thoracic portions) vs VAMIE (MIE for thoracic and abdominal portions)		LOS: 13.8 (2) Overall complication rate: 10 (37) Pulmonary complications: 5 (18.5) Chylothorax: 0 Arrhythmia: 1 (3.7) Anastomotic leak: 3 (11.1) Bleeding: 1 (3.7) RLN palsy: 4 (14.8) 90-day mortality: 0	LOS: 12.8 (2.7) Overall complication rate: 9 (33.3) Pulmonary complications: 2 (7.4) Chylothorax: 1 (3.7) Arrhythmia: 0 Anastomotic leak: 1 (3.7) Bleeding: 1 (3.7) RLN palsy: 3 (11.1) 90-day mortality: 1 (3.7)		NR	NR
He 2020[15] N RCT N Single institution/ NR surgeons N N	Robot-assisted esophagectomy and thoraco-laparoscopic esophagectomy		LOS (median): 12 (5-78 range) Readmissions: NR ICU stay: 1.5 (1-24) Pulmonary complications: 18 Chylothorax: 2 MACE: NR Mortality: 2 Anastomotic leak: 7 All complications: 30 (32.6)	LOS (median): 13 (8-125) range Readmissions: NR ICU stay: 1.5 (1-20) Pulmonary complications: 24 Chylothorax: 2 MACE: NR Mortality: 1 Anastomotic leak: 9 All complications: 38 (39.6)		Overall survival: NR Recurrence: 14 Recurrence free: 1-yr: 92.4 3-yr: 87.3 followup time: 15 (9-42)	Overall survival: NR Recurrence: 25 Recurrence free: 1-yr: 81.7 3 -r: 67.9 followup time: 9 (3-42)

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Short-term Outcomes LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			Long-term Outcomes Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
			Complications: Grade ≥2 directly related to surgery: NR Grade >2 overall: NR Reoperations: NR RLN palsy: 6	Complications: Grade ≥2 directly related to surgery: NR Grade ≥2 overall: NR Reoperations: NR RLN palsy: 9			
Jeong 2016[21] N Retrospective Y Single institution N N	Robot: 3-hole or 3-field (laparotomy; only thoracic portion is robotic) Open: Ivor-Lewis, 3-hole, or 3-field	LOS (med/IQR): 13 (12-16) ICU stay (hours; med/IQR): 1.9 (1.8-2) Complications (at least 1): 56 (35) Pneumonia: 11 (7) Anastomotic leak: 3 (2) Afib: 9 (6) Vocal cord palsy: 1 (0.6) Death: 1 (0.6)	LOS (med/IQR): 12 (10-15) ICU stay (hours; med/IQR): 1.8 (1.8-1.9) Complications (at least 1): 14 (16) Pneumonia: 3 (3.4) Anastomotic leak: 1 (1.1) Afib: 2 (2.3) Vocal cord palsy: 1 (1.1) Death: 1 (1.1)		NR	NR	
Meredith 2019[27] N Retrospective (prospectively maintained database) N Unknown Y N	Six approaches compared. The only robotic approach is Ivor-Lewis. Comparable methods using other approaches in this study are open Ivor-Lewis	LOS (med/range): 10 (1-115) Complication rate: 145 (30.5) Pulmonary complication: 81 (17.1) Pneumonia: 72 (15.2) PE: 9 (1.9)	LOS (med/range): 10 (4-66) Complication rate: 34 (23.6) Pulmonary complication: 14 (9.7) Pneumonia: 10 (6.9) PE: 3 (3.2) Chylothorax: 1 (0.7)	LOS (med/range): 9 (6-60) Complication rate: 28 (29.5) Pulmonary complication: 18 (18.9) Pneumonia: 8 (8.4) Chylothorax: 1 (1.1) MI: 3 (3.2)		NR	NR

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Short-term Outcomes LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			Long-term Outcomes Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
	and MIE transthoracic.	Chylothorax: 5 (1.1) MI: 6 (1.3) Arrhythmia: 55 (11.6) Anastomotic leak: 23 (4.8) Reoperation: 12 (2.5) 90-day mortality: 7 (1.5)	MI: 1 (0.7) Arrhythmia: 25 (17.4) Anastomotic leak: 4 (2.8) Reoperation: 0 90-day mortality: 2 (1.4)	Arrhythmia: 17 (17.9) Anastomotic leak: 4 (4.2) Reoperation: 2 (2.1) 90-day mortality: 2 (2.1)			
Motoyama 2019[30] N Retrospective N Single institution N N	Robot: transthoracic (unclear how abdominal portion was performed) MIE: transthoracic (unclear how abdominal portion was performed)		Chylothorax: 1 (5) Pneumonia: 0 Anastomotic leak: 1 (5) Right RLN palsy: 2 (10) Left RLN palsy: 5 (24)	Chylothorax: 1 (3) Pneumonia: 0 Anastomotic leak: 3 (8) Right RLN palsy: 12 (32) Left RLN palsy: 18 (47)		NR	NR
Naffouje 2019[22] Y (NSQIP 2016-2017) Retrospective Y Many Y N	Open vs MIE (robot and all other MIE) Ivor-Lewis Secondary analysis compared laparoscopic vs robotic (2:1 propensity match)		LOS (median, IQR): 7 (7-9.5) Readmissions: 6 (14.6) Pneumonia: 3 (7.3) PE: 1 (2.4) Transfusion: 1 (2.4) Reintubation: 4 (9.8) Superficial SSI: 0 Deep SSI: 0	LOS (median, IQR): 8 (7-12.25) Readmissions: 12 (14.6) Pneumonia: 16 (19.5) PE: 2 (2.4) Transfusion: 2 (2.4) Reintubation: 9 (11) Superficial SSI: 2 (2.4)			

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Short-term Outcomes LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			Long-term Outcomes Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
			Organ space SSI: 3 (7.3) Overall complications (patients with at least one complication): 12 (29.3) Mortality: 0 Anastomotic leak: 6 (14.6) Reoperation: 5 (12.2)	Deep SSI: 1 (1.2) Organ space SSI: 14 (17.1) Overall complications (patients with at least one complication): 28 (34.6) Mortality: 2 (2.4) Anastomotic leak: 17 (20.7) Reoperation: 15 (18.3)			
Osaka 2018[32] N Retrospective N Single institution N N	Robot (thoracic) with unknown method for abdomen vs thoracotomy and unknown for abdomen	LOS (med, range): 30 (22-35) Pulmonary complications: 3 (10) Anastomotic leak: 6 (20) SSI: 3 (10) Vocal cord palsy: 5 (16.7)	LOS (med, range): 17 (10-38) Pulmonary complications: 2 (6.7) Anastomotic leak: 3 (10) SSI: 0 Vocal cord palsy: 5 (16.7)		NR	NR	
Park 2016[31] N Retrospective N Single Institution N N	Transthoracic robot vs transthoracic VATS. In the robot cohort, 90% were McKeown and 10% were Ivor-Lewis. Abdominal portion in the robotic cohort was done		LOS: NR Readmissions: NR ICU stay: NR Respiratory complication: 9 (14.5) Anastomotic leak: 5 (8.1) RLN palsy: 8 (12.9)	LOS: NR Readmissions: NR ICU stay: NR Respiratory complication: 6 (14) Anastomotic leak: 1 (2.3) RLN palsy: 10 (23.8) Complication ≥		Median follow-up: 17 months 5-year survival: 69% 5-year freedom of locoregional recurrence: 88% 5-year freedom	Median follow-up: 26 months 5-year survival: 59% 5-year freedom of locoregional recurrence: 74% 5-year freedom of

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)	Short-term Outcomes LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			Long-term Outcomes Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
	robotically in 58%. In the MIE cohort, abdominal portion was laparoscopic in 49%, 19% were Ivor-Lewis, and 81% were McKeown.		Complication ≥ Clavien Dindo IIIa: 10 (16.1) 30-day mortality: 1 (1.6)	Clavien Dindo IIIa: 9 (20.9) 30-day mortality: 0		of distal recurrence: 72%	distal recurrence: 71%
Rolff 2017[33] N Retrospective N Single Institution N N	Open Ivor-Lewis vs Hybrid minimally invasive Ivor-Lewis (Robot in abdomen + thoracotomy)	LOS (med, range): 11.5 (8-101) Complications (Clavien-Dindo): ≥1: 122 (76) ≥2: 91 (57) ≥3: 51 (32) Pulmonary complications: 81 (51) Anastomotic leak: 11 (7) 30-day mortality: 3 (2) 90-day mortality: 5 (3)	LOS (med, range): 10 (8-69) Complications (Clavien-Dindo): ≥1: 37 (65) ≥2: 22 (39) ≥3: 14 (25) Pulmonary complications: 24 (43) Anastomotic leak: 4 (7) 30-day mortality: 0 90-day mortality: 3 (5)		NR	NR	
Sarkaria 2019[28] N Non-randomized prospective trial N Single	Robotic Ivor-Lewis (62/64) and McKeown (2/64) vs open Ivor-Lewis (103/106) Thoracoabdominal (3/106)	Readmissions: 17 (16) LOS (med, range): 11 (6-131) ICU admission: 19 (19.8) Complication (≥	Readmissions: 13 (20.4) LOS (med, range): 9 (5-17) ICU admission: 5 (7.8) Complication (≥		Functional Assessment of Cancer Therapy–Esophageal (FACT-E): no difference	Functional Assessment of Cancer Therapy–Esophageal (FACT-E): no difference	

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Short-term Outcomes** LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			**Long-term Outcomes** Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
institution/8 surgeons (2 performed robotic) Y N	"All but 1 patient who underwent MIE did so via a total RAMIE approach."	grade 3): 55 (51.9) Pulmonary complication: 36 (34) Chylothorax: 1 (0.9) MACE (afib): 2 (1.9) Infection (any): 38 (35.8) Anastomotic leak: 10 (9.4) RLN palsy: 0 (0) 30-day mortality: 2 (1.9) 90-day mortality: 4 (3.8)	grade 3): 25 (39.1) Pulmonary complication: 9 (14.1) Chylothorax: 0 (0) MACE (afib): 1 (1.6) Infection (any): 11 (17.2) Anastomotic leak: 2 (3.1) RLN palsy: 2 (3.1) 30-day mortality: 1 (1.6) 90-day mortality: 1 (1.6)		between surgical approach	between surgical approach	
Tagkalos 2019[23] N Retrospective study of prospectively collected database Y Single institution/Single surgeon N N	Robot (thoracic and abdominal) Ivor-Lewis vs minimally invasive (VATS and laparoscopy) Ivor-Lewis		Matched LOS (med, range): 12 (7-59) ICU stay (med, range): 1 (1-43) Pneumonia: 6 (15) Anastomotic leak: 5 (12.5) Wound infection: 0 30-day mortality: 0 90-day mortality: 2 (5)	Matched LOS (med, range): 12.5 (9-54) ICU stay (med, range): 2 (1-17) Pneumonia: 7 (17.5) Anastomotic leak: 5 (12.5) Wound infection: 1 (2.5) 30-day mortality: 1 (2.5) 90-day mortality: 1 (2.5)		NR	NR

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Short-term Outcomes** LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			**Long-term Outcomes** Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
van der Sluis 2019[14] N RCT N Single institutions/2 surgeons N N	Open McKeown v Robot transthoracic with laparoscopic abdominal and open cervical portions	Readmissions: 4 (7.3) LOS (median): 16 ICU stay: 1 (median) Grade >2 complications overall: 44 (80) Grade >2 complications directly related to surgery: 44 (80) Pulmonary complications: 32 (58) Chylothorax: 12 (22) MACE: 26 (47) 30-day mortality: 0 (0) 60-day mortality: 1 (2) 90-day mortality: 1 (2) Anastomotic leak: 11 (20) Reoperations: 18 (32.7) Health-related QOL (6wk): 57.6 (50.6-64.6)	Readmissions: 6 (11.1) LOS (median): 14 ICU stay: 1 (median) Grade >2 complications overall: 34 (63) Grade >2 complications directly related to surgery: 32 (59) Pulmonary complications: 17 (32) Chylothorax: 17 (31.5) MACE: 17 (22) 30-day mortality: 1 (2) 60-day mortality: 3 (6) 90-day mortality: 5 (9) Anastomotic leak: 13 (24.1) Reoperations: 13 (24.1) Health-related QOL (6wk): 68.7 (61.5-75.9) Physical functioning		Median follow-up: 40 months for all both arms Median OS not reached in either arm (no differences between arms). Median DFS: 28 months	Median follow-up: 40 months for all both arms Median OS not reached in either arm (no differences between arms). Median DFS: 26 months	

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Short-term Outcomes** LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			**Long-term Outcomes** Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
		Physical functioning (6wk): 58.6 (51.1-66)	(6wk): 69.3 (61.6-76.9)				
Van Der Sluis 2018[35] N RCT N NR N N **Cost only**	Open transthoracic esophagectomy vs RAMIE	Cost: Euros: 39,463	Cost: Euros: 34,892				
Washington 2019[29] N Retrospective N Single institution/Single surgeon Y N	Robotic vs laparoscopic transhiatal esophagectomy		LOS: 9.9 (4) ICU stay: 1.7 (2.4) Anastomotic leak: 1 (5.6) Clavien Dindo ≥3: 2 (11.1) Mortality: 0 (0)	LOS: 9.8 (4.7) ICU stay: 2.7 (6.1) Anastomotic leak: 1 (5.6) Clavien Dindo >3: 1 (5.6) Morality: 1 (5.6)		Median OS not reached in either arm.	
Yang 2019[24] N Retrospective Y Single institution/Single surgeon	Robot McKeown (abd and thoracic portions) vs thoraco-laparoscopic McKeown		Matched LOS (med, range): 11 (6-54) ICU stay: 2 (0-15) Reoperation: 4 (1.5) Total complication: 122 (45) Pneumonia: 24 (8.9)	Matched LOS (med, range): 11 (4-94) ICU stay: 1 (0-61) Reoperation: 9 (3.3) Total complication: 101 (37.3) Pneumonia: 34 (12.5)		Matched N: 255 Total recurrence: 30 (11.8) Locoregional recurrence only: 9 (3.5)	Matched N: 254 Total recurrence: 26 (10.2) Locoregional recurrence only: 10 (3.9) Distal recurrence:

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Short-term Outcomes** LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			**Long-term Outcomes** Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
N N			Pleural effusion: 19 (7) Pneumothorax: 7 (2.6) Re-intubation/trach: 12 (4.4) Empyema: 9 (3.3) Arrhythmia: 9 (3.3) Cardiac arrest: 0 GI bleeding: 0 Anastomotic leak: 32 (11.8) RLN palsy: 79 (29.2) Wound infection: 2 (0.7) Chyle leak: 4 (1.5) 90-day mortality: 0	Pleural effusion: 31 (11.4) Pneumothorax: 11 (4.1) Re-intubation/trach: 12 (4.4) Empyema: 11 (4.1) Arrhythmia: 8 (3) Cardiac arrest: 2 (0.7) GI bleeding: 1 (0.4) Anastomotic leak: 39 (14.4) RLN palsy: 41 (15.1) Wound infection: 2 (0.7) Chyle leak: 2 (0.7) 90-day mortality: 2 (0.7)		Distal recurrence: 17 (6.7) Locoregional and distal: 4 (1.6) Mediastinal LN recurrence: 5 (2) Median follow up (med, IQR): 17.2 (1-33)	7 (2.8) Locoregional and distal: 9 (3.6) Mediastinal LN recurrence: 13 (5.3) Median follow up (med, IQR): 9.3 (1-33)
Yun 2019[25] N Retrospective (prospective database) Y Single institution/Single surgeon N N	Open (Ivor-Lewis 54.4%; McKeown 45.6%) vs robot-assisted (Ivor-Lewis 57.1%; McKeown 42.9%) (abdominal portion was either robot-assisted or laparoscopic)	Unadjusted LOS: 18.2 (15.4) ICU stay: 1.36 (1.97) 30-day mortality: 4 (1.7)	Unadjusted LOS: 16.5 (9.8) ICU stay: 1.08 (0.43) 30-day mortality: 0 (0)		IPTW-Adjusted 1-year disease-free survival: 53.2% 3-year disease-free survival: 45.6%	IPTW-Adjusted 1-year disease-free survival: 54.4% 3-year disease-free survival: 49.2%	
Zhang 2019[26] N	Robot-assisted Ivor-Lewis		LOS (med, IQR): 9 (8-12.3)	LOS (med, IQR): 9 (8-11.3)		NR	NR

Author Year Large Database (y/n) Study Design Propensity matching (y/n) #Institutions/ Surgeons US (y/n) VA (y/n)	**Comparisons (*eg*, open vs robot Ivor-Lewis; VATS vs robot McKeown, *etc*)**	**Short-term Outcomes** LOS, mean days (SD) Readmissions, (%) ICU stay Pulmonary complications (pneumonia, pneumothorax, PE, ARDS, pleural effusion) Chylothorax MACE Anastomotic leak, N (%) Reoperations, N (%) RLN palsy Mortality, N (%)			**Long-term Outcomes** Quality of life Overall survival Cancer-specific survival Follow-up time		
		Open	**Robot (RAMIE)**	**Other minimally invasive approach (VAMIE)**	**Open**	**Robot**	**Other minimally invasive approach (VAMIE)**
Retrospective Y Single institution/Single surgeon N N	(abdomen and thorax robot) vs thoraco-laparoscopic Ivor-Lewis		Total complications: 19 (28.8) Pneumonia: 4 (6.1) Chylothorax: 0 Anastomotic leak: 5 (7.6) RLN palsy: 4 (6.1) MACE: 5 (7.6) Wound infection: 1 (1.5) In-hospital mortality: 0 90-day mortality: 1 (1.5)	Total complications: 16 (24.2) Pneumonia: 5 (7.6) Chylothorax: 1 (1.5) Anastomotic leak: 3 (4.5) RLN palsy: 3 (4.5) MACE: 2 (3) Wound infection: 0 In-hospital mortality: 0 90-day mortality: 1 (1.5)			

APPENDIX H. OPERATIVE TECHNIQUES OF INCLUDED STUDIES

Study	Study Arm	Approach	Abdomen	Chest	Anastomosis
Chao 2018[16]	RAMIE	McKeown	Laparoscopic	Robotic	Circular stapled; cervical
	VAMIE	McKeown	Laparoscopic	VATS	Circular stapled; cervical
Chen 2019[17]	RAMIE	McKeown	NR	Robotic	Circular stapled; cervical
	VAMIE	McKeown	Laparoscopic	VATS	Circular stapled; cervical
Deng 2018[18]	RAMIE	McKeown	Robotic	Robotic	Circular stapled or handsewn; cervical
	VAMIE	McKeown	Laparoscopic	VATS	Circular stapled or handsewn; cervical
Espinoza-Mercado 2019[19]	RAMIE	NR	NR	NR	NR
	VAMIE	NR	NR	NR	NR
	Open	NR	NR	NR	NR
Gong 2020[34]	RAMIE	McKeown	Robotic	Robotic	Circular stapled; cervical
	VAMIE	McKeown	Laparoscopic	VATS	Circular stapled; cervical
	Open	McKeown	Laparotomy	Thoracotomy	NR
He 2018[20]	RAMIE	McKeown	Robotic	Robotic	End to side circular stapled; cervical
	VAMIE	McKeown	Laparoscopic	VATS	End to side circular stapled; cervical
He 2020[15]	RAMIE	McKeown	Robotic	Robotic	Cervical
	VAMIE	McKeown	Laparoscopic	VATS	Cervical
Jeong 2016[21]	RAMIE	McKeown	Laparotomy	Robotic	Cervical
	Open	Ivor-Lewis or McKeown	Laparotomy	Thoracotomy	Cervical or thoracic

Study	Study Arm	Approach	Abdomen	Chest	Anastomosis
Meredith 2019[27]	RAMIE	Ivor-Lewis	NR	NR	NR
	VAMIE	Ivor-Lewis	NR	NR	NR
	Open	Ivor-Lewis	NR	NR	NR
Motoyama 2019[30]	RAMIE	Ivor-Lewis	NR	Robotic	NR
	VAMIE	Ivor-Lewis	NR	VATS	NR
Naffouje 2019[22]	RAMIE	Ivor-Lewis	NR	NR	NR
	VAMIE	Ivor-Lewis	NR	NR	NR
Osaka 2018[32]	RAMIE	NR	NR	Robotic	NR
	Open	NR	NR	Thoracotomy	NR
Park 2016[31]	RAMIE	90% McKeown 10% Ivor-Lewis	58% robotic 42% open*	Robotic	90% cervical 10% thoracic
	VAMIE	81% McKeown 19% Ivor-Lewis	49% laparoscopic 51% open*	VATS	81% cervical 19% thoracic
Rolff 2017[33]	RAMIE	Ivor-Lewis	Robotic	Thoracotomy	NR
	Open	Ivor-Lewis	Laparotomy	Thoracotomy	NR
Sarkaria 2019[28]	RAMIE	62/64 Ivor-Lewis; 2/64 McKeown	NR	NR	NR
	Open	103/106 open Ivor-Lewis; 3/106 thoracoabdominal	NR	NR	NR
van der Sluis 2019[14]	RAMIE	McKeown	Laparotomy	Robotic	End to side handsewn; cervical
	Open	McKeown	Laparotomy	Thoracotomy	End to side handsewn; cervical
Tagkalos 2019[23]	RAMIE	Ivor-Lewis	Robotic	Robotic	Circular stapled; intrathoracic
	VAMIE	Ivor-Lewis	Laparoscopic	VATS	Circular stapled; intrathoracic

Study	Study Arm	Approach	Abdomen	Chest	Anastomosis
Washington 2019[29]	RAMIE	Transhiatal	Robotic	NA	Cervical
	VAMIE	Transhiatal	Laparoscopic	NA	Cervical
Yang 2019[24]	RAMIE	McKeown	Robotic	Robotic	Cervical
	VAMIE	McKeown	Laparoscopic	VATS	Cervical
Yun 2019[25]	RAMIE	57.1% Ivor-Lewis 42.9% McKeown	Robotic or Laparoscopic	Robotic	Circular stapled; cervical
	Open	54.4% Ivor-Lewis 45.6% McKeown	Laparotomy	Thoracotomy	Circular stapled; cervical
Zhang 2019[26]	RAMIE	Ivor-Lewis	Robotic	Robotic	End to end both circular stapled + handsewn; intrathoracic
	VAMIE	Ivor-Lewis	Laparoscopic	VATS	End to end circular stapled; intrathoracic

APPENDIX I. CITATIONS FOR EXCLUDED PUBLICATIONS

Intervention (n=6)

1. Luketich JD, Pennathur A, Franchetti Y, et al. Minimally invasive esophagectomy: results of a prospective phase II multicenter trial-the eastern cooperative oncology group (E2202) study. *Ann Surg.* 2015;261(4):702-707.

2. Miyasaka D, Okushiba S, Sasaki T, et al. Clinical evaluation of the feasibility of minimally invasive surgery in esophageal cancer. *Asian J Endosc Surg.* 2013;6(1):26-32.

3. Mu J, Yuan Z, Zhang B, et al. Comparative study of minimally invasive versus open esophagectomy for esophageal cancer in a single cancer center. *Chin Med J (Engl).* 2014;127(4):747-752.

4. Romero D. Hybrid minimally invasive surgery overtakes open surgery. *Nat Rev Clin Oncol.* 2019;16(3):144.

5. Xie MR, Liu CQ, Guo MF, et al. Short-term outcomes of minimally invasive Ivor-Lewis esophagectomy for esophageal cancer. *Ann Thorac Surg.* 2014;97(5):1721-1727.

6. Yanasoot A, Yolsuriyanwong K, Ruangsin S, et al. Costs and benefits of different methods of esophagectomy for esophageal cancer. *Asian Cardiovasc Thorac Ann.* 2017;25(7-8):513-517.

Comparison (n=3)

1. Mori K, Yamagata Y, Aikou S, et al. Short-term outcomes of robotic radical esophagectomy for esophageal cancer by a nontransthoracic approach compared with conventional transthoracic surgery. *Dis Esophagus.* 2016;29(5):429-434.

2. Na KJ, Park S, Park IK, et al. Outcomes after total robotic esophagectomy for esophageal cancer: a propensity-matched comparison with hybrid robotic esophagectomy. *J Thorac Dis.* 2019;11(12):5310-5320.

3. Worrell SG, Bachman KC, Sarode AL, et al. Minimally invasive esophagectomy is associated with superior survival, lymphadenectomy and surgical margins: propensity matched analysis of the National Cancer Database. *Dis Esophagus.* 2020.

Small sample size (n=1)

1. Raja K. Minimally invasive esophagectomy after neoadjuvant chemoradiotherapy using cross regimen for locally advanced esophageal cancer. *Gut.* 2019;68:A69.

Not original research (n=1)

1. Inderhees S, Dubecz A. [Hybrid minimally invasive esophagectomy for esophageal cancer-MIRO trial]. *Chirurg.* 2019;90(8):677.

Duplicate or studies with a large overlap of patients from the same data source (n=11)

1. Li B, Li Z. Early results of robot assisted esophagec-tomy compared with conventional thoracoscopic approach for esophageal cancer: A randomized clinical trial. *Diseases of the Esophagus.* 2018;31:2.

2. Tagkalos E, Goense L, Hoppe-Lotichius M, et al. Robot-assisted minimally invasive esophagectomy (RAMIE) compared to conventional minimally invasive esophagectomy (MIE) for esophageal cancer: a propensity-matched analysis. *Dis Esophagus.* 2020;33(4).

3. Lin Y, Deng H. Comparison of short-term outcomes between RAMIE and VAMIE in treatment middle thoracic esophageal cancer. *Diseases of the Esophagus.* 2018;31:112.

4. Grimminger PP, Tagkalos E, Hadzijusufovic E, et al. Change from Hybrid to Fully Minimally Invasive and Robotic Esophagectomy is Possible without Compromises. *Thorac Cardiovasc Surg.* 2019;67(7):589-596.

5. Deng HY, Huang WX, Li G, et al. Comparison of short-term outcomes between robot-assisted minimally invasive esophagectomy and video-assisted minimally invasive esophagectomy in treating middle thoracic esophageal cancer. *Dis Esophagus.* 2018;31(8).

6. Halpern AL, Friedman C, Torphy RJ, et al. Conversion to open surgery during minimally invasive esophagectomy portends worse short-term outcomes: an analysis of the National Cancer Database. *Surg Endosc.* 2019.

7. Meredith K, Blinn P, Maramara T, et al. Comparative outcomes of minimally invasive and robotic-assisted esophagectomy. *Surgical Endoscopy.* 2020;34(2):814-820.

8. Van Der Sluis PC, Van Der Horst S, May A, et al. Robot-assisted minimally invasive esophagectomy versus open transthoracic esophagectomy for esophageal cancer: A randomized controlled trial. *Surgical Endoscopy.* 2018;32:S475.

9. Weksler B, Sullivan JL. Survival After Esophagectomy: A Propensity-Matched Study of Different Surgical Approaches. *Ann Thorac Surg.* 2017;104(4):1138-1146.

10. Yerokun BA, Sun Z, Yang CJ, et al. Minimally Invasive Versus Open Esophagectomy for Esophageal Cancer: A Population-Based Analysis. *Ann Thorac Surg.* 2016;102(2):416-423.

11. Yun JK, Lee IS, Gong CS, et al. Clinical utility of robot-assisted transthoracic esophagectomy in advanced esophageal cancer after neoadjuvant chemoradiation therapy. *J Thorac Dis.* 2019;11(7):2913-2923.

Unavailable (n=1)

1. Götzky K, Jähne J. [Minimally invasive esophagus resection: Results of a prospective multicenter study]. *Chirurg.* 2015;86(9):898.