Minimally invasive esophagectomy for esophageal carcinoma

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Contributions: (I) Conception and design: Both authors; (II) Administrative support: Both authors; (III) Provision of study materials or patients: None; (IV) Collection and assembly of data: None; (V) Data analysis and interpretation: Both authors; (VI) Manuscript writing: Both authors; (VII) Final approval of manuscript: Both authors.

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Abstract: The incidence of esophageal cancer has been increasing, and in the last year alone it is estimated that there upwards of 20,000 new diagnoses of esophageal cancer and approximately 15,000 deaths. Most patients in this age receive neoadjuvant chemoradiotherapy prior to surgical resection in an attempt to achieve a cure. The major open approaches are an Ivor Lewis (transthoracic), transhiatal, left thoracoabdominal approach, and "three-hole" McKeown esophagectomy. It is a surgical procedure with high reported rates of morbidity and mortality. Given high rates of morbidity and mortality, minimally invasive approaches to esophagectomy [minimally invasive esophagectomy (MIE)] has gained momentum as potential alternative in an attempt to minimize morbidity without sacrificing oncologic outcomes. Although complex and perhaps more time consuming, perioperative results are encouraging and generally trend toward fewer pulmonary complications, lower blood loss, shower ICU and hospitalization time. Further, it appears the technical skills can be obtained, and appear the learning curve appears to be approximately 40 patients. With these considerations in mind, it is likely the MIE will continue to grow in favorability for patients with surgically resectable esophageal cancer.

Keywords: Esophagus esophagectomy surgical procedures; minimally invasive morbidity mortality; minimally invasive esophagectomy (MIE); esophageal cancer

Received: 07 January 2020; Accepted: 16 December 2020; Published: 20 December 2021.
doi: 10.21037/vats-2019-mie-02
View this article at: http://dx.doi.org/ 10.21037/vats-2019-mie-02

A historical perspective

The incidence of esophageal cancer has been increasing and in the last year alone, it is estimated that there upwards of 20,000 new diagnoses of esophageal cancer and approximately 15,000 dying from the disease (1). Most patients in this age received neoadjuvant chemoradiotherapy prior to surgical resection in an attempt to achieve a cure. The major open approaches are an Ivor Lewis transthoracic), transhiatal, left thoracoabdominal approach, and "three-hole" McKeown esophagectomy. It is a surgical procedure with high reported rates of morbidity and mortality (2). A review of the National Medicare/Nationwide Inpatient Sample revealed mortality rates for esophagectomy ranging between 8.1% and 23.1% (3). Furthermore, a review of the Society of Thoracic Surgeons General Thoracic Database estimates major morbidity around 24% and a mortality rate of 2.7% (4). Given high rates of morbidity and mortality, minimally invasive approaches to esophagectomy [minimally invasive esophagectomy (MIE)] has gained momentum as potential alternative in an attempt to minimize morbidity without sacrificing oncologic outcomes.

The earliest reports of minimally invasive esophagectomy (MIE) date back to 1992, when Cuschieri *et al*. reported a five-patient series describing a technique of esophagectomy via a right thoracoscopic approach (5). They noted "unmeasurable" blood loss in four patients and 300 cc in the fifth study participant. The mean procedure time was 5.5 hours, stay in the intensive care was 1 day, and overall length of stay was approximately 11 days. In 1995, DePaula *et al*. reported their experience involving twelve patients with benign and malignant disease treated with a transhiatal approach to esophageal resection, without thoracotomy, using minimally invasive abdominal and mediastinal dissection (6). Overall their results were similarly encouraging.

In 1998, Luketich *et al*. at the University of Pittsburgh Medical Center described their experiences with a minimally invasive technique involving a combined laparoscopic/thoracoscopic approach implementing thoracoscopic dissection in the chest with laparoscopic mobilization of the stomach and conduit creation, and a cervical anastomosis (7,8). Later, in 1999, Watson *et al*. detailed their results on a preliminary experience of 2 patients undergoing a minimally invasive Ivor Lewis procedure; a technique with a laparoscopic-assisted approach for gastric mobilization and a thoracoscopic approach for mediastinal dissection and esophagogastric anastomosis (9). Luketich reported a landmark series 222 minimally invasive esophagectomies, indicating the feasibility of the technique (10). Over the subsequent 18 years, the momentum has only increased for a minimally invasive approach to esophagectomy.

Indications

The primary indication for MIE is surgically resectable esophageal carcinoma (stage I–IIIa); however, there is a role for benign disorders including achalasia and reflux associated esophageal stenosis. At this point, there are no hard contraindications to the procedure, but it is worthwhile to emphasize the complexity of these operations supports only those with a high aptitude for minimally invasive approaches to perform them. Multiple studies validate MIE as an oncologic approach and can be a viable option for patients who have undergone neoadjuvant chemoradiation or who will require adjuvant therapy (11). Similar to other laparoscopic approaches, previous abdominal and chest surgery make minimally invasive approaches more challenging as does an obese body habitus.

Technical approach: minimally invasive Ivor Lewis esophagectomy

MIE/Ivor Lewis is completed in two stages: (I) laparoscopic dissection of the stomach and construction of the conduit and (II) thoracoscopic dissection of the esophagus, comprehensive mediastinal lymph node dissection, removal of the surgical specimen, retrieval of the gastric conduit, and construction of a reproducible esophagogastric anastomosis. It appears a minimally Ivor Lewis approach provides superior visualization of mediastinal structures and allows for and extensive abdominal and thoracic lymph node harvest. Further, this approach minimizes recurrent laryngeal nerve injuries and the creation of reproducible anastomosis.

The patient is placed supine on the operating table, with the surgeon to the patient's right and the assistant to the left. The procedure should begin with an on-table esophagogastroduodenoscopy to visualize the exact site of disease (location of tumor and the presence of Barrett's esophagus) and to inspect the stomach as a potential replacement for the esophagus.

Initially, five laparoscopic ports are placed in the upper abdomen. After gaining exposure to the peritoneal cavity, the abdomen is examined for metastatic disease. If a negative evaluation, dissection proceeds with taking down the lesser omentum and revealing the crus (right) of the diaphragm. The phrenoesophageal ligament is opened and the esophagus is mobilized through the hiatus. The omentum is subsequently open, with attention to preserving the right gastroepiploic artery which serves as blood supply to the conduit. Mobilization is continued along the stomach's greater curve, further dividing the short gastric arteries. The hiatus is dissected, and the esophagus mobilized gently into the mediastinum. We limit the amount of mediastinal dissection initially as to not cause a pneumothorax which may head to hypotension with pneumoperitoneum. Existing retro-antral and retro-fundal attachments are divided to the pylorus. Along the lesser curve, the left gastric artery is dissected towards its origin with nodal tissue included in the specimen. The base of the artery and vein and they are ultimately divided with a vascular stapler.

The gastric conduit is then created using endoscopic staplers, starting at the incisura and being mindful to preserve the right gastric artery. The stomach is divided up to the cardia, keeping a 5–6-cm-width to the conduit with respect to the greater curve. It is critical to remember to withdraw/remove the nasogastric tube prior to conduit creation.

Pyloroplasty is not part of our center's routine, as we have observed a low incidence of gastric outlet obstruction after esophagectomy in the cohort of patients not undergoing a pyloric drainage procedure. Furthermore, post-operative issues typically can be successfully managed conservatively or by means of endoscopic balloon dilatation. Should pyloroplasty be required, the pylorus is opened with ultrasonic shears and closed transversely. Alternatives to pyloroplasty include pyloromyotomy or botulinum toxin injection of the pylorus.

A jejunostomy is placed by first rotating the transverse colon up towards the hiatus and identifying the Ligament of Treitz (LOT). Next, a loop of jejunum (approximately 30 cm) distal to the LOT is tacked to the wall of the abdomen. Placement of an additional 12 mm port in the lower right quadrant facilitates the creation of the conduit as well as the placement of the jejunostomy. The laparoscopic jejunostomy is accomplished via a Seldinger technique, with a needle, guidewire and finally the tube advanced over the guidewire into the jejunum under laparoscopic vision. Proper placement of the catheter is confirmed before securing the feeding tube to the abdominal wall.

The abdominal portion of the procedure concludes with an extensive dissection into the mediastinum. If a pleural space is entered at this time, it is of less significance with the conclusion of the laparoscopic portion of the procedure. Finally, the most cephalad portion of the gastric tube is stitched to the esophagus in the mediastinum. This stitch aides in orienting the conduit in its delivery into the thorax. In certain circumstances, a crural stitch maybe required to avoid herniation of abdominal contents into the chest postoperatively.

The thoracoscopic portion initially starts with repositioning the patient in the left lateral decubitus position. After lung isolation is achieved, five thoracoscopic (VATS) ports are placed. A camera port is located in the 7th or 8th intercostal space, anterior to the midaxillary line. A 10 mm thoracoscopy port is placed at the 8th or 9th intercostal space, posterior to the posterior axillary line, for the ultrasonic coagulating shears. A thoracoscopy port is placed in the anterior axillary line at the 4th intercostal space, through which a fan shaped retractor retracts the lung anteriorly to expose the esophagus. A 5 mm port is placed just anterior to the tip of the scapula, and is used for retraction by the surgeon. A final port is placed at the sixth rib, at the anterior axillary line for suction and is critical in the creation of the anastomosis.

A stitch is placed in the central tendon of the diaphragm allowing for visualization of the gastroesophageal junction. Thoracic dissection begins by dividing the inferior pulmonary ligament. Next, the lung is retracted anteriorly and dissection moves along the pericardium completely removed all the subcarinal lymph nodes. Careful consideration to the membranous wall of the right mainstem bronchus is required as mobilization the subcarinal nodes commences. All periesophageal nodes and the entire subcarinal nodal package is removed with the specimen. The mediastinal pleura is opened superior the azygos vein and the vein divided with a vascular load of an endoscopic stapler.

Posteriorly, the pleura is divided which allows for access to free the esophagus from the chest wall and aorta. Any aortoesophageal vessels encountered should be clipped prior to division. Tissues suspicious for lymphatic branches arising from the thoracic duct are meticulously clipped and divided to prevent chylothorax. If concern of thoracic duct injury is present, the thoracic duct may be ligated en masse at the level of the diaphragm. After freeing the esophagus medially and laterally, the specimen and attached gastric conduit is pulled into the thorax. One only needs to bring in enough gastric tube to reach the proximal esophageal remnant; redundant supradiaphragmatic gastric conduit may result in delayed poor gastric emptying. Although obvious, it is critical that the gastric tube remain oriented to avoiding spiraling or 360 degree twisting of the conduit.

After extending the posterior incision, the esophagus is then transected. Next, the anastomosis is created using an EEA stapler. First the anvil (typically a 28 mm EEA) is positioned in the proximal esophagus and two "purse string" sutures are placed to secure the anvil in position. The gastric conduit is then pulled into the chest and the gastric conduit is opened at the tip, along the staple line. The EEA stapler is placed through the posterior, inferior thoracoscopic port and into the conduit. The stapler is passed out along the greater curve of the gastric conduit to join the anvil. Prior to creating the anastomosis, we carefully ascertain the amount of conduit that will lie in the chest as too much tension may result in ischemic injury while redundancy in the conduit can result in emptying complications. Once a proper orientation is determined, the stapler and the anvil are docked and then fired ideally at or above the level of the azygos vein.

Laparoscopic transhiatal esophagectomy

As in open transhiatal esophagectomy, a minimally invasive transhiatal esophagectomy is optimal for early stage tumors without significant intrathoracic lymphadenopathy. Laparoscopic transhiatal esophagectomy is an operation of two stages: (I) an abdominal portion in which the conduit is created and dissection of the esophagus and paraesophageal lymph nodes is carried through the diaphragmatic hiatus and (II) a cervical portion which allows for dissection of the proximal esophagus and anastomosis creation.

Positioning and port placement are similar to the Ivor

Lewis approach. After entering the abdomen, the esophagus is mobilized at the hiatus, and the greater curve is freed from the omentum providing careful attention to preservation of the right gastroepiploic artery. The lesser curve is then mobilized with division of the gastric artery and vein, and the gastric conduit created. A jejunostomy should be placed to provide enteral access. In the final portion of the abdominal portion, the mediastinal esophagus is freed circumferentially via the hiatus. This dissection should be carried high enough to reach the cervical dissection plane. In the case of a difficult mobilization, the crus can be opened to enlarge the hiatus which can aide in exposure and subsequent delivery of the specimen. Before leaving the abdomen, the proximal portion of the conduit is sutured to the surgical specimen as in the Ivor Lewis approach.

The cervical portion of procedure is started with a horizontal left neck incision, through which the platysma is divided and the sternocleidomastoid muscle is retracted laterally. This should provide visualization of the inferior thyroidal vessels and the omohyoid muscle, which is divided. Next dissection of the esophagus is carried out bluntly and inferiorly until joining the laparoscopic mediastinal plan. After the esophagus is fully mobilized, the specimen is removed via the cervical incision; which ultimately pulls up the gastric conduit. The laparoscope is replaced in the abdomen to confirm that the gastric conduit is free of trauma and confirm a non-volvulized orientation. Once this is confirmed, the esophagus is divided approximately 4 cm distal to the upper esophageal sphincter. After negative resection margins have been obtained (both for Barrett's and carcinoma), the cervical esophagogastric anastomosis is created in the neck using either a hand-sewn or staple technique.

McKeown transthoracic esophagectomy

The three-hole McKeown esophagectomy combines aspects of the transhiatal and Ivor Lewis approaches, and allows for removal of tumors mid esophageal tumors as well as distal esophagus/gastroesophageal junction lesions with bulky intrathoracic lymph node burden. This procedure consists of 3 steps: (I) a thoracic portion which allows for esophageal mobilization, (II) an abdominal portion which allows for conduit creation and distal tumor resection, and (III) a cervical portion that allows for proximal esophageal dissection and anastomosis creation. This approach provides an opportunity for an extensive intrathoracic lymph node dissection as well as determining resectability of the tumor in the chest prior to creating gastric conduit.

The procedure begins in the left lateral decubitus position and mobilization of the thoracic esophagus which is carried out in a fashion similar to the second portion of a minimally invasive Ivor Lewis esophagectomy. A point of difference is that the dissection is carried to the thoracic inlet with circumferential mobilization of the esophagus. Once resectability is determined and the esophagus is free to the apex of the chest, the patient is repositioned supine for the abdominal portion. This portion of the procedure is similar to the previously described gastric mobilizations. Lastly, the neck dissection is completed in a similar fashion as that described for a minimally invasive transhiatal approach. After completing the cervical anastomosis, the surgeon returns to the laparoscopic view and gently retracts the pyloroantral area to minimize excess intra-thoracic gastric. Lastly, the gastric conduit is tacked to the hiatus.

Results

Surgical resection of the esophagus is associated with high morbidity and mortality and is often performed in elderly individuals with comorbidities which further affects outcomes (12). To this end, there has been growing interest within the surgical community to adopt minimally invasive approaches in hopes to enhance postoperative outcomes. A minimally invasive approach offers theoretical possibility of a less demanding postoperative recovery, as well as less respiratory/cardiovascular morbidity as compared to traditional open approaches (13). Further, laparoscopic and thoracoscopic approaches offer opportunity for improved visualization of abdominal and mediastinal structures which minimizes damage to adjacent organs, and improved node retrieval and improved hemostasis.

These theoretical benefits have been described in multiple retrospective series. The largest report to date was recently published in 2012 by Luketich *et al.* at UPMC (14). In this report of 1,011 patients undergoing to MIE, the overall operative mortality of was 1.68%, with a median ICU time of 2 days, and a median hospitalization of 8 days. From an oncologic perspective, median number of lymph nodes resection was 21. This report also evaluated outcomes between three field and Ivor Lewis MIE, and noted no observable difference among the approached with regard to length of ICU stay, hospitalization and overall morbidity and mortality. Interestingly, the 30-day mortality was 0.9% in the Ivor Lewis group and 2.5% in the three-field group (P=0.08). Lastly, there was a slightly decreased rate of recurrent laryngeal nerve injury in the MIE Ivor Lewis group than the three-field group (P<0.001).

Although technical feasibility as described in Luketich's report is encouraging, oncologic efficacy as a cancer operation remains primary importance. As in other reports, in our institution's experience we have found no difference between open esophagectomy and MIE approaches with regards to perioperative oncologic outcomes (15). To further elaborate, the median number of lymph nodes harvested with MIE were comparable with open approaches (21 *vs*. 19; P=0.71). The trend of positive margins was in fact found to be higher in open approaches versus minimally invasive approaches (6.6% *vs*. 0%; P=0.163). Intraoperatively, there was less blood loss and a lower requirement for intraoperative fluid resuscitation. Interestingly, there no statistically different times intraoperatively between the two groups. Most importantly, echoing other reports, MIE significantly decreased postoperative pulmonary complications with rates with MIE *vs*. open being 2.6% and 43.4%, respectively (P<0.001). Pulmonary complications in this study included need for intubation, postoperative pneumonia, pleural effusion requiring drainage or pulmonary embolus. MIE was also connected with a diminished median length of ICU stay and hospitalization. In addition to these encouraging initial results, the 60-day mortality rate favored MIE over open esophagectomy (0% *vs*. 2.6%; P=0.552).

The previously mentioned studies are just a few of the handful of reports touting the benefits of MIE. Despite this growing enthusiasm, the majority of this data comes from single center experiences, and little data exists in the form of meta-analyses. To date the largest meta-analysis compiled by Dantoc *et al*. in 2012 consists of 16 studies, which includes a total of 1,212 patients undergoing esophagectomy (16). The specific aim of this paper was to delineate the oncologic potential of MIE *vs*. open approaches. They noted a higher lymph nodes harvest in the MIE group *vs*. the open group (16 *vs*. 10; P=0.04). Positive resection margins were not commented on. In terms of long-term data, the trend for survival favored MIE for all time intervals, although this difference was statistically not significant. Other smaller meta-analyses generally favor this trend, and demonstrate associates of lower morbidity and mortality associated with MIE (17-19).

To date, there remains only a single randomized controlled trial evaluating open esophagectomy *vs*. MIE (12). In this 5-center study, 115 patients (ages 18–75 years) with resectable esophageal or gastroesophageal junction tumors were randomly assigned to open or minimally invasive Ivor Lewis esophagectomy. Fifty-six patients were randomized open esophagectomy and 59 to MIE. The primary outcome was pulmonary infection (defined as pneumonia confirmed by X-ray or CT, and associated with a positive sputum) within the first two postoperative weeks. Within the initial post-procedure hospitalization 19% of patient undergoing open procedures had pulmonary infections as compared to 12% of those undergoing minimally invasive approaches (P=0.05). The authors found that this trend persisted throughout the first 2 post-operative weeks with 16% of patients in the open group having pulmonary infection versus 9% in the MIE group (P=0.005). The authors noted longer operative times associated with MIE (329 *vs*. 299 min; P=0.002); however, MIE was found to be significantly associated with almost a 2.5 lower intraoperative blood loss (P<0.001). The rate of vocal-cord paralysis was also significantly lower in the MIE group as compared to the open group (2% *vs*. 14%; P=0.01). The time in ICU, leak rate, pulmonary embolus rate, and need for reoperation were similar between both groups.

Although preliminary results associated with MIE are encouraging, these procedures are undoubtedly among the most technically challenging operations in the general thoracic surgery. They require mastery of laparoscopic and thoracoscopic surgical techniques, and like any new procedure, a learning curve is encountered. When examining our center's first 80 patients undergoing MIE (the first 40 patients were termed "early experiences", and the subsequent 40 patients termed "later experiences"), we were able to extrapolate a learning curve of 35 to 40 patients (13). It was noted at the conversion rate within was approximately 2% in the early group *vs*. 0% in later patients. The mean surgical time decreased with experience from 364 to 316 min (P<0.01). Intraoperative estimated blood loss also trended favorably with experience from 205 *vs*. 176 cc (P<0.14). The median hospitalization decreased from 7 *vs*. 6 days (P<0.01). This supports the notion that, although complex, with persistence these procedures can be done successfully.

Conclusions

Esophageal cancer remains a growing problem in the United States, and surgical resection provides the only approach to offer cure for these patients. Traditional open approaches are burdened with high levels and morbidity and mortality, and MIE has been proposed as an alternative approach. Although complex and perhaps more time consuming, perioperative results are encouraging and generally trend toward fewer pulmonary complications, lower blood loss, shower ICU and hospitalization time. This appears to be at little cost in terms of oncologic efficacy. Further, MIE is technically demanding but it appears the learning curve is approximately 40 patients. With these considerations in mind, it is likely the MIE will continue to grow in favorability for patients with surgically resectable esophageal cancer.

Acknowledgments

Funding: None.

Footnote

Provenance and Peer Review: This article was commissioned by the Guest Editor (Robert E. Merritt) for the series "Minimally Invasive Esophagectomy for Esophageal Carcinoma" published in *Video-Assisted Thoracic Surgery*. The article has undergone external peer review.

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form, available at: http://dx.doi.org/10.21037/vats-2019-mie-02. The series "Minimally Invasive Esophagectomy for Esophageal Carcinoma" was commissioned by the editorial office without any funding or sponsorship. Both authors have no other conflicts of interest to declare.

Ethical Statement: Both authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/vats-2019-mie-02
Cite this article as: Predina JD, Morse CR. Minimally invasive esophagectomy for esophageal carcinoma. Video-assist Thorac Surg 2021;6:34.

