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Minimally Invasive Ivor Lewis Esophagectomy with Linear Stapled Anastomosis Associated with Low Leak and Stricture Rates

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Abstract

Background: Minimally invasive foregut surgery is increasingly performed for both benign and malignant diseases. We present a retrospective series of patients who underwent minimally invasive Ivor Lewis esophagectomy (MIE) with linear stapled anastomosis performed at two centers in the United States, with a focus on evaluating leak and stricture rates.

Methods: Patients treated from 2007 to 2018 were included, and data on demographics, oncologic treatment, pathology, and outcomes were analyzed. The surgical technique utilized laparoscopic and thoracoscopic access, with an intrathoracic esophagogastric anastomosis using a 6-cm linear stapled side-to-side technique.

Results: A total of 124 patients were included and 114 resections (91.9%) were completed in a minimally invasive fashion with a 6-cm linear stapled side-to-side anastomosis. Patients were

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predominantly male (90.7%) with a median age of 66.0 years and body mass index of 28.8 kg/m^2. Of 121 patients with malignancy, negative margins were obtained in 94.3% and median lymph node yield was 15 (IQR 12–22). In the intention to treat analysis, median operative time was 463 minutes (IQR 403–515), blood loss was 150 mL (IQR 100–200), and length of stay was 8 days (IQR 7–11). Postoperative complications were experienced by 64 patients (51.6%) including respiratory failure in 14 (11.3%) and pneumonia in 12 (9.7%). In patients who successfully underwent a 6-cm stapled side-to-side anastomosis, anastomotic leaks occurred in 6 patients (5.1%) **without need for operative intervention**, and anastomotic strictures occurred in 6 patients (5.1%) **requiring endoscopic management**.

Conclusions: Ivor Lewis MIE with a 6-cm linear stapled anastomosis can be completed with a high technical success rate, and **low rates of anastomotic leak and stricture**.

Keywords

minimally invasive esophagectomy; Ivor Lewis esophagectomy; intrathoracic anastomosis; esophageal cancer

Introduction

The incidence of esophageal and gastric malignancies in 2019 in the United States (US) will be an estimated 45,160 cases, with 27,220 deaths[1]. There has been increasing interest in minimally invasive surgery (MIS) due to improved time to functional recovery and return to normal activities.

A randomized trial that compared minimally invasive esophagectomy (MIE) to open esophagectomy for cancer found a decreased rate of pulmonary complications in the MIE group (9% MIE versus 29% open) with no differences in anastomotic leak rates and 30-day mortality[2]. Randomized trials comparing robotic[3] and hybrid esophagectomy[4] to open esophagectomy also favored the robotic and hybrid approaches. A US single-institution series of 1,033 consecutive patients undergoing MIE likewise showed favorable results with a median yield of 21 lymph nodes, 1.7% operative mortality, and length of stay of 8 days[5]. Patients in this series who underwent Ivor Lewis esophagectomy compared to a McKeown approach had a lower postoperative mortality rate of 0.9%.

Despite the increasing adoption of minimally invasive techniques for esophageal cancer surgery, there is no accepted ideal approach for creating an anastomosis between the stomach conduit and the esophagus. The largest reported series of MIEs with intrathoracic anastomoses utilized a stapled end-to-end (EEA) technique, most commonly with a 28-mm EEA stapler[5]. Anastomotic leak requiring reoperation was reported in 4% of patients in that series. Limitations with the use of the EEA stapler during a MIE include the need to make a several centimeter incision to place the stapler between the ribs, difficulty placing and securing the anvil into the divided esophagus, and a small luminal anastomotic opening, with leak rate of 9.8% and stricture rate of 28% reported in one series using an intrathoracic EEA anastomosis[6]. A linear stapled anastomosis has potential benefits but there are little reported data concerning its application to minimally invasive resection techniques for esophageal cancer.

A previously published series of 315 patients who underwent MIE by the current authors demonstrated a median yield of 16 lymph nodes, 1.0% perioperative mortality, length of stay of 8 days, and leak rate of 7.6%[7]. The vast majority (80%) of patients previously reported had a cervical anastomosis and a side-to-side anastomosis was performed in most patients through an extracorporeal approach. In this current manuscript, we focus on reporting our experience for minimally invasive Ivor Lewis esophagectomy with an intrathoracic stapled 6-cm side-to-side anastomosis, describing outcomes in 124 patients. The technique associated with this approach has been previously published[8]. The data presented here represents postoperative outcomes including leak and stricture rates from the largest Western series of patients, reported to date, undergoing this operation.

Methods

This retrospective study was approved by the Institutional Review Boards of the participating institutions including Shands Hospital at the University of Florida and Roswell Park Comprehensive Cancer Center. Consecutive patients treated between January 2007 and August 2018 who were scheduled for MIE and planned for a stapled side-to-side intrathoracic anastomosis were included. During this time period, MIS was the preferred approach for esophagectomy. Prior to 2014, our default approach for MIE was a three-field (McKeown) esophagectomy with a cervical anastomosis, with a limited number of patients undergoing Ivor Lewis esophagectomy due to contraindications to cervical anastomosis including prior gastric surgery and anticipated short gastric conduit, and prior neck surgery or irradiation. Starting in 2014, we switched to Ivor Lewis MIE with a stapled side-to-side 6-cm linear intrathoracic anastomosis as the default technique with a small minority of patients undergoing transhiatal or McKeown esophagectomies with cervical anastomoses for specific indications such as mid or proximal esophageal cancers or extensive Barrett's metaplasia, or for patients with a relative contraindication to single lung ventilation due to poor pulmonary function.

Prospectively maintained databases were queried to obtain data on demographics, diagnosis, operative and postoperative outcomes, pathology, and long-term outcomes. Missing data were obtained by review of the electronic medical record when feasible.

Patients with a preoperative cancer diagnosis were staged using positron emission tomography coupled with computed tomography (PET-CT) or endoscopic ultrasound (EUS). Neoadjuvant chemoradiotherapy was routinely recommended to patients with T2 or more advanced primary tumors or node positive disease. Patients were restaged with PET-CT or CT after completion of neoadjuvant therapy.

The technical details of the Ivor Lewis MIE technique used by the authors in this study has been previously described[8]. MIE was performed starting with laparoscopic mobilization of the stomach, nodal dissection, and creation of the gastric conduit in the supine position. Pyloroplasty was not routinely performed. Botulinum toxin was injected into the pylorus at the discretion of the treating surgeon. During the latter years of this study, approximately six patients were enrolled in a separate study which randomized patients to injection of 100 units of botulinum toxin into the pylorus versus no drainage procedure. Any patient without

a prior jejunostomy tube underwent tube placement at the time of esophagectomy. The patient was then repositioned into the left lateral decubitus position for the completion of the resection and nodal dissection via a right thoracoscopic approach. The esophagogastric anastomosis was performed in a side-to-side fashion using a 60-mm linear stapler. A nasogastric tube was routinely left across the anastomosis and a drain was placed by the anastomosis. The common channel was closed with sutures using the Endo Stitch (Ethicon, Cincinnati, OH) or with a linear stapler. A modification developed since publication of our previous technique, includes closure of the common esophagogastric channel using endosutures to approximate the walls of the esophagus and stomach and then closure with the use of a linear stapler. The specimen was extracted through a 3-cm anterior intercostal incision.

Pain control was provided by use of non-narcotic analgesia perioperatively, intercostal nerve blocks and local anesthetic intraoperatively, and intravenous narcotic analgesia postoperatively for severe breakthrough pain. The nasogastric tube was removed on post-operative day (POD) 3 and an esophagram or CT esophagram was routinely performed on POD 4. Patients without evidence of a leak or delayed conduit emptying were advanced to a clear liquid diet. Patients were typically discharged tolerating full liquid diet and nocturnal tube feeds.

Pathology was reported by pathologists specializing in gastrointestinal pathology and according to the College of American Pathologists protocol for carcinoma of the esophagus[9]. Pathologic response and grading were routinely reported in later years of the study.

Patients followed up with their surgeon within two weeks of their discharge and were subsequently followed every 3–6 months with clinical history and physical, as well as staging CT of the chest, abdomen, and pelvis.

Data were summarized using counts and percentages, or medians and interquartile ranges, and no comparisons were performed. Demographic and preoperative data are reported for the group as a whole. Staging and pathologic outcomes are reported for patients treated for malignancy. Operative and postoperative outcomes are reported for all patients.

Results

Preoperative Characteristics

A total of 124 patients were included in the intention to treat analysis, with 50 patients from the University of Florida and 74 patients from Roswell Park Comprehensive Cancer Center. Demographic and historical details are provided in Table 1.

One hundred and twenty-one patients were treated for malignancy and the staging and pathologic details for those patients are detailed in Table 2. All lesions originated in the distal esophagus or at the gastroesophageal junction and neoadjuvant therapy was administered in 90 patients (74.4%).

Operative Outcomes

Conversions were required in five cases including three thoracotomies, and two patients required both laparotomy and thoracotomy. A total of 119 operations (96.0%) were completed both laparoscopically and thoracoscopically, and a 6-cm side-to-side linear stapled anastomosis was performed in 118 patients (95.2%). Five patients had intraoperative complications including one with splenic bleeding, one injury to the right gastroepiploic artery requiring use of a colonic conduit, one patient with ST elevation, and two patients with hypoxia on single lung ventilation.

Operative and postoperative outcomes for the intention to treat group are detailed in Table 3.

Postoperative Outcomes

Postoperative outcomes for the intention to treat group are included in Table 3. The median overall length of stay was 8 days (IQR 7–11). Sixty-four patients (51.6%) experienced at least one postoperative complication with incidence of specific complications detailed in Table 3. Early anastomotic leak within 90 days of surgery occurred in 9 patients (7.3%), although only six of these patients had undergone a 6-cm side-to-side anastomosis. All leaks were managed non-operatively with endoscopic stent placement and percutaneous drainage. Reoperation was required for an incarcerated umbilical hernia in one patient, and laparoscopic lysis of adhesions and gastropexy in four patients for conduit obstruction, and in one patient for a delayed leak at three months. Fifteen patients (12.1%) were readmitted within 30 days. Overall 30-day mortality was 0.8% and 90-day mortality was 2.5%.

A total of 118 patients underwent a side-to-side stapled intrathoracic anastomosis. In the per treatment group, six patients (5.1%) had anastomotic leaks diagnosed within 90 days of surgery. Twenty-three patients (19.5%) underwent EGD within 90 days of surgery for symptoms or conduit dilation on imaging and 6 patients (5.1%) were found to have anastomotic strictures treated with endoscopic dilation. Eighteen patients (15.3%) underwent EGD after 90 days, with anastomotic strictures diagnosed in another 3 patients (2.5%), treated endoscopically.

Pathology

Pathologic details for the 121 patients treated for malignancy are summarized in Table 2. Margin negative resections were obtained in 99 of 105 patients (94.3%), and the median nodal yield was 15.5 lymph nodes (IQR 12.0–22.0). Of 63 patients who underwent neoadjuvant therapy and had available treatment effect grading, 19.0% experienced a complete pathologic response and another 27.0% had a moderate response.

Discussion

Minimally invasive esophagectomy is a technically challenging operation associated with morbidity in approximately half of patients, and a mortality rate of 1–5% at experienced centers. It is controversial whether minimally invasive Ivor Lewis esophagectomy with an intrathoracic anastomosis is associated with more or less postoperative morbidity and mortality than a McKeown procedure with a cervical anastomosis[5, 10]. Luketich *et al.*[5]

reported a migration over time from a McKeown to an Ivor Lewis approach as experience with the operation progressed. However, their predominant anastomotic technique is with an EEA. We have long avoided this type of anastomosis due to the possibility for higher leak and stricture rates compared to other anastomotic techniques[6]. Our outcomes with a consecutive series of patients undergoing Ivor Lewis MIE with a linear stapled side-to-side intrathoracic anastomosis demonstrate lower leak and stricture rates compared to reported outcomes of alternative techniques.

Application of minimally invasive techniques to esophageal cancer has been gradually gaining favor around the world. A randomized trial comparing open to minimally invasive esophagectomy demonstrated lower rates of pulmonary infection in the MIE group, with no significant differences in margin status, nodal yield, mortality[2] or survival[11]. A recent trial comparing robotic-assisted MIE (RAMIE) to open esophagectomy showed fewer surgical and cardiopulmonary complications in the RAMIE group with equivalent pathologic and oncologic outcomes[3]. From a functional standpoint, MIE can be associated with faster recovery of quality of life[12].

A number of techniques can be utilized for MIE, including an Ivor Lewis approach with intrathoracic anastomosis and McKeown or transhiatal approaches with cervical anastomosis. Intrathoracic anastomoses are associated with a lower rate of recurrent laryngeal nerve injuries and improved functional outcomes[10, 13]. We prefer Ivor Lewis esophagectomy with an intrathoracic 6-cm side-to-side anastomosis due to our prior success with the technique. We introduced a linear side-to-side stapled technique in our practice due to promising early data that showed a lower anastomotic leak rate with thoracic compared to cervical anastomosis, both utilizing a side-to-side stapled technique (4.4% thoracic vs. 8.5% cervical)[7]. The theoretical benefits of a 6-cm side-to-side anastomosis over an end-to-end anastomosis include improved vascular supply of both the esophagus and stomach by using the sides rather than the ends for the anastomosis, larger anastomotic lumen, and smaller thoracic incisions to accomplish the linear anastomosis. Since the linear stapler does not have to be introduced separately between the ribs, the specimen can typically be removed through a 3-cm anterior incision which anecdotally decreases postoperative pain and improves postoperative respiratory function. Our postoperative clinical pathway includes assistance from nursing and physical therapists to aide patients with ambulation starting on POD 1. With use of intercostal blocks, local anesthetic, and acetaminophen, most patients require only breakthrough doses of intravenous narcotics without need for epidurals or patient controlled analgesia (PCA).

There is no clear best anastomotic technique with Ivor Lewis esophagectomy. A meta-analysis of Ivor Lewis versus McKeown MIE showed no difference in anastomotic leak rates, although did find a shorter length of stay in the Ivor Lewis group[10]. The stricture rate was found to be significantly lower in the Ivor Lewis group in a retrospective analysis of 356 patients from the Netherlands (6.2% vs. 43.8%)[13]. Reviews of side-to-side, end-to-side, or end-to-end stapling techniques for Ivor Lewis MIE showed no difference in outcomes[14, 15]. The question of the best MIE approach will be addressed in a prospective fashion by a currently accruing randomized trial comparing cervical versus intrathoracic anastomosis after MIE for esophageal cancer[16].

Previously published series of patients undergoing Ivor Lewis MIE with linear stapled anastomoses are limited. A technique paper described early results in 31 patients utilizing a 4-cm stapled anastomosis[17]. Anastomotic leak was identified in only one patient, but the stricture rate was not reported. A report from Sweden utilizing prone positioning in 46 patients and a 45-mm linear stapled anastomosis reported a 8.7% leak rate and 2.2% stricture rate[18]. Larger series are lacking with regards to technical details and complete follow up information.

In our series, intraoperative complications were rare and conversions were required in 5 patients (4.0%), which is consistent with the 4.5% rate reported by Luketich *et al.*[5] and lower than the 12% rate reported from the National Cancer Database (NCDB)[19]. Pathologic outcomes were also within expected limits with a median of 15 lymph nodes harvested and margin negative resections in 94.3% of patients, which is comparable to an average of 16.3 lymph nodes harvested and 93.9% margin negative rate reported from the NCDB[19].

Our rates of post-operative complications are also comparable to the experience reported in the literature. The rates of aspiration (11.3%), pneumonia (9.7%), and respiratory failure (11.3%) were slightly lower than the 16.3% pulmonary complication rate reported in a meta-analysis of Ivor Lewis MIE[10].

Early anastomotic leaks in patients who underwent a side-to-side intrathoracic anastomosis occurred in 6 patients (5.1%) in the current series, all managed non-operatively. One additional patient experienced a delayed leak that required reoperation three months after the index operation. The leak rate of 5.1% for intrathoracic anastomoses in the current series is lower than the 8.5% leak rate for cervical anastomoses that we have previously reported[7]. No early reoperations were required using our side-to-side anastomotic technique, more favorable than the 4.3% leak rate requiring operative intervention reported in the largest published series of 530 patients[5] using an EEA stapled anastomosis. In the current series, in those few patients who developed a leak, the large anastomotic lumen size allowed for maintenance of an adequate anastomotic opening despite the presence of a leak. Complete disruption of the stomach conduit from the esophagus was not seen. The 30-day mortality rate of 0.8% in our series is also in line with the previously reported mortality rate of 1.3% in our series including cervical side-to-side anastomosis[7], 1.0% in a meta-analysis[10], and 0.9% in patients undergoing Ivor Lewis MIE reported by Luketich *et al.*[5].

Long-term anastomotic strictures after esophagectomy requiring dilation continues to be an obstacle with a 15–30% rate reported in some series[7] and 18% in a meta-analysis of Ivor Lewis MIEs which did not differentiate between EEA versus side-to-side technique[10]. Utilizing a side-to-side linear stapled technique, we have previously reported an anastomotic stricture rate of 4.1% in a series of patients where the vast majority had undergone a cervical anastomosis[7]. Similar to our previous report, the rate of anastomotic stricture requiring endoscopic intervention within 90 days of operation in the current series was 6 patients (5.1%) with most patients requiring only one endoscopic procedure. An additional three patients (2.5%) were diagnosed with anastomotic strictures after 90 days. The stricture rate for Ivor Lewis MIE with an EEA anastomosis was not reported in the largest series previously published[5]. Although the authors involved in the current study have

collectively performed over 500 MIEs, the data reported in the current study concerns a consecutive series of patients undergoing an Ivor Lewis approach with a stapled side-to-side anastomosis. The rate of anastomotic leak and stricture reported in these patients includes those treated during the learning curve of our minimally invasive program and compares favorably to other reports in the literature. A recent study indicated that the learning curve for Ivor Lewis MIE is over 100 cases per hospital, based on trends in anastomotic leak rates[20]. As our group has now surpassed this mark for the learning curve, the leak and stricture rates would be expected to further decrease.

One limitation of this study is the lack of a comparison group but the data presented represent a realistic reflection of a real-world transition. Since the practice change was fairly abrupt, it is challenging to provide a comparison group as patients who did not undergo the preferred technique in either time period were selected due to specific indications or contraindications to the default practice.

Conclusion

In the current era, minimally invasive oncologic surgery is being widely adopted by surgeons and embraced by patients. Our experience demonstrates that an Ivor Lewis MIE with an intrathoracic 6-cm linear stapled side-to-side anastomosis can be safely performed with a high technical success rate. Early leaks occurred in 5.1% of patients, none requiring operative intervention. Anastomotic strictures were diagnosed in 5.1% and these patients required only endoscopic dilation with good outcomes.

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Table 1:

Demographic and Preoperative Characteristics

	n=124
Gender: Male	68/75 (90.7)
Race: White	71/74 (95.9)
Age (years)	66.0 [60.8,71.0]
Body mass index (kg/m^2, n=53)	28.8 [27.0,31.6]
Smoking history	54/75 (72.0)
Alcohol history	25/65 (38.5)
GERD history	33/73 (45.2)
Barrett's	18/74 (24.3)
Prior abdominal surgery	61/109 (56.0)

Reported as number (percent) or median [IQR]. If data were not available or not applicable for the entire cohort, reported as number/total (percent).
GERD, gastroesophageal reflux disease.

Table 2:

Staging and Pathologic Outcomes for Cancer Patients

	n=121
Pretherapy clinical stage	
I	20 (16.5)
II	19 (15.7)
III	52 (42.0)
IVA	9 (7.4)
Unknown	21 (17.4)
Diagnosis	
Adenocarcinoma	114 (94.2)
Squamous cell carcinoma	6 (5.0)
Adenosquamous carcinoma	1 (0.8)
Neoadjuvant Therapy	
Chemoradiation	80 (66.1)
Chemotherapy	7 (5.8)
None	31 (25.6)
Other/Unknown	3 (2.5)
Pathology	
T stage	
T0	18(14.9)
Tis	3(2.5)
T1	38(31.4)
T2	17 (14.0)
T3	44 (36.4)
T4	0
Unknown	1 (0.8)
N stage	
N0	81(66.1)
N1	25(21.4)
N2	10(6.3)
N3	2(0.9)
Unknown	3 (2.7)
Number of nodes retrieved	15.5 [12.0,22.0]
Margin negative	99/105 (94.3)
Treatment effect grade	n=63
0 (complete)	12 (19.0)
1 (moderate)	17 (27.0)
2 (minimal)	26 (41.3)
3 (poor)	4 (6.3)
Response not graded	4 (6.3)

Reported as number (percent) or median [IQR]. If data were not available for the entire cohort, reported as number/total (percent).

Table 3:

Operative and Postoperative Outcomes

	n=124
Completed minimally invasive	119 (96.0)
Side-to-side 6-cm anastomosis	118 (95.2)
EBL (mL, n=109)	150 [100,200]
Operative time (min, n=102)	463 [403,515]
Pyloric botulinum injection	80/108 (74.1)
Any postoperative complication	64 (51.6)
Delayed gastric emptying	23 (18.5)
Respiratory	
Failure requiring intubation	8 (6.5)
Failure not requiring intubation	6 (4.8)
Aspiration	14 (11.3)
Pneumonia	12 (9.7)
Pneumothorax	6 (4.8)
Arrhythmia	15 (12.1)
Anastomotic leak	9 (7.3)
RLN paresis	3 (2.4)
Pulmonary embolism	4 (3.2)
Surgical site infection	3 (2.4)
Chyle leak	2 (1.6)
Deep vein thrombosis	2 (1.6)
Reoperation	7 (5.6)
Length of stay (days)	8 [7,11]
Disposition to home	94/114 (82.5)
30-day readmission	15 (12.1)
Mortality	
30-day	1/123 (0.8)
90-day	3/122 (2.5)

Reported as number (percent) or median [IQR]. If data were not available for the entire cohort, reported as number/total (percent).

EBL, estimated blood loss; RLN, recurrent laryngeal nerve.