Minimally Invasive Ivor-Lewis Esophagectomy (MIILE): A Single-Center Experience

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Abstract With the development of minimally invasive procedures, minimally invasive Ivor-Lewis esophagectomy (MIILE) has been proposed as a safe and feasible surgical choice for the treatment of esophageal cancer. This retrospective study evaluated MIILE results from a single medical center. A total of 619 patients were selected as candidates for Ivor-Lewis esophagectomy from December 2011 to May 2015, in which 334 patients accepted MIILE and 285 patients accepted open Ivor-Lewis esophagectomy (OILE). General characteristics, surgical data, complication rates, and survival were analyzed. Differences in general characteristics between groups were not significant. Intraoperative blood loss ($P < 0.01$), postoperative volume of drainage for the first day ($P < 0.01$), time to drain removal ($P \leq 0.01$), wound infection rate ($P = 0.04$), and length of hospital stay ($P < 0.01$) were significantly reduced in the MIILE group. There were no statistically significant differences in general morbidity ($P = 0.56$), the total swept lymph nodes ($P = 0.47$), mortality ($P = 0.34$), and survival rate at 3 years ($P = 0.63$). MIILE is a safe and feasible method for the treatment of esophageal cancer, in which good outcomes were reported and some advantages were found over the open procedure.

Keywords MIILE · OILE · Thoracic anastomosis · Comparative analysis

Introduction

Esophageal cancer is the fourth most frequently diagnosed cancer. It is also the fourth leading cause of cancer death in China, ranking in the eighth place worldwide [1]. When surgical approach is selected for esophageal cancer, radical esophagectomy is the procedure of choice [2]. Traditional open esophagectomy procedures for esophageal cancer are associated with large surgical wounds and slow and painful recovery [3]. Since the introduction of minimally invasive esophagectomy, which was reported by Cuschieri and colleagues in 1992, many variations in techniques have been reported by various medical organizations [4]. Our center has been conducting minimally invasive Ivor-Lewis esophagectomy (MIILE) procedures since 2011 [5]. In order to assess its safety, feasibility, surgical characteristics, and outcomes, compared to the open approach, we retrospectively compared 334 patients who accepted MIILE and 285 patients who accepted OILE in our medical center.

Methods

The present study was approved by the Ethics Committee of Anhui Provincial Hospital. Before the operation, signed informed consent was obtained from all patients. A total of 619 patients who accepted esophagectomy from December 2011 to May 2015 were included. Inclusion criteria were the following: (1) esophageal cancer located in the middle or inferior esophagus; (2) preoperative clinical staging T:1–3, N:0–1, M:0; (3) excluded acceptance of neoadjuvant therapy; (4)

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accepted MIILE or OILE; (5) postoperatively confirmed with esophageal squamous cell carcinoma confirmation. Exclusion criteria were the following: (1) palliative surgery; (2) confirmation esophageal carcinoma other than squamous cell carcinoma; (3) incomplete medical records. After selection, clinical data of 619 patients were recorded (Table 1). Preoperative laboratory exams included routine blood examination, blood biochemistry, coagulogram, and urinalysis. Special examinations included endoscopy and biopsy, upper gastrointestinal contrast series, chest and upper-abdomen enhanced CT scan, abdominal ultrasound, electrocardiogram, heart Doppler ultrasound, and lung function test.

Surgical Technique

Laparoscopic surgery: Patients were placed in the supine position. After general anesthesia, five ports were utilized for gastric mobilization. A 10–12-mm port was placed in the inferior border of the umbilicus for the laparoscope (A). Three 5-mm ports are placed: one at the subxiphoid (E), one in the left midline clavicular line 3 cm above the umbilicus level (D), and one at the right subcostal margin (B). A 10–12-mm port was placed in the right midline clavicular line 3 cm above the umbilicus level as the principal work port (C) (Fig. 1a).

Table 1 Characteristics of patients

Characteristics	MIILE (<i>n</i> = 334)	OILE (<i>n</i> = 285)	<i>P</i> value
Age, years, mean ± SD	61.6 ± 7.1	61.8 ± 7.0	0.84
Gender			
Male	205 (61.4)	187 (65.6)	0.28
Female	129 (38.6)	98 (34.4)	
Tumor location			0.62
Middle third	197 (59.0)	174 (61.1)	
Lower third	137 (41.0)	111 (38.9)	
Preoperative smoker			0.74
Yes	139 (41.6)	123 (56.8)	
No	195 (58.4)	162 (43.2)	
Comorbidity			
Hypertension	26 (7.8)	18 (6.3)	0.53
Diabetes	13 (3.9)	15 (5.3)	0.44
COPD	11 (3.3)	10 (3.5)	1.00
Preoperative T stage			0.81
T1	85 (25.5)	79 (20.7)	
T2	128 (38.3)	105 (50.9)	
T3	121 (36.2)	101 (28.4)	
Preoperative N stage			0.32
N0	196 (58.7)	179 (62.8)	
N1	138 (41.3)	106 (37.2)	

Data are *n* (%)

MIILE minimally invasive Ivor-Lewis esophagectomy, OILE open Ivor-Lewis esophagectomy, COPD chronic obstructive pulmonary disease

The gastro-hepatic ligament was divided to expose the right crus. The gastro-esophageal junction was freed from the hiatus by dissection including phrenoesophageal ligament take down. The right gastroepiploic arcade was identified and the gastroduodenal ligament was divided along the greater curvature including the short gastric arteries.

The stomach was retracted, and the celiac and gastric nodal tissues were dissected free and left with the specimen. The left gastric artery was isolated and divided.

Then, a Heineke-Mikulicz pyloroplasty was performed.

The Kocher maneuver was performed to achieve adequate mobilization of the gastric tube, which should allow the pylorus to easily reach the right crus.

The stomach was divided above the cardias with an Endo-GIA and exteriorized through the extended subxiphoid incision (Fig. 1b) to complete the gastric tube construction with the preservation of right gastric vessels. Then, the gastric tube was stitched to the lower the esophagus with silk stitches and returned to the abdomen with a simple abdominal wall closure.

A duodenostomy was performed to facilitate postoperative feeding.

Thoracoscopic surgery: The patient was placed in the left lateral decubitus position. The position of the double-lumen tube was confirmed and the right lung was immediately isolated. The operating table was flexed to expand the intercostal spaces.

Three 10-mm ports are placed in the midaxillary line in the seventh intercostal space, between the posterior axillary and scapular line in the seventh intercostal space and in the anterior axillary line in the fourth intercostal space (Fig. 1c).

Dissection began by taking down the inferior pulmonary ligament. The mediastinal pleura were dissected along the plane between the lung and esophagus. Subcarinal lymph nodes are taken with the esophagus. Dissection was carried out to the azygos vein, which was divided with an Endo-GIA stapler. Tributaries from the thoracic duct and aorto-esophageal attachments are isolated, clipped, and divided carefully. After the azygos was divided, the vagus nerve was isolated, and the dissection was performed close to the esophagus. When the esophagus was mobilized to the desired proximal extent, the gastric tube was delivered in the chest. The proximal esophagus was dissected and divided. The specimen was obtained by extension of the anterior axillary port to 5 cm in length. Through this port, the appropriate-sized end-to-end anastomosis anvil was placed in the proximal esophagus cut edge, and the suture was placed around the anvil (Figs. 1e and d). The proximal end of the gastric conduit was opened and the tip of the stapler was delivered to the chest, gently working into the open gastric conduit, brought along the line of the greater curve distal to the opening point, attached to the anvil anastomosis created, and the open-edge of the gastric conduit is closed with an additional Endo-GIA stapler (Fig. 1f). A 28-Fr straight chest tube was placed through the camera port.

Fig. 1 **a** Location of ports for the laparoscopic approach. **b** Gastric tube extracorporeal configuration. **c** Location of ports for the thoracoscopic approach. **d** Anvil placement in the proximal esophagus. **e** Esophageal suture around the anvil. **f** End-lateral esophagogastric anastomosis in the thorax

Surgical Methods of OILE

Patients were kept in the horizontal position after general anesthesia, a median incision below the xiphoid to the umbilicus (10–15 cm) was selected, and the same operating procedures

as MIILE were realized. After the abdominal approach, the patient was moved to the left lateral decubitus position, and an anterior thoracotomy incision in the fifth intercostal space was performed. The same surgical procedures as MIILE were carried out.

Fig. 2 Survival rate after esophagectomy

Statistical Analysis

Statistical analysis was conducted with SPSS 20.0 software (SPSS, Chicago, IL, USA). χ^2 and t test were used to compare groups with 95 % confidence interval. $P < 0.05$ was considered statistically significant. Cox-Meier regression test was used to analyze survival rates.

Results

From December 2011 to May 2015, 619 patients accepted Ivor-Lewis esophagectomy in our center, including 334 patients who underwent MIILE and 285 patients who underwent OILE. General characteristics such as age, gender, comorbidities, tumor location, smoking history, and preoperative TNM stage had no statistical difference (Table 1). Operation time, intraoperative blood loss, total lymph nodes dissected, first day postoperative drainage volume, time to chest drain removal, length of hospital stay, paregoric use after operation, postoperative stage, and 1-, 2-, or 3-year survival rate after operation were recorded (Table 2). Post-surgical complications are recorded in Table 3.

In the MIILE group, the operation in five patients was changed from the thoroscopic approach to thoracotomy for chest compact adhesion (two patients), trachea laceration (one patient), pre-cava bleeding (one patient), and anastomotic bleeding (one patient).

Two cases for laparoscopic surgery were changed to laparotomy, including one case for splenic arterial bleeding and one case secondary to left gastric arterial bleeding.

The difference in operation time, total lymph nodes dissected, postoperative case staging, and 3-year survival rate between the MIILE and OILE groups was not statistically significant.

However, the difference in blood loss, postoperative first day drain volume, postoperative analgesics use, chest drain removal, and length of hospital stay was statistically significant, in which better results were observed in the MIILE group.

Concurrent pulmonary and wound infection were significantly reduced in the MIILE group ($P = 0.02$ and $P = 0.04$, respectively). Postoperative concurrent chylothorax slightly increased compared with the OILE group but was not statistically significant; while the difference in anastomotic fistula, anastomotic bleeding, chest internal hemorrhage, heart rate abnormality, injury of recurrent nerve, delayed gastric emptying, incisional hernia, and death during the perioperative period in both groups was not statistically significant (Table 3).

Average postoperative follow-up time was 26 months (range, 1–47 months), in which 334 patients were from the MIILE group (11 patients lost follow-up) and 285 patients were from the OILE group (14 patients lost follow-up).

Survival at 1 year was 99 % for MIILE and 99 % for OILE; survival at 2 years was 96 % for MIILE and 97 % for OILE; survival at 3 years was 90 % for MIILE and 89 % for OILE; and median survival time was 43.5 months for MIILE and 42.8 months for OILE ($P = 0.631$).

Discussion

Esophagectomy could be a life-saving procedure for esophageal cancer or end-stage functional disorders, with the open procedure as the standard of care for esophageal resections [6]. A 10-year systematic review of open esophagectomy experience in the Veterans Affairs system reports a morbidity of 50 % and a mortality of 10 % [7]. For this reason, since the first total laparoscopic esophagectomy documented by De Paula in 1996, many studies have compared the results of open vs. laparoscopic esophagectomy, with good results favoring the laparoscopic approach [8, 9]. In 2000, Nyugen et al. compared minimally invasive esophagectomy with open transthoracic and transhiatal esophagectomy; reporting shorter operation times, less blood loss, and shorter ICU stays for the first one, with no increase in morbidity or mortality [10]. Other reports of minimally invasive chest surgery revealed some advantages over open procedures including small wounds, less pain, faster operative recovery, and lower occurrence of complications [11]. However, the popularity of MIILE continues to spread [12–15], especially for the longer learning curve and technology required. Most T4 esophageal cancers are not amenable to open or minimally invasive surgery, but all other T stages are potentially amenable to minimally invasive esophagectomy in experienced hands [6].

At present, most thoracic surgeons prefer to apply open esophagectomy or a hybrid technique with extracorporeal anastomosis [11]. However, we believe that the method used by our group with extracorporeal phases has the following advantages: (1) avoids the cervical approach and cervical esophagus dissection; (2) reduces recurrent laryngeal nerve injury risk; (3) allows a tension free anastomosis; (4) simplifies gastric tube fashioning with an extracorporeal step; (5) uses abdominal incision to place the duodenal feeding tube during operation, avoiding percutaneous endoscopic jejunostomy.

In this study, we confirm a statistically significant reduction in bleeding, postoperative drainage time, and length of hospital stay in the MIILE group. These data reaffirms the main characteristics of minimally invasive esophagectomy, including smaller trauma and faster recovery, as other similar studies [12–16].

In the complications analysis, the MIILE group presented with reduced incidence of postoperative pneumonia (33 patients in the MIILE group vs. 61 patients in the OILE group, $P = 0.02$) and reduced incidence of wound

Table 2 Intraoperative and postoperative surgical data

Characteristics	MIILE (<i>n</i> = 334)	OILE (<i>n</i> = 285)	<i>P</i> value
Mean operating time (minutes)	251.2 ± 26.4	240.1 ± 26.4	0.74
Blood loss (ml)	178.0 ± 55.0	181.1 ± 64.8	<0.01
Total lymph nodes dissected	20.3 ± 4.1	20.6 ± 3.9	0.47
Postoperative first day drain volume (ml)	246.6 ± 61.0	268.2 ± 75.4	<0.01
Postoperative analgesic (times)	9.5 ± 2.6	13.8 ± 6.8	<0.01
Chest drain removal (day)	12.0 ± 3.7	13.0 ± 4.0	<0.01
Length of hospital stay (day)	12.9 ± 3.9	14.0 ± 4.0	<0.01
Postoperative stage			0.61
IA	39 (11.7 %)	29 (10.2 %)	
IB	65 (19.5 %)	42 (14.7 %)	
IIA	104 (31.1 %)	93 (32.6 %)	
IIB	85 (25.4 %)	76 (26.7 %)	
IIIA	37 (11.1 %)	40 (14.0 %)	
IIIB	4 (1.2 %)	5 (1.8 %)	
Mean survival time (months)	43.5 ± 0.6	42.8 ± 0.6	0.63
1-year survival	99 %	99 %	0.51
2-year survival	96 %	97 %	0.42
3-year survival	90 %	89 %	0.69

Data are *n* (%)

MIILE minimally invasive Ivor-Lewis esophagectomy, OILE open Ivor-Lewis esophagectomy

infection (one patient in the MIILE group vs. 12 patients in the OILE group, *P* = 0.04). Some factors that influence these results include the following: (1) avoidance from the influence of thoracotomy on lung function; (2) reduction in damage of thoracic wall muscles; (3) reduction in postoperative incision pain (use of postoperative analgesics

after operation in the MIILE group was less than in the OILE group); which become beneficial to postoperative expectoration [17]. In other complications of esophagectomy, there was no statistical difference between both groups. Postoperative anastomotic fistula in esophagectomy has been a serious complication and is also one of the

Table 3 Postoperative complications

Complications	MIILE (<i>n</i> = 334)	OILE (<i>n</i> = 285)	<i>P</i> value
Total complications	92 (27.5 %)	133 (46.7 %)	0.56
Pneumonia	33 (9.9 %)	61 (21.4 %)	0.02
Wound infection	1 (0.3 %)	12 (4.2 %)	0.04
Chylothorax (reoperation)	4 (1.2 %)	2 (0.7 %)	1.00
Chylothorax (without reoperation)	5 (1.5 %)	5 (1.6 %)	1.00
Anastomotic leak	14 (4.2 %)	12 (4.2 %)	1.00
Anastomotic hemorrhage (reoperation)	2 (0.6 %)	2 (0.7 %)	0.61
Anastomotic hemorrhage (without reoperation)	4 (1.2 %)	3 (1.1 %)	0.61
Thoracic hemorrhage (reoperation)	3 (0.9 %)	2 (0.7 %)	1.00
Arrhythmia	10 (3.0 %)	15 (5.3 %)	0.47
Recurrent laryngeal nerve damage	8 (2.4 %)	10 (3.5 %)	1.00
Functional delayed gastric emptying	5 (1.5 %)	3 (1.1 %)	0.72
Ventral incisional hernia	0 (0)	2 (0.7 %)	0.34
Sudden death	3 (0.9 %)	4 (1.4 %)	0.34

Data are *n* (%)

MIILE minimally invasive Ivor-Lewis esophagectomy, OILE open Ivor-Lewis esophagectomy

main causes of death [18]. In this study, there was no difference in anastomotic fistula (14 patients in the MIILE group vs. 12 patients in the OILE group, $P=1$) or chylothorax incidence ($P=1$) between the MIILE and OILE groups.

Lymph node dissection can provide more accurate pathological staging and prognosis for patients. Some previous studies have reported that there was no obvious difference in the range of lymph node dissection between minimally invasive esophagectomy and open operations [19]. In this study, all patients in both groups underwent two-field lymph node dissection. The difference in the number and range of lymph node dissection between these both groups was not statistically significant ($P=0.47$). We believe laparoscopy and thoracoscopy allows us to clearly expose lymph nodes and other tiny structures such as recurrent laryngeal nerves, offering better tissue dissection and reducing the incidence of associated complications; although the difference in laryngeal recurrent nerve injury in both groups was not statistically significant ($P=1$).

Three and four patients died in the MIILE and OILE groups, respectively; and the difference was not statistically significant. In the MIILE group, two patients died for anastomotic and tracheal fistula, and one died for pneumonia. In the OILE group, two patients died for pneumonia, one patient died for anastomotic fistula combined with empyema, and one patient died for anastomotic fistula combined with aortic hemorrhage. In the long-term survival rate at 1 (99 % for MIILE and 99 % for OILE), 2 (96 % for MIILE and 97 % for OILE), and 3 years (90 % for MIILE and 89 % for OILE), the difference between both groups was not statistically significant ($P=0.63$, Fig. 2). This result is consistent with reports in previous studies [20–22]; thus, MIILE would not impact long-term survival rates.

Conclusion

MIILE has the same operative effects, lymph node dissection scope, and long-term survival rates as open esophagectomy; and this technique reduces pulmonary infection, wound complications, bleeding during operation, postoperative drainage time, and length of hospital stay. Therefore, MIILE is a safe and feasible minimally invasive surgery with some advantages, compared to the open approach in appropriately trained groups.

Compliance with Ethical Standards

Conflicts of Interest The authors declare that they have no conflict of interest.

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