#### ORIGINAL ARTICLE

# Comparison of perioperative outcomes between open and minimally invasive esophagectomy for esophageal cancer

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#### Keywords

Esophageal cancer; esophagectomy; laparoscopy; thoracoscopy.

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#### Abstract

**Background:** To compare surgical outcomes of thoracoscopic and laparoscopic esophagectomy with open esophagectomy in order to study the learning curve of minimally invasive surgery for esophageal cancers.

**Methods:** Among 109 esophageal cancer patients retrospectively studied, 59 patients underwent minimally invasive esophagectomy (MIE) and 50 underwent open surgery (OE). In the MIE group, the first 30 patients received hybrid procedures, including 16 thoracoscopic esophagectomies and 14 laparoscopic maneuvers. The later 29 patients received thoraco-laparoscopic esophagectomy (TLE).

**Results:** The overall morbidity of MIE and OE was 42.4% (25/59) and 44.0% (22/50), respectively, with no statistical difference. However, the MIE group had a significantly lower incidence of functional complication (1.79%, 1/59) than the OE group (32.0%, 16/50, P < 0.01). The technical complication rate was not significantly different between the two groups (14/59, 23.7% vs. 6/50, 12.0%, P = NS), nor was the overall complication rate between the 30 early period cases and the 29 later cases (P = NS); although the later cases had TLE and there was no recurrent laryngeal nerve injury.

**Conclusion:** Minimally invasive approaches may help to decrease the risk of functional complication but not technical problems, after esophagectomy. For esophageal cancer patients to benefit from this minimally invasive surgery, an extended learning curve is necessary to avoid technical problems, such as anastomotic leakage and recurrent laryngeal nerve palsy.

### Introduction

China has a high incidence of esophageal carcinoma, with a mortality rate ranking fourth of all malignant tumors. Complete resection remains the only chance of cure, and subtotal esophagectomy with systematic lymphadenectomy has been recognized as a standard procedure for esophageal cancers. Traditionally, this is achieved through Ivor-Lewis or McKeown approaches and is associated with significant morbidity. The mortality rate from experienced centers has been reported to be in the range of 6–7%, and in low-volume centers it may be as high as 23%.<sup>1</sup> With the improvements in videoscopic surgery, minimally invasive esophagectomy has gained more and more attention in recent years. We hereby compare clinical data and perioperative morbidity after open esophagectomy (OE) and minimally invasive esophagectomy (MIE) and analyze the learning curve of MIE at our institute.

### **Material and methods**

Between 1 January 2012 and 30 June 2013, 59 patients with esophageal cancer received MIE at the Shanghai Chest Hospital, while 50 matched OE patients were chosen as the control (including 1 case converted from MIE to open surgery as a result of dense peritoneal adhesion). Histological diagnosis of esophageal cancers was confirmed by esophagoscopy in all patients prior to surgery. Preoperative work-up included chest and abdominal computed tomography scans, upper gastrointestinal barium swallow, cervical ultrasonography, and positron emission tomography or single photon emission computed tomography scans. Only patients with a clinical stage of T3N1M0 (IIIa) or lower were considered surgical candidates; otherwise they were given induction chemotherapy or chemoradiation.

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 Table 1
 Demographic and tumor characteristics

	MIE	OE	<i>P</i> value
Number of patients	59	50	
Gender (male/female)	44/15	37/13	NS
Mean age (year)	61.5	60.2	NS
Comorbidity (n/%)	16/37.25	24/48%	NS
T stage $(T_{1-2}/T_3)$	45/14	20/30	<0.05

MIE, minimally invasive esophagectomy; OE, open surgery.

All patients received subtotal esophagectomy with systematic lymphadenectomy. In the MIE group, there were 16 cases of thoracoscopic esophagectomy (TE) with laparotomy, 14 cases of laparoscopic esophagectomy (LE) with open thoracotomy, and 29 cases of combined thoracoscopiclaparoscopic esophagectomy (TLE). Thoracoscopic positions included lateral decubitus and lateral semi-prone (60° forward), according to the surgeons' preference. In all laparoscopic cases, a small subxiphoid incision was used to make a gastric tube for reconstruction. In the MIE group, esophagogastric anastomosis was accomplished in the neck by circular stapler or hand suture. Only one case was converted to open surgery because of dense peritoneal adhesion. In the OE group, 32 cases underwent Ivor-Lewis and 18 cases underwent McKeown procedures.

Perioperative mortality and morbidity were compared between the two groups. Postoperative complications were divided into two types: functional complications and technical complications. The former referred to those not directly related to surgical maneuvers, including arrhythmia, pulmonary infection, acute lung injury (ALI), ileus, acute renal failure or acute hepatic failure. Technical complications included those related directly to surgery, such as perioperative bleeding, chylothorax, recurrent laryngeal nerve palsy (RLNP), and anastomotic leakage.

Statistical analysis was performed using SPSS version 17.0 for windows (SPSS Inc., Chicago, IL, USA). Continuous and categorical data were analyzed by  $\chi^2$  test and *t* test, respectively. All *P* values were two-sided and only those less than 0.05 was considered statistically significant.

#### Results

Apart from one basal cell, one neuroendocrine, and one adenocystic carcinoma, all 106 patients had squamous cell carcinoma. Sixteen tumors were located in the upper, 59 in the middle, and 34 in the lower thoracic portion. The MIE and OE groups were comparable in gender, age, or preoperative comorbidities (hypertension, chronic obstructive pulmonary disease, diabetes, obesity, malnutrition, arrhythmia, etc.); however, the MIE group had a higher rate of early-stage patients (T1-2) (see Table 1).

The overall morbidity rate was 43.1% (47/109), with 42.4% (25/59) for the MIE and 44% (22/50) for the OE group

**Table 2** Comparison of recurrent laryngeal nerve injury (P = NS)

	Number of patients	Number of RLNP (%)
MIE group	59	5 (8.5%)
OE group	50	3 (6%)
TE + TLE	45	5(11.1%)
LE + OE	64	3 (4.7%)

LE, laparoscopic esophagectomy; MIE, minimally invasive esophagectomy; OE, open surgery, RLNP, recurrent laryngeal nerve injury; TE, thoracoscopic esophagectomy; TLE, thoracoscopic-laparoscopic esophagectomy.

(P = NS). Only one patient (1.7%) in the MIE group had a functional complication (atrial fibrillation on the first postoperative day). In contrast, 16 patients (32.0%) experienced functional morbidities after OE, including 10 atrial fibrillations, two ALI, one atrial fibrillation combined with ALI, one ileus, one acute renal failure, and one acute hepatic failure. The incidence of functional complications was significantly lower in the MIE than in the OE group (P < 0.01).

Technical complications occurred in 14 patients (23.7%) in the MIE group, including five RLNP, 14 anastomotic leakages (2 of them required subsequent surgery), and one substernal bleeding (requiring subsequent surgery). There were six cases (12.0%) of technical complications in the OE group, including three RLNP, one intrathoracic anastomotic leakage (mended by subsequent surgery), and two cervical leakages. There was no significant difference in incidences of technical complication between the two groups (P = NS). No chylothorax occurred in either group. All patients were managed successfully. There was no in-hospital mortality in this series.

Because the two most common types of technical complications were RLNP and anastomotic leakage, they were analyzed separately. The rate of RLNP was slightly higher in the MIE group than in the OE group, but no statistical significance was observed. The rate of RLNP in patients receiving thoracoscopy (TE or TLE) was 11.1% (5/45). It was higher than the 4.7% (3/64) of RLNP in patients receiving open thoracotomy (LE or OE); however, the difference was not statistically significant (P = NS, Table 2). The leakage rate in the MIE group was significantly higher than in the OE group, while there was no significant difference among the three MIE sub-groups (TE, LE, and TLE, Table 3).

According to the operation date, MIE patients were further divided into the early (30 cases) and the later groups (29 cases) in order to study the learning curve. All TE and LE cases were in the early group, while all patients in the later group had TLE. There was no significant difference (P = NS) in either functional (3.3% vs. 0) or technical complications (8, 27.6% vs. 14, 46.7%). However, all five cases of RLNP were in the early group (16.7% vs. 0, P < 0.05).

Table 3 Comparison of anastomotic leakage

	Number of patients	Number of Leaks (%)
OE group†	50	6 (12%)
MIE group	59	14 (23.7%)
TE	16	3 (18.8%)
LE	14	3 (21.4%)
TLE	29	8 (27.6%)

+MIE versus OE, P < 0.05. LE, laparoscopic esophagectomy; MIE, minimally invasive esophagectomy; OE, open surgery; TE, thoracoscopic esophagectomy; TLE, thoracoscopic-laparoscopic esophagectomy.

### Discussion

Our results suggest that overall morbidity and mortality were comparable after MIE or OE. There were less functional complications after MIE than after OE. Technical complications were similar between the two groups; however, the MIE group needed more secondary intervention to manage technical complications. These results were consistent with a report by Mamidanna *et al.*, in which they investigated the short-term outcomes following open *versus* minimally invasive esophagectomy in England, and also found that MIE might help decrease functional morbidity, but not technical problems.<sup>2</sup>

Standard Ivor-Lewis or McKeown esophagectomy are extensive procedures associated with a high incidence of functional complications, especially acute lung injury and cardiac arrhythmia. In fact, pulmonary complications are the leading cause of in-hospital mortality after open esophagectomy. With the help of minimally invasive techniques, this scenario has gradually changed. Kinjo et al. reported that MIE might decrease the occurrence of functional complications.<sup>3</sup> Zingg et al. also observed that the risk of pulmonary infection and respiratory failure was significantly lower after MIE than after OE.<sup>4</sup> Luketich et al. retrospectively reviewed a large series of 222 MIE cases.<sup>5</sup> There were 12.5% cardiopulmonary complications and the mortality rate was 1.4%. However, in their historical control of OE, the rate of cardiopulmonary complication was as high as 37%.6 In our study, the incidence of functional complication in the MIE group was significantly lower than in the OE group (1.7% to 32.0%, P < 0.01). There was no pulmonary complication and only one atrial fibrillation, in contrast to three ALI and 11 atrial fibrillations in the OE group. Apart from the decreased size of the incisions, two other factors may have contributed to the diminished adverse impact of esophagectomy on patients' cardiopulmonary system. First, contusion of lung parenchyma is spared in the case of MIE, as traction of the right lung is no longer necessary. Second, in total thoracoscopic surgery, rib spread is avoided so that incisional pain is significantly reduced. Consequently, other functional morbidity may also be decreased as a result of improved cardiopulmonary stability after MIE.

Unlike the results reported by Mamidanna et al., we failed to detect a significant difference between the rates of technical complication after MIE or OE, although more patients in the MIE group required secondary intervention because of technical problems.<sup>2</sup> MIE is a modification of OE, intended to diminish surgical trauma. There is no way for MIE to decrease technical complications related to esophagectomy and associated lymph node dissection and reconstruction of the gastrointestinal tract, such as anastomotic leakage, RLNP, and chylothorax. On the contrary, the risk of increased technical problems when applying a new procedure is not uncommon, even in high volume centers where surgeons are experienced in the technique of OE. In the current study, the rate of anastomosis leakage in the MIE group was 23.7%, significantly higher than in the OE group (12%, P < 0.05). Similar findings have been reported in previous studies, and were contributed to the adverse impact on submucosal blood supply of the stomach, caused by forceps grasping during laparoscopic maneuver.<sup>7-9</sup> We did not find a decrease in the rate of leakage between the two time periods. Lin et al. reported their retrospective experience of MIE and suggested that the learning curve of MIE required at least 40 cases.<sup>10</sup> All patients in the later period received total thoracoscopic laparoscopic esophagectomy versus hybrid procedures in the early phase of the study, either TE with laparotomy or open thoracotomy with laparoscopy. Our data showed no significant difference between the two groups regarding RLNP (8.5% vs. 6.0%, P >0.05). Nonetheless, when lymphadenectomy at superior mediastinum was performed via thoracoscopy, the rate of RLNP (TE + TLE, 11.1%) was significantly higher than in the thoracotomy group (LE +OE, 4.7%, P < 0.05), as has been reported in previous studies.<sup>6,8</sup> However, all RLNP in the thoracoscopic group occurred in the earlier time period of our series (16.7%), with no further RLNP in the later period. No chylothorax occurred in any of our patients. The thoracic duct was exposed during surgery and carefully examined at the end of thoracic maneuvers in both MIE and OE. The magnifying effect of thoracoscopy provided better exposure and identification of the thoracic duct in the case of MIE. Therefore, the incidence of chylothorax in our study was lower than previously reported.6

#### Conclusion

In conclusion, our initial experience shows that MIE is safe and feasible for early stage esophageal cancers. It helps to reduce the risk of functional complication, especially cardiopulmonary morbidities associated with this extensive procedure. However, the learning curve of MIE is comparatively long and it is less likely for MIE to decrease technical problems associated with lymph node dissection and reconstruction of the digestive tract, even in experienced hands. Consequently, further attention should be paid to prevent technical problems, especially the risk of anastomotic leakage and recurrent laryngeal nerve injury, in order for minimally invasive techniques to fully benefit patients with esophageal cancer.

# Disclosure

No authors report any conflict of interest.

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