Thoracic Cancer

Open Access

Thoracic Cancer ISSN 1759-7706

ORIGINAL ARTICLE

Comparison of short-term outcomes and three year survival between total minimally invasive McKeown and dual-incision esophagectomy

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Keywords
Complication; dual-incision; minimally invasive surgery; survival.

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Received: 19 August 2016;
Accepted: 7 October 2016.

doi: 10.1111/1759-7714.12404

Thoracic Cancer **8** (2017) 80–87

Abstract

Background: The aim of this study was to compare the short-term outcomes and three-year survival between dual-incision esophagectomy (DIE) and total minimally invasive McKeown esophagectomy (MIME) for esophageal cancer patients with negative upper mediastinal lymph nodes requiring esophagectomy and neck anastomosis.

Methods: One hundred and fifty patients underwent DIE, while 361 patients received total MIME. Perioperative outcomes and three-year survival were compared in unmatched and propensity score matched data between two groups.

Results: Both unmatched and matched analysis demonstrated that there were no significant differences in the number of lymph nodes harvested, or major or minor complication rates between the DIE and MIME groups. Compared with patients who underwent DIE, patients who underwent total MIME had longer operation duration (310 minutes vs. 345 minutes; $P = 0.002$). However, there was significantly less intraoperative blood loss in the total MIME compared with the DIE group (191 mL vs. 287 mL, respectively; $P < 0.001$). Kaplan-Meier analysis demonstrated a trend that patients who underwent MIME had longer overall (79.5% vs. 64.1%; $P = 0.063$) and disease-free three-year survival (65.3% vs. 82.8%; $P = 0.058$) compared with patients who underwent DIE.

Conclusions: Both total MIME and DIE are feasible for the surgical treatment of esophageal cancer patients with negative upper mediastinal lymph nodes requiring esophagectomy and neck anastomosis. However, MIME was associated with better overall and disease-free three-year survival compared with DIE.

Introduction

It is estimated that 455 800 new esophageal cancer (EC) cases and 400 200 deaths occurred in 2012 worldwide.[1] China has the highest incidence and death from EC in the world, with rates of 21.62 per 100 000 person-years and 16.25 per 100 000 person-years in 2011, respectively.[2] Surgery remains the main treatment modality for resectable carcinoma of the esophagus.[3–5]

The choice of surgical approach is based not only on the location of the lesion, allowing complete planned intervention, but also the specific character of surgical trauma taking into account the patient's functional status.[3] There are two main approaches for middle and lower third EC: Ivor Lewis and Sweet. An international survey on EC showed that Ivor Lewis was the most commonly used approach in Western countries, while the Sweet approach was the most common in China.[6,7] For middle and upper third EC, the open McKeown approach is the most commonly used approach, with the advantage of complete resection of the esophagus and regional lymph nodes (LNs), which may improve long-term; although the overall perioperative complication rate and pulmonary complications using the McKeown approach are over 45% and 20%, respectively.[8] Recently, a study showed that minimally invasive McKeown esophagectomy (MIME) was superior to open McKeown esophagectomy with reduced estimated intraoperative blood loss, despite comparable short-term and long-term survival.[9]

For EC patients with enlarged LNs in the upper mediastinum who are in need of an esophagectomy, the Ivor Lewis and McKeown are both reasonable approaches. However, for EC patients with negative upper mediastinal LNs who are in need of esophagectomy, there is debate over the optimal approach. For example, a recent study comparing right and left transthoracic approaches on the survival of patients with LN negative esophageal squamous cell carcinoma demonstrated that the left transthoracic approach is superior to the right in terms of surgical and oncological outcomes.[10]

Dual-incision esophagectomy (DIE) has been used as an alternative approach for McKeown esophagectomy in our hospital for EC patients with negative LNs in the upper mediastinum.[11] Recently, Yu *et al.* reported that DIE through the left chest and neck achieved comparable short-term outcomes and long-term survival compared with Ivor Lewis esophagectomy.[12] However, no studies have been conducted to compare the outcome between MIME and DIE for EC patients with negative LNs in the upper mediastinum requiring esophagectomy and neck anastomosis. Therefore, the aim of this study was to summarize the surgical results between DIE and total MIME for EC patients with negative LNs in the upper mediastinum in our center.

Methods

The study included 115 consecutive patients who underwent DIE between January 2005 and October 2015 and 361 patients who received total MIME between January 2009 and July 2015 in the Department of Thoracic Oncologic Surgery in our hospital. Preoperative staging work-up included chest computed tomography (CT), abdominal ultrasonography, head CT, and bone scan. A positron emission tomography (PET)/CT scan is not included in the preoperative workup because medical insurance does not cover the expense. Patients with enlarged LNs in the upper mediastinum or with incomplete data were excluded.

The institutional review board of our hospital approved the study. The procedures followed were in accordance with ethical standards for human experimentation and with the Helsinki Declaration of 1975, as revised in 2000.

The clinical variables included age, gender, body mass index (BMI), Charlson score, use of neoadjuvant therapy, tumor location, duration of surgery, estimated intraoperative blood loss, number of harvested LNs, differentiation, American Joint Committee on Cancer (AJCC) stage, postoperative morbidity rate, length of hospital stay, locoregional and distant recurrence, and three-year overall survival (OS) and disease-free survival (DFS). All patients were diagnosed with squamous cell carcinoma by postoperative pathology.

In 2012, a randomized, controlled trial of neoadjuvant treatment showed survival benefit in locally advanced EC compared with esophagectomy alone.[13] Since then, we have adopted chemotherapy or chemoradiotherapy as an alternative for locally advanced EC.

A Charlson comorbidity index (CCI) was determined according to Charlson *et al.*'s definition.[14] EC staging was assessed according to 2009 AJCC staging.[15] Postoperative complications were recorded based on international consensus on the standardization of data collection for complications associated with esophagectomy.[16,17] Nine categories of complications were included: pulmonary, cardiac, gastrointestinal, urologic, thromboembolic, neurologic/psychiatric, infection, wound/diaphragm, and other. The major and minor complication data were scored using Clavien–Dindo classification.[18] OS was calculated from the day after surgery, while DFS was calculated from the day after surgery to the last follow-up without evidence of residual and metastatic cancer.

For EC patients with no enlarged LNs in the upper mediastinum, both DIE involving left transthoracic and neck incison and McKeown approaches are acceptable in our medical center, as long as the primary lesion and LNs can be completely removed. Young patients with good functional status tend to be treated using the McKeown approach, while older patients with poor functional status undergo dual incision.

Surgical technique

Dual-incision esophagectomy (DIE)

Dual-incision esophagectomy includes the left posterolateral thoracotomy incision and left neck anastomosis. The left transthoracic procedure is similar to the Sweet approach. First, the tumor in the thoracic esophagus is mobilized and then the diaphragm is cut, which liberates the stomach. The stomach is then pulled to the neck, and an anastomosis is performed through the left neck incision. Thoracic and abdominal LN dissections are routinely performed; however, pyloroplasty and cervical LN dissection are not routinely performed.[11]

Total minimally invasive McKeown esophagectomy (MIME)

The details of total MIME have been described in our previous study.[9,19,20] In short, the patient is placed in the left lateral decubitus position. Four thoracoscopic ports are established. The thoracic esophagus, along with the periesophageal tissue and mediastinal LNs, is circumferentially mobilized from the diaphragm to the level of inlet of the thorax. Mediastinal lymphadenectomy is performed in every patient, including the left recurrent and right subclavian, paratracheal, subcarinal, left and right bronchial, lower posterior mediastinum, para-aortic, and para-esophageal LN regions. The chest is inspected closely, and hemostasis is verified. A chest tube is routinely placed. The patient is then placed in a supine position. A pneumoperitoneum (12–14 cm H_2O) is established by CO_2 injection through an umbilical port. A total of five abdominal ports (three 5 mm and two 10 mm) are used. The stomach is mobilized and the abdominal/distal esophagus is dissected as far as possible toward the distal end. The gastric conduit is then made extracorporeally. Pyloroplasty or gastric drainage procedures were not routinely performed in our study and a feeding jejunostomy tube was not created. Instead, we inserted a duodenal nutrition tube before anastomosis. The abdomen is inspected to make sure that hemostasis is adequate and the incisions are closed. After the laparoscopic and thoracoscopic phases, a 4–6 cm horizontal neck incision is made. The cervical esophagus is exposed. After the specimen is removed from the field, an anastomosis is performed between the cervical esophagus and gastric tube using standard techniques (mechanical stapled or handsewn anastomosis in an end-to-side fashion).

Statistical analysis

SPSS version 16.0 (SPSS Inc., Chicago, IL, USA) was used for statistical analysis. Data were presented as mean value ± standard deviation for continuous variables and percentages for dichotomous variables. Continuous variables were analyzed using the *t*-test, and categorical variables were analyzed using Fisher's exact test. We first performed overall unmatched analysis for all patients. We then conducted propensity score matching analysis according to Austin's technique.[21] For propensity score matching analysis, we first created a logistic regression model that calculated matched propensity scores using the approach (MIME or DIE) as an outcome with age, gender, BMI, CCI, tumor location, and neoadjuvant radiotherapy and/or chemotherapy. Patients with scores lower than 0.10 (high chance of undergoing DIE) and higher than 0.90 (high chance of undergoing MIME) were excluded. We reported the absolute difference for variables after matching rather than statistical significance testing. We then performed analysis for all matched patients. Survival rates were estimated using the Kaplan–Meier method and log-rank tests were used to analyze differences between curves. Statistical significance was set as $P < 0.05$.

Results

Clinical characteristics

Compared with patients who underwent DIE, patients who underwent total MIME were older (57.41 ± 8.56 vs. 59.88 ± 7.94; $P = 0.005$), more often had middle third EC (49.6% vs. 67.9%; $P < 0.001$), and had low BMI (23.76 ± 2.35 vs. 23.16 ± 2.86; $P = 0.025$). There were no significant differences in gender, CCI, and neoadjuvant therapies between the groups (Table 1).

Perioperative outcomes of patients

Compared with patients who underwent DIE, patients who underwent total MIME had longer surgical duration (310 minutes vs. 353 minutes; $P < 0.001$) and greater hospital expenses (¥65 600 vs. ¥103 000; $P < 0.001$). However, there was significantly less intraoperative blood loss (208 mL vs. 287 mL; $P < 0.001$) in the total MIME group compared with the DIE group. There were no significant differences in the number of LNs harvested, major or minor complication rates, and the length of hospital stay between the groups (Table 2).

Table 1 Preoperative features of patients underwent esophagectomy

Clinical variables	Total MIME (*n* = 361)	DIE (*n* = 115)	*P*
Age (years)	59.88 ± 7.94	57.41 ± 8.56	0.005
Male (%)	286 (79.2)	93 (80.9)	0.703
Body mass index (kg/m^2)	23.16 ± 2.86	23.76 ± 2.35	0.025
Charlson comorbidity index	0.34 ± 0.82	0.29 ± 0.71	0.529
Location (%)			<0.001
Upper third	74 (20.5)	48 (41.7)	ND
Middle third	245 (67.9)	57 (49.6)	ND
Lower third	42 (11.6)	10 (8.7)	ND
Neoadjuvant CT and/or RT (%)	33 (9.1)	5 (5.2)	0.182

CT, chemotherapy; DIE, dual incision esophagectomy; MIME, minimally invasive McKeown esophagectomy; ND, no data; RT, radiotherapy.

Table 2 Postoperative features of patients who underwent esophagectomy

Clinical variables	Total MIME (*n* = 361)	DIE (*n* = 115)	*P*
Duration of surgery (min)	353 ± 101	310 ± 75	<0.001
Estimated blood loss (mL)	208 ± 169	287 ± 76	<0.001
Number of lymph nodes harvested	24 ± 11	23 ± 11	0.366
T category (%)			<0.001
T0–1	89 (24.7)	36 (31.3)	ND
T2	115 (31.9)	15 (13.0)	ND
T3	145 (40.2)	30 (26.1)	ND
T4	12 (3.3)	34 (29.6)	ND
N category (%)			<0.001
N0	218 (60.4)	106 (92.2)	ND
N1	107 (29.6)	8 (7.0)	ND
N2	24 (6.6)	0	ND
N3	12 (3.3)	1 (0.9)	ND
Differentiation (%)			0.308
Well differentiated	35 (9.7)	17 (14.8)	ND
Moderately differentiated	223 (61.8)	66 (57.4)	ND
Poorly differentiated	103 (28.5)	32 (27.8)	ND
AJCC staging (%)			0.037
Stage 0	1 (0.3)	2 (1.7)	ND
Stage I	90 (25.0)	33 (28.7)	ND
Stage II	173 (47.9)	40 (34.8)	ND
Stage III	97 (26.9)	40 (34.7)	ND
Complications (%)			
Major	19 (5.3)	4 (3.5)	0.437
Minor	55 (15.2)	17 (14.8)	0.906
Pulmonary complications (%)	11 (3.0)	4 (3.5)	0.818
Cardiac complications (%)	1 (0.3)	0	0.572
Gastrointestinal complications (%)	52 (14.4)	12 (10.4)	0.277
Neurologic/psychiatric complications (%)	1 (0.3)	0	0.572
Infection (%)	1 (0.3)	2 (1.7)	0.084
Wound/diaphragm complications (%)	13 (3.6)	8 (7.0)	0.127
Other complications (%)	4 (1.1)	2 (1.7)	0.597
Mortality (%)	9 (2.5)	3 (2.6)	0.6945
Length of hospital stay (days)	21 ± 12	23 ± 11	0.073
Hospital expenses (¥)	103 000 ± 27 932	96 200 ± 31 784	<0.001

AJCC, American Joint Committee on Cancer; DIE, dual incision esophagectomy; MIME, minimally invasive McKeown esophagectomy; ND, no data.

Propensity score matching results

In order to eliminate the confounding effects of preoperative variables on the outcomes of EC patients, we conducted propensity score matching analysis. The logistic regression model calculated propensity scores using the approach (MIME or DIE) as the outcome with age, gender, BMI, CCI, tumor location and neoadjuvant radiotherapy and/or chemotherapy, which showed good predictive capacity (c = 0.71). By excluding patients with scores lower than 0.10 (high chance of undergoing DIE) and higher than 0.90 (high chance of undergoing MIME), we achieved 1:1 matching, which resulted in a subgroup of 230 patients with a predicted preoperative chance of undergoing esophagectomy. In this subgroup, 115 patients underwent MIME, and 115 patients underwent DIE.

The preoperative characteristics after matching are displayed in Table 3. There were no significant differences in age, gender, BMI, CCI, tumor location, and neoadjuvant radiotherapy and/or chemotherapy between the groups.

Propensity score matching analysis demonstrated that compared with patients who underwent DIE, patients who underwent total MIME had longer surgical duration (310 minutes vs. 345 minutes; $P = 0.002$) and greater hospital expenses (¥65 600 vs.¥99 400; $P < 0.001$). However, there was significantly less intraoperative blood loss (191 mL vs. 287 mL; $P < 0.001$) and shorter hospital stay (20 days vs. 23 days; $P = 0.025$) in the total MIME group compared with the DIE group. There were no significant differences in number of LNs harvested, or major or minor complication rates between the groups (Table 4).

Three-year survival

As shown in Figure 1, there were no significant differences in the three-year OS (64.1% vs. 73.8%; $P = 0.101$) or DFS

Table 3 Propensity score matching results of preoperative features of patients who underwent esophagectomy

Clinical variables	Total MIME (*n* = 115)	DIE (*n* = 115)	*Absolute difference*
Age (years)	57.67 ± 7.70	57.41 ± 8.56	0.2
Male (%)	286 (79.2)	93 (80.9)	ND
Body mass index (kg/m^2)	23.81 ± 3.01	23.76 ± 2.35	0.1
Charlson comorbidity index	0.34 ± 0.84	0.29 ± 0.71	0.1
Location (%)			
Upper third	46 (40.0)	48 (41.7)	1.7
Middle third	58 (50.4)	57 (49.6)	0.8
Lower third	11 (9.6)	10 (8.7)	0.9
Neoadjuvant CT and/or RT (%)	6 (5.2)	5 (5.2)	0

CT, chemotherapy; DIE, dual incision esophagectomy; MIME, minimally invasive McKeown esophagectomy; ND, no data; RT, radiotherapy.

Table 4 Propensity score matching results of postoperative features of patients who underwent esophagectomy

Clinical variables	Total MIME (*n* = 115)	DIE (*n* = 115)	*P*
Duration of surgery (min)	345 ± 95	310 ± 75	0.002
Estimated blood loss (mL)	191 ± 128	287 ± 176	<0.001
Number of lymph nodes harvested	24 ± 11	23 ± 11	0.540
T category (%)			<0.001
T0–1	35(30.5)	36(31.3)	ND
T2	33(28.7)	15(13.0)	ND
T3	43(37.4)	30(26.1)	ND
T4	4(3.5)	34(29.6)	ND
N category (%)			<0.001
N0	76(66.1)	106(92.2)	ND
N1	28(24.3)	8(7.0)	ND
N2	5(4.3)	0	ND
N3	6(5.2)	1(0.9)	ND
Differentiation (%)			0.453
Well differentiated	12(10.4)	17(14.8)	ND
Moderately differentiated	64(55.7)	66(57.4)	ND
Poorly differentiated	32(27.8)	32(27.8)	ND
AJCC staging (%)			0.069
Stage 0	1(0.9)	2 (1.7)	ND
Stage I	33 (28.7)	33 (28.7)	ND
Stage II	58 (50.4)	40 (34.8)	ND
Stage III	23 (20.1)	40 (34.7)	ND
Complications (%)			
Major	5 (4.3)	4 (3.5)	0.734
Minor	14 (12.2)	17 (14.8)	0.562
Pulmonary complications (%)	2 (2.6)	4 (3.5)	0.701
Cardiac complications (%)	0	0	—
Gastrointestinal complications (%)	13 (11.3)	12 (10.4)	0.832
Neurologic/psychiatric complications (%)	0	0	—
Infection (%)	0	2 (1.7)	0.155
Wound/diaphragm complications (%)	3 (2.6)	8 (7.0)	0.122
Other complications (%)	0	2 (1.7)	0.155
Mortality (%)	3 (2.6)	3 (2.6)	1.000
Length of hospital stay (days)	20 ± 10	23 ± 11	0.014
Hospital expenses (¥)	99 400 ± 18 290	65 600 ± 32 000	<0.001

AJCC, American Joint Committee on Cancer; DIE, dual incision esophagectomy; MIME, minimally invasive McKeown esophagectomy; ND, no data.

(78.8% vs. 97.2%; $P = 0.314$) between the groups in unmatched analysis. However, after matching, there was a trend of longer three-year OS (64.1% vs. 79.5%; $P = 0.063$) and DFS (65.3% vs. 82.8%; $P = 0.058$) in the patients who underwent MIME compared with the patients who underwent DIE (Fig 2).

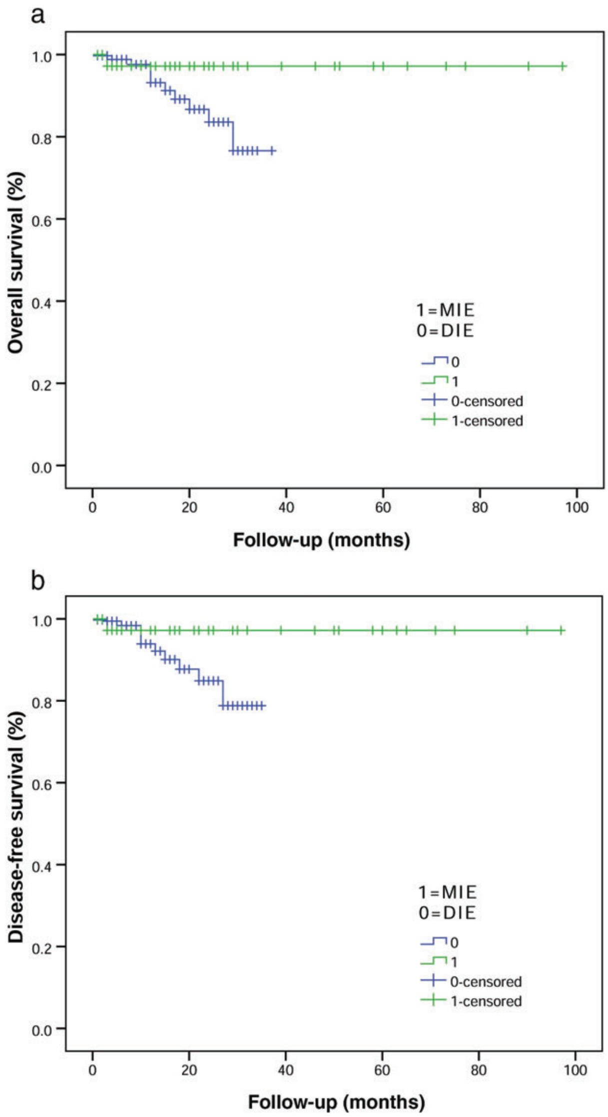

Figure 1 Survival analysis in unmatched patients after esophagectomy according to surgical procedures. In unmatched analysis, overall three-year survival rates were 76.6% and 97.2% ($P = 0.298$) in esophageal cancer patients who underwent dual incision esophagectomy (DIE) and minimally invasive esophagectomy (MIE), respectively. Three-year (**a**) overall survival and (**b**) disease-free survival.

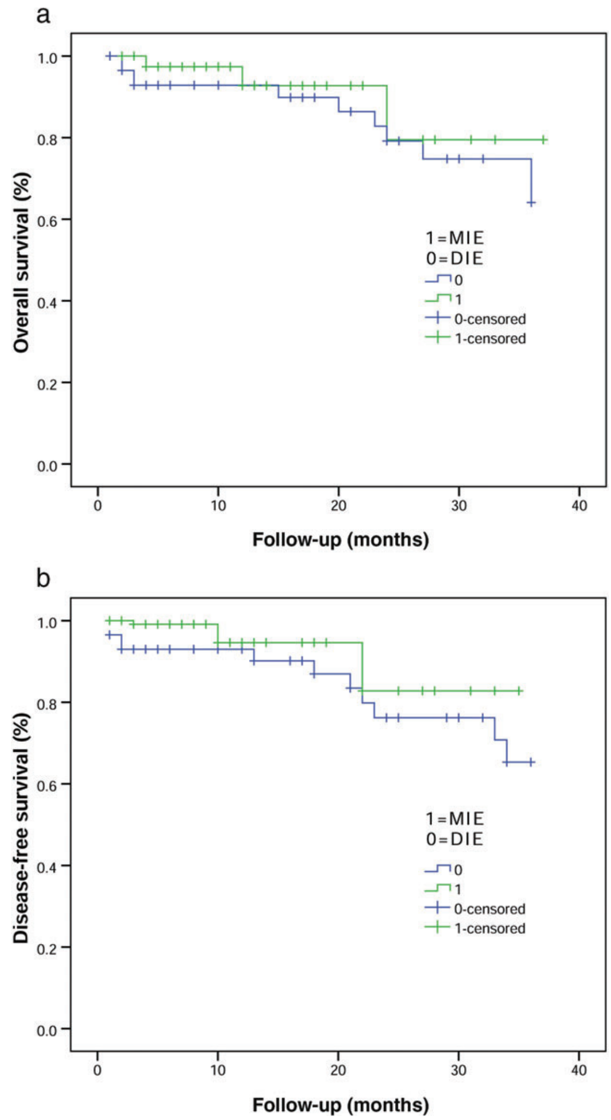

Figure 2 Survival analysis in matched patients after esophagectomy according to surgical procedures. After matching analysis, three-year overall survival rates were 64.1% and 79.5% ($P = 0.063$) in esophageal cancer patients who underwent dual incision esophagectomy (DIE) and minimally invasive esophagectomy (MIE), respectively. The three-year (**a**) disease-free survival was 65.3% and (**b**) overall survival was 82.8% ($P = 0.058$).

Discussion

In this study, we found that short-term outcome and three-year OS and DFS were comparable between the total MIME and DIE groups. However, total MIME was associated with less intraoperative blood loss and shorter hospital stay compared with the DIE approach. The DIE approach was associated with shorter surgical duration and lower hospital expenses. Most importantly, a trend indicated that MIME was associated with better three-year OS and DFS compared with DIE.

There was no significant difference in postoperative morbidity between the total MIME and DIE groups. Recent meta-analyses have demonstrated that minimally invasive esophagectomy (MIE) is superior to open esophagectomy for resectable EC with reduced morbidities.[22,23] However, the samples in the meta-analyses were relatively small, with fewer than 500 patients in the open and MIE groups, respectively. Two national studies compared over 800 cases of MIE with over 2000 cases of open esophagectomy, and over 1000 MIE with over 6000 open esophagectomy, respectively, and concluded that MIE resulted in comparable rates of morbidity and mortality as open esophagectomy.[24,25] Therefore, open esophagectomy currently remains the gold standard for most surgical teams.[5]

In unmatched data, we found that DIE achieved similar oncologic clearance compared with McKeown esophagectomy in EC patients with negative upper mediastinal LNs, which was reflected by a similar number of LNs harvested and similar three-year OS. Yu *et al.* also found no significant difference in the five-year OS and DFS between Ivor Lewis and DIE techniques.[12] However, after matching, our study results indicated that MIME had longer three-year OS and DFS compared with patients who underwent DIE, although no significant difference was reached. Further study is required to investigate the effects of MIME versus DIE for esophageal patients with negative upper mediastinal LNs requiring esophagectomy and neck anastomosis.

Total MIME was associated with less intraoperative blood loss and shorter hospital stay compared with DIE in our study. Recently, Xing *et al.* reported that esophagectomy Surgical Apgar Score (eSAS) was strongly associated with 30-day major morbidity after esophagectomy, and the eSAS is based on the intraoperative lowest heart rate, lowest mean arterial pressure, and estimated blood loss intraoperatively.[26] From this point of view, less intraoperative blood loss during MIE may decrease the postoperative morbidity rate. On the other hand, less intraoperative bleeding may lessen the need for perioperative transfusion, which may improve long-term survival in patients who received MIE.[27] However, further study is required to clarify the mechanisms that result in less intraoperative blood loss, leading to favorable short-term outcome and improved long-term survival in patients undergoing MIE.

The DIE approach was associated with shorter surgical duration and lower hospital expenses compared with total MIME in our study. Not surprisingly, MIE was associated with longer surgical duration in most studies, as a result of the learning curve.[20,24] However, with experience and practice, surgeons should quickly overcome the learning curve.[9] MIE requires longer time and consumes greater disposable instrumentation, which results in greater overall cost. Therefore, hospital expenses were significantly higher in cases of MIE compared with open esophagectomy, despite the shorter hospital stay.[28] Efforts to reduce the costs associated with the minimally invasive approach are warranted, not only in developed countries but also in developing countries.

The most common surgical approaches to accomplish resection of EC include transhiatal, Ivor Lewis, and McKeown esophagectomy in most Western countries and in Japan.[3,29] In contrast, in China, the most commonly used surgical approaches for the resection of EC include the McKeown and Sweet approaches.[7,11,30] Recently, the Ivor Lewis and MIE approaches have been increasingly adopted in China.[10,20,31,32] Different surgical approaches between China and other countries may be multifactorial. We agree with the National Comprehensive Cancer Network guidelines, in that the choice of esophageal resection procedure is dictated by the location of the tumor, the available choices for the conduit, the surgeon's experience and preference, and the patient's preference.[33]

There were two limitations to the current study. Firstly, as this was a retrospective study, the results were obtained from a single medical center, which may limit the generalization of these results. Secondly, only three-year OS and DFS were compared between the two approaches. Longer follow-up may be needed to define whether one approach is superior to another.

In conclusion, MIME and DIE yielded comparable short-term outcomes. However, MIME was associated with better three-year OS and DFS compared with DIE.

Acknowledgment

This study was supported by funding from the Capital Health Technology Development Priorities Research project, No. 2014–1-4021.

Disclosure

No authors report any conflict of interest.

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