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ORIGINAL ARTICLE

Comparison of perioperative outcomes following open versus minimally invasive Ivor Lewis oesophagectomy at a single, high-volume centre†

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Abstract

OBJECTIVES: With the increasing popularity of minimally invasive oesophageal resections, equivalence, if not superiority, to open techniques must be demonstrated. Here we compare our open and minimally invasive Ivor Lewis oesophagectomy (MIE) experience.

METHODS: A prospective database of all oesophagectomies performed at Massachusetts General Hospital in Boston, MA between November 2007 and January 2011 was analysed. A total of 38 MIE and 76 open Ivor Lewis (OIE) oesophagectomies were performed for oesophageal carcinoma. Sixty-day surgical, oncological and postoperative outcomes were examined between the two groups.

RESULTS: Groups had similar demographics in terms of age, gender, tumour histology, clinical stage, preoperative comorbidities and neoadjuvant therapy. No difference was found with respect to adequacy of oncological resections. The median number of lymph nodes retrieved (OIE: 21, inter-quartile range (IQR): (16, 27) versus MIE: 19, IQR: (15, 28)), resection margins (OIE: 6.6% positive versus MIE: no positive margins) and 60-day mortality (OIE: 2.6% versus MIE: no deaths) were comparable. However, rates of pulmonary complications were significantly lower in the MIE group (OIE: 43.4 versus MIE: 2.6%, $P < 0.001$). Additionally, the median length of ICU and hospital stay, intraoperative blood loss and amount of intravenous fluids infused intraoperatively were also significantly decreased with MIE, while median operative times and the requirement for intraoperative blood transfusion were not significantly different between the two groups. Multivariate logistic regression analysis identified MIE as the only variable associated with a significant reduction in the rate of pulmonary complications in our study, while pre-existing pulmonary comborbidity was associated with an increased risk of pulmonary complications.

CONCLUSIONS: Open and MIE appear equivalent with regard to early oncological outcomes. A minimally invasive approach, however, appears to lead to a significant reduction in the rate of postoperative pulmonary complications. Length of ICU and hospital stay, as well as intraoperative blood loss and intravenous fluid requirements are also reduced in the setting of MIE. Long-term survival data will need to be followed closely. A large, multi-centred, randomized, controlled trial is warranted to confirm these results.

Keywords: Oesophagectomy • Minimally invasive • Outcomes • Oesophageal cancer

INTRODUCTION

According to the National Cancer Institute, it was estimated that, in 2010, 16 640 individuals were diagnosed with oesophageal cancer, and 14 500 died as a result (http://seer.cancer.gov/statfacts/html/esoph.html). Oesophagectomy in the treatment of oesophageal cancer is a complex and technically demanding operation that is often associated with high morbidity and mortality [1]. Recently, a minimally invasive approach to oesophagectomy has become more popular in attempts to improve early postoperative outcomes. Minimally invasive Ivor Lewis oesophagectomy (MIE), in particular, may allow for better visualization of mediastinal structures, a lower frequency of recurrent laryngeal nerve injuries, a more extensive thoracic and abdominal lymph node harvest and the creation of a tension-free anastomosis [2–4].

In terms of postoperative outcomes, pulmonary complications remain among the most frequent following open oesophagectomy, ranging from ∼20 to 40% of patients, and leading to increased lengths of hospital stay, costs and, ultimately, mortality [5]. Many factors, including age, pulmonary comorbidity, compromised pulmonary function, tobacco use, performance status and trans-thoracic incision, have been previously identified as contributing to a high pulmonary complication rate following open oesophagectomy [6]. Further contributing to an increased

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pulmonary complication rate may be the growing frequency of induction therapy in the management of locally advanced oesophageal cancer [7], though this remains controversial. The aim of the present study is to compare a minimally invasive Ivor Lewis approach to a traditional open Ivor Lewis oesophagectomy (OIE), as originally described in [8], for oesophageal carcinoma with respect to early surgical outcomes, adequacy of oncological resection and incidence of perioperative complications at a high-volume centre.

MATERIALS AND METHODS

Patients

Using a prospective database, all oesophagectomies performed by the Division of Thoracic Surgery between November 2007 and January 2011 at Massachusetts General Hospital in Boston, MA were reviewed. Institutional Review Board approval was obtained from the Partners Human Research Committee, and specific patient consent was waived for this study. A total of 181 oesophagectomies were performed during this time period. Forty were attempted using a MIE technique (combined laparoscopic and thoracoscopic approach as described below), all by a single surgeon. Two were converted to an open procedure and were included in the open group, yielding a total of 38 patients in the MIE group. Indication for MIE was based on surgeon preference, but otherwise did not differ from open cases. Eighty-four OIE were performed among seven surgeons using laparotomy and thoracotomy. Six patients had a diagnosis of benign disease and two patients underwent a hybrid (combined open and minimally invasive procedure) and were excluded from the analysis, leaving 76 patients in the OIE group. Staging of all malignant lesions was based on preoperative endoscopic evaluation with biopsy, endoscopic ultrasound and positron-emission computed tomography (CT) imaging.

In addition to neoadjuvant therapy, which included chemotherapy and/or radiation therapy, relevant preoperative comorbidities were also taken into consideration as either present or absent. Cardiac comorbidity was defined as present if a patient had a history of coronary artery disease diagnosed by echocardiogram or cardiac catheterization, or a history of coronary bypass grafting and/or arrhythmia requiring oral medication, intervention or pacemaker. Similarly, pulmonary comorbidity was considered present if a patient had a documented history of any of the following diagnoses: chronic pulmonary obstructive disease, asthma, emphysema, chronic bronchitis or pulmonary fibrosis in their medical record. Tobacco use was defined as positive if lifetime usage was >5 pack-years. Previous abdominal surgery included either open or laparoscopic procedures performed for any indication. All data were collected via manual review of the preoperative history and physical, operative and discharge reports, and the longitudinal electronic medical record.

Surgical approach

MIE was performed in a manner similar to that previously described by Dr Luketich and colleagues in [9]. Briefly, with the patient supine and following flexible endoscopic evaluation, five abdominal laparoscopic ports are placed. The liver and peritoneal surfaces are inspected for evidence of metastatic disease. The gastrohepatic ligament is opened and the right crus of the diaphragm is identified, facilitating anterior dissection and mobilization of the oesophagus. Short gastric vessels are ligated using an ultrasonic energy device, while taking care to preserve the right gastroepiploic arcade. The fundus of the stomach is then mobilized up to the left crus and all retrogastric attachments are taken down. The left gastric artery and vein are divided using an endoscopic stapling device: endo-GIA stapler (Covidien, Norwalk, CT, USA). All nodal tissue is resected en bloc with the specimen. After the stomach is completely mobilized, an additional port is placed in the right lower quadrant to facilitate the creation of a gastric conduit. An endoscopic stapler is used to produce a gastric conduit ~4–6 cm in width. A laparoscopic jejunostomy is placed in all patients. The gastric conduit is tacked to the specimen maintaining proper orientation. The patient is then turned to the left lateral decubitus position. A total of five thoracoscopy ports are used. The central tendon of the diaphragm is retracted and the inferior pulmonary ligament is mobilized. All peri-oesophageal lymph nodes and subcarinal lymph nodes are removed, skeletonizing the right and left main-stem bronchi. The azygous vein is divided. With the oesophageal dissection complete, it is divided sharply and removed via the inferior, lateral port, which is enlarged to 5 cm. The oesophago-gastric anastomosis is created using an EEA stapler with the anvil placed in the oesophagus and the handle of the stapler brought through the tip of the gastric conduit and out along the greater curve as in [10]. The gastrostomy is closed with a linear Endo-GIA stapler (Covidien, Norwalk, CT, USA). A 19 Fr Blake drain (Ethicon, Somerville, NJ, USA) and 28 Fr chest tube are placed. The patient is then extubated in the operating room and transferred to the ICU.

Outcomes

Sixty-day oncological, surgical and perioperative outcomes were compared between MIE and OIE groups. Lymph node retrieval, resection margins and 60-day mortality served as surrogate endpoints for oncological outcomes, as long-term survival data were not yet available for most patients in our study.

Pulmonary complications were defined as one or more of the following: (i) respiratory failure necessitating re-intubation; (ii) pneumothorax or pleural effusion/oedema requiring either a chest tube, thoracentesis or readmission to the hospital or ICU for diuresis; (iii) pulmonary embolus diagnosed by CT angiography; (iv) pneumonia, diagnosed either by (a) positive sputum culture, (b) chest X-ray or spiral CT imaging and/or (c) leucocytosis combined with empiric antibiotic therapy and (v) prolonged ventilator dependence >48 h. Cardiac complications included atrial fibrillation, myocardial infarction and ventricular arrhythmia. Atrial fibrillation was only considered a complication in patients with no prior history of atrial or ventricular arrhythmia and was diagnosed by electrocardiogram.

Statistical analysis

Rates of complications were calculated as numbers of patients who had a complication (either single or multiple depending on category) divided by the total number of patients in the group. All data were tested for normality and presented either as mean ± SD or median and inter-quartile range (IQR) where indicated. Student's *t*-test or a Wilcoxan rank sum test was used to

compare continuous variables with an alpha of 0.05 according to whether the variable was normally distributed. Chi-square or Fisher's exact tests were used to evaluate dichotomous and categorical variables as appropriate, also with an alpha of 0.05. Logistic regression modelling was used to determine univariate and multivariate odds ratios (OR) with a 95% confidence interval (CI) and *P*-value reported. Independent or explanatory variables were selected based on clinical relevance and included in the multivariate analysis using a stepwise forward selection algorithm. Two-tailed *P*-values are reported universally, and the significance threshold was designated at a *P*-value of 0.05. STATA Statistical Software, Release 12 (2011 StataCorp LP) was used for all statistical analyses.

RESULTS

Patient characteristics

Between November 2007 and January 2011, 38 MIE and 76 OIE were performed for malignant oesophageal disease. No significant difference was found between MIE and OIE patients with respect to age, sex, comorbidities including history of cardiac and pulmonary disease, tobacco use, baseline pulmonary function as measured by the % predicted forced expiratory volume in 1 second (FEV1) and diffusion capacity of carbon monoxide (DLCO) or neoadjuvant therapy (Table 1). The average age of patients in the MIE group was 61.4 ± 8.1 years and 63.3 ± 9.3 years in the OIE group. The majority of patients in both groups were male (80.2% in the OIE group versus 76.3% in the MIE group). OIE patients did have a higher frequency of previous abdominal surgery, either open or laparoscopic, than patients in the MIE group, though this was not statistically significant (35.5 versus 18.4%, $P = 0.060$). Indications for oesophageal resection included high-grade dysplasia, adenocarcinoma and squamous cell carcinoma. Tumour histology did not differ significantly between groups ($P = 0.416$). Clinical stage ranged from stage 0 to stage III in both groups preoperatively. Overall, there was no significant difference between the MIE and OIE groups with respect to clinical staging of tumours ($P = 0.451$). Given the majority of locally advanced tumours in our database, >60% of patients in both groups underwent neoadjuvant chemotherapy and/or radiation therapy prior to surgical resection.

Table 1: Patient characteristics

Variable	MIE	OIE	*P*-value
n	38	76	
Age (mean ± SD), years	61.4 ± 8.1	63.3 ± 9.3	0.287
Sex, M:F, *n* (%)	29:9 (76.3:23.7)	61:15 (80.2:19.8)	0.626
Comorbidities			
Cardiac, *n* (%)	6 (15.8)	16 (21.1)	0.502
Pulmonary, *n* (%)	8 (21.1)	13 (17.1)	0.608
Tobacco use, *n* (%)	28 (73.7)	52 (68.4)	0.563
FEV1 (mean ± SD), % predicted	88.5 ± 17.5	88.4 ± 20.7	0.991
DLCO (mean ± SD), % predicted	76.8 ± 22.0	78.2 ± 23.7	0.765
Previous abdominal surgery, *n* (%)	7 (18.4)	27 (35.5)	0.060
Neoadjuvant therapy, *n* (%)	25 (65.8)	46 (60.5)	0.585
Histology, *n* (%)			
High-grade dysplasia	2 (5.3)	1 (1.3)	0.416
Adenocarcinoma	31 (81.6)	66 (86.8)	
Squamous cell carcinoma	5 (13.2)	9 (11.8)	
Clinical stage, *n* (%)			
Stage 0	4 (10.5)	8 (10.5)	0.451
Stage I	15 (39.5)	19 (25.0)	
Stage II	10 (26.3)	26 (34.2)	
Stage III	9 (23.7)	23 (30.3)	
Stage IV	0 (0)	0 (0)	

FEV1: forced expiratory volume in 1 s; DLCO: diffusion capacity of carbon monoxide.
P-values calculated using Student's *t*-test for continuous variables, and Chi-square or Fisher's exact tests for categorical and dichotomous variables as appropriate.
*$P < 0.05$.

Surgical outcomes

Surgical and hospital measures, including length of ICU and hospital stay, were found to be significantly different between OIE and MIE (Table 2). Median length of both ICU and hospital stay was significantly greater with OIE when compared with MIE (Table 2). Patients undergoing both MIE and OIE remained in the ICU for a median length of 1 day following surgery, though the IQR for OIE patients indicates that approximately half of OIE patients spent an additional day in the ICU in comparison with MIE patients ($P = 0.001$). Patients who underwent MIE stayed in the hospital overall for a median length of 7 (7–7) days, as opposed to 9 (9–13) days for those who underwent OIE ($P < 0.001$). Not surprisingly, the duration of nasogastric tube decompression and time until oral intake following oesophagectomy was also found to be significantly greater with OIE when compared with MIE.

Operative times were not significantly different between MIE and OIE, as median operative times in MIE cases were found to be only 5 min shorter than for OIE cases (MIE: 360.5 (318–391) min versus OIE: 365.5 (316.5–440.5) min). Estimated intraoperative blood loss and intravenous fluid infusion, however, were found to be greater for OIE cases in comparison with MIE cases. OIE cases had a median blood loss of 250, (200–400) ml and intravenous fluid infusion of 3.6 (2.0–4.5) l in comparison with MIE, which had a median blood loss of 200 (150–250) ml and intravenous fluid infusion of 2.8 (2.0–3.8) l ($P < 0.001$). This difference does achieve statistical significance, but may be less clinically significant overall, especially as the number of patients who required intraoperative blood transfusion did not significantly differ between the two groups. The vast majority of patients in both groups were extubated in the operating room at the end of surgery (MIE: 100%, OIE: 93.4%). In OIE patients, 92.1% received an epidural catheter for postoperative analgesia, while no patients in the MIE group received an epidural catheter, and instead received a patient-controlled analgesic pump.

Oncological outcomes

Adequacy of oncological resection was measured in terms of number of lymph nodes retrieved, frequency of positive resection margins and 60-day mortality. No significant difference was found between the OIE and MIE groups with respect to any of

Table 2: Surgical outcomes

Variable	MIE	OIE	*P*-value
Operative time, median (IQR), min	360.5 (318–391)	365.5 (316.5–440.5)	0.542
Estimated blood loss, median (IQR), ml	200 (150–250)	250 (200–400)	<0.001*
Intraoperative IV fluids, median (IQR), l	2.8 (2.0–3.8)	3.6 (3.0–4.5)	<0.001*
Intraoperative transfusions, *n* (%)	3 (7.9)	11 (14.5)	0.379
Epidural analgesia, *n* (%)	0 (0)	70 (92.1)	<0.001*
Extubated in operating room, *n* (%)	38 (100)	71 (93.4)	0.167
Length of hospital stay, median (IQR), day	7 (7–7)	9 (9–13)	<0.001*
Length of ICU stay, median (IQR), day	1 (1–1)	1 (1–2)	0.001*
Duration of NGT, median (IQR), day	5 (5–5)	7 (6–7)	<0.001*
Time until oral intake, median (IQR), day	6 (5–6)	7 (6–8)	<0.001*

IQR: inter-quartile range; IV: intravenous; NGT: nasogastric tube.
P-values calculated using the Wilcoxan rank sum test for continuous variables, and Chi-square or Fisher's exact tests for categorical and dichotomous variables as appropriate.
*$P < 0.05$.

Table 3: Oncological outcomes

Variable	MIE	OIE	*P*-value*
Lymph nodes, median (IQR), nodes	19 (15–28)	21 (16–27)	0.740
Resection margins, *n* (%), positive	0 (0)	5 (6.6)	0.163
60-day mortality, *n* (%), deaths	0 (0)	2 (2.6)	0.552

IQR: inter-quartile range.
**P*-values calculated using the Wilcoxan rank sum test for continuous variables, and Chi-square or Fisher's exact tests for categorical and dichotomous variables as appropriate.

Table 4: Perioperative complications

Variable, *n* (%)	MIE	OIE	*P*-value
Atrial fibrillation	5 (13.2)	12 (15.8)	0.710
All cardiac complications	5 (13.2)	17 (22.4)	0.240
Pneumothorax	1 (2.6)	3 (3.9)	0.719
Effusion/oedema	0 (0)	19 (25.0)	<0.001*
Pneumonia	0 (0)	16 (21.1)	0.001*
Pulmonary embolus	0 (0)	2 (2.6)	0.552
Respiratory failure	0 (0)	4 (5.3)	0.299
Ventilatory support >48 h	0 (0)	4 (5.3)	0.299
All pulmonary complications	1 (2.6)	33 (43.4)	<0.001*
Anastomotic leak	0 (0)	2 (2.6)	0.552
Thoracic duct leak	2 (5.3)	2 (2.6)	0.600

P-values calculated using Chi-square or Fisher's exact tests for categorical and dichotomous variables as appropriate. 'All' cardiac and pulmonary complications were calculated as the number of patients that experienced any type of cardiac or pulmonary complication divided by the total number of patients.
*$P < 0.05$.

these parameters (Table 3). In both groups, the median number of lymph nodes retrieved during the procedure was comparable (MIE: 19 (15–28) nodes versus OIE: 21 (16–27) nodes). With MIE, no positive margins were identified, while within the OIE group, 6.6% of all margins, proximal and distal, were positive. Sixty-day mortality was not significantly different between the two groups (two deaths in the OIE group and no deaths in the MIE group). Long-term survival data were not yet available for most patients.

Perioperative complications

We examined the 60-day postoperative complication rate for all cardiopulmonary complications, as well as anastomotic and thoracic duct leaks (Table 4). We observed no significant difference in the rate of perioperative anastomotic or thoracic duct leaks between the OIE and MIE groups. None of 38 MIE patients experienced an anastomotic leak within 60 days, and only 2.6% of OIE patients had an anastomotic leak ($P = 0.552$). The rate of atrial fibrillation and all other cardiac complications did not differ significantly between MIE and OIE. Following MIE, 13.2% of patients developed new onset atrial fibrillation, and this was the only cardiac complication that was observed in this cohort within 60 days of surgery. In the OIE group, 15.8% of patients developed postoperative atrial fibrillation, and a total of 22.4% of patients developed a cardiac complication of any type, also inclusive of myocardial infarction, demand ischaemia with elevated troponin, ventricular or atrial arrhythmias or heart block.

A highly significant difference in the rate of pulmonary complications was identified between OIE and MIE (Table 4). Most notably, rates of pulmonary effusion/oedema requiring intervention or re-hospitalization and rates of pneumonia were significantly higher in the OIE group. Of OIE patients, 25.0% developed pulmonary effusion or oedema and 21.1% developed a clinically significant pneumonia, while no patients in the MIE group developed either of these complications ($P < 0.001$). Two patients in the OIE group were diagnosed with a pulmonary embolus within 60 days of surgery, while no patients in the MIE group were diagnosed with a pulmonary embolus in the same time period despite the use of pneumoperitoneum. In the OIE group, 3.9% of patients developed a pneumothorax requiring chest tube placement, and a single patient in the MIE group (2.6%) required intervention for pneumothorax due to persistent postoperative air leak. This patient was eventually discharged from the hospital with a Heimlich valve in place. Thus, the difference in overall rates of pulmonary complications observed in this study was highly significant. In the OIE group, 43.4% of patients

Table 5: Risk factors for pulmonary complications

Variable	Univariate		Multivariate	
	OR (95% CI)	*P*-value	OR (95% CI)	*P*-value
Age	1.05 (1.00–1.11)	0.030*	1.05 (1.00–1.11)	0.074
Sex	1.04 (0.39–2.80)	0.937		
MIE	0.04 (0.01–0.27)	0.001*	0.03 (0.00–0.26)	0.002*
Pulmonary comorbidity	3.35 (1.26–8.90)	0.015*	6.64 (1.65–26.68)	0.008*
FEV1	0.97 (0.95–1.00)	0.030*	0.97 (0.94–1.01)	0.236
DLCO	0.98 (0.96–1.00)	0.069		
Tobacco use	1.56 (0.62–3.93)	0.340		
Neoadjuvant therapy	0.97 (0.42–2.22)	0.941		
Tumour histology	0.92 (0.31–2.71)	0.878		
Tumour stage	1.36 (0.89–2.08)	0.159		
Operative time	1.00 (1.00–1.01)	0.363		
Intraoperative blood loss	1.00 (1.00–1.00)	0.018		
Intraoperative IV fluids	1.00 (1.00–1.00)	0.002*	1.00 (1.00–1.00)	0.149

IV: intravenous; CI: confidence interval; OR: odds ratio.
P-values calculated using univariate or multivariate logistic regression as indicated.
*$P < 0.05$.

experienced a pulmonary complication of any kind within 60 days of surgery, while only 2.6% of patients in the MIE group experienced a pulmonary complication within the same time frame ($P < 0.001$). Of note, a single patient may have had more than one complication including pneumonia, followed by respiratory failure, re-intubation and ventilator dependence for >48 h. However, the rate of all pulmonary complications (Table 4) is calculated as the number of patients who experienced any pulmonary complication (single or multiple) divided by the total number of patients in the group.

Predictors of pulmonary complications

To identify risk factors for pulmonary complications, univariate and multivariate logistic regression analysis was used to assess clinically relevant parameters in our study. Age, sex, tumour histology, clinical stage, history of tobacco use, pulmonary comorbidity, pulmonary function (% predicted FEV1 and DLCO), neoadjuvant therapy, procedure type (MIE versus OIE), operative time, and amount of intraoperative blood loss and intravenous fluid infusion were selected as variables of interest for which data were available. In our univariate model, history of pulmonary comorbidity significantly increased risk of developing a pulmonary complication (OR: 3.35, 95% CI: (1.26, 8.90), $P = 0.015$), along with age and amount of intravenous fluids infused intraoperatively (Table 5). MIE was associated with a significantly decreased the risk of developing a pulmonary complication (OR = 0.04 (95% CI: 0.01, 0.27), $P = .001$). In multivariate model, MIE and pulmonary comorbidity remained the only variables that achieved statistical significance, again associated with a significantly decreased and increased risk of developing a pulmonary complication, respectively.

Discussion

With the advent of laparoscopic anti-reflux procedures, significant experience has been gained with a minimally invasive approach to the lower oesophagus and stomach. A result of this growing experience is a minimally invasive approach to oesophageal resection for cancer. An Ivor Lewis technique is commonly employed by surgeons in our group, as well as others [2], as it allows for improved visualization of mediastinal structures, decreased frequency of recurrent laryngeal nerve injuries, a comprehensive thoracic lymph node harvest and the creation of a tension-free anastomosis between the remnant oesophagus and the gastric conduit. Perioperative outcomes and the development of complications following open oesophagectomy have been previously attributed to a variety factors including age, pulmonary comorbidities, preoperative performance status, nutrition status and neoadjuvant therapy [7, 11–13]. We hypothesized that a MIE may lead to fewer early perioperative complications, when compared with an OIE in a similarly matched group of patients.

In the present study, patient demographics, in terms of age and sex, preoperative comorbidities, and tumour stage and histology, mirrored epidemiological trends typically observed among patients with oesophageal carcinoma [14]. In both groups, >60% of patients underwent neoadjuvant chemotherapy and/or radiation therapy, which reflects the current emphasis on a multidisciplinary treatment approach to more advanced oesophageal cancers [15, 16]. We did find that patients in the MIE group tended to have a greater proportion of stage I tumours than in the OIE group though, overall, tumour histology or clinical stage did not differ significantly between the two groups.

Intraoperatively, MIE and OIE appeared to be equivalent with regard to operative times, but a significant difference was noted in terms of greater intraoperative blood loss and intravenous fluid infusion with OIE. Length of ICU stay and overall hospital stay were significantly shorter with MIE, in keeping with the idea that minimally invasive surgery may lead to a shorter recovery period [17]. Importantly, there was no difference in the adequacy of oncological resection with respect to lymph node retrieval and resection margins between the two groups. Both of these outcomes served as surrogates for long-term survival in our study. Lymph node retrieval is an important component of a complete resection, as well as staging, which leads to an

appropriate subsequent treatment course and improved survival outcomes [18]. Positive resection margins signify an inadequate resection or a non-curative operation, and are also correlated with worse survival outcomes [19]. Finally, there was no difference in short-term survival up to 60 days between the MIE and OIE groups.

Interestingly, we did not observe a significant difference in the rate of cardiac complications, but rather a highly significant difference in the rate of pulmonary complications between the two groups. Approximately 40% of patients who underwent an open operation experienced a pulmonary complication, when compared with only 3% in the MIE group. Clinically significant pneumonia, pleural effusion and oedema were the most prevalent complications that distinguished the two groups. Postoperative pleural effusions occurred most commonly in the left chest, and a left-sided chest drain was not typically left in place following OIE or MIE. In a univariate analysis, intraoperative intravenous fluid infusion, age and pre-existing pulmonary disease significantly increased the risk of developing a pulmonary complication, while MIE significantly lowered the risk of developing a pulmonary complication. In a multivariate analysis, MIE and pulmonary comorbidity remained the only statistically significant variables, however. Previous studies suggest that any type of oesophagectomy, especially those that involve a thoracotomy incision in particular, is associated with a significant risk of pulmonary complication [11, 12]. Several recent reports of MIE, however, have demonstrated a trend towards decreased rates of pulmonary complications with this approach [20–22], and our analysis supports these findings.

Also, of note, none of the MIE patients in our study received an epidural catheter for postoperative pain control. A patient-controlled analgesic device was used instead. We postulate that the avoidance of an epidural may allow for less frequent episodes of hypotension requiring systemic vasopressor therapy and/or excess fluid resuscitation during postoperative management of MIE patients, which may contribute to a lower pulmonary complication rate. Despite the lack of an epidural catheter, our results suggest that pulmonary toilet and clearance of secretions were likely adequate in these patients.

We acknowledge several limitations in this study. Our analysis is limited to patients treated at a single institution, and all minimally invasive cases were performed by a single surgeon, while open cases were performed among seven different surgeons in the group. This inevitably introduces an element of bias in our data, and outcomes may be improved over the course of time as this surgeon became more experienced and proficient with a minimally invasive technique [23]. Findings could also reflect some individual differences in management style, rather than technique only. Postoperative care, for example, of MIE patients typically followed an algorithmic pathway, which aims for transfer from the ICU within 24 h of surgery and discharge from the hospital within a week of surgery. This factor may have influenced our length of ICU and hospital stay measurements, in particular. Use of an epidural catheter for pain management is another example. However, there is no standardized protocol in place with respect to intraoperative intravenous fluid management or blood transfusion at our institution.

Our preliminary experience with MIE when compared with OIE indicates that it can be performed safely with reasonable operative times, markedly less morbidity and mortality, excellent anastomotic integrity and with consistent initial oncological outcomes. As pulmonary complications carry a poor prognosis and are difficult to anticipate [24–26], the ability to decrease and eliminate them is of critical importance in improving outcomes of oesophageal resection. We demonstrate a highly significant decrease in pulmonary complications in our MIE cohort, even without the use of epidural analgesia. Although long-term oncological outcomes still need to be evaluated, initial short-term results indicate that MIE is, at least, equivalent, if not superior with regard to perioperative morbidity when compared with OIE. Further prospective studies are needed to confirm these results, such as a large multi-centred, randomized, controlled trial [27].

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REFERENCES

[1] Atkins BZ, Shah AS, Hutcheson KA, Mangum JH, Pappas TN, Harpole DH Jr *et al*. Reducing hospital morbidity and mortality following esophagectomy. Ann Thorac Surg 2004;78:1170–6.
[2] Pennathur A, Zhang J, Chen H, Luketich JD. The "best operation" for esophageal cancer? Ann Thorac Surg 2010;89:S2163–7.
[3] Pennathur A, Awais O, Luketich JD. Technique of minimally invasive Ivor Lewis esophagectomy. Ann Thorac Surg 2010;89:S2159–62.
[4] Bizekis C, Kent MS, Luketich JD, Buenaventura PO, Landreneau RJ, Schuchert MJ *et al*. Initial experience with minimally invasive Ivor Lewis esophagectomy. Ann Thorac Surg 2006;82:402–6.
[5] Karl RC, Schreiber R, Boulware D, Baker S, Coppola D. Factors affecting morbidity, mortality, and survival in patients undergoing Ivor Lewis esophagogastrectomy. Ann Surg 2000;231:635–43.
[6] Ferguson MK, Celauro AD, Prachand V. Prediction of major pulmonary complications after esophagectomy. Ann Thorac Surg 2011;91:1494–500.
[7] Reynolds JV, Ravi N, Hollywood D, Kennedy MJ, Rowley S, Ryan A *et al*. Neoadjuvant chemoradiation may increase the risk of respiratory complications and sepsis after transthoracic esophagectomy. J Thorac Cardiovasc Surg 2006;132:549–55.
[8] Lewis I. The surgical treatment of carcinoma of the oesophagus: with special reference to a new operation for growths of the middle third. Br J Surg 1946;34:18–31.
[9] Levy RM, Wizorek J, Shende M, Luketich JD. Laparoscopic and thoracoscopic esophagectomy. Adv Surg 2010;44:101–16.
[10] Campos GM, Jablons D, Brown LM, Ramirez RM, Rabl C, Theodore P. A safe and reproducible anastomotic technique for minimally invasive Ivor Lewis oesophagectomy: the circular-stapled anastomosis with the transoral anvil. Eur J Cardiothorac Surg 2010;37:1421–6.
[11] Avendano CE, Flume PA, Silvestri GA, King LB, Reed CE. Pulmonary complications after esophagectomy. Ann Thorac Surg 2002;73:922–6.
[12] Law S, Wong KH, Kwok KF, Chu KM, Wong J. Predictive factors for postoperative pulmonary complications and mortality after esophagectomy for cancer. Ann Surg 2004;240:791–800.
[13] Atkins BZ, D'Amico TA. Respiratory complications after esophagectomy. Thorac Surg Clin 2006;16:35–48.
[14] Pera M, Manterola C, Vidal O, Grande L. Epidemiology of esophageal carcinoma. J Surg Oncol 2005;92:151–9.
[15] Merkow RP, Bilimoria KY, McCarter MD, Chow WB, Ko CY, Bentrem DJ. Use of multimodality neoadjuvant therapy for esophageal cancer in the United States: assessment of 987 hospitals. Ann Surg Oncol 2012;19:357–64.
[16] Pennathur A, Luketich JD, Landreneau RJ, Ward J, Christie NA, Gibson MK *et al*. Long-term results of a phase II trial of neoadjuvant chemotherapy followed by esophagectomy for locally advanced esophageal neoplasm. Ann Thorac Surg 2008;85:1930–6.

[17] Parameswaran R, Blazeby JM, Hughes R, Mitchell K, Berrisford RG, Wajed SA. Health-related quality of life after minimally invasive oesophagectomy. Br J Surg 2010;97:525–31.
[18] Darling G. The role of lymphadenectomy in esophageal cancer. J Surg Oncol 2009;99:189–93.
[19] Yu E, Tai P, Malthaner R, Stitt L, Rodrigues G, Dar R *et al*. What are the factors that predict outcome at relapse after previous esophagectomy and adjuvant therapy in high-risk esophageal cancer? Curr Oncol 2010; 17:46–51.
[20] Biere SS, Cuesta MA, van der Peet DL. Minimally invasive versus open esophagectomy for cancer: a systematic review and meta-analysis. Minerva Chir 2009;64:121–33.
[21] Verhage RJ, Hazebroek EJ, Boone J, Van Hillegersberg R. Minimally invasive surgery compared to open procedures in esophagectomy for cancer: a systematic review of the literature. Minerva Chir 2009;64: 135–46.
[22] Nafteux P, Moons J, Coosemans W, Decaluwé H, Decker G, De Leyn P *et al*. Minimally invasive oesophagectomy: a valuable alternative to open oesophagectomy for the treatment of early oesophageal and gastro-oesophageal junction carcinoma. Eur J Cardiothorac Surg 2011;40: 1455–64.
[23] Song SY, Na KJ, Oh SG, Ahn BH. Learning curves of minimally invasive esophageal cancer surgery. Eur J Cardiothorac Surg 2009;35:689–93.
[24] Grotenhuis BA, Wijnhoven BP, Grüne F, van Bommel J, Tilanus HW, van Lanschot JJ. Preoperative risk assessment and prevention of complications in patients with esophageal cancer. J Surg Oncol 2010;101:270–8.
[25] Nagawa H, Kobori O, Muto T. Prediction of pulmonary complications after transthoracic esophagectomy. Br J Surg 1994;81:860–2.
[26] Nishi M, Hiramatsu Y, Hioki K, Hatano T, Yamamoto M. Pulmonary complications after subtotal esophagectomy. Br J Surg 1988;75:527–30.
[27] Biere SS, Maas KW, Bonavina L, Garcia JR, van Berge Henegouwen MI, Rosman C *et al*. Traditional invasive vs. minimally invasive esophagectomy: a multi-center, randomized trial (TIME-trial). BMC Surg 2011;11:2.

APPENDIX. CONFERENCE DISCUSSION

Dr A. Lerut *(Leuven, Belgium)*: I have a few comments and then a few questions. Since the revival of the concept of minimally-invasive oesophagectomy through the pioneering publications by Dr. Luketich at the beginning of this millennium, I think that we are now beginning to see, as a fallout, a massive switch towards minimally-invasive oesophagectomy all over the world, and I think that your presentation is yet another centre of excellence switching over to this technique. Most remarkable in this presentation to me is the fantastic, I would say unrivalled by any other centre, the near-zero pulmonary complication rate in your minimally-invasive oesophagectomy group. Precisely this outstanding figure may be a reflection of some biases in your patient material through selection. There was more abdominal surgery in the open group, more advanced stage in the open group, 7 surgeons performing open surgery versus one surgeon in the MIE. Also there might be a bias in the perioperative management. Resuming oral intake, despite the fact that you had only one anastomotic leak, after 7.9 days versus 4.9 days in MIE is unusually long. That probably also explains the difference in length of stay between the two groups, as today in most centres with some experience it takes less than 5 days to resume oral intake. So that's one question, why such a long time? It's also my impression that the favourable outcome of the MIE in relation to the pulmonary complication issue is perhaps reflecting a surrogate for the different policy in intraoperative fluid administration, which was again significantly higher in the open surgical group despite the fact that the need for blood transfusion was the same. We all know that an excess in fluid administration is a risk factor for pulmonary complications. In our centre we have done a lot of work on this and we now restrict our intraoperative fluid administration both in open and in minimally-invasive surgery to 1.5 L, at a maximum 2 L. So my question is, what was the reason for such high, a mean of 3.6 L, intraoperative fluid administration despite, again, the low volume of blood loss in both open and minimally-invasive surgery, being 300 cc in the open group?

My last question relates a bit more to the future strategy at MGH. In the open surgery group you had 7 different surgeons performing the open surgery versus only one in the MIE group. We all know when starting up totally minimally-invasive oesophagectomy, that the learning curve is very steep and difficult. So what's going to be your policy? Is it something that will be restricted to one surgeon with the high-volume experience versus the difficult issue of teaching the 6 other members of the staff?

Dr Sihag: Your first question with regard to intraoperative intravenous fluids, I know of no specific policy of fluid restriction in our operating rooms. However, I can hypothesize that we tend to treat patients in the operating room with intravenous fluid when we experience episodes of hypotension in the operating room, and my hypothesis is that patients undergoing minimally-invasive surgery tend to experience potentially lower haemodynamic instability during the operation. That would be my hypothesis.

Dr Lerut: Would it also be the issue of no epidural anaesthesia?

Dr Sihag: Yes. That is our other hypothesis. The patients did not have an epidural catheter, which we believe does cause episodes of hypotension in the perioperative period, not just in the intraoperative period. Unfortunately, we do not have specific data to look at regarding the amount of intravenous fluid received throughout the patient's hospital stay or even initial 3 days. That's something we are certainly interested in trying to gather data on in the future and look at more closely.

Dr Lerut: But your anaesthesiologist will be able to counter that by administering vasopressors, right?

Dr Sihag: Yes. I think that in sort of the short term between hypotension and vasopressor action, we do usually see an increase in the administration of intravenous fluids. Again, that would be my hypothesis as to why we observed such a finding. In terms of your next question of comparing minimally-invasive and the open technique among a group of surgeons where only one may be sufficiently trained to carry this out in their practice, I do see a movement, especially among the younger generation, to try and learn these procedures. However, I think that to expect surgeons who are already well trained in open techniques to adopt a minimally-invasive technique may or may not be realistic.

Dr Lerut: The nasogastric tube?

Dr Sihag: I'm sorry, what was your question with regard to the nasogastric tube?

Dr Lerut: The question about the duration of leaving in the nasogastric tube in the open group being significantly longer than in the MIE group despite the fact that there were no anastomotic leaks.

Dr Sihag: Yes, correct. I think that this parameter also is probably a reflection of the difference in management style and the more aggressive management style with minimally-invasive patients, as you observed, to remove the nasogastric tube at an earlier time point and to initiate oral intake if the barium swallow did not show any evidence of a leak or obstruction on films.

Dr M. Mulligan *(Seattle, WA, USA)*: I have one quick follow-up to that. It strikes me that you may have a surgeon who is very specific in what he wants, with a heavily protocoled postoperative management notion, and in centres where this is the case, the results are virtually identical to this. This looks very much like the Michigan outcomes data. I wonder whether or not you can attribute most of the benefit to that protocolized perioperative management scheme that he has'

Dr Sihag: I certainly think that some of the benefit can be attributed to management style. There's probably no question about that. In terms of how to analyse that specifically in our data becomes a little bit more complicated.

Dr D. Wood *(Seattle, WA, USA)*: This is similar to Dr. Mulligan's question, actually. I think that the difference that you have demonstrated in pulmonary complication outcomes is incontrovertible. The rest might be individual management. So taking Dr. Mulligan's question one step further, if you've learned the ability to manage patients in a different way, in maybe a more aggressive style with the minimally-invasive approach, can one then convert the same advances in management perhaps to the open techniques and capture some of the same benefits for even those patients who are undergoing open surgery?

Dr Sihag: I think that that's certainly a valid point. As surgeons who practice open operations predominantly look at data like this, I would say that moving to a more regimented or protocolized management style postoperatively may indeed lead to some patient benefit, and that would be a good way to be able to compare and tease out the effects of management style versus minimally-invasive technique alone, absolutely.

Dr P. Ugalde *(Salvador, Brazil)*: Could you comment on the type of oesophago-gastric anastomosis that is done? The surgeon that practices the minimally-invasive, does he do the anastomosis just as Dr Luketich does? Has he changed compared to what the other 7 surgeons do? Could you also comment on the incidence of fistula, your thoughts about that in both groups?

Dr Sihag: Sure. The minimally-invasive technique adopted by our group is extremely similar to that described by Dr. Luketich. It is a stapled anastomosis using an EEA stapler. In terms of fistula data, I do not have specific data on that. I didn't look at that in particular. However, my general sense is that I don't think that there was a significant difference between the two groups.

Dr Ugalde: And for the open technique?

Dr Sihag: The open technique varied. Some prefer stapled anastomosis, whereas others may prefer a hand-sewn.

Dr D. Mathisen *(Boston, MA, USA)*: Being the person who probably influenced the length of stay for the patients and the duration of nasogastric tubes, representing the most conservative approach amongst the group, I think it's just a stylistic difference. I tend to be much more conservative about those sorts of issues. I would also say that the one individual who did the minimally-invasive surgery owes a lot of this to Jim Luketich, having spent eight months with him. It reflects somebody who had an intense experience and brought that back with him. To answer Toni's question about that, when I left Boston this past week, I was in the operating room as Cam Wright was in watching Chris Morse do one of these. My sense is that the purpose of this paper was to show "not inferiority", that it was a comparable technique, that it didn't have reasons not to pursue it. I think we were gratified by the outstanding results, and it's clear to me that patients, referring doctors, and individual surgeons recognize that there will be a movement to that, not as a superior approach necessarily, but certainly an equivalent. If you notice the per cents, I think about 25% of these cases were done by a single surgeon, which reflects other people recognizing the value of that procedure. So it's gratifying to see, at least in these early analyses, that it can be done safely, effectively, with few complications. I know there were no anastomotic leaks in the minimally-invasive group. To reiterate, it's really an observational study and we're very pleased with the observations that we made.

Dr Lerut: If I may, I think that you made a very important point. You shouldn't start this kind of experience unless you have somebody who is really properly trained in a centre with a large experience. That is the key issue in the progress that we are going to make in this field. I do believe that MIE has a future, but the learning curve is extremely difficult and proper training is the name of the game.

Dr Mathisen: I would just amplify that by saying when Chris Morse decided to do this, his first notion was pick it up as he went along. It really gets to Toni's point. He's a very good surgeon and he had a lot of experience in open surgery, which I think is also essential. The learning curve was accelerated by an intense period of focusing on that kind of surgery, whereas it might have taken 5 to 10 years to pick it up along the way. So I would echo what Toni said. It is a technically-demanding procedure. It's still a big operation. Even though it's labelled, maybe mistakenly, as minimally invasive, it's still a maximal surgical procedure.