Minimally Invasive Versus Open Esophagectomy for Patients With Esophageal Cancer

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GENERAL THORACIC

Background. **Minimally invasive esophagectomy (MIE) compared with open esophagectomy (OE) has been shown to have clinical advantages, but selection bias is present.**

Methods. **All patients undergoing MIE or OE for cancer between 1999 and 2007 were eligible for analysis. To minimize selection bias, only patients who also met the selection criteria for the thoracoscopic approach were included in the open esophagectomy group.**

Results. **Fifty-six patients underwent MIE and 98 OE. No significant differences in demographics or pathologic data between groups occurred, with the exception of thoracic epidural analgesia (OE 98%, MIE 71.1%, $p < 0.001$), and neoadjuvant treatment (OE 50.5%, MIE 71.4%, $p = 0.016$). Morbidity and in-hospital death were not significantly different. Duration of surgery was longer in MIE (250 vs 209 minutes, $p < 0.001$) and blood loss less (320 mL vs 857 mL, $p < 0.001$). Intensive care unit stay was shorter in MIE (3.0 vs 6.8 days, $p = 0.022$). The relative risk (RR) for in-hospital death was 0.57 ($p = 0.475$) if the patients underwent MIE. After adjusting for thoracic epidural analgesia, the RR was 0.29 ($p = 0.213$) for the MIE group. The RR for surgical morbidity was 1.47 ($p = 0.154$) for patients undergoing MIE. Neoadjuvant treatment increased the RR for surgical morbidity to 1.78 ($p = 0.028$). No difference between the two groups concerning survival occurred.**

Conclusions. **The MIE is comparable with the OE. In MIE, neoadjuvant treatment increased the risk of surgical morbidity. Thoracic epidural analgesia in MIE reduced the risk of in-hospital death and should be considered for all patients undergoing esophagectomy.**

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Esophagectomy remains the gold standard for curative treatment of esophageal cancer. Despite advances in surgical, anesthetic, and intensive care techniques, hospital morbidity and mortality are still substantial, with rates up to 70% and 14%, respectively [1]. A number of approaches have been introduced in an attempt to decrease morbidity and mortality. As well as careful patient selection, standardized postoperative pathways and thoracic epidural analgesia, minimal invasive esophagectomy (MIE) has been advocated as a safe technique with comparable results to open esophagectomy (OE) such as the Ivor Lewis operation or the open cervico-thoraco-abdominal approach [2–6].

A number of different minimally invasive techniques have been described. Commonly, this entails thoracoscopic mobilization of the esophagus in either the prone or left lateral decubitus position, with or without laparoscopic-assisted mobilization of the stomach, followed by an anastomosis in the neck [4–8]. Alternatively, a transhiatal laparoscopic approach has been described, again with an anastomosis in the neck [9].

The potential advantage of a minimally invasive approach is the avoidance of a thoracotomy, thus causing less surgical access related trauma. However, the evidence that MIE is comparable with OE or even superior is based largely on case series that included a variable number of patients [3–6, 10–15]. Comparative studies with large numbers are scarce and no randomized trial has been reported. Most comparative studies showed clinical advantages such as shorter operation times, less blood loss, shorter intensive care unit (ICU) and hospital stays, and a similar survival [7, 8, 16–19]. However, only three of these studies included a large number of patients and only four analyzed survival. One of the problems arising when comparing MIE with OE is the effect of selection bias in nonrandomized studies. The aim of the present study was to compare the postoperative outcome and survival in patients with esophageal cancer undergoing MIE or OE, after minimizing the impact of selection bias.

Patients and Methods

Data Acquisition

This study was approved by the Flinders Clinical Research Ethics Committee and the Royal Adelaide Hospital Clinical Research Ethics Committee. From 1999 on-

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ward, details for all patients undergoing esophagectomy in two University hospitals and two associated private hospitals in South Australia were prospectively entered into a database (FileMaker Pro, Version 8; FileMaker Inc, Santa Clara, CA). These patients all underwent operation by one or more of six surgeons, who each worked together across several sites. The surgeons performing minimally invasive esophagectomy had each performed more than 20 procedures before 1999. All patients undergoing either MIE or OE for cancer between 1999 and 2007 were eligible for analysis. During this time, if specific selection criteria were met, two of the surgeons routinely undertook esophagectomy using a thoracoscopic technique (with or without a laparoscopic abdominal phase). The other four surgeons undertook esophagectomy through an open thoracotomy. No transhiatal esophagectomies were performed in this study. The selection criteria for the minimally invasive approach were the following: esophageal tumors not extending below the gastroesophageal junction, and no previous thoracic, hiatal, or bariatric surgery. All patients who underwent an attempted MIE during the study period were included in a "minimal access" esophagectomy group according to the intention to treat principle. For comparison, patients who underwent an OE were included in an "open" esophagectomy group. These patients all underwent surgery by one of the surgeons who did not undertake MIE.

Matching of Patients

To minimize the effect of selection bias, only patients who had undergone an OE and who also met the selection criteria MIE were included in the OE group in this study. One of the authors (DIW) selected these patients by identifying from the database all patients who met the selection criteria for MIE, but who had undergone an OE. Selection was undertaken without any knowledge of the perioperative or postoperative clinical outcome. Patients were excluded if they had undergone previous thoracic

Table 1. Descriptive Parameters

Variables	Open (n = 98)	Minimally Invasive (n = 56)	*p* Value
Mean age (SEM)	67.8 (1.1)	66.3 (1.3)	0.384[a]
Mean weight (SEM)	80.1 (2.0)	82.3 (3.1)	0.544[a]
Gender			
Male	71 (72.4%)	45 (80.4%)	0.274[b]
Female	27 (27.6%)	11 (19.6%)	
TEA			
Yes	96 (98%)	32 (57.1%)	<0.001[b]
No	2 (2%)	24 (42.9%)	
Neoadjuvant treatment			
Yes	48 (50.5%)	40 (71.4%)	0.016[b]
No	47 (49.5%)	16 (28.6%)	
Location of tumor			
Upper	5 (5.1%)	0	0.057[b]
Mid	18 (18.4%)	6 (10.7%)	
Lower	72 (73.4%)	44 (78.6%)	
Gastroesophageal junction	3 (3.1%)	6 (10.7%)	
Comorbidity			
Cardiac			
Yes	17 (17.3%)	4 (7.1%)	0.076[b]
No	81 (82.7%)	52 (92.9%)	
Respiratory			
Yes	35 (35.7%)	13 (23.2%)	0.107[b]
No	63 (64.3%)	43 (76.8%)	
Renal			
Yes	3 (3.1%)	2 (3.6%)	0.864[b]
No	95 (96.9%)	54 (96.4%)	
Diabetes			
Yes	12 (12.2%)	6 (10.7%)	0.776[b]
No	85 (87.8%)	50 (89.3%)	
Obesity			
Yes	17 (17.3%)	10 (17.9%)	0.936[b]
No	81 (82.7%)	46 (82.1%)	

[a] Student *t* test. [b] χ^2 test.

SEM = standard error of the mean; TEA = thoracic epidural analgesia.

Table 2. Details of the Operations Performed Including Stage of Disease According to UICC and Frequency of Pretreatment

Variables	Ivor Lewis	Three Stage	Thoracoscopic/ Laparoscopic Abdominal	Thoracoscopic/ Open Abdominal	*p* Value
Number of patients (total n = 154)	88 (57.1%)	10 (6.5%)	30 (19.5%)	26 (16.9%)	
UICC stage					0.349[a]
0	13 (15.5%)	1 (11.1%)	8 (26.7%)	7 (26.9%)	
I	12 (14.3%)	3 (33.3%)	4 (13.3%)	5 (19.2%)	
IIA	20 (23.8%)	2 (22.2%)	6 (20.0%)	5 (19.2%)	
IIB	12 (14.3%)	3 (33.3%)	5 (16.7%)	5 (19.2%)	
III	27 (32.1%)	0	7 (23.3%)	4 (15.5%)	
Pretreatment					0.090[a]
Yes	43 (50.0%)	5 (55.6%)	21 (70.0%)	19 (73.1%)	
No	43 (50.0%)	4 (44.4%)	9 (30.0%)	7 (26.9%)	

[a] χ^2 test.

UICC = International Union Against Cancer.

surgery, previous hiatal or bariatric surgery, or had a tumor which involved the gastroesophageal junction type II and III according Siewert and Stein [20]. Patients who had significant cardiac or respiratory comorbidity were also excluded from this study.

Demographics, comorbidity, tumor pathology, morbidity, and mortality were retrieved from the database. Any missing data were sought subsequently from the case records, and survival data were obtained from the South Australia State Cancer Registry and the South Australia State Births, Deaths and Marriages Registry.

Postoperative morbidity was separated into surgical, pulmonary, and medical. Surgical morbidity included anastomotic leak, thoracic empyema, chyle leak, and relaparotomy or rethoracotomy. A leak was defined as contrast extravasation during a contrast swallow study.

Table 3. Histopathologic Parameters

Variables	Open (n = 98)	Minimally Invasive (n = 56)	*p* Value
Histology			0.060[a]
Adeno	65 (66.3%)	46 (82.1%)	
Squamous	29 (29.6%)	10 (17.9%)	
Undifferentiated	4 (4.1%)	0 (0.0%)	
UICC stage			0.459[a]
0	14 (15.7%)	15 (28.8%)	
I	15 (16.9%)	9 (16.1%)	
IIA	18 (20.2%)	11 (19.6%)	
IIB	15 (16.9%)	10 (17.9%)	
III	27 (30.3%)	11 (19.6%)	
G stage			0.867[a]
Well differentiated	11 (12.0%)	8 (17.4%)	
Moderately differentiated	34 (37.0%)	15 (32.6%)	
Poorly differentiated	43 (46.7%)	21 (45.7%)	
Undifferentiated	4 (4.3%)	2 (4.4%)	
Proximal tumor free margins			
Yes	94 (95.9%)	53 (94.6%)	0.715[a]
No	4 (4.1%)	3 (5.4%)	
Distal tumor free margins			
Yes	96 (96.9%)	54 (94.8%)	1.000[a]
No	2 (2.0%)	2 (3.6%)	
Circumferential free margins			
Yes	80 (81.6%)	44 (78.6%)	0.801[a]
No	18 (18.4%)	12 (21.4%)	
Mean number of harvested lymph nodes (SEM)	6.7 (0.5)	5.7 (0.4)	0.144[b]

[a] Exact χ^2 test. [b] Student *t* test.

SEM = standard error of the mean; UICC = International Union Against Cancer.

Table 4. Intraoperative and Postoperative Outcome

Variables	Open (n = 98)	Minimally Invasive (n = 56)	*p* Value
Mean duration of surgery (SEM)	209.4 (7.8)	250.2 (7.2)	<0.001[a]
Mean blood loss in milliliters (SEM)	857 (82)	320 (49)	<0.001[a]
Patients requiring red blood cell transfusion	32 (32.7%)	8 (9.5%)	0.032[b]
Overall surgical morbidity			
Yes	20 (23.5%)	19 (34.5%)	0.156[b]
No	65 (76.5%)	36 (65.5%)	
Leak			
Yes	11 (12.8%)	11 (20.0%)	0.341[b]
No	75 (87.2%)	44 (80.0%)	
Thoracic empyema			
Yes	2 (2.4%)	2 (3.6%)	0.656[b]
No	83 (97.6%)	53 (96.4%)	
Chyle leak			
Yes	2 (2.4%)	2 (3.6%)	0.656[b]
No	83 (97.6%)	53 (96.4%)	
Relaparotomy			
Yes	4 (4.7%)	2 (3.6%)	0.771[b]
No	82 (95.3%)	53 (96.45)	
Rethoracotomy			
Yes	5 (5.8%)	3 (5.5%)	0.928[b]
No	81 (94.2%)	52 (94.5%)	
Overall pulmonary morbidity			
Yes	33 (38.8%)	17 (30.9%)	0.340[b]
No	52 (61.2%)	38 (69.1%)	
Overall medical morbidity			
Yes	20 (23.3%)	8 (14.5%)	0.206[b]
No	66 (76.7%)	47 (85.5%)	
In hospital death			
Yes	6 (6.1%)	2 (3.6%)	0.467[b]
No	92 (93.9%)	54 (96.4%)	
Mean ICU stay in days (SEM)	6.8 (1.4)	3.0 (0.8)	0.022[a]
Mean hospital stay in days (SEM)	21.9 (2.0)	19.7 (1.97)	0.463[a]

[a] *t* test. [b] χ^2 test.

ICU = intensive care unit; SEM = standard error of mean.

Pulmonary morbidity included postoperative pneumonia, pleural effusion needing intervention, and adult respiratory distress syndrome or respiratory failure. Medical morbidity included cardiac complications such as arrhythmias needing intervention or renal failure.

Preoperative Assessment

All patients underwent staging with endoscopy, biopsy, abdominothoracic computed tomography, endoscopic ultrasound, and positron emission tomography after it became available in 2001 and 2002, respectively. Operative fitness was evaluated by clinical assessment, spirometry, and echocardiography.

Patients with advanced tumors were considered for neoadjuvant combination chemoradiotherapy treatment. Patients with early stage tumors (T1 N0 or T2 N0) underwent surgery without pretreatment. In general, neoadjuvant treatment consisted of two courses of 5-fluorouracil and cisplatin in combination with 40 to 45 Gy of radiotherapy. Surgery was performed 4 to 8 weeks after pretreatment.

Surgery

The technique for MIE has been described in detail elsewhere [6, 21]. In brief, esophageal mobilization was performed in the first stage of the operation with patients in a fully prone position. Three ports were placed in the fifth, seventh, and ninth right intercostal space at the level of the posterior axillary line. The right lung was deflated using a double-lumen endotracheal tube. Mobilization was performed with a diathermy hook and a vascular stapler was used to divide the azygos vein. Patients were repositioned in a supine position with the head tilted toward the right side. Gastric mobilization was performed using either a hand-assisted laparoscopic technique (total minimally invasive) or an open technique with an upper abdominal midline laparotomy (thoracoscopically assisted), depending on the individual

Table 5. Results of Log Binomial Generalized Linear Models for the Nominated Outcome. Results are Shown for the Unadjusted (Crude) Model, and Results Adjusted for Neoadjuvant (Neoadj.) Treatment and Thoracic Epidural Analgesia, Respectively

Variable	RR	Standard Error	95% Confidence Interval		*p* Value
In-hospital death					
Group	0.57	0.45	0.12	2.71	0.475
Group	0.58	0.47	0.12	2.85	0.501
Neoadj. treatment	0.78	0.54	0.20	3.1	0.718
Group	0.29	0.29	0.04	2.05	0.213
TEA	0.27	0.27	0.04	1.87	0.187
Overall surgical morbidity					
Group	1.47	0.40	0.87	2.49	0.154
Group	1.78	0.47	1.06	2.98	0.028
Neoadj. treatment	0.45	0.12	0.26	0.78	0.004
Group	1.43	0.44	0.79	2.61	0.239
TEA	0.94	0.33	0.47	1.88	0.867
Overall pulmonary morbidity					
Group	0.80	0.19	0.49	1.28	0.349
Group	0.81	0.20	0.49	1.31	0.385
Neoadj. treatment	0.98	0.23	0.62	1.55	0.926
Group	0.68	0.20	0.38	1.22	0.2
TEA	0.71	0.24	0.36	1.38	0.312
Overall medical morbidity					
Group	0.63	0.24	0.30	1.32	0.218
Group	0.65	0.25	0.30	1.40	0.271
Neoadj. treatment	0.93	0.33	0.47	1.85	0.845
Group	0.54	0.24	0.22	1.31	0.172
TEA	0.71	0.37	0.25	1.96	0.505

RR = relative risk; TEA = thoracic epidural analgesia.

surgeon's preference. For the hand-assisted laparoscopic approach, an 8 cm right upper quadrant transverse incision was made for the hand port (different models used). In both the open and laparoscopic approach, the stomach was mobilized preserving the right gastric and gastroepiploic arteries. The left gastric artery was transected at its base and the associated lymph nodes were resected en bloc. After performing a separate neck incision on the left side and mobilization of the esophagus, it was then transected and the whole specimen was delivered to the abdomen. In the hand-assisted approach, the esophagus and stomach were delivered through the hand port incision and the gastric tube fashioned externally using staplers. A pyloromyotomy was performed under direct vision. In the open approach, the same technique to fashion the gastric tube was used. The anastomosis in the neck was performed with interrupted single layer resorbable sutures. A feeding jejunostomy was routinely placed.

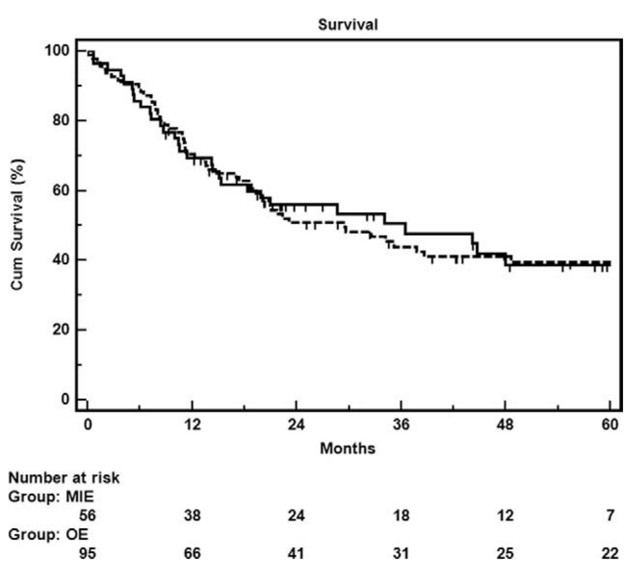

Fig 1. Kaplan-Meier survival analysis with no significant difference between groups (log-rank test; p = 0.826). (— = minimally invasive esophagectomy [MIE]; --- = open esophagectomy [OE].)

In the OE, a synchronous combined abdominal and thoracic Ivor Lewis procedure was performed using a previously described technique [22]. This entailed a midline laparotomy and right-sided anterolateral thoracotomy, with two surgical teams operating at the same time in the thoracic and abdominal cavities. Anastomosis was performed in the chest using an interrupted single layer suture. In a minority of cases, a three-stage thoraco-abdomino-cervical approach was used and the anastomosis performed in the neck in the same fashion as for the minimal invasive approach.

In both MIE and OE the lymph nodes adjacent to the esophagus, to the base of the left gastric artery and below the tracheal bifurcation, were removed. A radical en bloc lymphadenectomy was not performed with either technique.

Statistical Analysis

Comparison of data between the two patient groups was undertaken using the χ^2 test for categoric data, and the Student *t* test or Mann-Whitney *U* test for continuous data. To calculate the relative risk of each outcome by group, log binominal generalized linear models were used. Survival was calculated with the Kaplan-Meier method and differences between groups with the log-rank test. Statistical significance for each model was set at $p < 0.05$. Statistical analyses were performed with SPSS Version 16 for Windows and Stata Version 10 (SPSS Inc, Chicago, IL).

Results

From 1999 to 2007, 273 patients underwent an esophagectomy procedure. One hundred and fifty four (56%) met the selection criteria for this study. Of these, 56 patients underwent an attempted MIE and 98 underwent an OE. For the surgeons who performed the thoracoscopic operation, these represent 64% of patients undergoing esophagectomy, compared with 53% for the surgeons who only performed open esophagectomy procedures. In the MIE group, 30 patients (53.6%) underwent a combined laparoscopic and thoracoscopic procedure and 26 (46.4%) a thoracoscopically assisted esophagectomy. In the OE group, 88 patients (89.8%) underwent an Ivor Lewis esophagectomy and 10 (10.2%) a cervico-thoraco-abdominal esophagectomy. Demographic details are summarized in Table 1 and details about the type of surgery, including disease stage and the frequency of neoadjuvant therapies, are shown in Table 2. There were no significant differences between groups with the exception of the frequency of use of thoracic epidural analgesia, which was more frequent in the OE group (98% vs 71.1%, $p < 0.001$), and neoadjuvant chemoradiotherapy, which was more frequent in the MIE group (71.4% vs 50.5%, $p = 0.016$). Pathologic data are summarized in Table 3. No significant differences between groups were detected.

The MIE took approximately 40 minutes longer (mean 250.2 minutes versus mean 209.4 minutes, $p < 0.001$) than OE. Blood loss was significantly less during MIE (mean 320 mL vs 857 mL, $p < 0.001$) and fewer patients underwent blood transfusion (32 vs 8, $p = 0.032$). In two patients (3.6%) the laparoscopic phase was converted to an open abdominal approach, one due to bleeding from a splenic tear and one due to technical difficulties during dissection of the stomach. Three patients (5.5%) required conversion from thoracoscopy to thoracotomy, two due to bleeding and one due to technical difficulties when dissecting the esophagus. Surgical, pulmonary, and medical morbidity and in-hospital death were not significantly different as summarized in Table 4. The length of ICU stay was significantly shorter in patients who underwent MIE (3.0 days vs 6.8 days, $p = 0.022$). Hospital stay was similar (19.7 days vs 21.9 days, $p = 0.463$).

The calculation of the relative risk (RR) is shown in Table 5. There were no significant mortality differences between the study groups. For in hospital death, the RR was 0.57 (standard error 0.45, 95% confidence interval [CI] 0.12 to 2.71, $p = 0.475$) if the patients underwent MIE. After adjusting for neoadjuvant treatment, which was significantly more frequent in the MIE group, the RR did not change significantly (0.58). After adjusting for thoracic epidural analgesia, again a variable with significant difference in frequency between groups, the RR decreased by almost 50% in favor of MIE compared with OE with a RR of 0.29 (standard error 0.29, 95% CI 0.04 to 2.05, $p = 0.213$). The RR for surgical morbidity was 1.47 (standard error 0.4, 95% CI 0.87 to 2.49, $p = 0.154$) for patients undergoing MIE. Neoadjuvant treatment increased the RR for surgical morbidity to 1.78 (standard error 0.47, 95% CI 1.06 to 2.98, $p = 0.028$), whereas no change after adjusting for thoracic epidural analgesia was seen. Adjustment for neoadjuvant treatment or thoracic epidural analgesia did not show any change of RR of MIE versus OE for pulmonary or medical morbidity.

The Kaplan-Meier survival curve is shown in Figure 1. Three patients in the OE group were lost to follow-up. Median follow-up time was 32 months (95% CI 19.1 to 45.0 months). The log-rank test showed no difference between the two groups ($p = 0.826$). Median survival for patients with open surgery was 29 months (standard error 6.4, 95% CI 16.7 to 41.5) compared with 35 months (standard error 15.1, 95% CI 6.3 to 65.6) in the minimally invasive group. The Kaplan-Meier analysis of the subgroups within the OE and MIE procedure groups again demonstrated no differences (log-rank test, $p = 0.789$).

Comments

The results from our study show that MIE and OE have comparable morbidity, mortality, and overall survival. Survival was not different between the MIE and OE groups, and also not different between the surgical technique subgroups (open Ivor Lewis, open three-stage, thoracoscopic-laparoscopic and thoracoscopic-open).

Preselection of patients for inclusion in the OE group ensured that all of the patients in this case control study met consistent selection criteria for a minimally invasive approach. The group who underwent an OE was selected from patients operated on by four surgeons who did not undertake MIE during the time of this study. All of the surgeons worked collaboratively across the four hospital sites included in this study, and they applied similar operative techniques and protocols. The surgeons performing MIE had performed more than 20 procedures before 1999, when this study commenced, and this is likely to have reduced the impact of a learning curve for MIE. This preselection was designed to minimize the selection bias, which is inherent in any nonrandomized study comparing MIE and OE [7, 18, 19].

The two groups showed no significant differences for the descriptors used, except for the frequency of use of neoadjuvant treatments and thoracic epidural analgesia. There might be different reasons for the difference in frequency of neoadjuvant treatment. First, the indication for pretreatment might have been given more liberally when a MIE was planned. Second, neoadjuvant treatment was generally applied when the tumor was staged to be advanced (T3) or suspicion of lymph node metastasis (N1) was present. Patients in which the preoperative staging was not decisive and a MIE was planned might also have been more likely to undergo neoadjuvant treatment. Third, the two surgeons who undertook MIE may have applied different criteria for selecting patients for neoadjuvant treatment, indicating that despite our best attempts to define a comparable control group in this study, there remain some limitations due to the nonrandomized case-control methodology used.

Overall, neoadjuvant treatment was used in 88 patients with a major response, defined as a Mandard tumor regression grade of 1 or 2, in 27 patients [23]. Nineteen (70.4%) of these 27 patients underwent MIE. To assess the influence of neoadjuvant treatment on the outcomes, a log binominal generalized linear model was used. The RR for a nominated outcome in patients undergoing MIE compared with OE adjusted for neoadjuvant treatment increased only for surgical morbidity, but not for in-hospital death, pulmonary or medical morbidity. Patients undergoing MIE had a RR for surgical morbidity of 1.47 compared with patients who underwent OE. After adjusting for neoadjuvant treatment, this risk increased to 1.78, and this was statistically significant. To our knowledge, no study has evaluated the influence of radiochemotherapy in these two surgical approaches. Whether neoadjuvant treatment has an influence on perioperative mortality and morbidity is unclear. A number of studies did not detect higher perioperative mortality [24–26]. A meta-analysis of randomized controlled trials showed a trend toward higher operative mortality in pretreated patients (odds ratio of 1.72; 0.96, 3.07; 95% CI, $p = 0.07$) [27].

Thoracic epidural analgesia was used significantly more often in OE than in MIE. This might be explained by the fact that a number of anesthetists did not consider thoracic epidural analgesia to be necessary when a minimally invasive approach is used or it might have involved some selection bias between anesthetists. The log binominal generalized linear model suggested an advantage in RR for in-hospital death for patients who underwent MIE after adjusting for thoracic epidural analgesia (RR decreasing from 0.57 to 0.27). Additionally, the RR for pulmonary morbidity was positively influenced by thoracic epidural analgesia. The role of thoracic epidural analgesia has been clearly established in open abdominal and thoracic surgery with better analgesia and lower risk of postoperative respiratory failure [28, 29]. In minimally invasive surgery, however, it is less well-established with only a few studies showing a benefit in thoracoscopic surgery [30, 31]. To our knowledge, no study so far addressed the efficacy of thoracic epidural analgesia in MIE. The data of this study indicate that thoracic epidural analgesia should be administered also in MIE, especially as adverse events related to thoracic epidural analgesia are rare [28].

Duration of surgery was significantly longer and blood loss significantly lower in MIE and this is consistent with the literature [7, 8, 17, 18]. The lower blood loss is reflected by fewer patients requiring blood transfusion. Only one report with a small number of patients and long mean operation times of up to 430 minutes for transthoracic esophagectomy presented shorter operation times for minimally invasive procedures [16]. The ICU stay was significantly shorter after MIE. Total hospital stay was shorter by two days, but this difference did not reach significance. The ICU and hospital stays from other centers might differ from the outcomes we report, and criteria for transfer from ICU to a normal ward (with or without intermediate stay in a high dependency unit), as well as hospital discharge criteria, may be different in different health care systems in different countries. The surgeons performing esophagectomy in our study applied similar criteria for transfer from ICU to a ward, and the study has shown a difference in ICU stay between the two groups. This is consistent with other studies which also show an advantage for MIE [7, 16, 17].

Postoperative morbidity and in-hospital mortality did not differ significantly between the groups, thus showing that MIE is a safe procedure with acceptable complication rates. Again, these results are consistent with the literature, where morbidity and mortality have been described as similar between the two approaches [5, 7, 17, 18]. Of note, the anastomotic leak rate was higher in MIE but this difference was not significant. With the thoracoscopic approach, all anastomoses were performed in the neck, and it is widely thought that cervical anastomoses have a higher leak rate than intrathoracic anastomoses [32, 33], although this view has been challenged by a recent prospective randomized trial [34]. Surprisingly, overall pulmonary morbidity was not different in the two study groups. The groups did not differ in preoperative respiratory comorbidity. Any reduction in access related morbidity by avoiding a thoracotomy might have been offset by the longer operation time and the prone position. In both groups the right lung was deflated. Furthermore, almost all patients who underwent an OE received thoracic epidural analgesia, and this has been shown to decrease postoperative respiratory failure [28].

Concerning the pathologic analysis, no differences in location of tumors, frequency of histologic subgroups, International Union Against Cancer (UICC) stage, histologic differentiation, rate of proximal or distal tumor free margins, and number of lymph nodes harvested occurred. Most of the tumors arose in the distal third of the esophagus. In the open group, 5 patients had tumors of the upper third of the esophagus compared with none in the minimally invasive group. The radicality of the resection, defined as the absence of microscopic tumor at the proximal, distal, and circumferential margins, is comparable with the literature with an R0 rate of around 80% [9, 35, 36]. The number of lymph nodes harvested was smaller than in some other Western and Japanese series

[7, 17, 18]. The number of lymph nodes harvested is dependent on the extent of dissection and the technique of pathologic examination. In this study, no radical en bloc lymphadenectomy was performed and 88 patients (56%) received preoperative radiochemotherapy. However, this less radical approach to lymph node resection seems not to have influenced overall survival. Median survival for both groups was comparable with other studies in the Western literature and a log-rank test did not show a significant difference in the overall survival between groups [7, 33].

It is important to recognize the limitations of our study. This is a retrospective analysis, based on data which were prospectively entered into a database. As discussed above, despite the matching process, there remains a risk of some selection bias, and within the MIE group some patients underwent a laparoscopically assisted abdominal phase and others an open abdominal phase. However, all patients underwent thoracoscopic mobilization of the esophagus, thus avoiding a thoracotomy.

In conclusion, MIE incorporating thoracoscopic esophageal dissection is comparable with OE in terms of morbidity, mortality, and oncologic survival. This study suggests benefits for the minimally invasive approach in terms of less blood loss, shorter ICU stay, and possibly a shorter length of hospital stay. Patients who have undergone neoadjuvant treatment and who underwent a MIE had an increased risk of surgical morbidity but not in-hospital death. Patients who underwent MIE with a thoracic epidural analgesia had a reduced relative risk of in-hospital death. This raises the question of whether a thoracic epidural analgesia should be considered for all patients undergoing esophagectomy, irrespective of the choice of surgical technique.

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