Introduction of Minimally Invasive Esophagectomy in a Community Teaching Hospital

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ABSTRACT

Background and Objectives: The safety of minimally invasive esophagectomy (MIE) outside of high-volume centers has not been studied. Therefore, we evaluated our experience with the introduction of MIE in the setting of a community teaching hospital.

Methods: A retrospective cohort of all elective esophagectomy patients treated in a community hospital from 2008 through 2015 was evaluated (n = 57; open = 31 vs MIE = 26). Clavien-Dindo complication grades were recorded prospectively.

Results: Mean age was 63 ± 11 years (range, 30–83), mean Charlson comorbidity index was 4.5 ± 1.7 and proportion of ASA score ≥ 3 was 87%. The groups did not differ in age, gender distribution, or comorbidity indices. There were 108 complications observed, including 2 deaths (3.5%, both coronary events). Postoperative complication rate was 77.1% and serious complication rate (grades 3 and 4) was 50.8% in the entire cohort. The rate of serious complications was similar (58% for open vs 42% for MIE group; 2-sided P = .089). MIE operations were longer (342 ± 109 vs 425 ± 74 minutes; P = .001). Length of stay trended toward not being significantly shorter among MIE cases (15 ± 13 vs 12 ± 12 days; P = .071). Logistic regression models including MIE status were not predictive of complications.

Conclusions: Introduction of MIE esophagectomy in our community hospital was associated with prolonged operative time, but no detectable adverse outcomes. Length of stay was nonsignificantly shortened by the use of MIS esophagectomy.

Key Words: Community hospital, Minimally invasive esophagectomy, Open esophagectomy.

INTRODUCTION

Adoption of minimally invasive esophagectomy (MIE) remains constrained, even some 20 years after its initial report. The hesitancy to use the method is likely relative to operative complexity and perhaps oncological efficacy concerns when compared to the traditional open esophagectomy (OE).

Earlier randomized studies demonstrated decreased perioperative morbidity among patients randomized into MIE or hybrid MIE (laparoscopy + thoracotomy), as compared to those with OE. Because of its demonstrated decreased morbidity while preserving oncological adequacy, MIE remains an enticing option, and it is increasingly accepted as standard of care, along with OE.

All evaluations of MIE to date are reported out of the high-volume tertiary centers with highly specialized multidisciplinary teams. A parallel trend for esophageal surgery centralization is noted, although opinions against such centralization have been expressed. In our view, geographical, economic, insurance network restrictions, and the logistic realities of the United States remain significant barriers to such full centralization, and, thus, the means to deliver high-quality care closer to patients’ homes must be pursued. Meanwhile, evidence supporting the safety of the esophagectomies being performed in selected low-volume institutions is available.

As in many community settings, our surgical oncology practice is not limited to esophageal disorders, but rather covers a wide spectrum of complex oncological scenarios. We began offering MIE in 2010 after supplementary training. The main objective of the present study was to assess overall safety of introducing an MIE program into our community teaching hospital. Consequently, we have retrospectively examined all patients that underwent elective esophagectomy at our hospital during a 7-year period (2008 through 2015), comparing short- and medium-term outcomes between MIE and OE.

METHODS

We retrospectively reviewed all elective esophagectomy cases performed between July 2008 and June 2015 at...
Mercy Medical Center in Des Moines, Iowa (578-bed community teaching general hospital with cardiovascular, transplant, and trauma surgery programs) after our Institutional Review Board approval. A total of 57 cases were evaluated (OE = 31, MIE = 26, including both fully minimally invasive procedure and hybrid cases of thoracoscopy/laparotomy). Open esophagectomy was performed, mostly by a transhiatal approach (transhiatal 29, Ivor Lewis 2). Our default technique for MIE has been a 3-field McKeown procedure as described by others.\textsuperscript{5,17} The MIE approach was offered to all patients, except those with poor pulmonary reserves who were not expected to tolerate single-lung ventilation based on preoperative evaluation. We did not consider the patient’s body habitus or body mass index in the decision for any approach. Exceptions were 3 patients with a very long thorax early in our experience, who had planned thoracoscopic esophageal mobilization combined with open gastric conduit creation. Three additional cases started as MIE and were converted to transhiatal esophagectomy. Of these, 2 did not tolerate single-lung ventilation long enough to complete mediastinal dissection, and 1 had successful thoracoscopic mobilization but difficulty with abdominal dissection requiring laparotomy. These 6 hybrid cases are included in the MIE group in this report. All operations were performed by surgical oncologists (JF or CG), assisted by a general surgery resident without fellows participating. Postoperative pain control was achieved with liberal use of surgeon-performed local anesthetic blocks and analgesics, but without neuraxial/regional anesthesia.

Clavien-Dindo complication grades were recorded and analyzed prospectively for quality control.\textsuperscript{18} Anastomotic leak was aggressively sought after and defined by CROSS study criteria, either clinical evidence of a salivary fistula or radiological findings on esophagogram.\textsuperscript{19} Clinical suspicion of vocal cord paralysis was counted as paralysis, unless ruled out by direct laryngoscopy. Any unplanned operation at the same site within the first 90 days was considered a return to OR.

Operative time was defined as total time between the first incision and final dressing application, not including anesthesia induction or initial patient positioning. Patient repositioning between thoracic and abdominal phases of MIE was included in the operative time. Overall survival was measured from the date of diagnosis. Neoadjuvant therapy was provided for most patients with cancer as chemoradiation to a total dose of 50.4 Gy in 28 fractions, whereas all but 1 patient received various chemotherapy agents concomitantly.

Primary outcome measures were 30-day postsurgical morbidity and mortality, and long-term overall survival. The secondary objective was the number of resected lymph nodes. Continuous variables were tested by the Mann-Whitney test. Proportions were compared by Pearson’s $\chi^2$ test or Fisher’s exact test, as appropriate. Logistic regression models were used to analyze binary outcomes, and goodness of fit was assessed by the Hosmer-Lemeshow test and Pearson’s test. We required both tests to be negative to accept the model as consistent with data ($P > .05$ for each test). Survival was assessed by Kaplan-Meier estimates. Point estimate and 95% confidence interval (CI) are reported. Statistical significance was considered at $P < 0.05$. The STATA 10 package (Tulsa, OK, USA) was used for analysis.

**RESULTS**

**Demographic, Clinical, and Operative Information**

There were 57 patients in total, with 31 cases of open esophagectomy and 26 cases of MIE. No statistically significant baseline differences were observed between both groups (Table 1). Lymph node stage, age, preoperative serum albumin level, and comorbidities (Charlson comorbidity index, Seattle comorbidity index, American Society of Anesthesiologists (ASA) score) were similar in both groups.

Length of operation has remained relatively consistent for both OE and MIE (test for trend $P = .406$; Figure 1). MIE operations were significantly longer in comparison to OE ($P = .001$), in part reflecting the time needed to reposition the patient from lateral to supine. The average postoperative length of stay for OE patients was 15 $\pm$ 13 days vs 12 $\pm$ 12 days among MIE patients ($P = .198$). A similar nonsignificant trend toward decreasing length of stay among the MIE patients was observed when analyzing the subpopulation with complications of Clavien-Dindo grade $\leq 2$ (n = 28; 10.8 $\pm$ 9.5 vs 7.4 $\pm$ 2.9 days; 2-sided $P = .197$).

**Thirty-day Perioperative Complication Analysis**

There were 108 complications observed among the 57 cases (Table 2, Figure 2). The overall complication rate was 77.1%, and the serious complication rate (grades 3 and 4) was 50.8% in the whole cohort. The rate of serious complications was statistically similar between the groups, albeit a favorable trend was noted among patients who underwent MIE (58% for the OE group vs 42% for MIE group; 2-sided $P = .089$; 1-sided $P = .059$ for MIE superiority). OE had an average of 2.1 $\pm$ 1.9 complications as compared to 1.7 $\pm$ 1.4 in the MIE group ($P = .552$). We observed,
on average, 1.0 ± 1.1 serious complications (grades 3 and 4) in the open group compared to 0.7 ± 0.9 in the MIS group \((P = .362)\). There was one 30-day perioperative mortality in each group \((P = .999; \text{Table 2, Figure 2})\).

We fitted a stepwise logistic regression model \((P > .2\) for factor removal) in an attempt to predict factors contributing to the occurrence of grade 3 or 4 complications. The entry model included gender, Charlson comorbidity index, ASA score, age, body mass index, preoperative albumin, and use of the minimally invasive approach. The final model was not predictive of serious complication development \((P = .156, \text{pseudo } R^2 = 0.074)\), and receipt of MIE surgery was not associated with increased risk of serious complications \((OR 0.298; 95\% \text{ CI } 0.666–1.335; P = .114)\).

**Survival**

Survival analysis was limited to the 54 cases with malignant diagnoses. Overall, median survival was 25.1

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**Table 1.**

Demographic and Clinical Data

| Male: female, n | Overall | Open Esophagectomy | MIE | \(P\) |
|----------------|---------|--------------------|-----|------|
| Male: female, n | 46:11 | 25:6 | 21:5 | 0.629† |

**Age (years)**

| Mean ± SD | Overall | Open Esophagectomy | MIE | \(P\) |
|-----------|---------|--------------------|-----|------|
| 63.1 ± 10.6 | 60.7 ± 11.6 | 66.1 ± 8.5 | 0.093* |

**CCI**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 4.5 ± 1.7 | 4.5 ± 1.9 | 4.5 ± 1.6 | 0.993* |

**SCI**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 8.6 ± 3.1 | 8.3 ± 3.4 | 9.0 ± 2.9 | 0.634* |

**ASA class ≥3**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 48 (87) | 25 (86) | 23 (88) | 0.563‡ |

**Current smoking**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 11 (20) | 8 (25) | 3 (13) | 0.319† |

**Diabetes mellitus**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 21 (36) | 12 (37) | 9 (36) | 0.907‡ |

**COPD**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 19 (33) | 11 (34) | 8 (32) | 0.539‡ |

**Preoperative serum albumin (g/dl) mean ± SD**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 3.4 ± 0.6 | 3.4 ± 0.5 | 3.5 ± 0.7 | 0.773* |

**BMI (kg/m²) mean ± SD**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 27.8 ± 4.9 | 27.3 ± 4.9 | 28.4 ± 4.9 | 0.671* |

**Histology, n**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| Adenocarcinoma | 52 | 30 | 22 |
| Squamous cell carcinoma | 2 | 0 | 2 |
| Benign | 3 | 2 | 1 |

**Neoadjuvant therapy (benign cases excluded)**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 50 (93) | 28 (93) | 22 (92) | 0.816† |

**cAJCC Stage**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| 9 (16) | 2 | 7 | 0.101† |
| 23 (43) | 13 | 10 | |
| 21 (39) | 14 | 7 | |
| 1 (2) | 1 | 0 | |

**Lymph node status (benign cases excluded)**

| Overall | Open Esophagectomy | MIE | \(P\) |
|---------|--------------------|-----|------|
| Proportion cN† | 24 (44) | 15 (50) | 9 (37) | 0.358‡ |
| Proportion pN† | 15 (28) | 10 (33) | 5 (21) | 0.370‡ |
| Total number examined LN | 11.8 ± 6.5 | 10.4 ± 634 | 13.6 ± 6.5 | 0.035* |
| Total number involved LN | 1.2 ± 3.0 | 1.8 ± 3.9 | 0.5 ± 1.2 | 0.147* |

Data are expressed as number (percentage of total group), unless otherwise noted. CCI, Charlson comorbidity index; SCI, Seattle comorbidity index; ASA, American Society of Anesthesiologists physical status class; LOS, postoperative length of stay; COPD, chronic obstructive pulmonary disease; LN, lymph node; CN+, clinically positive node; PN+, pathological node. *Mann-Whitney test; †Fisher or \(\chi^2\) test as required.
months. Three-year survival rate was 51% overall: 42% for OE and 62% for MIE, respectively. Length of follow-up for surviving patients was 28.3 months, not long enough to report 5-year survival rates. Median survival in OE was 21.7 months, as compared to 39.6 months in the MIE group. Survivorship was not significantly different between the groups (unstratified log rank test $P = .161$; log rank test stratified on pN-status $P = .080$; Figure 3). Cox proportional hazard model was built with a limited number of factors because of the small number of cases (overall model, $P = .043$). Age (HR = 1.068 per year, 95% CI 1.020–1.118, $P = .005$) and pretreatment nodal status (involved vs uninvolved nodes, HR = 2.864; 95% CI 1.017–8.068; $P = .046$) were significant predictors, while ASA class (ASA $\geq 3$ vs ASA $\leq 2$, HR = 0.566, 95% CI 0.152–2.108, $P = .397$) was not a predictor of overall survival. Receipt of MIE narrowly missed significance (HR = 0.392, 95% CI 0.143–1.068, $P = .067$).

**DISCUSSION**

Surgical outcomes of esophagectomy have been increasingly scrutinized. Surgical volume for complex procedures is a recognized surrogate marker of improved outcomes, and therefore centralization of high-risk procedures has been called for. Certain low-volume hospitals provide excellent esophagectomy care, and volume alone may not be an adequate proxy for quality. High-volume hospitals remain inaccessible to a significant proportion of patients, mainly for geographic and logistic reasons. In this context we deem that high-risk operations may be offered in certain well-prepared community hospitals with appropriate quality assurance. Consequently, we have examined our performance during MIE introduction in our relatively large community teaching hospital without university affiliation.

Although MIE has been previously reported from major academic institutions, process and outcomes related to starting an MIE program in community settings have not been studied so far. We performed this analysis to formally evaluate changes made in our practice and because no prior literature analyzed patient safety outcomes related to MIE introduction into a community teaching hospital. In the present study, we did not identify increased morbidity and mortality after the introduction of MIE into our practice.

At this juncture, the standard of care for use of MIE is evolving. Meaningfully lower perioperative morbidity is
an appealing reason for adoption of MIE, with significant support for lower complication rates being gleaned from 2 prospective randomized trials8,9 and from 1 meta-analysis.23 Improved quality of life and decreased pulmonary postoperative complications (RR/H11005 0.30) were observed in the earlier MIE trial.8 Pulmonary complications in turn have been recognized as a major driver of perioperative mortality and even long-term survival.2 A similar benefit has been observed, even in a hybrid MIE trial, where MIE consisted of thoracotomy and laparoscopy. Among 207 randomized patients, a significant improvement in perioperative morbidity (major complications in OE 64.4% vs 35.9% in the hybrid MIE) has been observed.9 Thus, it seems that both totally minimally invasive and hybrid MIE confer a measurable risk reduction of perioperative complications, both in randomized trials and meta-analysis.23 Other available retrospective pooled evidence regarding hybrid MIE suggests perioperative and oncologic noninferiority.5,6,24

Although it did not reach statistical significance, we noted a nonsignificant trend toward fewer complications among our MIE patients. Yet, we still report a considerable combined morbidity rate of 77% and serious morbidity of 50% (grades 3 and 4). To put this in context, the rate of pulmonary complications in this study (42.1%) is comparable to that reported by recent randomized trials (the Dutch CROSS Esophageal Cancer Trial 45.2% and Francophone de Cancérologie Digestive [FFCD]-9901 trial 46.7%). The same remains true for cardiovascular complications (24.5% reported herein vs 18.9% in the CROSS study) and anastomotic leak (22.8% reported herein vs 26.1% in the CROSS study). In regard to serious complications, the Eastern Cooperative Oncology Group (ECOG) 2202 prospective feasibility study reported a 49.5% rate of grade 3 and 4 perioperative complications, paralleling our 42% rate in the MIE group and 50% rate for the entire cohort. Assessing perioperative mortality, the Society of Thoracic Surgeons database review reported a 2.7% rate, whereas ECOG 2202 reported 2.9% and the CROSS study 4%.19 The perioperative mortality of our study cohort (3.5%) is well within this range.

It should be noted that there is a large variation in the reported complication rates for esophagectomy in the surgical literature. Notable differences have been seen among randomized trials and some retrospective studies (generally single-institution trials with a constrained number of surgeons performing the procedure), as well as among various databases reporting on quality of
For example, one report highlighted major differences in reported mortality between the General Thoracic Surgery Database maintained by The Society of Thoracic Surgeons, the National Surgery Quality Improvement Program and the Nationwide Inpatient Sample reporting mortality at 3.2% vs 2.6% vs 6.1%, respectively ($P < .001$). Our patient cohort is an unselected elective community-practice population with a very high rate of preoperative comorbidities. Most of our patients had ASA classification $\geq 3$ and age-unadjusted Charlson comorbidity index averaging 4.5, a figure considerably higher when compared to other studies. This comorbidity burden negatively impacts resilience, length of stay, and reported median length of overall survival. In addition, our group features a high rate of neoadjuvant therapy delivery (93%), nearly 3-fold higher as compared to that in the ECOG feasibility study. Although both studies featured a similar rate of clinical node positivity, around 40%, differences in T-stage may have influenced our need to deliver neoadjuvant therapy in most cases. Although neoadjuvant therapy has not been reported to increase perioperative complication rates in randomized studies, it may be associated with increased perioperative mortality, at least in early-stage esophageal cancer. Therefore, our high-rate of neoadjuvant therapy may have put our cohort at some additional disadvantage and, despite this, our demonstration of comparable mortality speaks to the ability to perform MIE safely outside of high-volume specialty center with the proper preparation and ongoing quality monitoring.

Kaplan-Meier survivorship function suggests a nonsignificant trend favoring the MIE group. Similar trends were seen by others, and we suppose may represent selection bias. Although comparing OE and MIE for survival should be done in a prospective fashion only, we remain comforted by the absence of obvious detriment and await reports of further randomized studies in this regard.

Figure 2. Complication rates compared between open and MIE esophagectomy. The $P$-values are shown for low-grade complications (grade 1 and 2), serious complications (grade 3 and 4), and death (grade 5). None of the comparisons was significantly different.
mance status. Going forward, we might also pursue a prospective quality of life assessment of the MIE patients to see whether we can capture the more subtle advantages of the approach.

Results of this study may not be generalizable to other similar hospitals. Both attending surgeons have significant prior experience with all aspects of gastroesophageal and other complex operations. Yet our group rarely reaches an annual esophagectomy volume ≥13 cases, considered high-volume by the Leapfrog Group. Our group also has a large experience with complex minimally invasive procedures. We hypothesize that significant cross-fertilization of technical skills contributed to outcomes that compare favorably to those reported in series from the tertiary centers and also served to hasten our mastery of the MIE procedure.

CONCLUSION

Introduction of minimally invasive esophagectomy in our community hospital was associated with prolonged operative time, but no detriment in terms of complications and overall survival. Length of stay was nonsignificantly shortened by the use of minimally invasive technique. Esophagectomy in this community hospital is associated with outcomes comparable to published standards despite a higher rate of preoperative comorbidities in this population.

References:

1. Cuschieri A, Shimi S, Banting S. Endoscopic oesophagectomy through a right thoracoscopic approach. J R Coll Surg Edinb. 1992;37:7–11.

2. Booka E, Takeuchi H, Nishi T, et al. The impact of postoperative complications on survivals after esophagectomy for esophageal cancer. Medicine (Baltimore). 2015;94:e1369.

3. Luketich JD, Alvelo-Rivera M, Buenaventura PO, et al. Minimally invasive esophagectomy: outcomes in 222 patients. Ann Surg. 238:486 – 494, 2003; discussion 494 – 485.

4. Luketich JD, Pennathur A, Franchetti Y, et al. Minimally invasive esophagectomy: results of a prospective phase II multicenter trial—the eastern cooperative oncology group (E2202) study. Ann Surg. 2015;261:702–707.

5. Dantoc MM, Cox MR, Eslick GD. Does minimally invasive esophagectomy (MIE) provide for comparable oncologic outcomes to open techniques? A systematic review. J Gastrointest Surg. 2012;16:486–494.

6. Singh RK, Pham TH, Diggs BS, Perkins S, Hunter JG. Minimally invasive esophagectomy provides equivalent oncologic outcomes to open esophagectomy for locally advanced (stage II or III) esophageal carcinoma. Arch Surg. 2011;146:711–714.
7. Nguyen NT, Nguyen XM, Reavis KM, Elliott C, Masoomi H, Stamos MJ. Minimally invasive esophagectomy with and without gastric ischemic conditioning. *Surg Endosc.* 2012;26:1637–1641.

8. Biere SS, van Berge Henegouwen MI, Maas KW, et al. Minimally invasive vs open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. *Lancet.* 2012;379:1887–1892.

9. Mariette C, Meunier B, Pezet D, et al. Hybrid minimally invasive vs open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomized phase III controlled trial, the MIRO trial. *J Clin Oncol.* 2015;33(suppl. 3): abstr 5.

10. Thirunavukarasu P, Gabriel E, Atwood K, Kukar M, Hochwald SN, Nurkin SJ. Nationwide analysis of short-term surgical outcomes of minimally invasive esophagectomy for malignancy. *Int J Surg.* 2016;25:69–75.

11. Kim JY, Correa AM, Vaporciyan AA, et al. Does the timing of esophagectomy after chemoradiation affect outcome? *Ann Thorac Surg.* 2012;93:207–212; discussion 212–203.

12. Tessier W, Gronnier C, Messager M, et al. Does surgery procedure after neoadjuvant chemoradiation affect outcomes in esophageal cancer? *Ann Thorac Surg.* 2014;97:1181–1189.

13. Ben-David K, Ang D, Grobmyer SR, Liu H, Kim T, Hochwald SN. Esophagectomy in the state of Florida: is regionalization of care warranted? *Am J Surg.* 2012;78:291–295.

14. Stitzenberg KB, Chang Y, Smith AB, Nielsen ME. Exploring the burden of inpatient readmissions after major cancer surgery. *J Clin Oncol.* 2015;33:455–464.

15. Funk LM, Gawande AA, Semel ME, et al. Esophagectomy outcomes at low-volume hospitals: the association between systems characteristics and mortality. *Ann Surg.* 2011;253:912–917.

16. Santin B, Kulwicki A, Price P. Mortality rate associated with 56 consecutive esophagectomies performed at a "low-volume" hospital: is procedure volume as important as we are trying to make it? *J Gastrointest Surg.* 2008;12:1346–1350.

17. Ben-David K, Sarosi GA, Cendan JC, Howard D, Rossidis G, Hochwald SN. Decreasing morbidity and mortality in 100 consecutive minimally invasive esophagectomies. *Surg Endosc.* 2012;26:162–167.

18. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240:205–213.

19. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. *N Engl J Med.* 2012;366:2074–2084.

20. Wright CD, Kucharczuk JC, O’Brien SM, Grab JD, Allen MS, Society of Thoracic Surgeons General Thoracic Surgery D. Predictors of major morbidity and mortality after esophagectomy for esophageal cancer: a Society of Thoracic Surgeons General Thoracic Surgery Database risk adjustment model. *J Thorac Cardiovasc Surg.* 2009;137:587–595; discussion 596.

21. Carrott PW, Markar SR, Kuppusamy MK, Traverso LW, Low DE. Accordion severity grading system: assessment of relationship between costs, length of hospital stay, and survival in patients with complications after esophagectomy for cancer. *J Am Coll Surg.* 2012;215:331–336.

22. Parekh K, Fairchild T, Natta TV, Lynch W, Iannettoni M. Timing of esophagectomy after completion of neoadjuvant therapy affects anastomotic leak rates. *Interact CardioVasc Thorac Surg.* 2008;7(suppl. 2):s185–s186.

23. Zhou C, Zhang L, Wang H, et al: Superiority of minimally invasive oesophagectomy in reducing in-hospital mortality of patients with resectable oesophageal cancer: a meta-analysis. *PloS One.* 2015;10:e0132889.

24. Sundaram A, Geronimo JC, Willer BL, et al. Survival and quality of life after minimally invasive esophagectomy: a single-surgeon experience. *Surg Endosc.* 2012;26:168–176.

25. Lapar DJ, Stukenborg GJ, Lau CL, Jones DR, Kozower BD. Differences in reported esophageal cancer resection outcomes between national clinical and administrative databases. *J Thorac Cardiovasc Surg.* 2012;144:1152–1157.

26. Markar SR, Schmidt H, Kunz S, Bodnar A, Hubka M, Low DE. Evolution of standardized clinical pathways: refining multidisciplinary care and process to improve outcomes of the surgical treatment of esophageal cancer. *J Gastrointest Surg.* 2014;18:1238–1246.

27. Murphy CC, Correa AM, Ajani JA, et al. Surgery is an essential component of multimodality therapy for patients with locally advanced esophageal adenocarcinoma. *J Gastrointest Surg.* 2013;17:1359–1369.

28. Charlson ME, Pompei P, Ales KL, MacKenzie CR. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chronic Dis.* 1987;40:373–383.

29. Walsh TN, Noonan N, Hollywood D, Kelly A, Keeling N, Hennessy TP. A comparison of multimodal therapy and surgery for esophageal adenocarcinoma. *N Engl J Med.* 1996;335:462–467.

30. Mariette C, Dahan L, Mornex F, et al. Surgery alone vs chemoradiotherapy followed by surgery for stage I and II esophageal cancer: final analysis of randomized controlled phase III trial FFCD 9901. *J Clin Oncol.* 2014;32:2416–2422.