Editorial Commentary

Minimally invasive transthoracic esophagectomy: pushing the boundaries to improve surgical outcomes

Jose M. Pimiento[1], Jacques P. Fontaine[2]

[1]Department of Gastrointestinal Oncology, [2]Department of Thoracic Oncology, Moffitt Cancer Center and Research Institute, Tampa, FL, USA

Correspondence to: Jose M. Pimiento, MD, FACS. Associated Professor, Gastrointestinal Oncology, Moffitt Cancer Center and Research Institute, 12902 Magnolia Dr, Tampa, FL 33612, USA. Email: Jose.pimiento@moffitt.org.

Provenance: This is an invited article commissioned by the Section Editor Dr. Lei Deng (Department of Medicine, Jacobi Medical Center, Albert Einstein College of Medicine, Bronx, NY, USA).

Comment on: Mariette C, Markar SR, Dabakuyo-Yonli TS, *et al.* Hybrid Minimally Invasive Esophagectomy for Esophageal Cancer. N Engl J Med 2019;380:152-62.

Submitted Mar 20, 2019. Accepted for publication Apr 02, 2019.
doi: 10.21037/jtd.2019.04.12
View this article at: http://dx.doi.org/10.21037/jtd.2019.04.12

Improving outcomes after major oncologic procedures remains a paramount goal for most health systems. Improvements in patient selection through updated risk assessment tools, more accurate preoperative staging, better definition of perioperative therapies and advances in adjuvant antineoplastic therapies are all tools that have contributed to superior long-term outcomes for patients. Despite these improvements, some surgical procedures remain associated with significant perioperative morbidity and mortality. Esophagectomy is certainly one of these procedures. Esophagectomies are associated with a morbidity ranging from 40–80% (including Clavien-Dindo II and above), and a 30-day mortality ranging from 2% to 6% (1). However, it has been hypothesized that recent advances in minimally invasive surgical techniques have improved surgical outcomes.

To test the hypothesis that minimally invasive techniques lead to better outcomes in esophagectomies, an open-label randomized control trial entitled "The Hybrid Minimally Invasive Esophagectomy for Esophageal Cancer" was conducted across 13 institutions in France (2). Patients were randomized to either a standard Ivor Lewis approach with laparotomy and right thoracotomy or to a hybrid minimally invasive esophagectomy (MIE) consisting in a laparoscopic mobilization of the stomach and a right thoracotomy—with both procedures necessitating an intrathoracic anastomosis. Of note, pyloric emptying procedures were not performed in either arm of the study. This trial was designed to compare short-term outcomes specifically focusing on major complications (Clavien-Dindo grade II or higher). Secondary end points included death within 30 days, tumor recurrence and overall survival. The trial was powered to find a 20% difference between the two surgical groups requiring 98 patients in each arm. From 2009 to 2012, 219 patients were eligible and 207 were randomized (103 patients to the hybrid-procedure group and 104 to the open-procedure group) with 204 eventually undergoing the assigned intervention. The most noteworthy patient characteristics were the following: 51% of patients had positive nodal disease, 59% had histologic diagnosis of adenocarcinoma, 69% of tumors were located in the lower third of the esophagus and 74% of patients had received neoadjuvant therapy. The results of the trial demonstrated a significant decrease in major complications from 64% in the open group to 36% in the hybrid group as well as a lower incidence of pulmonary complication 30% versus 18% respectively. The median hospital stay was the same in both groups at 14 days. The 30-day mortality (1% *vs.* 2%) and 90-day mortality (4% *vs.* 6%) were similar in both groups. At 3 years, overall and disease-free survival were not statistically different, but the trends seem to favor the hybrid group.

These results build on the results of the European multicenter TIME trial initially published in 2012 (3) which explored the outcomes of MIE versus open procedures. The TIME trial, which accrued between 2009 and 2011 across

five European hospitals, randomized 56 patients to open esophagectomy and 59 patients to MIE. Although most procedures were performed with a cervical anastomosis, the TIME trial also demonstrated similar improvements in pulmonary complications and identical long-term oncologic outcomes (overall and disease-free survival at 3 years) associated with the minimally invasive technique (3,4).

Dr. van der Sluis and his group from the Netherlands published in 2018 the results from their ROBOT trial (Robot-assisted Thoracolaparoscopic Esophagectomy *vs.* Open Transthoracic Esophagectomy trial), where 55 patients were randomized to an open three-field esophagectomy versus 54 patients randomized to a robotic-assisted three-field esophagectomy were the thorax was approached robotically and the abdomen laparoscopically. The overall complication rate (59% *vs.* 80%), median blood loss (400 *vs.* 568 mL), pulmonary complications (80% *vs.* 60%) favored the robotic-assisted group while demonstrating no difference in overall and disease-free survival between both groups. These results are similar to the ones seen in the French Hybrid technique trial as well as the TIME trial and the study by van Workum *et al.* (2,3,5,6).

At our institution, we have developed a comprehensive MIE program using robotic technology and have performed 344 MIE cases. Our published experience shows similar results to the aforementioned series with lower pulmonary complication rates compared to open procedures (14.5% *vs.* 29.4%) but identical mean length of stay (12 days) and overall survival (7).

In a recent publication by van Workum *et al.* (6), four European high-volume esophageal centers examined their MIE learning curve—reviewing the relationship between their surgical experience and surgical outcomes—specifically anastomotic leaks and operative times. The study included 646 patients. It is interesting to note that the number of cases required to achieve the lowest anastomotic leak rate (in other words to attain a plateau on the learning curve) and improved complication rate is about 119 surgical procedures (6). This data highlights that although minimally invasive hybrid techniques for an esophagectomy improve outcomes (2), the experience and volume of the individual surgeon and institution continues to play a major role. Thus, adoption of any new surgical technique will need to be taken in the context of high-volume institutions with high volume surgeons to lessen the learning curve and optimize outcomes (5,6).

It is therefore important to define "quality benchmarks" when reviewing a surgeon's or an institution's results after minimally invasive esophagectomy (MIE). Schmidt *et al.*, tried to define such quality benchmarks or "best possible" outcomes after trans-thoracic MIE (8). Their group reviewed outcomes of a selected cohort of 334 patients with low co-morbidities (age ≤65, American Society of Anesthesiologists score ≤2, ECOG score ≤1, body mass index 19–29 kg/m^2) out of a total of 1,057 patients who underwent trans-thoracic MIE across 13 high-volume centers over a 5-year period. The quality benchmark was set at the 75th percentile of the median outcome parameters in this highly selected group of low comorbidity (low-risk) patients. Quality benchmark values in this low-risk group were a 30-day overall and major complication (≥ grade III) rate of 56% and 31% respectively. The 30- and 90-day mortality were 1.0% and 4.6% respectively.

Another source of data for establishing quality benchmarks can certainly be the single institution extensive MIE experience from Dr. James Luketich's group at University of Pittsburgh. Their review of 1,011 consecutive patients undergoing elective MIE revealed a median length of stay of 8 days, a 5% anastomotic leak rate requiring surgical intervention and a 30-day operative mortality of 1.7% (9).

In conclusion, MIE, whether by laparoscopic or robotic technique, is associated with similar 30- and 90-day mortality but significantly less complication rates than open technique, mostly due to decreased cardiopulmonary complications and better pain control (2,5). Interestingly, although the rate of pulmonary complications are lower after MIE, several large series have shown that the median length of hospital stay remains unchanged regardless of surgical technique and this may be due to time required for patients to recuperate from the extent of internal dissection and changes in gastrointestinal physiology and functionality rather than the length of incisions. Although Palazzo *et al.* reported an improved in 5-year survival after MIE compared to open esophagectomy in a study with 172 patients (10), most other publications have reported no statistically significant differences in overall or disease-free survival (2). It must be noted that there is a significant learning curve associated with MIE which may be difficult to reach in low-volume centers. It is for this reason we must rely on "quality benchmarks" defined by the results of these high-quality randomized trials or large high-quality series when assessing our own surgical results. It is of utmost importance for surgeons to collect and analyze their own surgical data. One cannot improve unless one critically evaluates his or her own quality metrics. Lastly,

this clinical outcomes data, allows us to be more accurate and informative when discussing surgical treatment options with our esophageal cancer patients.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

References

1. van Hagen P, Hulshof MC, van Lanschot JJ, et al. Preoperative chemoradiotherapy for esophageal or junctional cancer. N Engl J Med 2012;366:2074-84.
2. Mariette C, Markar SR, Dabakuyo-Yonli TS, et al. Hybrid Minimally Invasive Esophagectomy for Esophageal Cancer. N Engl J Med 2019;380:152-62.
3. Biere SS, van Berge Henegouwen MI, Maas KW, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. Lancet 2012;379:1887-92.
4. Straatman J, van der Wielen N, Cuesta MA, et al. Minimally Invasive Versus Open Esophageal Resection: Three-year Follow-up of the Previously Reported Randomized Controlled Trial: the TIME Trial. Ann Surg 2017;266:232-6.
5. van der Sluis PC, van der Horst S, May AM, et al. Robot-assisted Minimally Invasive Thoracolaparoscopic Esophagectomy Versus Open Transthoracic Esophagectomy for Resectable Esophageal Cancer: A Randomized Controlled Trial. Ann Surg 2019;269:621-30.
6. van Workum F, Stenstra MHBC, Berkelmans GHK, et al. Learning Curve and Associated Morbidity of Minimally Invasive Esophagectomy: A Retrospective Multicenter Study. Ann Surg 2019;269:88-94.
7. Amaral M, Pimiento J, Fontaine JP. Robotic esophagectomy: the Moffitt Cancer Center experience. Ann Cardiothorac Surg 2017;6:186-9.
8. Schmidt HM, Gisbertz SS, Moons J, et al. Defining Benchmarks for Transthoracic Esophagectomy: A Multicenter Analysis of Total Minimally Invasive Esophagectomy in Low Risk Patients. Ann Surg 2017;266:814-21.
9. Luketich JD, Pennathur A, Awais O, et al. Outcomes after minimally invasive esophagectomy: review of over 1000 patients. Ann Surg 2012;256:95-103.
10. Palazzo F, Rosato EL, Chaudhary A, et al. Minimally invasive esophagectomy provides significant survival advantage compared with open or hybrid esophagectomy for patients with cancers of the esophagus and gastroesophageal junction. J Am Coll Surg 2015;220:672-9.

Cite this article as: Pimiento JM, Fontaine JP. Minimally invasive transthoracic esophagectomy: pushing the boundaries to improve surgical outcomes. J Thorac Dis 2019;11(Suppl 9):S1336-S1338. doi: 10.21037/jtd.2019.04.12

