Minimally Invasive Versus Open Esophagectomy for Esophageal Cancer: A Population-Based Analysis

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Background. **The objective of this study was to evaluate outcomes of minimally invasive approaches to esophagectomy using population-level data.**

Methods. **Multivariable regression modeling was used to determine predictors associated with the use of minimally invasive approaches for patients in the National Cancer Data Base who underwent resection of middle and distal clinical T13N03M0 esophageal cancers from 2010 to 2012. Perioperative outcomes and 3-year survival were compared between propensity-matched groups of patients with esophageal cancer who underwent minimally invasive esophagectomy (MIE) or open esophagectomy (OE). A subgroup analysis was performed to evaluate the impact of using robotic-assisted operations as part of the minimally invasive approach.**

Results. **Among 4,266 patients included, 1,308 (30.6%) underwent MIE. It was more likely to be used in patients treated at academic (adjusted odds ratio [OR], 10.1; 95% confidence interval [CI], 4.2–33.1) or comprehensive cancer facilities (adjusted OR, 6.4; 95% CI, 2.6–21.1). Compared with propensity-matched patients who underwent OE, patients who underwent MIE had significantly more lymph nodes examined (15 versus 13; $p = 0.016$) and shorter hospital lengths of stay (10 days versus 11 days; $p = 0.046$) but similar resection margin positivity, readmission, and 30-day mortality (all $p > 0.05$). Survival was similar between the matched groups at 3 years for both adenocarcinoma and squamous cell carcinoma ($p > 0.05$). Compared with MIE without robotic assistance, use of a robotic approach was not associated with any significant differences in perioperative outcomes ($p > 0.05$).**

Conclusions. **The use of minimally invasive techniques to perform esophagectomy for esophageal cancer is associated with modestly improved perioperative outcomes without compromising survival.**

(Ann Thorac Surg 2016;■:■–■)

Over the past decade, minimally invasive esophagectomy (MIE) has been used increasingly for the treatment of esophageal cancer [1]. Currently, MIE can be performed through the laparoscopic transhiatal, the laparoscopic-thoracoscopic McKeown, or the laparoscopic-thoracoscopic Ivor Lewis approach [2]. Although there are differences in the specific operative approach, supporters of MIE have cited reduced perioperative morbidity, shortened hospital stay, and improved patient satisfaction when compared with traditional open esophagectomy (OE) [3].

More recently, robotic-assisted minimally invasive esophagectomy (RAMIE) has been introduced to address the technical difficulties encountered in laparoscopic resections, but data comparing RAMIE versus standard MIE without robotic assistance (SMIE) are lacking. The only study comparing RAMIE versus SMIE found no differences in operative time, blood loss, number of resected lymph nodes, postoperative complications, days of mechanical ventilation, length of intensive care unit stay, or length of hospital stay [4].

Despite the ongoing adoption of MIE, data regarding the oncologic acceptability of using a minimally invasive approach in esophageal cancer is extremely limited. Most comparative effectiveness studies are single high-volume institutional experiences that lack generalizability [5–8]. The Traditional Invasive Versus Minimally Invasive Esophagectomy (TIME) trial is the only

Accepted for publication Feb 16, 2016.

Presented at the Forty-first Annual Meeting of the Western Thoracic Surgery Association, Whistler, British Columbia, Canada, June 24–27, 2015.

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Dr D'Amico discloses a financial relationship with Scanlan.

0003-4975/$36.00
http://dx.doi.org/10.1016/j.athoracsur.2016.02.078

Abbreviations and Acronyms

CI = confidence interval
MIE = minimally invasive esophagectomy
OE = open esophagectomy
RAMIE = robotic assisted minimally invasive esophagectomy
SMIE = standard minimally invasive esophagectomy without robotic assistance

multicenter randomized study comparing open esophagectomy versus MIE, but it lacks power to detect any oncologic difference [9]. Moreover, although 1 population study analyzed short-term outcomes between MIE and OE in the United Kingdom [10], no study to date has examined survival differences between MIE and OE on a national level in the United States.

Therefore the purpose of this study was to compare perioperative outcomes and survival in patients who underwent MIE versus traditional OE using population-level data. Furthermore, we aimed to assess any differences in using a robotic-assisted minimally invasive approach over the standard MIE approach. The primary hypothesis was that surgical approach would not be associated with perioperative outcomes or 3-year survival.

Patients and Methods

The Duke University Institutional Review Board approved this retrospective review of the National Cancer Data Base. The National Cancer Data Base is jointly administered by the American College of Surgeons and the American Cancer Society and collects data from greater than 1,500 cancer institutions. The database currently contains records of 30 million patient records and approximately 70% of newly diagnosed cancer cases in the United States.

Patients with clinical T1-3any NM0 esophageal cancers located in the middle and distal esophagus who underwent esophagectomy from 2010 to 2012 were included in the study. MIE was defined by intent-to-treat criteria as any operation involving either thoracoscopy or laparoscopy, including any hybrid or robotic-assisted approach. Patients with nonmalignant pathologic conditions or missing surgical approach data were excluded.

The primary end point of our study was 3-year survival. Secondary end points included positive surgical margins, lymph nodes examined, hospital length of stay, 30-day unplanned readmissions, 30-day mortality, and adjuvant therapy use.

Baseline characteristics between all cases of OE and MIE were compared using the Kruskal-Wallis and Pearson's χ^2 tests for continuous variable and categorical variables, respectively. Multivariable logistic regression models were developed to identify factors independently associated with the use of OE versus MIE; a backward variable elimination method was used to produce the most parsimonious model based on the lowest Akaike information criterion. To adjust for potential selection bias between the comparison of OE and MIE, we developed propensity scores, defined as the conditional probability of undergoing MIE. Patients were matched using a 1:1 nearest-neighbor algorithm, using the following variables: age, sex, race, insurance status, Charlson-Deyo comorbidity score, treatment facility type (community, comprehensive, or academic), location of the primary lesion (middle or lower third of the esophagus), American Joint Committee on Cancer clinical T and N stages, tumor size, and use of simultaneous neoadjuvant chemotherapy and radiotherapy. Outcomes were compared in propensity-matched groups. Survival was plotted using the Kaplan-Meier method.

To assess the effect of robotic assistance in MIE, a subgroup analysis was performed in a similar fashion comparing RAMIE versus SMIE. This method was repeated for both adenocarcinoma and squamous cell carcinoma. For all analyses, p values less than 0.05 were considered to indicate statistical significance. All analyses were performed using R, version 3.0.1 (The R Foundation for Statistical Computing, Vienna, Austria).

Results

Among 4,266 total patients identified, 2,958 (69.3%) underwent OE, whereas 1,308 (30.7%) underwent MIE. Among patients who received MIE, 231 (17.6%) underwent RAMIE.

Unadjusted baseline characteristics of patients who underwent OE and MIE are shown in Table 1. Patients who underwent MIE were more likely to be treated at an academic facility ($p < 0.001$), to have a lower clinical T stage ($p = 0.029$), to have a lower pathologic T stage ($p = 0.041$), and to have a smaller tumor size ($p = 0.007$) when compared with patients undergoing OE. Conversion to an open procedure within the entire MIE group was 11.6%. The use of MIE increased from 27.1% in 2010 to 37.5% in 2012. The median number of esophagectomies per center was 2. After accounting for patient, tumor, and hospital factors, we found that treatment at either a comprehensive facility (odds ratio [OR], 7.32, 95% confidence interval [CI], 2.28–23.47; $p = 0.001$) or an academic facility (OR, 11.24; 95% CI, 3.52–35.90; $p < 0.001$) was predictive of a patient undergoing MIE (Fig 1). Independent predictors of OE included the presence of a clinical stage T2 tumor (OR, 0.74; 95% CI, 0.58–0.96; $p = 0.023$) or a clinical stage T3 tumor (OR, 0.72; 95% CI, 0.56–0.93; $p = 0.011$), when compared with clinical stage T1 disease (Fig 1).

After propensity matching, no substantial differences in covariates remained between groups (Table 2). Within matched groups, we found that margin positivity, unplanned readmission, and 30-day mortality rates were not significantly different between OE and MIE groups (all $p > 0.05$). However, the MIE group was associated with a higher number of lymph nodes harvested (15 versus 13; $p = 0.016$) and a modest decrease in hospital length of stay (10 days versus 11 days; $p = 0.046$) (Table 3).