Minimal or maximal surgery for esophageal cancer?

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In recently published issues of the *Journal of Thoracic and Cardiovascular Surgery*, readers have had opportunities to examine a variety of studies focused on improving our understanding of the surgical management of esophageal cancer, including the potential advantages of minimally invasive approaches.¹⁻⁵ These articles provide an opportunity to review changes in the surgical management of esophageal cancer and the key factors influencing quality outcomes.

MINIMAL SURGERY FOR ESOPHAGEAL CANCER: THE ENDOSCOPIC APPROACH

Of the many advances and changes in the management of esophageal cancer, perhaps the most dramatic shift has been in the approach to high-grade dysplasia and superficially invasive disease. Over the past decade, endoscopic therapies for superficially invasive esophageal carcinomas have overtaken esophagectomy as the primary treatment modality. This has been based primarily on the high rates of disease control demonstrated in the published literature and the nearly nonexistent postprocedure morbidity associated with endoscopic procedures.^{6,7} Whether or not endoscopic resection (mucosal or submucosal) is adequate definitive therapy for superficially invasive cancers is based on the underlying risk of undetected nodal metastasis.⁸⁻¹⁷ The proportions of patients with lymph node metastasis associated with a T1a depth of invasion range widely, from <3% to ~9%, whereas the risk associated with T1b depth of invasion is substantially higher (>25%).^{8,11,18-22} As such, when considering endoscopic therapy as opposed to esophagectomy, the risk-to-benefit assessment must weigh the likelihood of undertreatment (endoscopic therapy alone in the setting of occult positive lymph nodes) against the potential morbidity and mortality associated with esophagectomy.

Unfortunately, clinical assessment of the depth of tumor invasion is quite poor, with up to 60% of superficially invasive

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Central Message

Available evidence supports a prominent role for minimal surgery (eg, endoscopic and minimally invasive) in esophageal cancer management.

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cases incorrectly characterized by endoscopic ultrasound.²¹ As a result, to optimize risk stratification in patients with apparently superficially invasive esophageal cancer, endoscopic mucosal resection should be performed, with careful assessment for the presence of high-risk characteristics.²³ In addition to depth of invasion (mucosal vs submucosal), predictors of lymph node metastasis in superficial esophageal cancer included tumor size >2 cm, the presence of lymphovascular invasion, and poorly differentiated tumor grade.^{9-11,13} When these high-risk characteristics are identified, patients should be counseled regarding the risks of nodal metastasis and recommended for either esophagectomy or definitive chemoradiation,^{24,25} depending upon their fitness for operative intervention as determined by a surgeon with expertise in esophagectomy.

MINIMAL VERSUS MAXIMAL SURGERY FOR ESOPHAGECTOMY

Similar to the drive for minimal surgery to achieve maximal benefit in lung surgery, an increasing number of surgeons are strong proponents for minimally invasive esophagectomy. Potential advantages include reduced blood loss, reduced morbidity during the perioperative phase with faster recovery, and decreased length of hospital stay.²⁶ Results from high-volume esophageal surgery centers have been excellent, with low mortality rates and acceptable

morbidity.²⁷ The oncologic adequacy of a minimally invasive approach was also established, with many single-center studies showing rates of complete resection, lymph node retrieval, and survival similar to the rates achieved with Ivor Lewis and McKeown esophagectomy.²⁸⁻³⁰ Detractors, however, cite a lack of prospective data supporting minimally invasive esophagectomy as superior to open esophagectomy and a wide variation in the definition of a minimally invasive esophagectomy³¹; indeed, until a few years ago there were few prospective studies and no randomized trials showing even equivalent outcomes, let alone superior ones. Prospective and randomized trial results are now available that clearly establish the safety of minimally invasive esophagectomy as primary treatment as well as following induction therapy.^{32,33} The first randomized controlled trial of minimally invasive versus open esophagectomy was published during 2012.³⁴ That multicenter trial from the Netherlands was powered to examine differences in pulmonary infection within the first 2 weeks after resection and found that the relative risk was 70% less after minimally invasive esophagectomy compared with an open approach. Length of hospital stay and complete resection also favored minimally invasive esophagectomy, as did pain scales and short-term quality of life (as measured by the Short-Form 36 and the European Organization for Research and Treatment of Cancer Quality of Life Questionnaire Cancer 30 and Esophagus 18 measures). There were no differences in pathologic stage or total lymph nodes retrieved. Mortality at 30 days and during hospital stay were not significantly different.³⁴ Although the trial was not powered to demonstrate a difference in quality of life, the early improvements in quality-of-life measures were sustained. At 1-year follow-up, measures of physical health, global health, and pain were all significantly better for the patients who were treated with a minimally invasive approach compared with an open esophagectomy.³⁵ Wang and colleagues,² using a propensity-matched comparison of open and minimally invasive esophagectomy, also found that scores were higher for physical function and global quality of life, with less fatigue, pain, and dyspnea in the minimally invasive cohort, especially during the first year of survival after esophagectomy.

PREDICTING MORBIDITY AND MORTALITY AFTER MINIMAL OR MAXIMAL ESOPHAGECTOMY

Despite the advantages offered by a minimally invasive approach to esophagectomy, there is still a significant risk of major complications and the potential for fatal outcomes. As such, appropriate patient selection continues to be vitally important. A number of authors from centers of excellence for esophageal surgery have examined a variety of predictors to aid surgeons in risk stratification for postoperative

morbidity and mortality. The majority of these efforts have focused on developing preoperative risk stratification tools, including the Charlson comorbidity index, frailty indices,³⁶ nutritional risk assessment,³⁷ and other preoperative clinical parameters.³⁸ Intraoperative risk stratification tools may also prove useful for patient-specific treatment protocols. For example, use of the intensive care unit may not be necessary for all patients, but may improve outcomes for patients with high preoperative or intraoperative risk score for postoperative morbidity and mortality. Using intraoperative heart rate, mean arterial blood pressure, and blood loss, Janowak and colleagues¹ found that a modified esophagectomy Surgical Apgar Score of 6 or less was strongly and independently associated with 30-day major morbidity and suggested that this score could be used to aid clinicians in postoperative decision making (eg, risk-stratified triage of patients and modification of postoperative care) to optimize outcomes and resource use. Increased use of these types of preoperative and intraoperative risk-stratification tools may aid clinicians in reducing postoperative complications and identifying patients who might be at increased risk for difficult-to-manage complications requiring a more intensive initial hospitalization. Indeed, hospital readmissions after esophagectomy, an increasingly important and influential quality measure, appear to be directly related to complications identified at the initial hospitalization, most commonly pulmonary issues, anastomotic complications, gastrointestinal complaints, and venous thromboembolism.³

MINIMAL OR MAXIMAL SURGERY FOR ESOPHAGEAL CANCER?

Although the ultimate answer to this question depends on the characteristics of the patient, the tumor, and the treating physicians, the available evidence increasingly favors a prominent role for minimally invasive approaches in the management of esophageal cancer. Endoscopic therapies and minimally invasive approaches offer at least equivalent oncologic outcomes, with reduced complications and improved quality of life compared with maximal surgery. When used in combination with established preoperative and intraoperative risk-stratification tools, treatment protocols, and postoperative pathways, minimal surgery for esophageal cancer can provide maximal patient benefit.

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