Surgical Approaches to Esophageal Cancer

Steven Teng, MD, and Richard Karl, MD

The optimal surgical treatment approach for esophageal cancer remains controversial.

**Background:** Esophageal cancer is a highly lethal malignancy. Esophageal resection remains the primary treatment in most centers. A number of approaches to esophageal resection have been described.

**Methods:** The authors review the current approaches to esophageal resection and adjuvant therapy for esophageal cancer.

**Results:** Transthoracic, transhiatal, and minimally invasive techniques are currently employed in esophageal surgery for malignancy. A number of authors favor extended mediastinal and cervical lymphadenectomy in hopes of improving survival. Combined chemotherapy and radiotherapy in the neoadjuvant setting appears to offer some promise.

**Conclusions:** No consensus of opinion exists regarding the optimal approach or extent of esophageal resection for cancer. Prospective, randomized trials of neoadjuvant therapy may determine its efficacy. Newer approaches may enhance quality of life.

**Introduction**

Esophageal cancer represents one of the most lethal malignances affecting mankind. This is compounded by the fact that adenocarcinoma of the esophagus is increasing in incidence at a rate exceeding that of any other neoplasm. At most centers, esophageal resection remains the therapeutic alternative of choice for patients who are considered to be surgical candidates. However, no consensus of opinion exists among surgeons as to the optimal approach to patients with carcinoma of the esophagus. Despite the numerous contributions to the surgical literature, esophageal resection remains a highly disputed topic. The following represents a review of the recent literature in an attempt to elucidate the modern surgical approaches to this lethal condition.

**Clinical Presentation**

The most common symptom of esophageal cancer at the time of presentation is dysphagia. Unfortunately, by the time that dysphagia manifests itself, most patients no longer have early-stage disease. A minority of patients may present with hemoccult positive stools, vague episodes of chest discomfort, or mild cases of odynophagia. Anemia and weight loss of varying degrees are also common findings. Chest pain, upper abdominal pain, tracheoesophageal fistula, hepatic dysfunction, neurologic changes, and bone pain are all associated with advanced-stage disease and portend a poor prognosis.

In the case of adenocarcinoma arising in Barrett’s esophagus, asymptomatic cancers may be detected by surveillance endoscopy. As many as 50% of patients undergoing esophagectomy for high-grade dysplasia noted on endoscopic biopsy will have evidence of invasive carcinoma in the resected specimen. It is in such patients with early-stage disease that resection offers the highest possibility of long-term survival and cure.

**Preoperative Evaluation**

Appropriate preoperative evaluation of patients with esophageal cancer is directed at accurately determining the stage of the disease, the technical feasibility of resection, and the adequacy of the patient’s physiologic reserve to withstand the operation. The existence of any comorbid conditions is particularly important in view of the fact that this population of patients is usually elderly and often has a significant history of alcohol or tobacco use.

The first diagnostic test in most patients with dysphagia is a barium swallow. This will usually define the presence and level of a mechanical obstruction. All patients should undergo esophagoscopy and computed tomography of the chest, upper abdomen, and possibly the neck. These studies should delineate the anatomic location and extent of the disease as well as provide the opportunity for tissue diagnosis. Of particular concern is the presence of lymph node involvement, metastatic disease, or local extension into surrounding structures, which might preclude curative resection. Bronchoscopy can be helpful in identifying tracheal involvement when the primary tumor is located in the proximal two thirds of the esophagus. Endoscopic ultrasound has also proven to be accurate in determining the local extent of disease and is discussed elsewhere in this issue.

Routine blood chemistries, urinalysis, and appropriate cardiac, respiratory, and nutritional evaluation are also performed as for any other major upper abdominal or thoracic surgical procedure.

**Techniques of Resection**

A number of approaches to esophageal resection have been described. Each has its supporters and detractors despite the lack of sufficient objective evidence to clearly support one over another. The two most often reported are a variant of the transthoracic approach as described by Lewis in 1946 and the transhiatal approach championed by Orringer (Figs 1 and 2). The left thoracoabdominal incision is rarely used in this country today. This is the result of the poor exposure of the proximal esophagus due to the position of the aortic arch and the associated morbidity of dividing the costal margin. The use of a left thoracotomy in combination with division of the left hemidiaphragm to accomplish the intra-abdominal portion of the procedure has been described with good results in 2,613 patients.

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The Ivor-Lewis approach to esophagectomy is performed through an upper abdominal incision and a right posterolateral thoracotomy. Its supporters point to the excellent exposure afforded for both the intra-abdominal and thoracic portions of the operation. Some believe that this exposure allows for a more definitive oncologic procedure with superior margins and improved clearance of regional lymph nodes. This has not been associated with significantly superior survival rates (Table 1).4,6-10

The transhiatal esophagectomy is accomplished via upper abdominal and cervical incisions. The esophagus is bluntly dissected from both above and below. Advocates of the transhiatal esophagectomy believe that avoiding a thoracotomy results in a less morbid procedure. In addition, many emphasize that the performance of a cervical anastomosis leaves the patient less vulnerable to a potentially devastating mediastinitis as a result of leakage of an intrathoracic anastomosis despite the overall higher rate of anastomotic leakage associated with a cervical anastomosis. For this reason, some surgeons perform transthoracic resection with a cervical anastomosis via a separate incision. Critics of the transhiatal approach emphasize the difficulty of performing an adequate oncologic operation and the potential for hemorrhage with the blunt mediastinal dissection. Significant differences between the two techniques regarding either operative morbidity or mortality have yet to be shown conclusively (Tables 2-3).4,6-12 A retrospective analysis of an institutional experience with 82 patients, however, demonstrated less morbidity and mortality in patients undergoing transhiatal esophagectomy despite the fact that those patients had been adversely selected for on the basis of anesthetic risk.11 The perception of

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>TTE</th>
<th>Number of Patients</th>
<th>Survival</th>
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<tbody>
<tr>
<td>Colinog et al.</td>
<td>1983</td>
<td>TTE</td>
<td>47</td>
<td>27% (3 y)</td>
</tr>
<tr>
<td>Mahal et al.</td>
<td>1982</td>
<td>TTE</td>
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<td>TTE</td>
<td>104</td>
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<tr>
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<td>1987</td>
<td>TTE</td>
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<td>Alexander et al.</td>
<td>1980</td>
<td>TTE</td>
<td>15</td>
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<tr>
<td>Cho et al.</td>
<td>1987</td>
<td>TTE</td>
<td>64</td>
<td>11.5 mo median</td>
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Table 1: - Survival by Different Surgical Approaches

<table>
<thead>
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</tbody>
</table>

TTE = transthoracic esophagectomy
TIE = transhiatal esophagectomy
ao = anatomico
es = esophagectomy
tax = transthoracic anastomosis
"prospective, nonrandomized"
the transhiatal esophagectomy as a less than optimal oncologic procedure with decreased morbidity has led some surgeons to reserve it use for patients with high-grade dysplasia arising in Barrett’s esophagus or those patients with high operative risk.

In addition to the numerous retrospective analyses regarding both procedures, at least two prospective, randomized trials have attempted to resolve the controversy. Neither Chu et al. nor Goldminc et al. were able to demonstrate significant differences between either approach in terms of survival, morbidity, or mortality. Both studies may have been hampered by inadequate sample size.

**Choice of Conduit**

The stomach, a segment of colon, and the jejunum have all been described as replacement conduits for the esophagus following resection (Fig 3). The most commonly used conduit in patients undergoing esophagectomy for malignancy is the formation of a gastric tube with either intrathoracic or cervical esophagogastrostomy. Most surgeons reserve the use of an isoperistalsic segment of colon for patients in whom the stomach is not suitable or for those whose favorable long-term prognosis justifies the longer operative time and creation of additional anastomoses. The use of a colonic interposition reduces the incidence of reflux esophagitis and stricture associated with esophagogastrostomy. The jejunum is rarely used in the United States today; it is most often employed as a free jejunal graft with microvascular anastomoses to replace the cervical esophagus.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Approach</th>
<th>Number of Patients</th>
<th>Operation Mortality</th>
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<td>Orange</td>
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<td>0%</td>
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<td>TTE</td>
<td>271</td>
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<td>Maloney</td>
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<td>TTE</td>
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<td>Yang</td>
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<td>R-TTE</td>
<td>150</td>
<td>2.5%</td>
</tr>
<tr>
<td>Goldminc</td>
<td>1999</td>
<td>TTE</td>
<td>35</td>
<td>0% (0%)</td>
</tr>
<tr>
<td>Chu</td>
<td>1998</td>
<td>TTE</td>
<td>95</td>
<td>0% (0%)</td>
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<tr>
<td>Brotelli</td>
<td>1994</td>
<td>TTE</td>
<td>34</td>
<td>0%</td>
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**Table 2** — Operation Mortality by Surgical Approach

**Table 3** — Complications by Surgical Approach

In some instances, an extracorporeal tube has been used to connect a cervical esophagostomy and a gastrostomy to allow the patient to consume solid food orally.
Extent of Operation

An additional area of controversy has been the extent of resection necessary to provide a potentially curative operation. How much of an esophageal margin should be obtained, and how extensive a lymphadenectomy should be performed? The question of adequate margins is important due to the propensity for intramural tumor spread via submucosal lymphatics.

Law et al\textsuperscript{14} addressed the importance of adequate proximal and distal margins by examining the significance of histologically involved margins in a group of 604 patients. Interestingly, histologically involved margins had no influence on anastomotic recurrence, but the gross margin of resection affected the incidence of anastomotic recurrence. Patients who developed an anastomotic recurrence had an average resection margin of 2.7 cm compared to 4.4 cm in those patients who did not. The use of postoperative radiation in some patients with involved margins may have influenced the observations. All margins were as measured in the fresh gross specimen, which the authors estimated to be 44\% of the length of the in situ margin. In contrast to previously published reports, these authors found no relationship between histologically involved margins and the anastomatic leak rate. The authors recommend in situ margins of 10 cm proximally and distally when feasible.\textsuperscript{15}

A number of reports from Japan have demonstrated impressive gains in survival with the use of extended lymphadenectomy when compared against historic controls. While there has not been a reported increase in mortality with these procedures, the authors have acknowledged significant increases in operative morbidity.\textsuperscript{16-19}

Extended lymphadenectomy is described as a three-field lymphadenectomy comprising extensive abdominal, mediastinal, and bilateral cervical lymph node dissections. At least one report indicates that such radical operations are of benefit only in patients with fewer than four involved lymph nodes.\textsuperscript{20}

The success reported with three-field lymphadenectomy in Japan has inspired some Western surgeons to try to duplicate these results. Altorki and Skinner\textsuperscript{21} reported that a prospective study of 30 patients undergoing three-field lymphadenectomy revealed that the cervical nodal regions were as likely to harbor involved lymph nodes as were mediastinal nodes. The therapeutic implications of this observation are controversial. It may reflect the wisdom of cervical node dissections, or it may merely point to the futility of extensive lymph node dissections due to the prevalence of systemic disease.

Furthermore, Altorki et al\textsuperscript{22} would go on to report that en bloc esophagectomy with extended lymph node dissection improved the survival of stage III disease based on their retrospective analysis of 128 patients. Of 54 patients with stage III disease, 33 underwent en bloc resection with an extended lymphadenectomy (two- or three-field). Median survival for those patients undergoing the more extensive procedure was 27 months vs a median survival of 12 months for those patients with a limited resection ($P=0.007$).\textsuperscript{23} Whether this represents stage migration due to the more extensive lymphadenectomy or a true improvement in survival is unclear.

The impact of three-field lymphadenectomy has been examined by a single-institution, prospective, randomized trial in Japan.\textsuperscript{23} Thirty-two patients received extended lymphadenectomy, and 30 patients received conventional lymphadenectomy. Five-year survival rates of 66.2\% and 48\%, respectively, were obtained. The survival advantage for patients who underwent extended lymphadenectomy did not reach statistical significance ($P=0.192$). The more extensive procedure was associated with increased morbidity. Recurrent nerve palsy occurred in 56\% compared with 30\% in the control group. A tracheostomy in the postoperative period was required in 53\% of patients undergoing extended lymphadenectomy compared with 10\% in the control group.\textsuperscript{23}

Minimally Invasive Techniques

The application of minimally invasive surgical techniques to a potentially morbid procedure such as esophagectomy is attractive and has been described by several authors. In 1997, Bonivina et al\textsuperscript{24} reported their experience with staging laparoscopy in 50 patients. Findings at the time of laparoscopy prompted a change in management in five patients (10\%). Three patients were found to have peritoneal carcinomatosis not identified by preoperative computed tomography scan. Advanced cirrhosis of the liver was identified in one patient, which precluded resection. In the remaining patient, a suspected liver metastasis was identified as a hemangiomia allowing the patient to undergo potentially curative resection.

Both thoracoscopic and laparoscopic techniques have been applied to esophageal resection as well as staging. Law et al\textsuperscript{25} published a prospective evaluation of their experience with thoracoscopic esophagectomy at the Queen Mary Hospital in Hong Kong. The thoracoscopic procedure was completed successfully in 18 patients. Conversion to open thoracotomy was necessary in one patient. Operative time, complication rate, and survival were not significantly different when compared to patients undergoing Ivor-Lewis resection during the same time frame. One patient developed recurrent cancer at a port site. Patients were selected for thoracoscopy based on their increased risk for thoracotomy. The authors report that they currently favor thoracoscopic resection over transhiatal esophagectomy in this subset of patients.

In summary, the appropriate role for minimally invasive techniques in patients with esophageal cancer has yet to be definitively established and will continue to evolve as both experience and technology improve.

Elderly Patients

As the percentage of elderly patients in the population increases, the incidence of esophageal cancer in elderly patients will likely increase as well. The role of esophageal resection in those patients with potentially resectable disease becomes increasingly important in light of the potential for higher morbidity and mortality in this population. This is further complicated by the extremely poor prognosis despite resection for all but the earliest stages of disease. Several authors have published their experiences with esophagectomy in elderly patients.

Poon et al\textsuperscript{26} retrospectively reviewed their experience with esophagectomy in 167 patients 70 years of age or greater. They found a significantly higher rate of medical complications compared with a group of 570 patients less than 70 years of age. The incidence of what were termed surgical complications did not differ between the two groups. Five-year survival in the more elderly patients (26\%) did not compare favorably with that of the younger patients (35\%). The authors found that the difference in long-term survival lost statistical significance when they excluded patients who succumbed in the perioperative period. In-hospital mortality for the older and younger groups of patients were 18\% and 14\%, respectively. Interestingly, while these authors favor the transthoracic approach to esophagectomy, they tended to reserve the transhiatal approach for the more elderly patients based on their belief that it represents a less morbid procedure.

Jougon et al\textsuperscript{27} reported no statistically significant differences in either morbidity or mortality for patients aged 70 years and older. These authors based their operative approach solely upon the anatomic extent of the disease. In most cases, their procedure of choice was resection via a left thoracoabdominal incision.

It would appear that elderly patients have the potential to benefit from esophageal resection for malignancy after having undergone a thorough preoperative risk
The Role of Adjuvant Therapy

The poor prognosis usually associated with esophageal cancer has led to attempts to improve outcome with the use of chemotherapy and radiation. To date, prospective, randomized trials of preoperative and postoperative chemotherapy or radiation have failed to affect patient survival. A number of phase II trials of chemoradiation in the neoadjuvant setting have produced complete pathologic response rates of approximately 25% and have increased median survival by more than 30%.[29] The improvement in survival appears limited to those patients who responded to the preoperative therapy. The interval between the completion of neoadjuvant therapy and surgery is usually reported to be between 18 days and six weeks.[30-32] At our institution, we prefer to schedule surgery four to six weeks following chemoradiation. Phase III trials of neoadjuvant chemoradiation are currently underway.

The incidence of complete pathologic response to combined chemotherapy and radiation has prompted some to question the utility of surgery. Concern about the role of resection is raised, especially in light of the potential for increased morbidity with the addition of neoadjuvant therapy.

Swisher et al[33] retrospectively analyzed the impact of neoadjuvant chemoradiation on esophagectomy in 312 patients (106 received neoadjuvant therapy). They found no significant difference in operative time, operative mortality, leak rates, and cardiopulmonary complications. Estimated blood loss was lower (1006 cc vs 1246 cc) in those patients receiving chemoradiation.

A phase II trial of neoadjuvant chemoradiation found that adjuvant therapy actually reduced operative time, blood loss, and transfusion requirements. Morbidity and mortality were not significantly different between the two groups. In addition, 50% of those patients who remained disease free at a median follow-up of 30 months had residual disease in the resected specimen. The authors suggest a continued role for resection in the treatment of esophageal cancer.[34]

Currently available data suggest that neoadjuvant multimodality therapy holds the promise of significantly impacting the survival of these patients without adding to the operative morbidity. Abandoning surgical resection at this time would be premature.

Conclusions

The current therapeutic options in the treatment of both squamous cell and adenocarcinoma of the esophagus are both numerous and confusing. The choice of surgical approach appears to be affected as much by the personal biases of surgeons as by available objective data. Many of the current questions regarding the various surgical techniques may never be answered by prospective, randomized trials of adequate sample size. Still, the possible applications of minimally invasive surgical techniques, extended lymphadenectomy, and preoperative multimodality therapy may have a positive impact on patient survival and quality of life.

No significant relationship exists between the authors and the companies/organizations whose products or services may be referenced in this article.

References


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