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TOPIC HIGHLIGHT

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Transhiatal versus transthoracic esophagectomy for esophageal cancer

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Abstract

Esophageal cancer continues to represent a formidable challenge for both patients and clinicians. Relative 5-year survival rates for patients have improved over the past three decades, probably linked to a combination of improved surgical outcomes, progress in systemic chemotherapy and radiotherapy, and the increasing acceptance of multimodality treatment. Surgical treatment remains a fundamental component of the treatment of localized esophageal adenocarcinoma. Multiple approaches have been described for esophagectomy, which can be thematically grouped under two major categories: either transthoracic or transhiatal. The main controversy rests on whether a more extended resection through thoracotomy provides superior oncological outcomes as opposed to resection with relatively limited morbidity and mortality through a transhiatal approach. After numerous trials have addressed these issues, neither approach has consistently proven to be superior to the other one, and both can provide excellent short-term results in the hands of experienced surgeons. Moreover, the available literature suggests that experience of the surgeon

and hospital in the surgical management of esophageal cancer is an important factor for operative morbidity and mortality rates, which could supersede the type of approach selected. Oncological outcomes appear to be similar after both procedures.

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Key words: Esophageal cancer; Transhiatal esophageal resection; Transthoracic esophageal resection

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INTRODUCTION

Esophageal cancer is the eighth most common cancer worldwide, with a wide variation in its frequency between high- and low-incidence regions. There are two main histopathological subtypes: squamous cell carcinoma (SCC) and adenocarcinoma. SCC is the most common subtype in several endemic regions of the world^[1], with a high correlation to smoking and alcohol abuse, as well as chronic inflammation^[2]. On the other hand, adenocarcinoma is commonly associated with Barrett's metaplasia, gastroesophageal reflux disease (GERD), and obesity^[3]. It has become the most common subtype in the western hemisphere, and frequently involves the gastroesophageal junction (GEJ) and proximal stomach. SCC and adenocarcinoma of the esophagus are distinct entities and should be considered as such when defining optimal therapy. As



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a result of its increasing incidence^[4] and relationship with GERD, the following review focuses on adenocarcinoma of the esophagus.

Despite improvements in systemic chemotherapy and radiotherapy, and the increasing acceptance of multimodality treatment that have resulted in enhanced survival rates over the past three successive decades^[5], surgical resection continues to be the mainstay of care for treatment of localized esophageal adenocarcinoma. Multiple approaches have been described for esophagectomy, and they can be thematically categorized under two major headings: transthoracic or transhiatal. The transthoracic procedure is performed more commonly by means of combined laparotomy and right thoracotomy (Ivor Lewis procedure). Other options include left thoracotomy with or without cervical incision, a single left thoracoabdominal incision, or a three-incision resection with a cervical anastomosis (McKeown procedure). The transhiatal approach is performed through midline laparotomy and left cervical incision. There has been considerable controversy about which procedure provides the best short- and longterm outcomes. The discussion centers around whether more extended resection through thoracotomy provides superior oncological outcomes than resection with relatively limited morbidity and mortality through a transhiatal approach. Decisions regarding surgical technique are frequently based on personal bias, surgeons' experience and comfort with a procedure. The issue of the extent of surgical resection is addressed first, with a brief description of each approach. The relevance of surgeon/hospital volume and its relationship with adequate outcomes after esophagectomy, and the role of surgery in the context of multimodality treatment are discussed separately.

TRANSTHORACIC ESOPHAGECTOMY

Transthoracic esophagectomy is most commonly performed *via* laparotomy followed by right thoracotomy and intrathoracic anastomosis (Ivor Lewis procedure). It was originally described in 1946 in two stages^[6], and historically, it is the standard procedure against which all other techniques are measured. Left thoracotomy or thoracoabdominal incision provides adequate exposure to the distal esophagus, but presents greater difficulty to access the upper and middle thirds and to perform an anastomosis high in the chest.

Ivor Lewis esophagectomy starts through a midline incision in the abdomen. The left lobe of the liver is mobilized and retracted laterally, and the stomach is fully mobilized and freed from its vascular attachments, including an upper abdominal lymphadenectomy, while preserving the right gastroepiploic and right gastric vessels on whose pedicle the reconstructive conduit is based. The duodenum is mobilized completely *via* a Kocher maneuver and a pyloric drainage procedure is performed, to diminish gastric stasis and minimize aspiration^[7,8]. The right diaphragmatic crus is divided with electrocautery to allow access to the mediastinum and to avoid constricting the transposed stomach. Placement of a feeding jejunostomy is commonly performed before abdominal closure and repositioning for the thoracic component of the procedure. Muscle-sparing right lateral thoracotomy is then performed through the fifth intercostal space. The mediastinal pleura that overlies the esophagus is incised, the azygos vein is divided, the intrathoracic esophagus is mobilized, and *en bloc* resection of the surrounding periesophageal tissue is performed, including mediastinal lymph node dissection.

After division of the proximal esophagus in the chest to ensure an adequate margin, the GEJ and stomach are transposed into the thoracic cavity. A gastric conduit is now created, with a linear stapler parallel to the greater curve, and the fundus is removed with a portion of the lesser curvature. The specimen is removed, and an esophagogastric anastomosis is performed. The McKeown procedure is an alternative three-incision approach, in which right thoracotomy is the initial stage of the procedure, followed by repositioning of the patient in the supine position for abdominal and left cervical incision, to achieve a cervical esophagogastric anastomosis.

The theoretical advantage of the transthoracic approach is a more thorough oncological operation as a result of direct visualization and exposure of the thoracic esophagus, which allows a wider radial margin around the tumor and more extensive lymph node dissection. However, the combined effects of an abdominal and thoracic incision might compromise cardiorespiratory function, especially in patients with coexisting lung or heart disease. The other disadvantage is that an intrathoracic anastomotic leak can lead to catastrophic consequences including mediastinitis, sepsis, and death. The three-incision modification of the procedure effectively eliminates the potential for complications associated with an intrathoracic esophagogastric anastomosis.

The perioperative mortality of transthoracic esophagectomy in experienced centers ranges from 9% to as low as 1.4%^[9-15]. Five-year survival in approximately 25% of patients who undergo transthoracic esophageal resection has been reported. These reports include heterogeneous populations of patients with esophageal cancer that underwent a variety of surgical approaches, the use of adjuvant treatment in some but not all patients, and combined histologies (SCC and adenocarcinoma).

TRANSHIATAL ESOPHAGECTOMY

Transhiatal esophagectomy was first performed by Turner in 1933 for esophageal carcinoma^[16]. During subsequent decades, it was not routinely performed since the transthoracic approach was preferred after general anesthesia became available. In 1978, Orringer described his initial series of blunt transhiatal esophagectomy, which kindled new interest in this procedure^[17]. It has gained favor among surgeons concurrent with the rising incidence of adenocarcinoma of the distal esophagus, which is readily approachable through the diaphragmatic hiatus.

The abdominal portion of the procedure duplicates that of the previously described transthoracic approach



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and includes mobilization of the stomach, pyloromyotomy and placement of a feeding jejunostomy. Again, cautery division of the right crus allows access to the mediastinum and dissection under direct vision of the distal and middle third of the esophagus. A left cervical incision along the anterior border of the sternocleidomastoid muscle provides exposure to the cervical esophagus. Circumferential dissection of the cervical esophagus is carried down to below the thoracic inlet, and blunt dissection is continued into the superior mediastinum to mobilize the upper thoracic esophagus, with care to avoid injury to the recurrent laryngeal nerve in the tracheoesophageal groove. The remainder of the dissection at the level of and superior to the carina is completed by blunt dissection through the esophageal hiatus. The cervical esophagus is then divided, the stomach and attached intrathoracic esophagus are delivered through the abdominal wound, and a gastric conduit is fashioned using a linear stapling device in the same manner as described above. The gastric tube is delivered through the posterior mediastinum to the cervical wound, where a cervical esophagogastric anastomosis is performed. The stomach is considered by most surgeons as the ideal replacement for the resected esophagus, although a segment of colon or a free flap of small bowel can be used as alternative conduits^[18,19].

The postulated advantages of the transhiatal approach to esophagectomy are avoidance of a thoracotomy incision, which thereby minimizes pain and subsequent postoperative pulmonary complications; elimination of potentially life threatening mediastinitis as a result of an intrathoracic anastomotic leak; and a shorter duration of operation, which potentially results in decreased morbidity and mortality^[17]. Leak of a cervical esophagogastric anastomosis can be handled in the vast majority of patients with opening of the cervical wound, followed by local wound care. Compared to transthoracic esophagectomy, transhiatal esophagectomy is associated with poor visualization of upper and middle thoracic esophageal tumors (potentially compromising the oncological integrity of the operation), increased anastomotic leak rate with subsequent stricture formation, and a higher risk of recurrent laryngeal nerve injury^[20,21].

The reported postoperative mortality after transhiatal esophagectomy in individual series tends to be slightly lower than that of the transthoracic approach, between 1% and 7.5%^[22-26], and 5-year survival rate is approximately 25%, which is not substantially different from that accomplished after the transthoracic approach. Orringer et al^[26] have reported the most extensive experience with transhiatal esophagectomy. Their latest report involved 2007 patients, of which 1525 had a diagnosis of cancer. Seventy-two percent had adenocarcinoma, and 38% received neoadjuvant chemoradiation, with a 5-year survival rate of 29%. Among this series, their most recent group of 944 patients had a hospital mortality of 1%. The anastomotic leak rate was 9% in this same group, and recurrent laryngeal nerve injury occurred in 2% of cases. These results reflect those reported from other surgical series of transhiatal esophagectomy.

Table 1 Meta-analysis comparing transthoracic and transhiatalesophagectomy

Meta-analysis	Rindani <i>et al</i> ^[20]	Hulscher <i>et al</i> ^[21]
No. of patients	5483	7527
Postoperative mortality (%)		
TT	9.5	9.2
TH	6.3	5.7
Intraoperative blood loss (mL)		
TT	1171	1001
TH	1311	728
Hospital stay (d)		
TT	19.8	21
TH	19.5	17.8
Pulmonary complications (%)		
TT	25	18.7
TH	24	12.7
Cardiac complications (%)		
TT	10.5	6.6
TH	12.4	19.5
Anastomotic leakage (%)		
TT	10	7.2
TH	16	13.6
Vocal cord paralysis (%)		
TT	4.8	3.5
TH	11.2	9.5
5-yr OS (%)		
TT	26	23
TH	24	21.7

TT: Transthoracic esophagectomy; TH: Transhiatal esophagectomy; OS: Overall survival.

STUDIES COMPARING TRANSTHORACIC VS TRANSHIATAL ESOPHAGECTOMY

The question of one approach being superior to the other continues to generate considerable controversy among surgeons. No definitive advantage in oncological outcome or postoperative morbidity and mortality can be concluded from the non-comparative case series mentioned above.

Two large meta-analyses have addressed these issues by utilizing collective reviews of numerous individual studies that have compared transhiatal esophagectomy to transthoracic esophagectomy^[20,21]. Most of the studies included in these meta-analyses were retrospective in nature and were not consistent with respect to the surgical technique utilized and which therapy in addition to surgery was delivered. Nevertheless, the results of both were very similar.

The meta-analysis by Rindani *et al*^{20]} included almost 5500 patients from 44 series published between 1986 and 1996 (Table 1). The statistical analysis was descriptive rather than comparative due to the diverse nature of the series, and there was only one prospective randomized trial included, with a small sample and short follow-up. Postoperative respiratory and cardiovascular complications were almost identical between the two groups. The transhiatal group had a higher incidence of anastomotic leaks and recurrent laryngeal nerve injuries. Thirty-day mortality was 6.3% after transhiatal and 9.5% after transhoracic resection, but survival at 5 years was equivalent between the two procedures.

The second meta-analysis, by Hulscher et al^[21], in-



Meta-analysis	Goldminc <i>et al</i> ^[27]	Chu <i>et al</i> ^[28]	Jacobi <i>et al</i> ^[29]	Hulscher et al ^[30,31]
No. of patients	67	39	32	220
Postoperative mortality (%)	07	39	52	220
TT	8.6	0	6	4
TH	6.2	0	6	4 2
Intraoperative blood loss (mL)	0.2	0	0	2
TT	¹ (2.3 units transfused)	671	2270	1900
TH	¹ (2.3 units transfused)	724	1000	1000
Hospital stay (d)	(2.5 units transfused)	724	1000	1000
TT	18	27	21	19
TH	20.5	18	23	15
Postoperative pneumonia (%)	20.0	10	20	10
TT	20	0	31	57 (atelectasis included)
TH	19	10	19	27 (atelectasis included)
Cardiac complications (%)		10		2) (aterectable included)
TT	1	15.8	19	26
TH	1	15	31	16
Anastomotic leakage (%)				
TT	9	0	12.5	16 (subclinical included)
TH	6	0	12.5	14 (subclinical included)
Vocal cord paralysis (%)				· · · · · · · · · · · · · · · · · · ·
TT	3	1	1	21 (transient)
TH	3	1	1	13 (transient)
Reported survival (%)				. ,
TT	22 at 3 yr	Median survival 13.5 mo	77 at 1 yr	36 at 5 yr
TH	30 at 3 yr	Median survival 16 mo	70 at 1 yr	34 at 5 yr

¹Data not reported or did not occur. TT: Transthoracic esophagectomy; TH: Transhiatal esophagectomy.

volved over 7527 patients derived from 50 studies from 1990 to 1999 (Table 1). Six were prospective comparative studies, three of which were randomized, all with a relatively small sample size. None of these three studies could demonstrate a significant difference in morbidity, mortality, or long-term survival^[27-29]. When all 50 studies were analyzed, no significant differences were demonstrated in the overall morbidity rate. Blood loss was higher after transthoracic esophagectomy, and it had a higher risk of pulmonary complications, chylous leakage (2.4% vs 1.4%) and wound infection (7.7% vs 4.3%). Similar to the previous meta-analysis, transhiatal esophagectomy had a higher incidence of anastomotic leakage and recurrent laryngeal nerve injury. Length of stay in the intensive care unit (ICU) and hospital were longer in the transthoracic group, and inhospital mortality was significantly higher as well. Again, there was no difference in 5-year survival rates.

There have been a total of four randomized trials that have compared both techniques (Table 2). Three of them, included in the previous meta-analyses described above, could not provide definitive conclusions and each was hampered by an extremely small sample size, with nonsignificant differences reported between the two arms^[27-29].

The fourth randomized trial, published in 2002 by Hulscher *et al*^{30]}, has provided level I evidence regarding this controversial issue. Two hundred and twenty patients were assigned to either transhiatal or transthoracic esophagectomy with cervical anastomosis. The transthoracic esophagectomy procedure included *en bloc* resection of the thoracic duct, azygos vein, ipsilateral pleura, and all peri-esophageal tissue in the mediastinum, including a formal lymphadenectomy. Transhiatal esophagectomy had

a shorter operative duration than transthoracic esophagectomy (3.5 h vs 6 h), with lower blood loss (1 L vs 1.9 L). Perioperative morbidity rate was also lower in the transhiatal group (pulmonary complications, 57% vs 27%; chylous leakage, 10% vs 2%). Duration of mechanical ventilation, ICU stay and hospital stay were all shorter in the transhiatal group. However, there was no significant difference in hospital mortality (transthoracic: 4%; transhiatal: 2%). Although initially a trend toward a survival benefit with transthoracic approach was seen, after longer follow-up, no difference in 5-year overall survival was found (transthoracic: 36%; transhiatal 34%). Notably, the transthoracic approach was of benefit in some subgroups; patients with 1-8 positive lymph nodes had better disease-free survival rate (64% vs 23%), and patients with tumors arising from the distal esophagus (rather than gastric cardia) tended towards a survival benefit (51% vs 37%, not statistically significant)^[31]. However, this phase III study was not adequately powered to address these subgroup analyses.

A large population-based study has been published recently, which has evaluated the results of both approaches through the Surveillance, Epidemiology and End Results (SEER) - Medicare linked database from 1992 to 2002^[32]. A lower operative mortality was found after transhiatal esophagectomy (6.7% vs 13.1%). Although observed 5-year survival was higher after transhiatal esophagectomy, after adjusting for stage, patient and provider factors, no significant 5-year survival difference was found.

These data suggest that perioperative and oncological outcomes are not substantially influenced by the surgical approach to esophagectomy, and that either procedure is associated with acceptable results in the hands of expe-



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rienced surgeons. Ideally, surgeons and hospitals treating patients with esophageal carcinoma should have expertise in both techniques. Some patients might even benefit from an individualized approach. For an older or higherrisk surgical patient, for whom perioperative recovery is an even greater concern than usual, a transhiatal approach could confer an advantage. In a fit patient with evidence of a limited number of involved lymph nodes, there is some evidence (although not level I evidence) that suggests a benefit in survival with the transthoracic approach. Still, available literature suggests that experience of the surgeon and hospital is likely to be a more important factor than is the type of approach selected.

SURGEON/HOSPITAL VOLUME AND ESOPHAGECTOMY

There is increasing evidence that confirms that patients who undergo complex oncological resections, such as esophagectomy, at high-volume hospitals by experienced surgeons have significantly lower rates of perioperative morbidity and mortality^[33-35]. This association has been shown for several surgical procedures in studies that have used health-services-linked databases. However, the association between volume and outcome for esophagectomy is one of the strongest among all complex cancer operations^[33-35]. Furthermore, a recent analysis of the SEER - Medicare linked data base^[36] suggests that long-term survival, and therefore oncological outcome, is also volume dependent. The probability of surviving 5 years following esophagectomy in high-volume hospitals was 34%, whereas 5-year survival probability in low-volume hospitals was only 17%. This 17% absolute difference in 5-year survival following esophagectomy between high-volume and lowvolume hospitals was the highest amongst all cancer resections surveyed. Volume-dependent discrepancy in 5-year survival could not be attributed to differences in the delivery of adjuvant therapy. Therefore, not only are short term procedure-related outcomes associated with surgical experience but long-term oncological outcomes might also be affected by surgeon and center volume/experience with esophageal resection. The basis for this improved survival has not been defined and requires further investigation.

ROLE OF SURGERY IN THE MULTIMODALITY THERAPY ERA

Relative 5-year survival rates for patients with esophageal cancer have improved over the past three successive decades^[5,37]. The reasons for this trend are surely multifactorial and could include the widespread acceptance and use of a multimodality treatment approach, improved surgical outcomes, and progress made in systemic chemotherapy and radiotherapy.

Based on the current level I evidence, it can be reasonably argued that the addition of surgery to an effective regimen of chemoradiotherapy in patients with SCC of the esophagus might not improve outcome. Two randomized trials have addressed the role of chemoradiotherapy alone *vs* chemoradiotherapy followed by surgery in patients with SCC. The German Esophageal Cancer Study Group^[38] has demonstrated better 2-year local, progression-free survival in the surgical group (64.3% *vs* 40.7%), although with increased treatment-related mortality (12.8% *vs* 3.5%), and equivalent overall survival between the two treatment groups. The FFCD 9102 trial^[39], in which 90% of the patients had a diagnosis of SCC, found a higher frequency of locoregional relapse in the chemoradiotherapy alone group, but with a lower 3 mo mortality rate. As in the German study, survival rates were similar in both groups.

In contrast to SCC, the controversy regarding patients with esophageal adenocarcinoma has been centered on the added value of preoperative combined modality therapy, and not the necessity of surgical resection. Despite the fact that numerous phase III trials^[14,40-43] have compared preoperative chemoradiotherapy followed by surgery to surgery alone, it is not clear that preoperative chemoradiotherapy can be declared as a standard of care.

One randomized trial from Ireland^[41] has shown a benefit in patients with adenocarcinoma, but definitive conclusions are hampered by the small sample size, unusually poor results with surgery alone, and short follow-up. More recently, the Cancer and Leukemia Group B initiated a trial that was closed prematurely due to poor accrual^[43]. The most common histological tumor subtype in this study was adenocarcinoma. Reported median survival (4.48 years *vs* 1.79 years) and 5-year survival (39% *vs* 15%) favored trimodality therapy. Its major limitation was the incredibly small patient sample size due to poor accrual, although the findings had statistical significance.

Although the survival benefits have not been consistent, the majority of patients are down-staged with preoperative chemoradiotherapy, and for those patients who have a substantial response (complete pathological or major partial response defined by residual microscopic disease in the resected specimen) to preoperative chemoradiotherapy, there is a survival advantage. Surgery appears to be a crucial component of combined modality therapy to eliminate residual disease following chemoradiotherapy that leads to improved locoregional control and improved long-term survival. However, failure at a distant site is common and is the most frequent cause of death.

Even though the evidence for the benefit of preoperative chemoradiotherapy in the treatment of patients with esophageal cancer is not compelling, the combined modality approach has gained acceptance in most centers in the United States, and is by far the most frequent therapeutic option offered to patients with cancer of the esophagus. A meta-analysis has reported that preoperative chemoradiotherapy improved 3-year survival by 13% over surgery alone with similar improvement identified in patients with either SCC or adenocarcinoma histology^[44]. Although the role of surgery has been questioned, especially for SCC, it can be reasonably concluded that esophageal resection remains an important, if not the most impor-

tant, therapeutic component of a combined modality approach to esophageal cancer. However further refinement of our treatment of patients with esophageal cancer is warranted. Patients who achieve a complete pathological response to combined chemoradiotherapy probably will obtain no advantage from undergoing esophagectomy, considering the substantial morbidity and mortality associated with the procedure. Unfortunately, current diagnostic methods are not reliable to identify this group of patients preoperatively. In contrast, it is reasonable to expect that patients with residual disease, either apparent or occult, following preoperative combined modality treatment will benefit from eradicating that residual disease with resection to give them the best opportunity for a long-term disease-free state. Surgeons interested in this lethal disease should direct their efforts to more accurate identification of those patients that will likely benefit from different single or combination treatment modalities, and tailor their therapeutic interventions accordingly.

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