

Chapter 16

Esophageal Cancer: Surgical Treatment

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Abstract Treatment approaches varies according to the stage of esophageal cancer and the majority of patients present with advanced disease. Despite being a challenging surgical procedure, historically associated with high morbidity and mortality, esophagectomy remains a central treatment component in patients with early-stage and loco regional esophageal cancer. This chapter describes the indications for esophagectomy, with an emphasis of the technical aspects of the surgical approaches available, common post-operative complications and outcomes following esophagectomy.

Keywords Esophageal cancer • Esophagectomy • Surgery • Indication • Complication

Introduction

Outcomes of treatment of esophageal cancer remain poor with an overall 5-year survival rate of 19 % [1]. As expected the treatment approach varies according to the stage of disease at presentation although the majority of patients present with advanced disease [2]. Esophageal resections in patients with esophageal cancer are

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challenging procedures, rated as high risk procedures by the Leapfrog Group, and are historically associated with high morbidity and mortality rates and concerns that the operation can negatively impact quality of life [3]. However, surgery remains the best option for cure in certain patients with early-stage disease and provides superior local control and improved survival for regional cancers [4]. Additionally, mortality rates have steadily declined over the past decades due to the improvement in staging techniques, patient selection, and the application of enhanced recovery protocols and standardized clinical pathways. Surgical approaches have also continued to evolve especially with the introduction of minimally invasive techniques [5].

In a US nationwide study assessing 57,000 esophagectomies between 1998 and 2006, a decrease in mortality rates from 12 to 7 % has been reported [6]. Furthermore, several studies showed a strong relationship between operative mortality when procedures are performed in high volume centers [7, 8]. In specialized high volume centers for esophagectomy, mortality rates of 0.3–5 % have been reported [9]. However, morbidity rates following esophagectomy continue to be appreciably higher when compared to other complex oncologic operations such as pancreatectomy, gastrectomy, or hepatectomy. Several studies have demonstrated that postoperative quality of life is negatively impacted by postoperative complications [10]. However, it has been shown that in the absence of major perioperative complications, a comparable normal baseline level of quality of life can typically be achieved 6 months after surgery [11, 12].

Indications for Esophagectomy

The current NCCN treatment guidelines for esophageal cancer recommend surgery for all physiological fit patients clinically staged with resectable cancers (T1b–T4a N0–3 M0) [4]. After accurate staging patients presenting with T1b N0 cancer are currently recommended to be treated with surgical resection, although certain specialized centers have advocated that selected “low risk” T1b N0 cancers can be treated endoscopically. These “low-risk” cancers are described as tumor infiltration only in the superficial submucosal layer (sm1), tumor differentiation grades 1 and 2, and no evidence of lymphovascular invasion [13]. However, the majority of high volume centers would recommend primary surgical resection due to the potential for inaccuracy in the assessment of depth of submucosal invasion and the risk of lymph node metastases. Clinically staged T3 and T4a cancers with or without suspected lymph node involvement are currently recommended for multimodality therapy which involves neoadjuvant therapy with either chemotherapy alone or in combination with radiation to improve local control and survival. The most appropriate treatment for patients clinically staged with T2 N0 cancers remains controversial with surgery alone or multimodality both identified as appropriate treatment [14]. However, up to 37 % of patients with clinically staged T2 N0 cancers will be found on final pathology to be understaged and would therefore potentially benefit from neoadjuvant treatment. If those patients are upstaged regarding the final surgical pathology, adjuvant chemotherapy can be considered.

Surgical Approach

Esophageal resection may be accomplished by a variety of different approaches, but no one technical approach will be appropriate for all patients. To understand the reasoning for selecting one approach over another, it is important to understand the fundamental aspects of various esophageal resection strategies. Factors involved in the choice of procedure include disease stage, tumor location and histology, patient-related factors such as comorbidities and previous surgeries, as well as personal preference and experience of the surgeon [2].

Transhiatal Esophagogastrectomy

The transhiatal esophagectomy is performed using a laparotomy and left cervical incision [15]. Mobilization of the stomach is performed with dissection of the celiac and left gastric nodes, division of the left gastric artery, and preservation of the right gastroepiploic and proximal right gastric arteries. The majority of the transthoracic esophageal dissection is performed through the hiatus. Much of the mediastinal component of the dissection is done manually without the ability to visualize the dissection or to do a directed lymph node dissection. The advantage of this approach is that it does not involve a separate thoracic incision. The left cervical incision allows mobilization of the cervical esophagus and transection of the esophagus at the thoracic inlet. Completion of the esophagectomy is achieved via the laparotomy and the gastric conduit is carefully drawn up through the mediastinum and externalized in the cervical incision where the esophagogastric anastomosis is performed (Fig. 16.1). The NCCN treatment guideline mentions that transhiatal approach is applicable for lesions at any thoracic location, but might not be feasible for dissection of bulky, mid esophageal cancers adjacent to the trachea. Other studies have suggested that transhiatal esophagectomy is best suited for tumors centered at the esophagogastric junction, as survival of true esophageal cancers is improved with transthoracic operations [16].

Ivor Lewis Esophagogastrectomy

This is the most common utilized approach worldwide. It involves a laparotomy followed by a right thoracotomy with the anastomosis typically done in the upper thorax at or above the level of the azygos vein. Gastric mobilization is performed as described for the transhiatal approach. This approach involves two standard incisions and all the dissection is done under direct vision including a directed lymph node dissection (Fig. 16.2). This approach is appropriate for most lower and lower middle level tumors and has the additional advantage that this approach can be performed with minimal cardiac manipulation, which is of hypothetical benefit in patients with cardiac comorbidities.

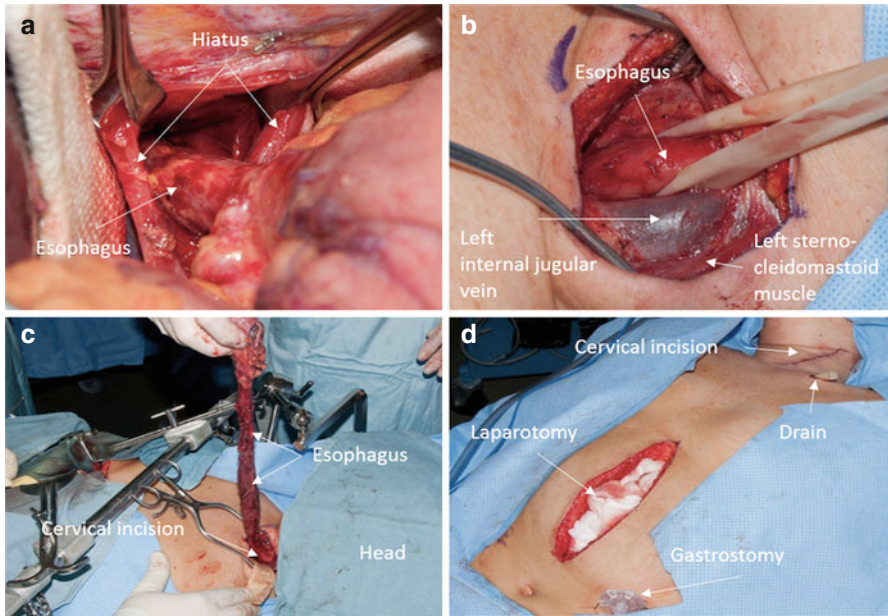


Fig. 16.1 Transhiatal esophagectomy. (a) Mediastinal esophageal dissection through the hiatus via midline laparotomy. (b) Preparation of cervical esophagus through left cervical incision. (c) Dissected esophagus completely excavated through cervical incision. (d) Upper midline laparotomy and closed left cervical incision after cervical anastomosis, placement of cervical wound drain, and gastrostomy tube

McKeown (Three-Stage) Esophagogastrectomy

This approach begins with a right-sided thoracotomy for complete mobilization of the esophagus and dissection of the thoracic lymph nodes under direct vision, followed by abdominal and left cervical incisions after repositioning the patient from the left lateral decubitus to the supine position. Gastric mobilization and cervical anastomosis are performed as described for the transhiatal approach. With this approach large mid and upper thoracic tumors can be mobilized under direct vision and resectability can be assured prior to gastric mobilization (Fig. 16.3).

Left Thoracoabdominal Esophagogastrectomy

The left thoracoabdominal esophagectomy utilizes a contiguous incision from the upper abdomen to the left thorax typically through the eighth intercostal space (Fig. 16.4). Mobilization of the stomach is similar to the description in previous procedures. Esophagectomy is accomplished through the left chest and the anastomosis can be performed in either the intrathoracic or cervical location. The anastomosis can be performed just inferior to the aortic arch, or following dissection under

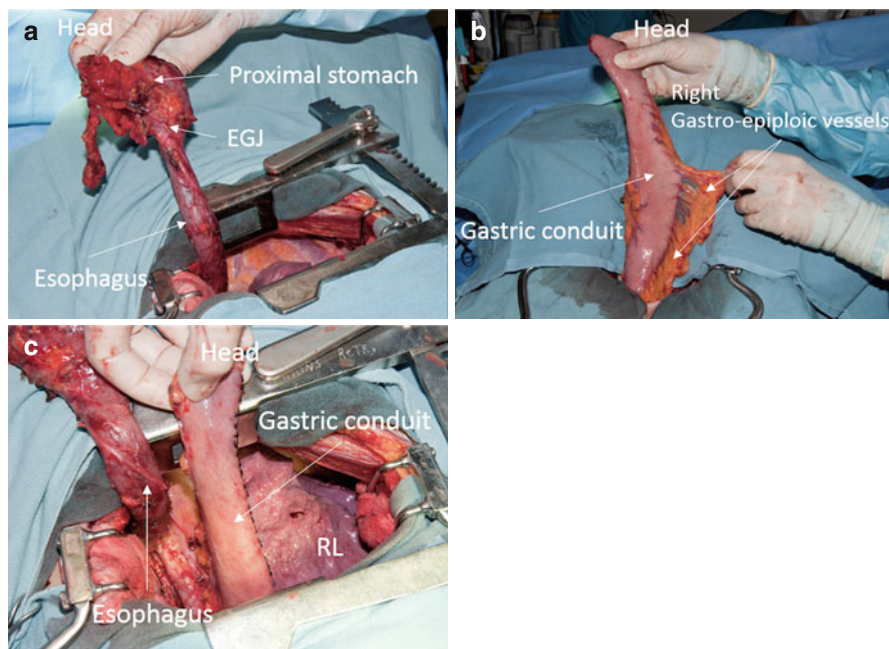


Fig. 16.2 Ivor Lewis esophagectomy. (a) Dissected esophagus and esophagogastric junction (*EGJ*) excavated through the right thoracotomy. (b) Upper midline laparotomy; prepared gastric conduit after resecting cardia and portion of lesser curvature to provide a 5–10 cm resection margin around the esophagogastric junction (*EGJ*); preserved right epiploic vessels. (c) Gastric conduit pulled through hiatus and dissected esophagus, both excavated through thoracotomy. Right lung (*RL*) deflated

the aorta can be accomplished above the arch. The intrathoracic dissection can be continued into the neck through a window made in the pleura above the aortic arch and lateral to the subclavian artery. The dissection separates the vagus nerves from the esophagus making the mobilization in the neck more straightforward and decreasing the incidence of recurrent nerve injuries. This approach provides superior exposure to the distal esophagus and allows a complete abdominal and thoracic lymph node dissection. It also provides the significant advantage of providing exposure to the chest and abdomen at the same time which facilitates modifying the operation according to intraoperative findings. Specifically not only can the level of the anastomosis be changed but also the colon or small bowel can be used if the stomach is found to be unavailable or inappropriate.

Transhiatal Esophagectomy Versus Transthoracic Esophagectomy

Several studies have compared the outcomes between transthoracic and transhiatal approaches. The only randomized trial showed significantly higher pulmonary morbidity and wound infections in patients who underwent a transthoracic resection

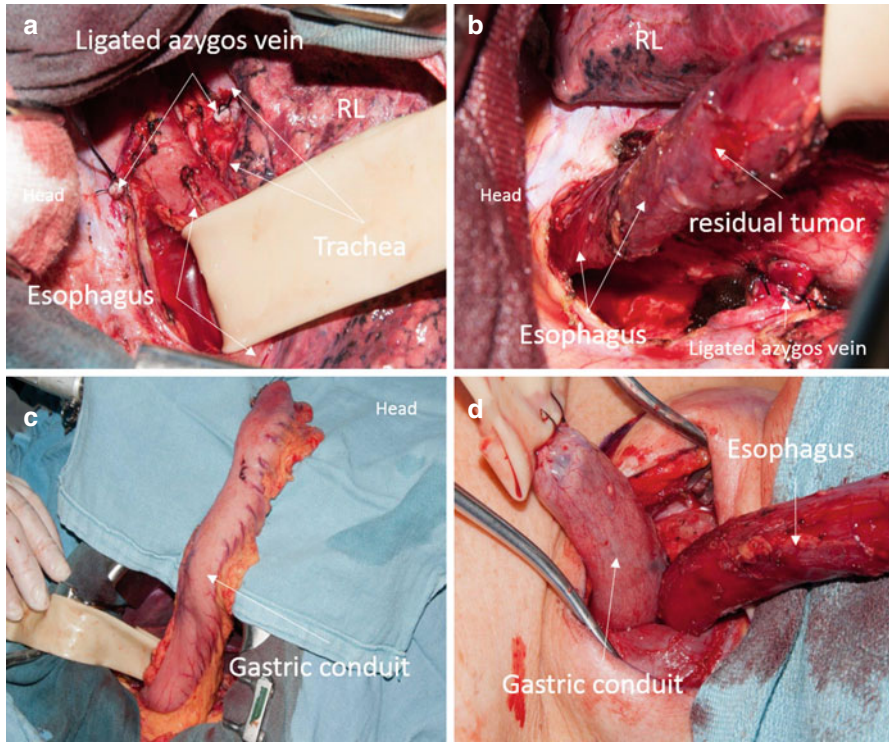


Fig. 16.3 McKeown esophagectomy after neoadjuvant chemoradiotherapy for a previously bulky squamous cell esophageal cancer with extensive contact plane to posterior trachea. (a) Right thoracotomy, esophagus partly dissected and secured with loop, ligated azygos vein, deflated right lung (RL), extensive adherence to trachea. (b) Complete dissection of the esophagus into the apex of the thorax, proximal location of residual tumor at the level of the azygos vein. (c) Prepared gastric conduit excavated through upper midline laparotomy. (d) Gastric conduit and dissected esophagus seen through the cervical incision before performing cervical anastomosis

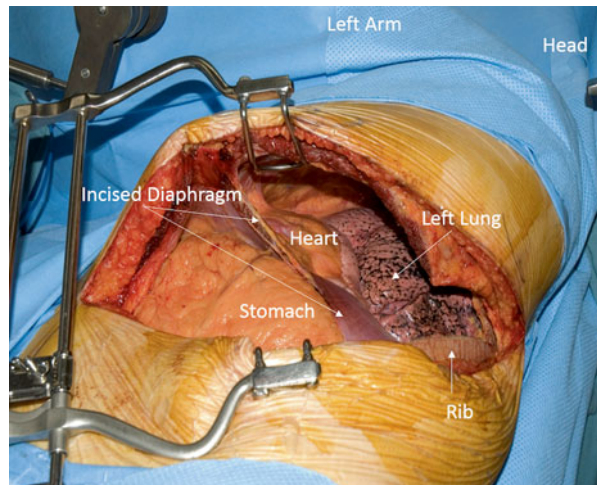


Fig. 16.4 Left thoracoabdominal esophagectomy: Patient in right semi-lateral decubitus position. View through contiguous incision from the upper abdomen to the left thorax in abdominal and thoracic cavity. The diaphragm has been incised

[17]. Additionally perioperative mortality rates were nonsignificantly higher when compared to transhiatal esophageal resections. However, transhiatal resections were associated with higher incidences of recurrent laryngeal nerve palsy as well as anastomotic leak and stricture rates. Despite a higher average lymph node harvest in the transthoracic approach, no difference was demonstrated in overall survival between the transhiatal and the transthoracic patients. These results may reflect a selection bias as patients who underwent transhiatal resections had significantly lower tumor stages and tumors were more commonly located in the distal esophagus. This was given added credibility following a subsequent subanalysis which revealed a survival advantage of 14 % for the subgroup of patients undergoing transthoracic resection for esophageal cancers not including those cancers at the esophagogastric junction [16].

Minimally Invasive Esophagectomy

In the last decade the utilization of minimally invasive and hybrid techniques for esophageal resections has increased. National and international audits suggest that currently 15–30 % of all esophageal resections are performed with at least a component of the operation utilizing minimally invasive approaches [18]. Decreased blood loss, lower incidence of respiratory complications, as well as shorter hospital stay have been described in the literature as potential advantages of the minimally invasive approach over the transhiatal or transthoracic operations [19]. Initial concerns as to whether minimally invasive resections would negatively impact the integrity of the oncologic resection have not been proven as there has been no differences identified between open and minimally invasive studies comparing in-hospital mortality, complete resection rates, and total number of lymph nodes harvested. Additionally studies have shown no difference in overall survival between minimally invasive and open procedures [19–21]. Patients with more advanced diseases or those who have undergone extensive prior abdominal and/or thoracic surgery are currently felt to be less suitable for minimally invasive surgery.

Salvage Esophagectomy

The best initial management for early and locoregional esophageal squamous cell carcinoma continues to evolve. Studies have shown no overall survival benefit between surgery and definitive chemoradiation in patients with squamous cell cancer [22, 23]. These reports have resulted in many patients undergoing definitive chemoradiation and reserving salvage esophagectomy for patients with persistent or recurrent disease [24, 25]. This treatment course is currently not well established and at the present time no definitive methodology for identifying patients with

complete response after definitive chemoradiotherapy is available. In addition the majority of publications suggest that secondary to the late effects of radiotherapy salvage esophagectomy is associated with significant higher levels of perioperative morbidity and mortality [26, 27].

Summary

The most appropriate approach will continue to vary between centers and surgeons. Specialized centers capable of providing a diversified surgical approach, depending on physiologic factors and tumor characteristics, while applying standardized recovery pathways and enhanced recovery programs will be in the best position to provide superior outcomes.

Technical Aspects of Esophageal Resection

Lymphadenectomy

Discussion continues as to whether the extent of lymph node dissection has a therapeutic and survival benefit rather than being of only prognostic significance as a marker for systemic disease. Several studies support both a therapeutic and prognostic benefit as they document a link between the number of lymph nodes removed at the time of surgery and survivorship [28–31]. One study using the SEER database identified the total nodal count as an independent predictor of overall survival regardless of the extent of lymphatic metastasis and independently of tumor histology [28]. Subsequently, there have been several studies targeting the appropriate extent of nodal dissection and although opinions continue to vary one paper indicates that removal of 23 or more nodes provides the optimal threshold for survival [30]. Another report based recommendations for the optimal number of resected lymph nodes on the T-stage, ranging from 10 to 12 nodes for pT1 tumors to 30–50 nodes for pT3/4 tumors [31].

These targets raised the question as to which of the approaches to esophageal resection provides the most appropriate opportunity for adequate nodal dissection. Multiple papers have advocated the single-field (transhiatal) versus two-field (Ivor Lewis) versus three-field (McKeown) lymphadenectomy and failed to demonstrate a clear superiority for any one approach. One randomized trial comparing single-field versus two-field dissection showed a nonsignificant trend for the transthoracic two-field en bloc approach [17]. Analysis of the subset of adenocarcinomas of the distal tubular esophagus showed a significant improvement in survival for the more extensive transthoracic procedure [32]. Three-field lymphadenectomy has been advocated mainly in Asia in studies dominated by squamous cell cancer. A Japanese

randomized trial comparing two- and three-field dissections showed a nonsignificant improvement in 2- and 5-year survival following three-field dissection [33]. However, incidences of tracheostomies and phrenic and laryngeal nerve palsies were increased following three-field dissection.

The current NCCN treatment guideline recommends a two-field lymphadenectomy with the goal of resecting at least 15 nodes. The optimum number of nodes that should be removed after neoadjuvant therapy is currently unknown, although similar lymph node resection is recommended.

Resection Margins

Although there is a lack of data addressing the adequacy of resection margins, evidence from large retrospective case series demonstrates that R1 (microscopic tumor at margin) and R2 (macroscopic tumor at margin) resection margins are associated with a poor prognosis [34–36]. There is general agreement that achieving negative proximal and distal margins is considered a prerequisite for a curative esophagectomy. Squamous cell carcinoma is associated with intramural cancer spread and satellite lesions in up to 30 % of patients [37] and in adenocarcinoma a similar incidence in submucosal lymphatic spread has been found [35]. In a prospective study including only SCC patients, an intraoperatively measured proximal margin of 5 cm was associated with a 20 % recurrence probability at the anastomosis. Recurrence rate decreased with extended resection margins with recurrence probabilities of 8 % for 5–10 cm margins and 0 % for >10 cm margins [38]. The resection margins in adenocarcinoma were assessed in a retrospective study including 500 patients. In this series all tumors were located at the esophagogastric junction and an intraoperatively measured resection margin of 7 cm or more was independently associated with survival in patients who had R0 resections and at least 15 lymph nodes resected [35]. The current NCCN treatment guideline recommends, where feasible, resection margins of at least 10 cm proximally and 5 cm distally regardless of tumor histology [36].

The assessment of the circumferential resection margins (CRM) in esophageal cancer remains unclear and currently two different definitions for CRM from the College of American Pathologists (CAP) and the Royal College of Pathology (RCP) are utilized. CRM is generally defined as the distance of the outer tumor edge to the lateral surface of the surgical specimen in millimeters. While the CAP defines a positive CRM as tumor presence at the circumferential transection margin, the RCP defines positive CRM as tumor cells within a 1 mm radius of the surface. Irrespective of which pathologic criteria are used, it has been shown that positive CRM is associated with increased local recurrence rates and decreased survival [39–42]. It remains unclear to what extent surgery can affect CRM and the impact of positive CRM after neoadjuvant treatment needs to be further evaluated (Fig. 16.5). Current guidelines recommend the pathologic assessment of CRM in all cases.

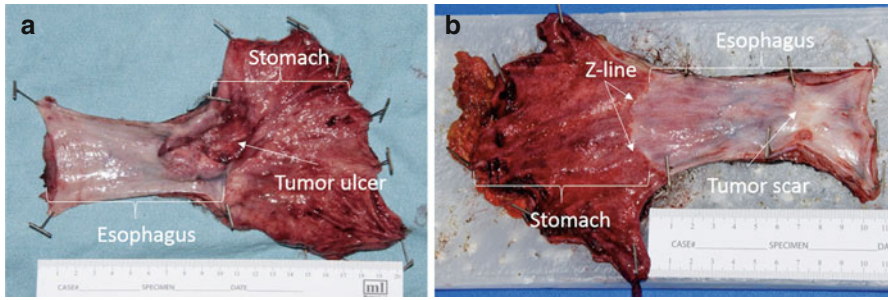


Fig. 16.5 Surgical specimen after esophagectomy. **(a)** Esophagogastric junction with ulcerated tumor, no previous neoadjuvant therapy. **(b)** Distal esophageal scarring in the region of primary tumor after neoadjuvant chemoradiotherapy

Choice of Conduit

Surgery in esophageal cancer patients aims to remove all primary and residual cancer and to provide a functional reconstruction of upper gastrointestinal continuity. Most commonly the stomach is utilized for reconstruction; however, no randomized trials currently exist. Clear advantages for the utilization of the stomach are the requirement for only one anastomosis, shorter operative time, and quicker return to oral alimentation. The most appropriate width of the gastric conduit has been debated and remains unclear with most surgeons preferring a wide tube of at least 5 cm. Potential disadvantages of the use of a gastric conduit are loss of gastric reservoir function with the risks of early satiety, dumping syndrome, and most commonly gastroesophageal reflux. Reflux symptoms can be reduced by performing a cervical anastomosis or a high intrathoracic anastomosis above the level of the azygos vein. After reconstruction with a gastric conduit, postoperative delayed gastric emptying is common and has been shown to increase pulmonary complications. A meta-analysis comparing outcomes in patients with and without a pyloric drainage procedure showed a nonsignificant benefit for those who underwent a drainage procedure with regard to gastric emptying, ability to eat, and postoperative nutrition [43]. Additionally no increase in complications associated with that procedure was reported. However, pyloric drainage did not affect late complications such as dumping or bile reflux. More recently the utilization of a botulinum toxin injection into the pylorus and endoscopic pyloric balloon dilation for the treatment of delayed gastric emptying has been reported, but none of these procedures has yet been compared to surgical division of the pylorus [44–46].

If the stomach is not available or inappropriate as a conduit, other alternatives include pedicled or free jejunal conduits or the left and the right colon. Utilizing a bowel interposition will always result in multiple anastomoses and add to the complexity of the procedure. As colonic blood supply is generally robust, ischemic complications are reduced. Colonic grafts can be associated with the development of redundancy over time which can impact oral nutrition and quality of life.

The application of pedicled jejunal grafts is largely limited due to the extent to which the jejunal segment can be mobilized into the mediastinum [47]. Although depending on the mesenteric blood supply and the fatty content of the small bowel mesentery, pedicled jejunal grafts can typically extend up to the inferior pulmonary vein. The Merendino procedure, first described in 1955, interposes a pedicled jejunal segment as a reconstruction following a limited distal esophageal resection. Primarily introduced for the treatment of benign strictures of the distal esophagus, very few case reports describe the utilization of the Merendino procedure in the setting of early limited disease in patients with esophageal cancer [48–51]. Possible advantages that have yet to be proven are to achieve free margins and removal of underlying Barrett's esophagus with a limited resection as well as a near total preservation of functional and anatomic upper GI continuity. The authors of one case report describe an evolutionary laparoscopic vagal-sparing procedure and propose that the Merendino procedure may play a greater role in early adenocarcinoma of the distal esophagus and the esophago-gastric junction [51]. Additionally it may fill the gap of a limited resection when endoscopic mucosal resection is not feasible and limited esophageal resection is appropriate. Free jejunal grafts have been utilized for reconstruction of the cervical esophagus to interpose short segments. However, no randomized trials comparing the outcomes of different conduits are available. The decision regarding the most suitable conduit will most often be based on type and location of tumor and the availability of conduit options. High volume centers should be familiar with all of the reconstructive options to be able to apply appropriate approaches when the stomach is not available.

Anastomosis

Previous studies have compared cervical and intrathoracic anastomoses (Figs. 16.6 and 16.7) regarding leak and stricture rates. A recent meta-analysis including 267 patients showed a significantly higher risk of anastomotic leakage and recurrent nerve injuries in cervical anastomoses [52]. Pulmonary complications, perioperative mortality, and anastomotic stricture rates were comparable with intrathoracic anastomoses. However, the choice of the location of the anastomoses is dictated by the surgical approach utilized, which varies according to a variety of factors but mainly on tumor location. It must be highlighted that a low intrathoracic anastomosis should be avoided whenever possible as impaired gastric emptying as well as severe gastroesophageal reflux and the development of peptic strictures are common sequels.

A meta-analysis of five randomized trials found that in contrast to circular stapled anastomoses, hand-sewn anastomoses were associated with higher risks of anastomotic leakage and anastomotic strictures [53]. Another meta-analysis including 1,407 patients compared hand-sewn versus circular stapled anastomoses showed no difference in anastomotic leak rates or mortality rates [54]. Contrary to the previous review, this study showed that circular stapled anastomoses were associated with a higher stricture rate. Two studies reviewed the outcomes of a hybrid approach, with a longitudinal

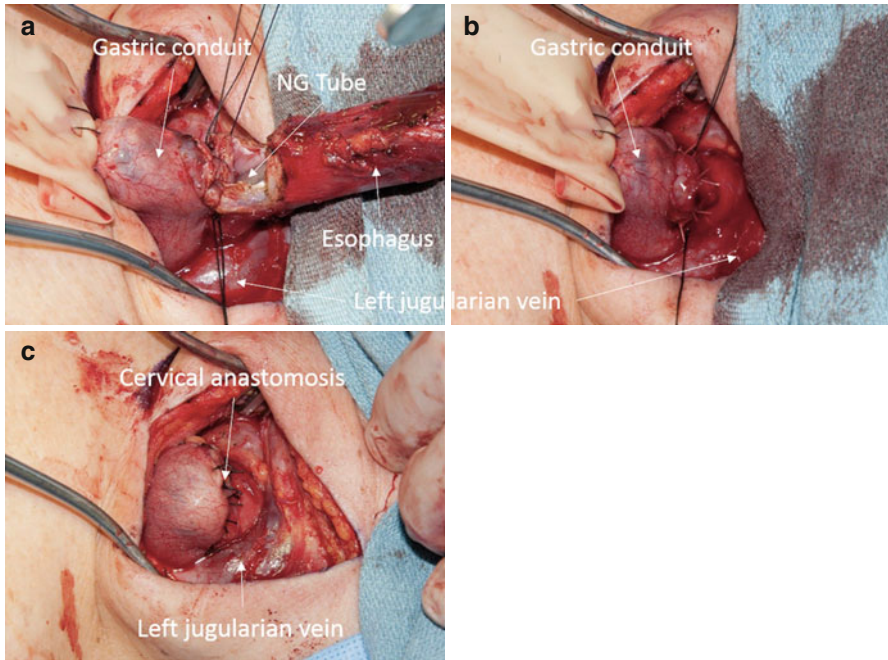


Fig. 16.6 (a) Begin of cervical anastomosis through a 5–6 cm incision anterior to the left sternocleidomastoid muscle. (b) Completed first layer of anastomosis with interrupted sutures. (c) Completed cervical esophagogastric anastomosis, hand sewn in two layers. The anastomosis is placed back into the prevertebral space following completion of the anastomosis

stapled back wall and a hand-sewn front wall (Fig. 16.7), with a low incidence of anastomotic complications [55, 56]. This technique has found a wide adaption among esophageal surgeons and a recent randomized trial comparing stricture rates at 3 months after hand-sewn, circular stapled, or hybrid anastomoses showed no strictures in the hybrid anastomoses whereas the circular stapled anastomoses had the highest stricture rate of 19 % [57]. Results of both hand-sewn and stapled anastomoses are acceptable. Although randomized trials are not consistent, postoperative stricture rates seem more common in hand-sewn anastomoses. Circular stapled anastomoses may be associated with a higher complication rate than linear stapled anastomoses.

Complications and Outcome

Common Major Complications Associated with Esophageal Resection

Esophagectomy is historically associated with high morbidity rates and remains one of the most demanding surgical procedures in thoracic surgery. Although mortality rates are decreasing in the United States, morbidity rates remain high at

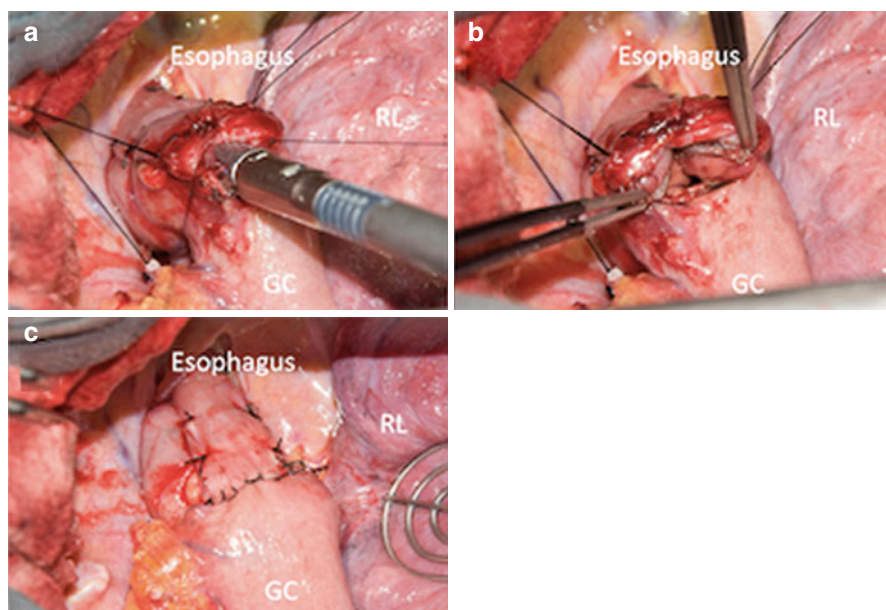


Fig. 16.7 Intrathoracic hybrid chest anastomosis during Ivor Lewis esophagectomy, deflated right lung (*RL*). **(a)** Linear stapler with upper arm in the esophageal lumen and lower arm in the gastric conduit (*GC*) lumen. **(b)** Completed stapled common wall of esophagogastric anastomosis. **(c)** Hand sewn front wall of the completed esophagogastric anastomosis

approximately 50 % [58]. The most common complications associated with esophagectomy are pneumonia, atrial arrhythmia, and anastomotic leakage [59]. Pulmonary complications are the most common complications and are thought to be responsible for 50–65 % of mortalities associated with esophagectomy [60]. Patients who develop pneumonia have a sixfold increased risk of perioperative mortality [61]. The incidence of pneumonia is directly linked to technical complications associated with the surgical procedure and is lower in transhiatal procedures and, more recently, in minimally invasive approaches [62]. Other factors associated with increased respiratory complications are recurrent nerve injuries and poor gastric emptying [43]. Perioperative factors that have been highlighted to decrease pulmonary complications include advanced regional anesthetic techniques, especially thoracic epidurals, minimizing blood loss and transfusion requirements and restricting perioperative fluid administration as well as avoidance or early recognition of vocal cord dysfunction [63–66]. Currently there is no evidence that neoadjuvant chemoradiotherapy increases the incidence of short-term pulmonary complications or overall morbidity [67].

Atrial arrhythmia occurs in up to 17 % of cases during the perioperative period and appears to occur more commonly in elderly patients and in those who are undergoing neoadjuvant therapy [68, 69]. Reports demonstrated an association between the occurrence of atrial fibrillation and perioperative complications, specifically anastomotic leakage and pneumonia as well as an increased mortality [70, 71].

Therefore, the appearance of atrial arrhythmias should lead to a careful assessment of other complications. Electrolytes correction, antiarrhythmic medication, and defibrillation are recommended as the impact of atrial fibrillation on the conduit perfusion is currently poorly understood. There has been evidence that prophylactic amiodarone and minimally invasive surgery may reduce atrial arrhythmias [72, 73].

Anastomotic leakages are reported in 3–21 % of cases and associated with mortality rates varying from 0 to 35 % [74]. The incidence of leaks does not seem to be directly related to prior induction therapy. The manifestation of anastomotic leaks and their treatment can be extremely diverse due to the location, extent of leak, and the presence of a systemic sepsis. Anastomotic leaks have been reported between postoperative day 1 and 30, but are most commonly seen between day 4 and 8. There is increasing evidence that cervical anastomoses are associated with a higher leak rate.

Effects of Complications on Outcome After Esophageal Resection

Evolving evidence has shown a direct impact of complications on perioperative outcomes such as mortality, length of stay, and postoperative quality of life [61, 68, 75, 76]. Many studies assessing the impact of complications on survival have shown an effect on timing and incidence of cancer recurrence as well as long-term survival [77]. However, disease-free survival seems less affected by complications [61].

The evolution of staging modalities leading to an improved patient selection as well as the performance of the operation in high volume centers or by high volume surgeons has been linked to decreased complications and improved outcomes [9]. The Leapfrog Group (<http://www.leapfroggroup.org>) currently defines high volume surgeons or units as those performing 13 or more cases per year. However, this definition remains elusive as other international groups set the definition of “high volume” at 20–50 cases per year [6, 78].

Standardized Clinical Pathway and Enhanced Recovery

Although surgery remains an important component to the management of early and locoregional esophageal cancer, standardized clinical pathways and enhanced recovery programs are now recognized as an important framework for optimizing the treatment process and improving recovery [5, 79]. These pathways should ideally include all participating disciplines in the treatment of esophageal cancer such as surgery, anesthesiology, gastroenterology, medical oncology, radiology and oncologic radiology, pathology, nurses, dietary services, and physical therapy. The pathway should include standardized approaches to all key factors associated with improved recovery, starting from the perioperative management with the utilization of thoracic

epidurals, restrictive fluid management, as well as approaches to shorten operation time and minimize blood loss to the postoperative management including early nutritional support, early mobilization, and effective pain control. It has been shown that standardized pathways specifically developed for esophagectomy led to a significant improvement in length of stay, mortality rates, and complications [80].

Quality of Life Following Esophagectomy

Overall the 5-year survival rate of esophageal cancers remains poor; however, an increasing number of patients are presenting with early disease making evaluation of quality of life measures following esophagectomy more important. Historically there was the general impression that quality of life remains poor after surgical resection, due to the extent and invasiveness of the procedure. Multiple studies have shown that after initial postoperative deterioration of quality of life, an improvement at 3 months and return to a comparable baseline at 6 months after surgery can be expected [81]. However, it has also been shown that the occurrence of perioperative complications had significant deleterious effects on quality of life [76]. These data suggests that comparable levels of quality of life following esophageal resection can be achieved most likely in high volume and experienced centers, where complication rates tend to be lower.

References

1. Siegel R, Naishadham D, Jemal A. Cancer statistics, 2012. *CA Cancer J Clin*. 2012;62(1):10–29.
2. D’Amico TA. Outcomes after surgery for esophageal cancer. *Gastrointest Cancer Res*. 2007;1(5):188–96.
3. Varghese Jr TK, Wood DE, Farjah F, Oelschlager BK, Symons RG, MacLeod KE, et al. Variation in esophagectomy outcomes in hospitals meeting Leapfrog volume outcome standards. *Ann Thorac Surg*. 2011;91(4):1003–9.
4. Ajani JA, Barthel JS, Bekaii-Saab T, Bentrem DJ, D’Amico TA, Fuchs CS, et al. Esophageal cancer. *J Natl Compr Canc Netw*. 2008;6(9):818–49.
5. Low DE. Evolution in surgical management of esophageal cancer. *Dig Dis*. 2013;31(1):21–9.
6. Kohn GP, Galanko JA, Meyers MO, Feins RH, Farrell TM. National trends in esophageal surgery – are outcomes as good as we believe? *J Gastrointest Surg*. 2009;13(11):1900–10.
7. Birkmeyer JD, Dimick JB. Potential benefits of the new Leapfrog standards: effect of process and outcomes measures. *Surgery*. 2004;135(6):569–75.
8. Birkmeyer JD, Siewers AE, Finlayson EV, Stukel TA, Lucas FL, Batista I, et al. Hospital volume and surgical mortality in the United States. *N Engl J Med*. 2002;346(15):1128–37.
9. Markar SR, Karthikesalingam A, Thrumurthy S, Low DE. Volume-outcome relationship in surgery for esophageal malignancy: systematic review and meta-analysis 2000–2011. *J Gastrointest Surg*. 2012;16(5):1055–63.
10. Derogar M, Orsini N, Sadr-Azodi O, Lagergren P. Influence of major postoperative complications on health-related quality of life among long-term survivors of esophageal cancer surgery. *J Clin Oncol*. 2012;30(14):1615–9.

11. Moraca RJ, Low DE. Outcomes and health-related quality of life after esophagectomy for high-grade dysplasia and intramucosal cancer. *Arch Surg.* 2006;141(6):545–9.
12. Parameswaran R, McNair A, Avery KN, Berrisford RG, Wajed SA, Sprangers MA, et al. The role of health-related quality of life outcomes in clinical decision making in surgery for esophageal cancer: a systematic review. *Ann Surg Oncol.* 2008;15(9):2372–9.
13. Pech O, Manner H, Ell C. Endoscopic resection. *Gastrointest Endosc Clin N Am.* 2011;21(1):81–94.
14. Rice TW, Mason DP, Murthy SC, Zuccaro Jr G, Adelstein DJ, Rybicki LA, et al. T2N0M0 esophageal cancer. *J Thorac Cardiovasc Surg.* 2007;133(2):317–24.
15. Orringer MB, Marshall B, Chang AC, Lee J, Pickens A, Lau CL. Two thousand transhiatal esophagectomies: changing trends, lessons learned. *Ann Surg.* 2007;246(3):363–72.
16. Hulscher JB, van Lanschot JJ. Individualised surgical treatment of patients with an adenocarcinoma of the distal oesophagus or gastro-oesophageal junction. *Dig Surg.* 2005;22(3):130–4.
17. Hulscher JB, van Sandick JW, de Boer AG, Wijnhoven BP, Tijssen JG, Fockens P, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med.* 2002;347(21):1662–9.
18. Boone J, Livestro DP, Elias SG, Borel Rinkes IH, van Hillegersberg R. International survey on esophageal cancer: part I surgical techniques. *Dis Esophagus.* 2009;22(3):195–202.
19. Hoppo T, Jobe BA, Hunter JG. Minimally invasive esophagectomy: the evolution and technique of minimally invasive surgery for esophageal cancer. *World J Surg.* 2011;35(7):1454–63.
20. Luketich JD, Schauer PR, Christie NA, Weigel TL, Raja S, Fernando HC, et al. Minimally invasive esophagectomy. *Ann Thorac Surg.* 2000;70(3):906–11.
21. Singh RK, Pham TH, Diggs BS, Perkins S, Hunter JG. Minimally invasive esophagectomy provides equivalent oncologic outcomes to open esophagectomy for locally advanced (stage II or III) esophageal carcinoma. *Arch Surg.* 2011;146(6):711–4.
22. Murakami M, Kuroda Y, Okamoto Y, Kono K, Yoden E, Kusumi F, et al. Neoadjuvant concurrent chemoradiotherapy followed by definitive high-dose radiotherapy or surgery for operable thoracic esophageal carcinoma. *Int J Radiat Oncol Biol Phys.* 1998;40(5):1049–59.
23. Chiu PW, Chan AC, Leung SF, Leong HT, Kwong KH, Li MK, et al. Multicenter prospective randomized trial comparing standard esophagectomy with chemoradiotherapy for treatment of squamous esophageal cancer: early results from the Chinese University Research Group for Esophageal Cancer (CURE). *J Gastrointest Surg.* 2005;9(6):794–802.
24. Smithers BM, Cullinan M, Thomas JM, Martin I, Barbour AP, Burmeister BH, et al. Outcomes from salvage esophagectomy post definitive chemoradiotherapy compared with resection following preoperative neoadjuvant chemoradiotherapy. *Dis Esophagus.* 2007;20(6):471–7.
25. Swisher SG, Wynn P, Putnam JB, Mosheim MB, Correa AM, Komaki RR, et al. Salvage esophagectomy for recurrent tumors after definitive chemotherapy and radiotherapy. *J Thorac Cardiovasc Surg.* 2002;123(1):175–83.
26. Marks J, Rice DC, Swisher SG. Salvage esophagectomy in the management of recurrent or persistent esophageal carcinoma. *Thorac Surg Clin.* 2013;23(4):559–67.
27. Markar SR, Karthikesalingam A, Penna M, Low DE. Assessment of short-term clinical outcomes following salvage esophagectomy for the treatment of esophageal malignancy: systematic review and pooled analysis. *Ann Surg Oncol.* 2014;21(3):922–31.
28. Schwarz RE, Smith DD. Clinical impact of lymphadenectomy extent in resectable esophageal cancer. *J Gastrointest Surg.* 2007;11(11):1384–93.
29. Groth SS, Virnig BA, Whitson BA, DeFor TE, Li ZZ, Tuttle TM, et al. Determination of the minimum number of lymph nodes to examine to maximize survival in patients with esophageal carcinoma: data from the Surveillance Epidemiology and End Results database. *J Thorac Cardiovasc Surg.* 2010;139(3):612–20.
30. Peyre CG, Hagen JA, Demeester SR, Altorki NK, Ancona E, Griffin SM, et al. The number of lymph nodes removed predicts survival in esophageal cancer: an international study on the impact of extent of surgical resection. *Ann Surg.* 2008;248(4):549–56.
31. Rizk NP, Ishwaran H, Rice TW, Chen LQ, Schipper PH, Kesler KA, et al. Optimum lymphadenectomy for esophageal cancer. *Ann Surg.* 2010;251(1):46–50.

32. Omloo JM, Lagarde SM, Hulscher JB, Reitsma JB, Fockens P, van Dekken H, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus: five-year survival of a randomized clinical trial. *Ann Surg.* 2007;246(6):992–1000.
33. Nishihira T, Hirayama K, Mori S. A prospective randomized trial of extended cervical and superior mediastinal lymphadenectomy for carcinoma of the thoracic esophagus. *Am J Surg.* 1998;175(1):47–51.
34. Law S, Wong J. What is appropriate treatment for carcinoma of the thoracic esophagus? *World J Surg.* 2001;25(2):189–95.
35. Barbour AP, Rizk NP, Gonen M, Tang L, Bains MS, Rusch VW, et al. Adenocarcinoma of the gastroesophageal junction: influence of esophageal resection margin and operative approach on outcome. *Ann Surg.* 2007;246(1):1–8.
36. Casson AG, Darnton SJ, Subramanian S, Hiller L. What is the optimal distal resection margin for esophageal carcinoma? *Ann Thorac Surg.* 2000;69(1):205–9.
37. Tsutsui S, Kuwano H, Watanabe M, Kitamura M, Sugimachi K. Resection margin for squamous cell carcinoma of the esophagus. *Ann Surg.* 1995;222(2):193–202.
38. Tam PC, Siu KF, Cheung HC, Ma L, Wong J. Local recurrences after subtotal esophagectomy for squamous cell carcinoma. *Ann Surg.* 1987;205(2):189–94.
39. Khan OA, Cruttenden-Wood D, Toh SK. Is an involved circumferential resection margin following oesophagectomy for cancer an important prognostic indicator? *Interact Cardiovasc Thorac Surg.* 2010;11(5):645–8.
40. Pultrum BB, Honing J, Smit JK, van Dullemen HM, Van Dam GM, Groen H, et al. A critical appraisal of circumferential resection margins in esophageal carcinoma. *Ann Surg Oncol.* 2010;17(3):812–20.
41. Dexter SP, Sue-Ling H, McMahon MJ, Quirke P, Mapstone N, Martin IG. Circumferential resection margin involvement: an independent predictor of survival following surgery for oesophageal cancer. *Gut.* 2001;48(5):667–70.
42. Deeter M, Dorer R, Kuppusamy MK, Koehler RP, Low DE. Assessment of criteria and clinical significance of circumferential resection margins in esophageal cancer. *Arch Surg.* 2009;144(7):618–24.
43. Urschel JD, Blewett CJ, Young JE, Miller JD, Bennett WF. Pyloric drainage (pyloroplasty) or no drainage in gastric reconstruction after esophagectomy: a meta-analysis of randomized controlled trials. *Dig Surg.* 2002;19(3):160–4.
44. Kent MS, Pennathur A, Fabian T, McKelvey A, Schuchert MJ, Luketich JD, et al. A pilot study of botulinum toxin injection for the treatment of delayed gastric emptying following esophagectomy. *Surg Endosc.* 2007;21(5):754–7.
45. Martin JT, Federico JA, McKelvey AA, Kent MS, Fabian T. Prevention of delayed gastric emptying after esophagectomy: a single center's experience with botulinum toxin. *Ann Thorac Surg.* 2009;87(6):1708–13.
46. Sebastian JJ, Pena E, Blas JM, Cena G, Diez M. Management of gastric outlet obstruction after esophagectomy using forced pyloric dilation. *Rev Esp Enferm Dig.* 2008;100(9):594–5.
47. Blackmon SH, Correa AM, Skoracki R, Chevray PM, Kim MP, Mehran RJ, et al. Supercharged pedicled jejunal interposition for esophageal replacement: a 10-year experience. *Ann Thorac Surg.* 2012;94(4):1104–11.
48. Gutschow CA, Schroder W, Wolfgarten E, Holscher AH. Merendino procedure with preservation of the vagus for early carcinoma of the gastroesophageal junction. *Zentralbl Chir.* 2004;129(4):276–81.
49. Staiger WI, Ronellenfitsch U, Kaehler G, Schildhaus HU, Dimitrakopoulou-Strauss A, Schwarzbach MH, et al. The Merendino procedure following preoperative imatinib mesylate for locally advanced gastrointestinal stromal tumor of the esophagogastric junction. *World J Surg Oncol.* 2008;6:37.
50. Holscher AH, Vallbohmer D, Gutschow C, Bollschweiler E. Reflux esophagitis, high-grade neoplasia, and early Barrett's carcinoma—what is the place of the Merendino procedure? *Langenbecks Arch Surg.* 2009;394(3):417–24.

51. Pring C, Dexter S. A laparoscopic vagus-preserving Merendino procedure for early esophageal adenocarcinoma. *Surg Endosc.* 2010;24(5):1195–9.
52. Biere SS, Maas KW, Cuesta MA, van der Peet DL. Cervical or thoracic anastomosis after esophagectomy for cancer: a systematic review and meta-analysis. *Dig Surg.* 2011;28(1):29–35.
53. Hsu HH, Chen JS, Huang PM, Lee JM, Lee YC. Comparison of manual and mechanical cervical esophagogastric anastomosis after esophageal resection for squamous cell carcinoma: a prospective randomized controlled trial. *Eur J Cardiothorac Surg.* 2004;25(6):1097–101.
54. Honda M, Kuriyama A, Noma H, Nunobe S, Furukawa TA. Hand-sewn versus mechanical esophagogastric anastomosis after esophagectomy: a systematic review and meta-analysis. *Ann Surg.* 2013;257(2):238–48.
55. Orringer MB, Marshall B, Iannettoni MD. Eliminating the cervical esophagogastric anastomotic leak with a side-to-side stapled anastomosis. *J Thorac Cardiovasc Surg.* 2000;119(2):277–88.
56. Collard JM, Romagnoli R, Goncette L, Otte JB, Kestens PJ. Terminalized semimechanical side-to-side suture technique for cervical esophagogastric anastomosis. *Ann Thorac Surg.* 1998;65(3):814–7.
57. Wang WP, Gao Q, Wang KN, Shi H, Chen LQ. A prospective randomized controlled trial of semi-mechanical versus hand-sewn or circular stapled esophagogastric anastomosis for prevention of anastomotic stricture. *World J Surg.* 2013;37(5):1043–50.
58. Bailey SH, Bull DA, Harpole DH, Rentz JJ, Neumayer LA, Pappas TN, et al. Outcomes after esophagectomy: a ten-year prospective cohort. *Ann Thorac Surg.* 2003;75(1):217–22.
59. Low DE, Bodnar A. Update on clinical impact, documentation, and management of complications associated with esophagectomy. *Thorac Surg Clin.* 2013;23(4):535–50.
60. Bakhos CT, Fabian T, Oyasiji TO, Gautam S, Gangadharan SP, Kent MS, et al. Impact of the surgical technique on pulmonary morbidity after esophagectomy. *Ann Thorac Surg.* 2012;93(1):221–6.
61. Hii MW, Smithers BM, Gotley DC, Thomas JM, Thomson I, Martin I, et al. Impact of postoperative morbidity on long-term survival after oesophagectomy. *Br J Surg.* 2013;100(1):95–104.
62. Ferri LE, Law S, Wong KH, Kwok KF, Wong J. The influence of technical complications on postoperative outcome and survival after esophagectomy. *Ann Surg Oncol.* 2006;13(4):557–64.
63. Law S, Wong KH, Kwok KF, Chu KM, Wong J. Predictive factors for postoperative pulmonary complications and mortality after esophagectomy for cancer. *Ann Surg.* 2004;240(5):791–800.
64. Tsui SL, Law S, Fok M, Lo JR, Ho E, Yang J, et al. Postoperative analgesia reduces mortality and morbidity after esophagectomy. *Am J Surg.* 1997;173(6):472–8.
65. Dumont P, Wihlm JM, Hentz JG, Roeslin N, Lion R, Morand G. Respiratory complications after surgical treatment of esophageal cancer. A study of 309 patients according to the type of resection. *Eur J Cardiothorac Surg.* 1995;9(10):539–43.
66. Kita T, Mammoto T, Kishi Y. Fluid management and postoperative respiratory disturbances in patients with transthoracic esophagectomy for carcinoma. *J Clin Anesth.* 2002;14(4):252–6.
67. Atkins BZ, Shah AS, Hutcheson KA, Mangum JH, Pappas TN, Harpole Jr DH, et al. Reducing hospital morbidity and mortality following esophagectomy. *Ann Thorac Surg.* 2004;78(4):1170–6.
68. Carrott PW, Markar SR, Kuppusamy MK, Traverso LW, Low DE. Accordion severity grading system: assessment of relationship between costs, length of hospital stay, and survival in patients with complications after esophagectomy for cancer. *J Am Coll Surg.* 2012;215(3):331–6.
69. Rao VP, Addae-Boateng E, Barua A, Martin-Ucar AE, Duffy JP. Age and neo-adjuvant chemotherapy increase the risk of atrial fibrillation following oesophagectomy. *Eur J Cardiothorac Surg.* 2012;42(3):438–43.
70. Stawicki SP, Prosciak MP, Gerlach AT, Bloomston M, Davido HT, Lindsey DE, et al. Atrial fibrillation after esophagectomy: an indicator of postoperative morbidity. *Gen Thorac Cardiovasc Surg.* 2011;59(6):399–405.

71. Murthy SC, Law S, Whooley BP, Alexandrou A, Chu KM, Wong J. Atrial fibrillation after esophagectomy is a marker for postoperative morbidity and mortality. *J Thorac Cardiovasc Surg.* 2003;126(4):1162–7.
72. Tisdale JE, Wroblewski HA, Wall DS, Rieger KM, Hammoud ZT, Young JV, et al. A randomized, controlled study of amiodarone for prevention of atrial fibrillation after transthoracic esophagectomy. *J Thorac Cardiovasc Surg.* 2010;140(1):45–51.
73. Turaga KK, Shah KU, Neill EO, Mittal SK. Does laparoscopic surgery decrease the risk of atrial fibrillation after foregut surgery? *Surg Endosc.* 2009;23(1):204–8.
74. Sarella AI, Tolan DJ, Harris K, Dexter SP, Sue-Ling HM. Anastomotic leakage after esophagectomy for cancer: a mortality-free experience. *J Am Coll Surg.* 2008;206(3):516–23.
75. Rizk NP, Bach PB, Schrag D, Bains MS, Turnbull AD, Karpeh M, et al. The impact of complications on outcomes after resection for esophageal and gastroesophageal junction carcinoma. *J Am Coll Surg.* 2004;198(1):42–50.
76. Viklund P, Lindblad M, Lagergren J. Influence of surgery-related factors on quality of life after esophageal or cardia cancer resection. *World J Surg.* 2005;29(7):841–8.
77. Lerut T, Moons J, Coosemans W, Van RD, De LP, Decaluwe H, et al. Postoperative complications after transthoracic esophagectomy for cancer of the esophagus and gastroesophageal junction are correlated with early cancer recurrence: role of systematic grading of complications using the modified Clavien classification. *Ann Surg.* 2009;250(5):798–807.
78. van Lanschot JJ, Hulscher JB, Buskens CJ, Tilanus HW, ten Kate FJ, Obertop H. Hospital volume and hospital mortality for esophagectomy. *Cancer.* 2001;91(8):1574–8.
79. Zehr KJ, Dawson PB, Yang SC, Heitmiller RF. Standardized clinical care pathways for major thoracic cases reduce hospital costs. *Ann Thorac Surg.* 1998;66(3):914–9.
80. Low DE, Kunz S, Schembre D, Otero H, Malpass T, Hsi A, et al. Esophagectomy – it’s not just about mortality anymore: standardized perioperative clinical pathways improve outcomes in patients with esophageal cancer. *J Gastrointest Surg.* 2007;11(11):1395–402.
81. Parameswaran R, Blazeby JM, Hughes R, Mitchell K, Berrisford RG, Wajed SA. Health-related quality of life after minimally invasive oesophagectomy. *Br J Surg.* 2010;97(4):525–31.