Evidence-Based Surgical Treatment of Esophageal Cancer: Overview of High-Quality Studies

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Evidence-based medicine is the conscientious, explicit, and judicious use of best available evidence in making decisions for individual patient care. The present review gives an evidence-based review of esophageal cancer surgery. The literature search was restricted to the highest level of evidence on the surgical treatment of esophageal cancer.


Only few adequately powered randomized controlled trials (RCTs) have been performed in esophageal cancer (EC) surgery. In a systematic review of other surgical procedures, less than 5% of reported studies had a prospective design [1–3]. Possibly, surgeons may not consider RCTs as a feasible strategy to resolve specific surgical questions. Indeed, standardization of surgical techniques, defining end points and study designs that are acceptable to both surgeons and patients may be problematic. Another problem is the number of resections performed. Although high-volume centers achieve better results [4, 5], only few hospitals perform esophageal surgery with sufficient frequency to exclude technical factors and overcome a learning curve in performing novel operations or techniques. Moreover, compared with pharmaceutical trials, fundraising for surgical trials is difficult. Finally, a commonly held view is that the timing is never right for RCTs. On the one hand, surgeons are reluctant to randomize while a procedure is being developed, and on the other hand they are reluctant after a steady state has been reached because they are already using the procedure on consecutive patients and are convinced of its value [6]. The present review gives an overview on evidence-based studies that focus on surgical topics related to the treatment of EC.

Material and Methods

Systematic reviews and RCTs are considered the highest level of evidence [1–3]. For the purpose of this overview, the literature search was restricted to this highest level of evidence related to the surgical treatment of EC. Non-surgical issues, such as (neo)-adjuvant chemo(radio)therapy, preoperative staging, and the value of a palliative resection are not addressed.

All available systematic reviews and RCTs were independently selected by two investigators (SML, BCV) by using PubMed, MEDLINE, and the Cochrane Controlled Trial register through November 2008. Electronic links to related articles and references of selected articles were hand searched as well. The present systematic review only includes studies published in English. The following search terms were used: esophageal cancer, adenocarcinoma/squamous cell carcinoma, and esophagus. Searches were restricted to randomized controlled trials, systematic reviews, and meta-analyses. Ideally, level 1a evidence was reviewed, if available, and if not, then evidence from the next level was reviewed [1–3].

Results

Surgical Approach

TRANSTHORACIC VERSUS TRANSHIATAL ESOPHAGECTOMY. Two major surgical strategies can be used to optimize outcome after esophagectomy. To improve cure, an en bloc transthoracic resection or an extended resection with two-field lymphadenectomy have been proposed. Alternatively, early postoperative morbidity and mortality may be decreased by limiting the extent of dissection using a transthiatal technique. English-language literature was systematically reviewed. With only three small RCTs (including a total of 138 patients) published at that time [7–9], 50 studies were reviewed including 7,527 patients. There were no important differences between perioperative complications, although blood loss was significantly higher after transthoracic resection. Transthoracic resections had a higher risk of pulmonary complications, chylous leakage, and wound infection. Anastomotic leakage and vocal cord paralysis were more frequent after transhiatal resections. Intensive care unit stay and hospital stay was significantly longer after transthoracic resection. Furthermore, in-hospital mortality was significantly higher after transthoracic resections (9.2% vs 5.7%). There was no significant difference in 5-year survival (23.0% vs 21.7%) after transthoracic and transhiatal resections, respectively. Although transthoracic resections had significantly higher early morbidity and mortality rates, it was concluded that 5-year survival was comparable [10]. However, this meta-analysis merely...
compared surgical access rather than extent of dissection, limiting these conclusions.

Subsequently, a RCT was conducted. Patients were randomized to either transhiatal (106 patients) or transthoracic resection with two-field en bloc lymphadenectomy (114 patients) for adenocarcinoma of the distal esophagus or cardia. Perioperative morbidity was higher after transthoracic esophagectomy without significant difference in-hospital mortality. After transhiatal and transthoracic resection, 5-year survival was 34% and 36%, respectively. The median number of quality-adjusted life-years after transhiatal resection was not significantly different (p = 0.26). The cost of treatment with transthoracic resection was 56% higher. It was concluded that transhiatal esophagectomy was associated with lower morbidity than transthoracic esophagectomy. There appeared a trend toward improved long-term survival at 5 years with the extended transthoracic approach [11, 12]. Randomization was stratified according to tumor location. In a subgroup analysis based on post-surgery classification, the long-term benefit of transthoracic esophagectomy was more substantial in patients with esophageal tumors. In 90 patients with an adenocarcinoma located in the esophagus, a survival benefit of 14% was seen with the transthoracic approach compared with the transhiatal approach (51% vs 37%). No overall survival benefit for either surgical approach was seen in 115 patients with junctional or cardiac tumors [12]. Therefore, the authors now consider transthoracic esophagectomy standard treatment for otherwise fit patients with potentially curable EC, whereas transhiatal esophagectomy is the preferred approach in patients with junctional or cardiac cancer [13].

**Two-Field Versus Three-Field Lymphadenectomy**

Only one small RCT (62 patients) compared extended cervical and superior mediastinal lymphadenectomy with conventional two-field dissection and demonstrated a slightly (not significantly) better survival in the extended lymphadenectomy group at 2 years (83% vs 66%) and 5 years (65% vs 48%), respectively. The patients undergoing three-field dissection had significantly more phrenic nerve palsy (13% vs 0%) and tracheostomies (53% vs 10%), but fewer anastomotic leakages (6% vs 20%). The authors stated that larger RCTs were needed to establish the value of cervical lymphadenectomy [14]. Therefore, there is no evidence to support the routine use of a three-field lymphadenectomy.

**Two-Stage or Synchronous Two-Team Transthoracic Approach**

Hayes and colleagues [15, 16] randomized 27 patients with esophageal carcinoma to a standard two-stage Lewis-Tanner transthoracic subtotal esophagectomy or a synchronous two-team approach. Although the synchronous operations were completed significantly more quickly (230 vs 305 minutes), they produced a higher incidence of complications (7 vs 4 patients after standard esophagectomy), with significantly more blood transfusions (5 vs 3 units), and 3 postoperative deaths after the two-team approach. Therefore, use of the two-stage procedure is recommended.

**Minimally Invasive Resection**

Esophagectomies are associated with high risk postoperative morbidity. Therefore, minimally invasive esophagectomy is gaining in popularity, despite concerns of the learning curve and oncological results. No RCTs have been performed to compare minimally invasive surgery with open surgery. However, Gemmill and McCulloch [17] systematically reviewed the English-language literature. The review included relatively weak case studies and case-matched studies. There were 1,398 patients described who underwent some form of minimally invasive esophagectomy. There were 32 (2.3%) of these 1,398 patients who died within 30 days after the esophagectomy. There were 628 (46%) who had a reported complication. Anastomotic leakage affected 106 (7.7%) of 1,381 patients. Respiratory infections occurred in 167 (13%) of 1,268 patients. Mean blood loss was 316 mL. The duration of operation was 281 minutes 56 (4.9%). There were 1,138 esophagectomies that were converted to open surgery. Only in 222 patients, the complete resection rate was stated clearly. Overall the complete resection rate was 91.0%, and the mean number of resected nodes was 17.6 (607 patients). It can be concluded that the quality of the studies is poor; therefore, the data must be analyzed with caution. The reports describe a variety of different techniques. However, in experienced hands, minimally invasive surgery seems feasible and safe, but its generalizability should be questioned. Potential bias is that patients selected for minimally invasive surgery are not representative of the population of patients with cancer (eg, patients with smaller tumors and avoidance of candidates with serious co-morbidity). Moreover, surgeons whose results were unsatisfactory may have been less inclined to publish their results (publication bias). Until large randomized studies are available, minimally invasive resection should be seen as investigational.

**Technical Surgical Aspects**

**ROUTE OF RECONSTRUCTION.** The stomach is the method of reconstruction in most patients. The esophageal substitute can be placed in the anatomical prevertebral position or in an extra-anatomical (retrosternal or subcutaneous) position. Extra-anatomical reconstruction could offer the advantage that a recurrent intrathoracic tumor mass will not invade the neo-esophagus. However, it may lead to increased anastomotic leakage rates and worse long-term functional results. A meta-analysis of RCTs to determine the effect of the route of reconstruction on patient outcomes was performed. Six RCTs containing 342 patients were reviewed [18–22, 23]. Relative risk, expressed as posterior versus anterior mediastinal route (treatment vs control) was 0.56 (95% CI, 0.17–1.82) for mortality, 1.01 (95% CI, 0.35–2.94) for anastomotic leaks, 0.43 (95% CI, 0.17–1.12) for cardiac complications, and 0.67 (95% CI, 0.34–1.33) for pulmonary complications. Systematic qualitative review of the data did not suggest any difference in other perioperative outcomes or con-
duct function for the two routes of reconstruction. Therefore, posterior and anterior mediastinal routes of reconstruction are considered to have similar functional outcome and quality of life. However, they erroneously included the RCT of Zieren and colleagues [23], who did not randomize for the route of reconstruction. More RCTs would be needed to definitively resolve the controversies [24]. At present, the commonly used prevertebral route seems safe and suffices for most situations. When a macroscopically incomplete (R2) resection is done, there are theoretical grounds to support extra-anatomical reconstruction, because the risk of developing a symptomatic locoregional recurrence is high [25].

Cervical or Thoracic Anastomosis?

Cervical anastomosis allows for a larger proximal margin of resection and is believed to result in less dangerous leakage, and an increased risk of injury to the recurrent laryngeal nerve compared with intrathoracic anastomosis. However, the technique of first choice remains controversial. Thus far, three RCTs have been published. Chasseray and colleagues [26] compared stapled intrathoracic with cervical anastomoses after esophagectomy. Transfusion requirements and operating time were similar for the 49 patients having a thoracic anastomosis (TA) and the 43 patients who had a cervical anastomosis (CA). A CA resulted in a greater median margin of macroscopically normal esophagus above the tumor (4.0 vs 1.5 cm for TA; \( p < 0.05 \)). One patient from each group had involvement of the resected proximal anastomotic doughnut. Overall, 41 patients (44%) sustained one or more complications (22 vs 19 patients). Leakage was significantly more frequent after cervical anastomosis (11 vs 2 patients; \( p < 0.02 \)). Thirty-day mortality rates were comparable: 7 deaths occurred after TA (14.3%) and 4 after CA (9.3%). Length of hospital stay was similar. Postoperative strictures occurred in 14% of TA and 23% of CA patients (\( p = \) not significant) and were most common after an anastomotic leak. Median survival time was comparable. The authors concluded that the greater length of tumor-free esophagus removed did not result in improved survival period, but was associated with a higher incidence of anastomotic leakage. This study is difficult to evaluate because of the variety of techniques used.

Ribet and colleagues [27] randomized 60 consecutive patients with cancer of the thoracic esophagus to undergo a cervical anastomosis (30 patients) or a thoracic anastomosis (30 patients). The surgical technique was identical. Proximal resection margins were more frequently involved in patients undergoing TA (10 vs 3 patients after CA). Morbidity consisted of 8 anastomotic leaks in the neck (4 of which were subclinical) and 3 in the chest (with one subclinical). Respiratory complications (21 vs 11 patients; \( p = 0.01 \)) and recurrent laryngeal trauma (6 vs 1 patient) were more frequently seen in patients having CA. Postoperative mortality was comparable (5 deaths after CA and 4 after TA). Median survival was comparable (9 months vs 12 months). Although mortality was comparable, the authors concluded that subclinical leaks, respiratory morbidity, and recurrent laryngeal nerve trauma were more prevalent after CA. However, it remained unclear as to what extent the neck dissection added to the morbidity.

Walther and colleagues [28] compared a manually sutured esophagogastric anastomosis in the neck with stapled anastomosis in the chest after transthoracic esophagectomy. Apart from anastomosis, surgical procedures were identical. No cervical lymphadenectomy was carried out. There were 83 patients who were randomized to receive an anastomosis in the neck (41 patients) or in the chest (42 patients). To evaluate selection bias, patients undergoing esophageal resection during the same period but not randomized (n = 29) were also followed and compared with those in the study (n = 83). The anastomosis was checked for leakage by roentgenograms with water-soluble contrast medium 5 days postoperatively. Anastomotic leakage was defined as extravasation of contrast or clinical symptoms of leakage, or both. Objective measurements of anastomotic level and diameter were assessed with an endoscope and balloon catheter at 3, 6, and 12 months after surgery. Two patients (1.8%) died in the hospital, and the remaining 110 patients were followed until death or for a minimum of 60 months. No differences were seen in operating time. The 5-year survival rate was comparable (29% for TA vs 30% for CA). The leakage rate was 1.8% (one radiologic and one clinical) with no relation to mortality or anastomotic method. All patients in the randomized group had tumor-free proximal and distal resection margins, but 1 patient in the nonrandomized group had tumor infiltrating into the proximal resection margin. At 3, 6, and 12 months after the operation, there was no difference in anastomotic diameter (\( p = 0.771 \)). Both increased with time (\( p = 0.004 \)). Experience of dysphagia, number of anastomotic dilatations and body weight were comparable. With similar results in randomized and nonrandomized patients, study bias was eliminated. The authors concluded that when neck and chest anastomoses are performed in a standardized way after esophageal resection, they are equally safe. The additional esophageal resection of 5 cm in the neck group did not increase tumor removal or survival; on the other hand, it did not adversely influence morbidity, anastomotic diameter, or eating as reflected by body weight development.

Considering the latter trial as the best available evidence at the present time, one could conclude that there are no major differences in clinical outcomes for anastomoses in the neck or chest after transthoracic esophagectomy. Hospital mortality was not influenced by the site of the anastomosis in any of the RCTs. One can hardly imagine that the resection of 5 cm of (uninvolved) proximal esophagus will result in a detectable survival benefit. The increased incidence of anastomotic complications after neck anastomosis is not uniformly confirmed. Therefore, it seems prudent to advice surgeons to use the anastomotic site with which they are best familiar.
Hand-Sewn or Stapled Anastomosis?

Anastomoses can be fashioned by hand or mechanical. Early (leakage) and late (stricturing) patient outcomes may be influenced by the technique. A meta-analysis of RCTs to determine the effect of the anastomotic technique on patient outcomes was performed. Five RCTs containing 467 patients were reviewed [29–33]. Only one RCT compared hand-sewn and stapled esophagogastroduodenal anastomoses in the neck. Relative risk (expressed as hand-sewn versus stapled) was 0.45 (95% CI, 0.20–1.00) for operative mortality, 0.79 (95% CI, 0.44–1.42) for anastomotic leaks, 0.60 (95% CI, 0.27–1.33) for anastomotic strictures, 0.99 (95% CI, 0.55–1.77) for cardiac morbidity, and 0.93 (95% CI, 0.63–1.37) for pulmonary morbidity.

Outcomes examined by systematic qualitative review demonstrated that the hand-sewn methods led to a longer operating time in three of four studies, but only one was significantly longer. Although both techniques gave similar results for anastomotic outcomes, the stapled method seemed to be associated with an increased operative mortality, a finding which is difficult to explain [34].

More recently, Hsu and colleagues [35] randomized 63 patients with squamous cell cancer. Patients were randomized to receive either hand-sewn (32 patients) or circular stapled (31 patients) cervical anastomosis. Transhiatal esophagectomy with mediastinal lymphadenectomy was performed in 59 patients, 4 patients underwent transthoracic resection. The hand-sewn anastomosis was accomplished using a double layer of interrupted sutures. The mean operating time was 37 minutes longer when the hand-sewn method was used (524 vs 447 min; p < 0.001). Anastomotic leakage (7 in the hand-sewn versus 8 patients in the stapler group), hospital mortality (4 vs 3 patients), and benign esophageal stricture (4 vs 5 patients) were comparable in both groups. The authors concluded that using a circular mechanical stapler shortens operating time with comparable outcome to the hand-sewn technique for cervical esophagogastric anastomoses.

Recently, another RCT was undertaken in 117 patients with squamous cell carcinoma of the thoracic esophagus who all underwent Ivor-Lewis esophagectomy. The results of this study showed that both the hand-sewn method and the staple method were safe. Hand-sewn anastomosis took 15 minutes longer to perform. The stapled method had a higher incidence of anastomotic strictureting in patients with a small diameter of the esophagus [36]. Another recently performed small RCT with 32 patients showed similar results. In this small study the incidence of recurrent laryngeal nerve injury was higher after handsewn anastomosis, and operation times were longer. This did not lead to a difference in postoperative symptoms and long-term survival [37].

In summary, the difference in operating times between hand-sewn and stapled groups is not consistent in the literature, probably because different methods of hand-sewn suturing were used. It seems that both methods have comparable results in experienced hands. Costs were not mentioned in these studies.

Hand-Sewn: One-Layer or Two-Layer Anastomosis?

Zieren and colleague [23] reported an RCT comparing one-layer and two-layer cervical anastomoses after esophagectomy. After transthoracic resection (24 patients) and palliative transthiatal resection (16 patients), the gastric tube was placed retrosternally and after "curative" transthiatal resection (67 patients) in the posterior mediastinum. Anastomotic leakage and late stricture were the study endpoints. On postoperative day 7, a water-soluble contrast study was carried out. The groups were comparable regarding patient characteristics. After 54 one-layer and 53 two-layer procedures, the rates of anastomotic leakage were comparable (10 patients in each group [19%]). After a mean follow-up of 44 weeks, 13 of 51 patients (25%) undergoing one-layer anastomosis and 28 of 50 (56%) undergoing the two-layer procedure complained of cervical dysphagia and required dilatation (p < 0.01). Strictures were malignant in 2 and 4 of these patients, respectively. The risk of developing a fibrotic (benign) stricture during the first year after the operation was 30% for one-layer anastomosis and 64% for two-layer anastomosis (p < 0.05). The authors concluded that based on comparable leakage rates, one-layer anastomosis is superior to the two-layer procedure because of the lower incidence of a benign, fibrotic stricture.

Single-Layer Anastomosis: Continuous or Interrupted Sutures?

Bardini and colleagues [38] carried out an RCT to compare the efficacy of a single layer of continuous absorbable monofilament with that of a single layer of interrupted Polyglactin sutures in the performance of cervical esophagogastric anastomoses. Forty-two patients were enrolled in the study (21 patients per group). A gastrografin swallow study was performed on postoperative day 10. There was no hospital mortality. One asymptomatic anastomotic leak (4.8%) and two early anastomotic strictures requiring dilation (9.5%) occurred in patients in whom the interrupted technique was used. No leaks or strictures were observed in the continuous technique group. Significantly less operative time to perform the anastomosis was required for the continuous technique compared with the interrupted technique (10 min vs 16 min; p < 0.0001), and the cost of the suture material was reduced markedly due to the lower number of sutures needed for each anastomosis. It was concluded that either a continuous or an interrupted single-layered esophagogastric anastomosis in the neck can give satisfactory results after esophagectomy. The continuous technique has the advantages of being somewhat time-saving and cheaper.

The Diameter of the Anastomosis

A wide cross-sectional area at the anastomatic site might help in reducing the incidence of anastomotic leakage and strictures. There were 100 consecutive patients who were randomized. Fifty patients underwent end-to-side (two-layer) cervical esophagogastric anastomosis after removal of a 3 × 2 cm gastric crescent from the anterior
width of the gastric tube. In the control group, an end-to-side (two-layer) cervical esophagogastric anastomosis was constructed on the anterior wall of the gastric tube without removal of a gastric tube crescent. All patients underwent water soluble contrast esophagography on postoperative day 8. Anastomotic stricture was defined as difficulty in swallowing solids or failure to pass a 12.8-mm endoscope through the anastomosis that necessitated bougie dilatation. The incidence of anastomotic leakage in the experimental arm was significantly less in comparison with the control group (2 patients [4.3%] vs 10 patients [20.8%]; \( p = 0.03 \)). Similarly, anastomotic stricture formation was significantly lower in the study group (4 patients [8.5%] vs 14 patients [29.2%]; \( p = 0.02 \)). They concluded that a wide cross-sectional area at the anastomotic site by removal of a gastric crescent resulted in significantly less anastomotic complications [39].

**Width of the Gastric Tube**

The (near)-total stomach can be used as the esophageal substitute after esophagectomy because of its abundant blood supply, its elasticity and reservoir function, and the advantage of only one anastomosis. The advantages of a narrow gastric tube are its excellent elasticity and the ease with which it can be pulled up into the neck without tension. On the other hand, the whole stomach may have the advantage of the intact submucosal network, as reported by Pierie and colleagues [40]. Recently, in an RCT containing 44 patients, the size of the gastric tube on the blood flow at the anastomotic site, the frequency of leakage from esophagogastrostomy, and the postoperative nutritional status was evaluated. The patients were randomized to either reconstruction with a subtotal stomach (22 patients) or a slender gastric tube (22 patients) after esophagectomy (level 2b evidence). Esophagogastrostomies were hand-sewn in a one-layer method. Of 22 patients, although leakage occurred in 1 with subtotal stomach (5%) and 5 with slender gastric tube reconstruction (25%), the difference did not reach statistical significance (\( p = 0.19 \)). The mean blood flow at the anastomotic site, as measured with laser flow meters was comparable between the two types of esophageal substitutes. There was also no difference noted in the nutritional status at 6 and 12 months after the operation, as expressed by body mass index, serum albumin level, or total lymphocyte count. However, as stated by the authors, the number of patients in this study was small, and therefore its power was not enough to justify the no-difference outcome (risk of type II statistical error), especially for the frequency of leakage [41].

**The Use of Pedicled Omentum in Anastomosis**

Anastomotic leakage is a life-threatening complication. The use of a pedicled omentum in the esophageogastric anastomosis may lead to less anastomotic complications due to rapid adhesions and new blood vessel networks to the underlying tissues, thereby helping to seal microscopic leaks and helping with tissue remodeling. The mobile pool of histiocytes, monocytes, and granulocytes in the omentum, contain the local infective process and thereby protect the anastomosis. Using a pedicled omental wrap has been evaluated in an RCT. There were 194 patients who were randomized in two groups. In 97 patients, a pedicled omentum was wrapped around the esophageogastric anastomosis, and 97 patients did not have an omental graft. The use of a pedicled omental wrap was associated with a significant reduction in anastomotic leakage (3.7% vs 14.3%). However, mortality rates in the two groups of patients were not significantly different. The findings in this study should be taken with a little caution because hand-sewn anastomoses were performed with silk, which is known to increase the risk of infection because of potential bacterial harboring [42].

**The Use of a Pyloroplasty**

Because gastric emptying may be impaired after esophagectomy with gastric reconstruction, a pyloroplasty or pyloromyotomy may be performed. Urschel and colleagues [43] performed a meta-analysis of RCTs to determine the effect of pyloric drainage. Nine RCTs could be identified, including a total of 553 patients [44–52]. Early outcomes assessed included operative mortality, anastomotic leakage, pulmonary morbidity, pyloradic drainage complications, fatal pulmonary aspiration, and gastric outlet obstruction. Only three trials provided data on these early postoperative outcomes. The trials were not uniform in their patient inclusion criteria, outcome assessment, method of esophagectomy, extent of resection, pathology, route of reconstruction, specific characteristics of gastric conduit, and technique of pyloric drainage (pyloroplasty or pyloromyotomy). The diagnostic criteria for early postoperative gastric outlet obstruction often included clinical findings, such as aspiration, vomiting, postprandial fullness, and regurgitation, and radiological findings of gastric dilatation. The relative risk, expressed as pyloric drainage versus no drainage, was 0.92 (95% CI, 0.34–2.44) for operative mortality, 0.90 (95% CI, 0.47–1.76) for esophagogastrectomy anastomotic leaks, 0.69 (95% CI, 0.42–1.14) for pulmonary morbidity, 2.55 (95% CI, 0.34–18.98) for pyloradic drainage complications, 0.25 (95% CI, 0.04–1.60) for fatal pulmonary aspiration, and 0.18 (95% CI, 0.03–0.97) for early postoperative gastric outlet obstruction (favors pyloric drainage). Systematic semi-quantitative review showed a nonsignificant trend favoring pyloric drainage for the late outcomes like gastric emptying, food intake and nutritional status, and obstructive upper gastrointestinal symptoms. For the late outcome of bile reflux, however, there was a nonsignificant trend favoring the no-drainage group. The scintigraphic gastric emptying time, expressed as a ratio (pyloric drainage/no drainage), was 0.53 (shorter emptying with pyloric drainage). The authors concluded that pyloric drainage procedures reduce the occurrence of early postoperative gastric outlet obstruction after esophagectomy with gastric reconstruction, without affecting other early or late patient outcomes. Further trials with much larger numbers of patients would be needed to clarify the possible beneficial or detrimental impact of pyloric drainage on other early and late postoperative outcomes [53].
The Use of Neck Drainage
To evaluate the role of a closed-suction drain for esophagogastroduodenal anastomosis in the neck, an RCT in 40 patients who underwent esophagectomy with a (left-sided) cervical anastomosis was conducted. Half of the patients had a drain inserted at the end of operation. The output of neck drains was recorded every 4 hours; the neck wounds were inspected daily for any evidence of hematoma or seroma formation. The drain was removed when its output was less than 10 mL per day. The median duration of drainage was 46 hours (range, 36 to 88 hours). The median total output of neck drains was 63 mL (range, 15 to 210 mL). Hematoma or seroma formation did not occur in any patients in either group. Anastomotic leakage did not occur in any patient. The benefits of a drain could not be demonstrated, and therefore the investigators concluded that routine drainage was not necessary. Again, the number of patients in this trial may have been too small to detect a difference in outcome. In view of the low risk on hematoma or seroma formation in the neck, or both, such a difference would be of little clinical relevance [54].

The Use of Fibrin Glue to Reduce Lymph Leakage
Fibrin glue has been shown to be effective in improving postoperative chylothorax after various thoracic procedures and in reducing lymphorrhoea after axillary dissection. The value of using fibrin glue after esophagectomy was investigated in a randomized controlled trial. A series of 43 consecutive patients with thoracic EC who underwent extended esophagectomy were prospectively randomized to two groups; in 21 patients 3 mL of fibrin glue was applied to the dissected mediastinum, and in 22 patients fibrin glue was not applied. The daily volume from the thoracic drain was significantly larger (p < 0.05) on postoperative day 1 in patients who had the fibrin glue applied. Also the cumulative drainage volume was significantly larger on postoperative days 4 to 6, and 9, suggesting that the cumulative drainage volume in this group was consistently larger. Therefore, the authors concluded that the application of fibrin glue to the dissected mediastinum seems to induce postoperative lymph leakage and may thus be responsible for prolonged chest tube insertion in some patients. Hence, the use of fibrin glue can not be recommended for reducing lymph leakage [54].

Comment
In summary, with EC surgery there long has been a debate about the best surgical approach. Only one RCT addresses the concerns of the optimal extent of resection, in which the results suggest that fit patients are best treated by a transthoracic esophagectomy with extended en bloc (two-field) lymphadenectomy. For less fit patients or patients with junctional or cardiac tumors, transhiatal esophageal resection could suffice. Future and ongoing RCTs should establish the role of three-field lymphadenectomy. Currently, there is no evidence to support the routine use of a three-field lymph node dissection for EC. When performing a two-field resection, a synchronous two-team approach is associated with more complications. Although the results of minimally invasive surgery are promising, randomized studies are lacking in evidence, and therefore this type of surgery should be seen as investigational.

Esophagectomy is associated with a high rate of morbidity and considerable mortality. Most RCTs in this field concern technical aspects of the procedure, mainly to optimize the results (and minimize complications) of esophageal reconstruction. Diverse technical adaptations have been subject of investigation; however, again, limited randomized trials have been performed. Available evidence suggests that posterior and anterior mediastinal routes of reconstruction have similar functional outcome and quality of life after esophagectomy for cancer. There were no major differences found in clinical outcomes for anastomoses in the neck or chest after transthoracic esophagectomy. In addition, results of the hand-sewn and stapled anastomosis are comparable in experienced hands. When using a hand-sewn anastomosis, a continuous or an interrupted single-layered esophagogastric anastomosis in the neck can give satisfactory results after esophagectomy, although the latter takes more time and is slightly more costly. Therefore, it seems prudent to advice surgeons to use the technique in which they are best familiar.

Although leakage rates of one-layer anastomosis are similar to rates of the two-layer procedure, the first technique is superior due to a lower incidence of benign strictures. For cancers located in the thoracic esophagus, a wider anastomosis might be of benefit, and the use of pedicled omentum might decrease the rate of anastomotic leakage, but this should be confirmed in larger trials. Routine pyloroplasty and placement of a neck drain are unnecessary. There is no indication to use fibrin glue to prevent lymph leakage.

Altogether, the present review in EC surgery indicates that there is only limited high-quality evidence available. There is a need for large, multicenter randomized studies concerning many aspects of EC surgery.

References