

Evidence-Based Operative Details in Esophageal Cancer Treatment: Surgical Approach, Lymphadenectomy, Anastomosis

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Keywords

Esophageal cancer · Operative details · Lymphadenectomy · Surgical approach · Anastomosis · Neoadjuvant treatment

Summary

Background: This review depicts surgical treatment strategies in the management of esophageal cancer under the focus of evidence-based medicine. The main emphasis lies on technical details, i.e. surgical approach, lymphadenectomy, and current techniques of anastomosis. **Methods:** The current literature on operative details in esophageal cancer treatment was reviewed. Surgical approaches and different techniques of anastomotic reconstruction utilizing a gastric tube were compared. The grade of evidence regarding the necessity and extent of lymphadenectomy was discussed. **Results:** There is no level-1 evidence-based difference regarding the surgical approach for esophagectomy. The preferred anastomosis site is intrathoracic compared to the neck. Extended lymphadenectomy is still imperative in esophagectomy although neoadjuvant protocols might also result in a downstaging effect of lymph nodes. Neoadjuvant regimens have no negative influence on complication rate and anastomotic integrity. **Conclusion:** A tailored interdisciplinary approach to the patients' physiology and esophageal cancer stage is the most important factor that influences operative outcome and oncological results after esophagectomy.

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Introduction

Esophageal cancer is one of the leading causes of cancer-related deaths in the Western world, with a rising incidence especially for adenocarcinoma of the distal esophagus and the cardia.

Treatment options for esophageal cancer are based on i) locoregional treatment strategies with surgery and radiotherapy and ii) systemic therapy utilizing chemotherapy.

Surgery is the mainstay for achieving locoregional control in patients with esophageal carcinoma and offers the best chance for cure in localized and locally advanced disease [1].

For esophageal resection several approaches have been described [2]. Which approach is chosen depends on tumor location and the surgeon's ability to obtain a curative R0 resection and adequate lymphadenectomy (>25 lymph nodes (LNs)) [2, 3].

Approaches for Esophagectomy

- Transhiatal esophagectomy involves neck and abdominal incisions. By blunt dissection through the hiatus from the abdominal incision the esophagus is mobilized and an anastomosis is made via neck incision. As this procedure mostly avoids a thoracotomy, the practical disadvantage is a limited exposure of the tumor area with potentially fewer LNs for pathological examination. Performing an additional thoracotomy to the procedure described above, i.e. tri-incisional esophagectomy, allows an excellent lymphadenectomy of abdominal and thoracic LNs. The anastomosis is generally performed on the left side of the neck to decrease the risk of recurrent laryngeal nerve injury [2, 3].
- Abdominothoracic esophagectomy (Ivor-Lewis procedure) involves abdominal and right thoracic incisions. First, the stomach is mobilized by means of an abdominal incision. After re-

positioning the patient to the lateral position the esophagus is removed, and the LNs are collected through the chest incision. Finally, an intrathoracic esophagogastric anastomosis (EGA) is performed. The Ivor-Lewis procedure with a right-sided thoracotomy has the advantage of providing an excellent yield of LNs for pathologic examination and good exposure to the lesion, especially for cancers of the distal third of the esophagus [2].

- Minimally invasive esophagectomy (MIE) is the most recently described approach; it relies on thoracoscopic access to the chest and laparoscopic access to the abdomen to achieve excision of the esophagus [2, 4]. Advantages of MIE are an accelerated recuperation. It is furthermore claimed that in expert hands, MIE also provides adequate LN yield to assess for metastatic disease [5, 6].

Esophagectomy: Evidence for the Best Surgical Approach?

Which of the approaches described above is the best is still one of the hottest discussed issues in the surgical literature [2, 7–9].

As analyzed by Rubenstein et al. [2], there is no level-1 evidence that any approach increases survival times compared with the others. Randomized studies have associated a transhiatal approach with less morbidity than a transthoracic approach; however, percentages of patients with long-term survival did not differ significantly [10].

The significance and oncologic adequacy of MIE is also under debate [11]. The recently published TIME trial suggests equivalent LN retrieval rates between open esophagectomy and MIE. However, the overall LN retrieval rates in the trial were below the accepted minimum in both MIE and open groups [12]. Similarly, comparison of R0 resection rates between open and MIE techniques is based on few high-quality studies [11, 13].

Because to date no final decision could be reached on whether or not to apply an MIE approach, it should be made according to the operator's experience and the ability to provide adequate oncologic resection. In general, local expertise is probably a better predictor of outcome than approach [2].

Compared with the others, there is no level-1 evidence that any approach for esophagectomy increases survival times.

Impact of Lymphadenectomy

Esophageal cancer is associated with early and diffuse lymphatic dissemination into the neck, chest, and abdomen [14]. Consequently, lymphadenectomy is the main oncological factor that can be influenced by the surgeon, besides a complete resection of the primary tumor [14].

Noordman and van Lanschot [15] recently pointed out that although most studies have concluded that LN retrieval is associated with improved survival, the majority of these studies have been performed in patients undergoing surgery alone. This has led to recommendations regarding the optimal extent of lymphadenec-

tomy between 6 and 30 nodes [15–17]. Contrary to this, a nationwide population-based retrospective cohort study including 1,044 patients with esophageal cancer published in 2015 did not show any improved survival after extensive lymphadenectomy. As the published data shows conflicting results, however, it has become the subject of discussions [18].

Other studies investigated the designated fields of dissection, i.e. two-field versus three-field lymphadenectomy [19, 20]. Prospective trials have been performed comparing survival after transhiatal and transthoracic esophagectomy [10], but a recent meta-analysis did not show any difference in survival between limited transhiatal and extended transthoracic operations [21].

Finally, after publication of the CROSS trial comparing neoadjuvant chemoradiotherapy followed by surgery versus surgery alone in patients with esophageal cancer, this multimodal approach has become the standard of care in many countries [22]. Neoadjuvant chemoradiotherapy has a marked downstaging effect on the primary tumor as well as on the regional LNs [14, 22].

In the CROSS trial, the total number of resected nodes in those patients who underwent surgery alone had a positive association with overall survival [14]. This correlates with the already discussed international retrospective study published by Peyre et al. [16].

Interestingly, this relationship between the total number of resected nodes and overall survival was completely lost in the group receiving neoadjuvant chemoradiotherapy.

These data suggest that maximal LN retrieval is relevant in patients who undergo surgery alone, but question whether such an approach is necessary after neoadjuvant chemoradiotherapy.

Thus, the effect of the extent of lymphadenectomy on survival remains controversial. As proposed by Noordman and van Lanschot [15], future research should distinguish between patients treated with surgery alone and those who undergo neoadjuvant therapy before surgery. Neoadjuvant therapy has been suggested to abolish any positive effect of extensive lymphadenectomy on survival; however, this effect should be further explored, preferably in a randomized setting comparing transthoracic esophagectomy with transhiatal esophagectomy after neoadjuvant chemoradiotherapy, and focused on in truly esophageal (Siewert type-1) tumors [15].

Operative Details of Anastomosis

When performing esophagectomy, the stomach is the most common substitute. When the stomach is not adequate for reconstruction or when gastric reconstruction fails due to necrosis or ischemia, colon interposition is mostly used as a second option [23, 24].

Various surgical techniques exist for esophagogastric reconstruction. Besides hand-sewn anastomosis the use of stapler devices – circular-stapled (CS) and linear-stapled (LS) – are common alternatives [24, 25]. Circular-stapled anastomoses have become increasingly popular in the 1990s due to the reduction of leakage rates [23, 24, 26]. Linear anastomosis, which is claimed to reduce strictures, was first described by Collard [27] in 1998 and was later modified by Orringer et al. [28, 29].

As key to the formation of an ideal EGA the different technical parameters, i.e. surgical approach, location, and stapler device, have been discussed. However, the hitherto conducted studies and meta-analyses focused on these parameters individually, while none has shown one single approach or technique to be the most successful. In a pooled analysis of relevant randomized controlled trials and comparative studies, Markar et al. [30] analyzed the main technical parameters that affect the integrity of EGA:

- Hand-sewn versus stapled EGA: Pooled analysis revealed no significant difference between the groups regarding anastomotic leakage [24, 25, 29, 30].
- LS versus CS EGA: No significant difference between the groups regarding anastomotic leakage. However, a meta-analysis showed a non-significant trend towards a reduced rate of anastomotic strictures in the LS group compared to circular anastomosis [30, 31].
- Cervical versus thoracic EGA: Only subgroup analysis of randomized trials including four randomized controlled trials revealed that an anastomotic leak was more common in the cervical EGA than in the thoracic group ($p = 0.005$) [12, 30, 32].
- Anterior versus posterior mediastinal reconstruction: No significant difference between the groups regarding anastomotic leakage [30].
- Minimal versus open esophagectomy and EGA: No significant difference between the groups regarding anastomotic leakage [30].
- Ischemic conditioning of the gastric conduit: Ischemic conditioning of the gastric conduit is mainly performed by pre-operative vessel embolization or alternative laparoscopic vessel ligation [33]. Pooled analysis demonstrated no significant difference between the groups regarding the incidence of anastomotic leak [30].
- Influence of neoadjuvant treatment/radiation on EGA: There are concerns whether neoadjuvant chemotherapy or especially the addition of radiation in a combined regimen might increase anastomotic leakage and stenosis in patients with esophageal cancer treated with neoadjuvant regimens followed by esophagectomy.

There is no statistically proven evidence to support the theory that perioperative chemotherapy or radiochemotherapy increases the surgical complication rate after esophagectomy [22, 34–37].

Conclusion

Esophageal cancer still is a devastating diagnosis, with esophagectomy being the only procedure for cure.

Several approaches for resection have been described: transhiatal, abdominothoracic, and, most recently, minimally invasive resection. There is no level-1 evidence that any approach for esophagectomy increases survival times compared with the others.

Taking the spectrum of operative complications into consideration, anastomotic leakage still is a critical issue. Based on meta-analyses, the risk for leakage might be reduced by performing an intrathoracic anastomosis compared to cervical reconstruction (level-1

evidence). Besides higher leakage rates, the risk of recurrent nerve trauma is an additional drawback of reconstruction at the neck.

Both hand-sewn anastomosis and the use of a stapler device are valid alternatives. No randomized studies exist showing a clear benefit for either technique.

However, despite standardized techniques, leakage of the anastomosis or of the stapling line of the gastric tube is reported in 1.6–22% for hand-sewn and 4.9–26% for stapled anastomosis [24, 25].

The re-operation rate for anastomotic leakage is high, i.e. up to 70%; however, in the clinical routine as well as the literature a clear trend does exist toward the placement of an endoluminal stent combined with an interventional abscess drainage, which is associated with favorable outcome in most series [38].

Narrow gastric tubes might avoid ischemia due to the blood supply by the gastroepiploic arcade and simplify the possibility of endoluminal stent placement in case of an anastomotic leakage [39].

Similarly, endoluminal stent placement has been performed successfully for tracheobronchial fistulas, with the best results achieved by means of the double stenting procedure, helping to avoid re-operation with mostly discouraging results. Nevertheless, tracheobronchial fistulas remain a life-threatening complication with high mortality [38].

Besides complete tumor removal (R0 resection), lymphadenectomy is the main oncological factor that can be influenced by the surgeon [14]. The well-established opinion is that extensive lymphadenectomy increases the probability of radical removal of all tumor-positive LNs and thus might result in an improvement of long-term survival [15].

Based on the CROSS trial, comparing the strategies neoadjuvant chemoradiotherapy followed by surgery versus surgery alone, the paradigm of extended lymphadenectomy was confirmed only for the surgery alone group [22]. On the contrary, this relationship between total number of resected LNs and overall survival was lost in the neoadjuvant study arm [14, 16, 22]. Given that this data needs to be confirmed, the results imply that maximal LN retrieval is of relevance for the surgery only group. However, it is questionable whether such an approach is necessary after neoadjuvant chemoradiotherapy (level-II evidence). Until this is not confirmed, extended lymphadenectomy remains the gold standard.

Since the introduction of multimodal treatment strategies in esophageal cancer there has also been an ongoing discussion of adverse effects of neoadjuvant chemotherapy and especially of radiation on the operative outcome. Meanwhile, there exists level-1 evidence that neoadjuvant treatment does not increase mortality or the complication rate.

In order to reduce complications in esophageal surgery, patient selection parameters for the best individual therapy and optimization of interdisciplinary complication therapy are the goals for the future [36].

Disclosure Statement

There is no conflict of interest for all authors.

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