Transhiatal or Transthoracic Esophagectomy

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5.1 Introduction

A surgical resection remains the most important treatment modality for the cure of non-metastasized esophageal cancer. For many years, open esophagectomy was performed worldwide through two approaches: the transhiatal esophagectomy (THE) and transthoracic esophagectomy (TTE). Pertaining in-hospital mortality rates were between 3 and 10%, and the 5-year survival rate after surgery was 20–30%. Resulting contributions to improved patient-care and selection were the improvement of perioperative care, the introduction of neoadjuvant treatments, the centralization of surgery in high volume centres and the better imaging modalities. Hence, short and long-term outcomes of surgical resection have improved substantially.

Minimally invasive esophagectomy (MIE) was pioneered in the early nineties and popularized in the last decades by many surgeons. Three meta-analyses support the concept that MIE may be associated with less respiratory complications, a reduction of morbidity and a faster postoperative recovery [1–3]. At the same time, the procedure is technically demanding and programs to safely introduce these techniques are warranted. Two randomized trials compared open esophagectomy with MIE: the total (thoracolaparoscopic) MIE in the TIME-trial and the hybrid (laparoscopy and thoracotomy) esophagectomy in the MIRO-trial. Both studies show the short-term advantages of MIE: less blood loss, a lower rate of respiratory infection, a shorter hospital stay and a better quality of life in favour of the MIE. The quality of the specimen resected is similar to the open technique (radicality and number of lymph nodes). Long-term oncological outcome of the TIME trial at 1-year and 3-year showed no differences between the two groups concerning overall and disease-free survival [4].

In this chapter we review the transhiatal and transthoracic esophagectomy and discuss the comparison of the outcomes of these two open approaches by a randomized controlled study, the HIVEX trial.

5.2 Comparing THE with TTE: The HIVEX Trial

5.2.1 Transhiatal Esophagectomy

Via an upper abdominal incision, the distal esophagus and locoregional lymph nodes in the posterior mediastinum are dissected en bloc through a widened hiatus. The upper abdominal

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lymph nodes are dissected including the paracardial lymph nodes, the nodes along the lesser curvature and the nodes at the left gastric artery. A standard D1 plus or D2 lymphadenectomy of the celiac trunk is performed. The cervical esophagus is dissected via a left (or right) cervical incision and the intrathoracic esophagus dissected bluntly and stripped with the aid of a vein stripper. Creation of gastric tube and resection of the specimen is then followed by positioning the gastric tube in the prevertebral plane to the neck where the anastomosis is made [5].

5.2.2 Transthoracic Esophageal Resection

Several techniques are used: Ivor Lewis procedure (right thoracotomy and laparotomy), Mc Keown (three-stage with neck incision) and the Sweet procedure (left thoraco-abdominal incision). The three-stage and the two-stage open esophagectomy involves an esophageal resection, creation of a gastric tube, a two-field lymphadenectomy (celiac trunk and mediastinal lymphadenectomy) followed by a cervical anastomosis in the three-stage procedure and an intrathoracic anastomosis in the case of an Ivor Lewis procedure. The extent of the mediastinal lymphadenectomy is still debated, but the majority of the patients undergoes a total mediastinal lymphadenectomy.

5.2.3 Differences Between Open TTE and THE

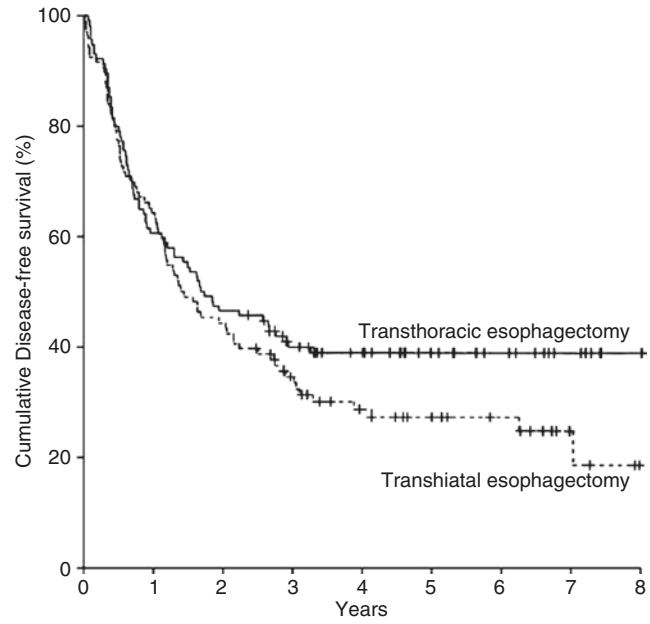
In 2001, Hulscher et al. published a meta-analysis on transthoracic and transhiatal esophagectomy [6]. Six prospective comparative studies including three control-randomized studies (RCT) and 18 retrospective comparative studies were included (all published between 1990 and 1999). The three RCTs in this meta-analysis were all underpowered and focused on squamous cell carcinoma [7–9]. In 2002, Hulscher et al. published the Dutch HIVEX trial, a RCT comparing TTE with THE [10]. In 2007, Omloo et al. published a long-term follow-up of this trial (5 years) [11].

The HIVEX trial included 220 patients with adenocarcinoma type I of the distal esophagus or adenocarcinoma type II of the gastric cardia involving the distal esophagus. Patients were randomized to THE or TTE with extended en bloc lymphadenectomy. Primary endpoints of this study were overall survival and disease-free survival. Secondary endpoints were the perioperative data and other parameters such as postoperative morbidity and mortality, the quality of the resected specimen, the number of lymph nodes involved and the number of quality-adjusted life-years gained.

Perioperative morbidity was higher after TTE, but there was no statistically significant difference between the groups THE and TTE regarding in-hospital mortality (2% in the transhiatal group and 4% in the transthoracic group, $p = 0.45$). In the TTE group, 57% of patients had pulmonary complications vs. 27% in the THE group ($p = <0.001$). Chyle leakage occurred more in the TTE group, 10% vs. 2% ($p = 0.02$). In the THE group, vocal-cord paralysis was more common but this difference was not significant (21% vs. 13%, $p = 0.15$). Mechanical ventilation time, ICU stay and hospital stay were significantly higher in the TTE group (postoperative ventilation time: 2 days vs. 1 day, $p = <0.001$; ICU stay: 6 days vs. 2 days, $p = <0.001$; and postoperative hospital stay: 19 days vs. 15 days, $p = <0.001$).

After a median follow-up of 4.7 years, 142 patients had died: 74 (70%) after THE and 68 (60%) after TTE ($p = 0.12$). Although the difference in survival was not statistically significant, there was at 5 years a trend toward a survival benefit holding for the extended approach. Disease-free survival was 27% in the THE group, as compared with 39% in the TTE group, whereas overall survival was 29% as compared with 39% (Figs. 5.1 and 5.2).

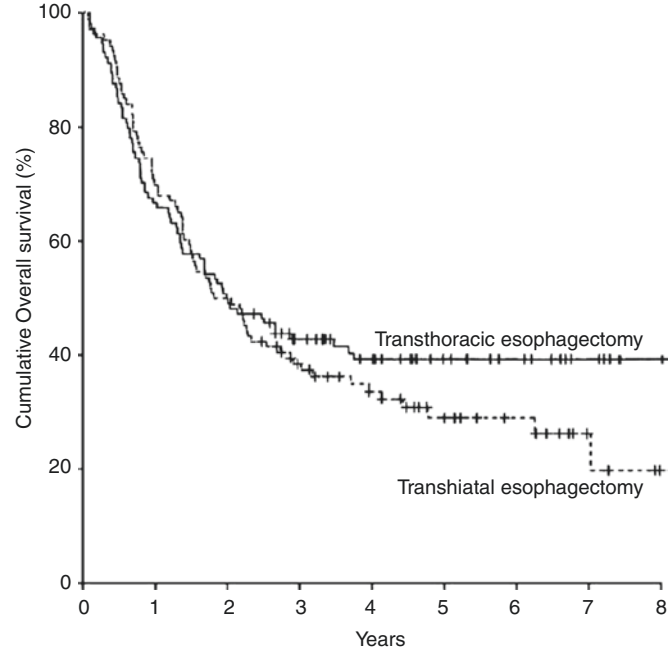
The conclusion of this HIVEX trial was that THE was associated with a lower morbidity rate than TTE with its extended en bloc lymphadenectomy. Although median overall, disease-free, and quality-adjusted survival did not differ statistically between the groups, there was at 5 years a



No. At Risk

Transhiatal esophagectomy	106	68	47	32	20	15	11	4
Transthoracic esophagectomy	114	69	53	39	31	20	13	7

Fig. 5.1 Kaplan Meier curves showing disease free survival among patients randomly assigned to transhiatal esophagectomy or transthoracic esophagectomy with extended en bloc lymphadenectomy. From Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus, Hulscher JB, van Sandick JW, de Boer AGEM et al., 347. Massachusetts Medical Society. Reprinted with permission



No. At Risk

Transhiatal esophagectomy	106	74	53	35	25	16	11	4
Transthoracic esophagectomy	114	76	57	42	31	20	14	7

Fig. 5.2 Kaplan Meier curves showing overall survival among patients randomly assigned to transhiatal esophagectomy or transthoracic esophagectomy with extended en bloc lymphadenectomy. From Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus, Hulscher JB, van Sandick JW, de Boer AGEM et al., 347. Massachusetts Medical Society. Reprinted with permission

trend toward improved long-term survival holding for the extended transthoracic approach.

The long-term follow-up of this randomized trial was published in 2007. Omloo et al., analysed a total of 95 patients who underwent a THE and 110 patients who underwent a TTE. After transhiatal and transthoracic resection, 5-years survival was 34% and 36%, respectively (p = 0.71).

5.2.3.1 Who May Benefit from TTE or THE?

In a subgroup analysis, based on the location of the primary tumour (classified after pathological examination of the resection specimen), no overall survival benefit for either surgical approach was seen in 115 patients with a type II tumour (p = 0.81). In 90 patients with a type I tumour, an absolute survival benefit of 14% was observed with the transthoracic approach (51% vs. 37%, p = 0.33). Moreover, there was evidence that depending on the number of positive lymph nodes in the resection specimen, the effect of treatment differed. In patients (n = 55) without positive nodes, the locoregional disease-free survival after THE was comparable to that of TTE (86% and 89%, respectively). A poor outcome was found for patients (n = 46) with more than eight positive lymph nodes in the resection specimen: the survival was 0% in both groups. Regarding patients (n = 104) with one to eight positive lymph nodes in the resection specimen, a 5-year locoregional disease-free survival advantage was seen for those patients operated via the transthoracic approach (64% vs. 23%, p = 0.02). The authors concluded that there is no significant overall survival benefit for either approach. However, when compared with THE, a TTE for type I esophageal cancer shows an ongoing trend towards a better 5-year survival rate. Moreover, patients with a limited number of positive lymph nodes (between one and eight) in their resection specimen also seem to benefit from TTE. In patients with a limited nodal burden, a more extensive nodal dissection may indeed cure the patient. However, when the number of positive nodes is very high, this reflects systemic disease and then more extensive surgery can not cure the patient. Moreover, in patients with a very limited nodal spread, the locoregional nodes can be removed by a THE as well as a TTE.

5.2.3.2 Post-Operative Morbidity

Most studies showed more complications for the TTE as compared to the THE. The meta-analysis of Hulscher et al. [2] showed more perioperative blood loss, pulmonary complications, chyle leakage, and wound infections in the transthoracic group. More anastomotic leakage and vocal cord paralysis were found in the transhiatal group. The in-hospital mortality rates for transthoracic resection in comparison with transhiatal were higher (9.2% vs. 5.7%, RR: 1.60, 95% confidence interval: 1.89–1.35). The question arises whether these differences still are representative because in recent years we see better patient selection, improvement of perioperative care and refinement of surgical techniques. Lacking recent RCTs we note a cohort study in 2014 by Davies et al. including 680 patients operated between 2000 and 2010, showing a shorter median hospital stay for transhiatal surgery (14 days vs. 17 days, p < 0.001). The in-hospital mortality rate also favoured THE (1.1% vs. 3.2% for THE and TTE respectively, p = 0.110). The results show a median of 20 nodes in the transthoracic group vs. 13 in the transhiatal group (p < 0.001) [12].

5.3 Minimally Invasive Esophagectomy (MIE)

Over the last decades, the safe and oncological-proficient operation termed MIE emerged. Ideally, minimally invasive techniques should be as radical as open approaches and not compromise oncological outcome [13]. It may be fair to say that during the early developmental phase of MIE a somewhat different oncological operation was performed—attributable to the enormous technical challenges and search for optimal techniques. More recent studies show, however, that indices of the number of lymph nodes dissected and surgical margins for MIE are similar or perhaps superior to open approaches. Two RCTs have been performed, one total MIE (TIME trial)

and the other hybrid, in which laparoscopy and right posterolateral thoracotomy are performed with intrathoracic anastomosis (MIRO trial) [14, 15]. The long-term follow-up of the TIME trial up to 3 years posits similar survival-outcomes for the open and the MIE groups [16].

Minimally invasive esophagectomy may harbour several advantages for the surgeons as well. The developments of high definition and 3D cameras with robotic platforms offer an excellent and detailed view of the operation field. This facilitates a careful dissection along the tissue planes enabling an increased radical nodal dissection with less blood loss. Also, ergonomics of the instruments has improved and the surgeon may feel more comfortable during MIE than at open surgery. The possible advantages of robotic surgery including esophageal cancer resections seems clear but this has yet to be evidenced by the ROBOT trial, which compares the open esophageal resection vs. the laparoscopy and thoracoscopy as assisted by robot [17].

Minimally invasive surgery—especially in prone position—is technically challenging and needs careful introduction using a structured program.

5.4 Influence of Neoadjuvant Therapy

The extended use of neoadjuvant therapy changed the prognosis of the resectable esophageal cancer cure. According to the long-term outcome of the CROSS trial, a better survival after neoadjuvant chemoradiotherapy is seen for both adenocarcinoma and squamous cell cancer (Carboplatin and Paclitaxel for 5 weeks with concurrent radiotherapy, 41.4 Gy given in 23 fractions, 5 days a week). Five-year overall and progression-free survival rates were 47 and 44% in the neo-adjuvant chemoradiotherapy-plus-surgery group while in the surgery-alone group 33% and 27%, respectively. Holding for the squamous cell cancer, it was 61% vs. 30% and 58% vs. 28%; whereas in the adenocarcinomas case it was 43% vs. 33% and 41% vs. 27%, respectively [18, 19].

The dissection of lymph nodes is important for the staging of esophageal cancer and the number of dissected lymph nodes is an important predictor of survival in patients with esophageal cancer.

Based on data from the CROSS study, Talsma et al. found that in the group of patients treated by surgery alone, the number of resected lymph nodes indeed had a prognostic impact on the survival rate [20]. But the therapeutic value of lymphadenectomy is still controversial in this study after CRT because the number of resected nodes was not associated with survival. Also, a cohort study by Lagergren et al. showed no significant influence of the number of resected nodes on the 5-year survival rates (disease specific and overall) in patients with the surgery-alone group [21].

As described above, an important distinction between the outcomes of transthoracic and of transhiatal esophagectomies concerns the differences in lymph-node yield and the possible influence on locoregional recurrent disease. Moreover, given the data on the association between the number of nodes dissected after neoadjuvant chemoradiotherapy, the question arises what the best surgical approach is for Gastro-esophageal junction tumours: either the transhiatal approach with limiting morbidity and inability to dissect the nodes from the middle and upper mediastinum, or the transthoracic MIE with extended mediastinal nodal dissection. The trend in the Netherlands is to operate distal oesophageal tumours (type I) totally minimally invasive by use of thoracoscopy and laparoscopy after neoadjuvant therapy. For type II tumours (cardia cancers) many Dutch surgeons prefer a thoracoscopic or transhiatal approach by laparoscopy after neoadjuvant therapy.

Discussions concern whether to organize a new trial, one comparable with the HIVEX trial, in which patients will be treated by neoadjuvant therapy and by minimally invasive surgery. This trial is yet to be accomplished.

Conclusion

Evidence concerning which approach is the best for distal esophageal and GEJ cancers was produced by the HIVEX trial that compared the

Transhiatal vs. Transthoracic approach without neoadjuvant therapy. Given the current use of neoadjuvant therapy, there is no comparison of cohorts or of randomized studies that compare MIE THE with MIE TTE for distal or GEJ types 1 and 2 tumours after neoadjuvant therapy. Such a study is crucial for improving the treatment of the distal and GEJ cancers.

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