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## Minimally invasive esophagectomy for cancer; beyond techniques

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# Summary

The global incidence of esophageal cancer has increased in the past two decades. Surgical resection with radical lymphadenectomy, after neoadjuvant therapy, is the cornerstone in the treatment of resectable esophageal cancer. Open esophagectomy (OE) is associated with a high morbidity rate, especially pulmonary infections, and long in-hospital recovery period. Minimally invasive esophagectomy (MIE), avoiding thoracotomy and laparotomy, may reduce the rate of pulmonary infections, thereby resulting in a shorter hospital stay. These perspectives in esophageal surgery encourage surgeons to search for an evidence based implementation the minimally invasive procedures. The aim of this thesis is chart different techniques, scientific evidence and the impact of minimally invasive esophagectomy.

## Chapter 1

The transhiatal approach for esophagectomy may reduce the respiratory infection rate in compromised patients with distal esophageal and gastro-esophageal (GE) cancers. Minimally invasive esophagectomy could further improve post-operative outcome. Two cohorts of laparoscopic and open transhiatal esophagectomy for cancer were compared for short- and long-term outcome. A total of 100 patients were included in the analysis. Both groups had the same oncological outcome, however significant less blood loss and shorter hospital stay was observed in patients undergoing laparoscopic transhiatal esophagectomy. Faster recovery without a significant longer operation time could be the major benefit of the laparoscopic transhiatal approach. This is a retrospective study and randomized trials are needed to further clarify the role of laparoscopic transhiatal approach for esophageal cancer.

## Chapter 2

Cervical anastomosis and thoracic anastomosis are used for gastric tube reconstruction after transthoracic esophagectomy for cancer. A systematic review was conducted in order to identify randomized trials that compare cervical with thoracic anastomosis. Cervical anastomosis could be associated with a higher leak rate and recurrent nerve trauma. However, the currently available randomized evidence is limited. Further randomized trials are needed to provide sufficient evidence for the preferred location of the anastomosis after esophagectomy.

## Chapter 3

Minimally invasive Ivor Lewis esophagectomy is one of the approaches used worldwide for treating esophageal cancer. Optimization of this approach and especially identifying the ideal intrathoracic anastomosis technique is needed. To date, different types of anastomosis have been described. A literature search on the current techniques and approaches for intrathoracic anastomosis was held. The studies were evaluated on leakage and stenosis rate of the anastomosis. This review has found no important differences between the two most frequently used stapled anastomoses: the transoral introduction of the anvil and the transthoracic. Clinical trials are needed to compare different methods in order to improve the quality of the intrathoracic anastomosis after esophagectomy.

## Chapter 4

The increasing incidence of distal carcinomas of the esophagus and the esophagogastric junction induce more interest in the two stage Ivor Lewis esophagectomy. The study reported in this chapter described a multicentre analysis of minimally invasive Ivor Lewis esophagectomy for achieving short-term results. A series of 103 patients operated in 5 different centers showed pulmonary complications and anastomotic leakage to be the most important complications. Though Ivor Lewis minimally invasive esophagectomy is increasingly implemented, important problems remain. Questions arise how to standardize the operative technique and most important the type of anastomosis and therefore decreasing the rate of anastomotic leakage. Nonetheless, we recognize the advantage of starting the operation abdominally and keeping a long segment of the patient's own esophagus as worthy reasons for continual improvement.

## Chapter 5

In this chapter we evaluated our own initial experience of a transthoracic esophagectomy with the thoroscopic procedure in prone position in 40 patients. The short-term results in this series of 40 patients show the safety and feasibility of a thoroscopic esophagectomy in prone position. A multicenter randomized trial, in which this approach will be compared with the standard open thoracotomy, is needed to establish the role of this approach in daily practice.

## Chapter 6

This first multicentre, randomised trial was performed to determine whether minimally invasive esophagectomy is associated with a reduced morbidity than with open esophagectomy. A total of 115 patients were included and randomized to receive either OE or MIE. A significant reduction of in the incidence of in-hospital respiratory infection of 25% was associated with MIE. Furthermore there was a shorter hospital stay and better quality of life after 6 weeks, whereas the quality of the resected specimen did not differ between the groups.

## Chapter 7

The minimally invasive esophagectomy is being implemented widely for treating esophageal cancer in order to reduce morbidity and improve quality of life. Non-randomized studies investigating long-term quality of life after MIE show conflicting results at one year follow-up. Therefore, we investigated whether MIE brings about an enduring better long-term one-year quality of life than does open esophagectomy indicating both a faster recovery and less procedure-related symptoms.

This first randomized trial shows that MIE is associated with a better long-term one year quality of life as compared to OE. Survival and long term complications are equal for both groups.

## Chapter 8

This study was performed as a substudy analysis of a randomized trial comparing conventional open esophagectomy by thoracotomy and laparotomy with minimally invasive esophagectomy by thoracoscopy and laparoscopy. This additional analysis focuses on the immunological changes and surgical stress response in these two randomized groups of a single center. In this substudy a significantly better preserved leukocyte counts and IL-8 levels were observed as compared to the open group. Both findings can be related to fewer respiratory infections found post-operatively in the MIE group. Moreover, significant differences in the prolactin levels at 168 hours post operation imply that the stress response is better preserved in the MIE group. These findings indicate that less surgical trauma could lead to better preserved acute-phase and stress responses and fewer clinical manifestations of respiratory infections.

## Chapter 9

Minimally invasive esophagectomy is associated with less pulmonary complications, shorter hospital stay, and better quality of life as compared to open esophagectomy. However, there are concerns about the likely higher costs for this procedure. Therefore, we carried out an economic evaluation of the randomized controlled TIME trial in MIE was compared to OE in patients with curable esophageal cancer. Total healthcare costs holding for MIE or OE procedures are similar. Minimally invasive esophagectomy is favored over the open procedure because of better quality of life effects and less postoperative complications.