General introduction and outline of thesis
GENERAL INTRODUCTION AND OUTLINE OF THESIS

The incidence of esophageal cancer is increasing in the western world. In the Netherlands, in the year 1990 807 patients were diagnosed with esophageal cancer, whereas in 2005, this number reached a staggering 1546.\(^1\) It is expected that this rise in incidence will continue in the years to come. This substantial increase in incidence can be accounted for by an increase in the number of adenocarcinomas diagnosed (figure 1). Moreover, approximately one third of the patients are considered candidates for curative resection.

Figure 1. The rising incidence of esophageal cancer caused by the rising incidence of adenocarcinoma. Data of the Netherlands Cancer Registry.\(^1\)

Surgical resection with radical lymphadenectomy remains the most important part of the treatment for resectable esophageal cancer. Surgery is considered when the tumor is staged as cT1-3 N0-1 Mo. Most patients present with stage III esophageal cancer which has a 5-year survival of approximately 15-20%. In addition, the possible value of neoadjuvant chemoradiotherapy is currently being investigated.

The three main surgical approaches utilized worldwide for esophageal cancer are: a three stage transthoracic resection (i.e. thoracotomy, laparotomy and cervicotomy) with a cervical anastomosis; the two stage transthoracic Ivor Lewis resection (i.e. laparotomy, thoracotomy) with an intrathoracic anastomosis; and a two stage transhiatal resection (i.e. laparotomy and cervicotomy).\(^2\) Transhiatal esophagectomy is generally performed for carcinoma of the gastro-esophageal junction in patients with moderate condition.\(^3\)-\(^4\) Traditional or open transthoracic esophageal resection is generally performed for carcinoma of the intrathoracic esophagus. This transthoracic procedure is however associated with a high morbidity and mortality rate of
approximately 50-70% and 5% respectively. The extensive nature of this open approach has a significant negative impact on the quality of life of these patients.

Surgery for cancer of the esophagus is considered to be one of the most extensive and traumatic oncological surgical procedures. Open resection not only involves a long operation time and large incisions but also necessitates post-operative care in the intensive care unit (ICU), a long in-hospital recovery and carries a significant risk of morbidity and death. Minimally invasive esophagectomy (MIE) can reduce the extensive nature of the required surgery. Furthermore, reduction of the post-operative morbidity shortens recovery time and could be associated with a better quality of life. A better short-term post-operative quality of life is even associated with a better survival. Evidence of the short term benefits of minimally invasive surgery over open procedures is accumulating. Faster post-operative recovery, less peri-operative complications and a shorter duration of hospital stay appear to be the main advantages. MIE involves a thoracoscopy and laparoscopy either with a cervical or intrathoracic anastomosis. The thoracic phase of this procedure can be performed through a lateral right thoracic approach with a right lung block by selective intubation. This can also be performed with a robot-assisted approach. However, this still results in a high percentage of respiratory complications. In order to further reduce the respiratory complications produced by the lung block and shuntig, the thoracic approach with the patient in prone-position has been introduced in the last years. No selective intubation is necessary in this approach.

Several centers report significantly lower respiratory complications with the thoracoscopic transthoracic esophagectomy. Furthermore, median length of ICU and hospital stay was shorter in these studies compared to open reports. Importantly, the resected specimens and survival reported for MIE and open resection are comparable. These landmark studies favor minimally invasive esophagectomy in terms of respiratory complications and recovery. However, to date no prospective randomized trial has been conducted to prove the beneficiary effects of minimally invasive esophagectomy. Confirmation of the advantages of minimally invasive approach for esophageal cancer in randomized trials is called for.

AIM OF THE THESIS

The aim of this thesis is to review current surgical treatment for esophageal cancer with the emphasis on minimally invasive esophagectomy and to compare the impact of open with minimally invasive esophagectomy on the patient with esophageal cancer.
OUTLINE OF THE THESIS

Part I of this thesis investigates the current available literature. In Chapter 1 the current evidence for diagnostic investigations, neoadjuvant therapy and minimally invasive esophagectomy are reviewed. This chapter was especially made for all Dutch healthcare practitioners who need an evidenced based update on esophageal cancer.

In Chapter 2 a systematic investigation is performed of current comparative studies comparing open esophagectomy with minimally invasive esophagectomy. The studies included are critically appraised. Also, the outcome parameters are pooled where appropriate.

Two transthoracic approaches are generally used worldwide for esophageal cancer: Ivor Lewis esophagectomy with a thoracic anastomosis and the three stage esophagectomy with a cervical anastomosis. Identifying the optimal site of anastomosis based on level 1 evidence was the aim of this review in Chapter 3. Besides a three stage minimally invasive esophagectomy, a two stage minimally invasive Ivor Lewis esophagectomy with an intrathoracic anastomosis is being performed nowadays. The variations in anastomosis techniques for minimally invasive Ivor Lewis esophagectomy are reviewed and discussed in Chapter 4.

In Part II of this thesis a retrospective analysis was performed of the outcome after minimally invasive esophagectomy in a single center. The outcome of a minimally invasive transhiatal esophagectomy was evaluated in Chapter 5. A historic open control group was used as a comparison. This study compares the short- and long-term results including the oncological consequences of two cohorts of 50 consecutive patients with cancer of the distal esophagus and gastro-esophageal junction.

In Chapter 6 an analysis was performed of the initial series of patients in the VU university medical center who underwent a minimally invasive transthoracic esophagectomy in prone position. This analysis included forty patients.

Prospective studies on minimally invasive esophagectomy are presented in Part III. The protocol of the first randomized trial of traditional invasive versus minimally invasive esophagectomy (TIME-trial) is presented in Chapter 7. The short-term results of this trial are discussed in Chapter 8.

Every gastro-intestinal surgical procedure has an immunological response. This has never been investigated in a randomized trial comparing open with minimally invasive esophagectomy. An analysis of the immunological consequences is therefore studied in Chapter 9.

Only one case-report has been published in literature describing a minimally invasive Ivor Lewis esophagectomy. The largest case-control study of the patients in the trial who had an open or minimally invasive Ivor Lewis esophagectomy are compared and analyzed in Chapter 10.

A sub-analysis of patients in the trial undergoing a esophagectomy with a cervical anastomosis are compared with patients who had a thoracic anastomosis in Chapter 11.

In order to identify factors which are associated with respiratory complications in the TIME-trial a logistic regression analysis was performed in Chapter 12.
REFERENCES