

Chapter 8

Prevention and Treatment of Major Complications After Esophageal Surgery

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Esophageal Surgery for Cancer

Introduction

Esophageal carcinoma is an aggressive disease with early lymphatic and hematogenous dissemination [1]. The incidence of esophageal carcinoma has been rising steadily over the past decades, which seems mainly to be a result of the sixfold increase in the number of patients with esophageal adenocarcinoma [2]. Surgical resection remains the most important part of a potentially curative treatment; however, even after esophagectomy, a substantial proportion of patients will develop local or distant recurrent disease, [3, 4] and 5-year survival rates rarely exceed 40 % [5, 6]. Esophagectomy can be performed by means of a transthoracic or transhiatal resection. Over the past few years, minimally invasive techniques for esophagectomy have been developed in an attempt to decrease invasiveness without compromising the extent of dissection and consequent survival.

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Table 8.1 Complication rate in 940 patients who underwent esophagectomy at the Academic Medical Center

	All patients <i>N</i> (%)
No. of patients	940 (100)
Overall complications	636 (68)
<i>Non-surgical complications</i>	
Pulmonary total ^b	285 (30)
Pneumonia	262 (28)
Cardiac	97 (10)
<i>Surgical complications</i>	
Anastomotic leakage	
Clinical	103 (11)
Subclinical ^a	80 (9)
Chylous leakage	51 (5)
Recurrent laryngeal nerve paralysis	98 (10)
In-hospital mortality	31 (3)

Adapted from van Heijl et al. [10]

^aOnly on radiological examination

^bPulmonary: pneumonia, atelectasis, pleura-empyema

Centralization of surgical resections, advances in surgical techniques, and improvements in perioperative care have reduced the risk of esophagectomy to an acceptable level [7]. Esophageal surgery is however still associated with substantial morbidity. Early postoperative complication rates vary between 40 and 80 %, depending on the applied criteria and the type of resection [5, 8]. Centralization of esophageal surgery in high-volume centers has reduced in-hospital mortality to approximately 1–4 % [9].

This chapter will discuss the incidence, diagnosis, and treatment of the most important complications that are associated with surgical resection of the esophagus.

Complications: Classification and Prognostication

The overall incidence of complications after esophagectomy as reported in the literature varies between 40 and 80 %. In one of the largest series regarding esophagectomy for esophageal carcinoma, the incidence of individual complications that are associated with surgical resection of the esophagus was described. This series included almost 1,000 patients over a period of 16 years (Table 8.1) [10].

Classification of complications facilitates the evaluation and comparison of surgical outcomes among different surgeons, centers, and therapies. The severity of postoperative complications can be graded according to the morbidity scale proposed by Dindo et al. [11]. This classification system is based on the therapy used to treat the complication, and it consists of five grades (Table 8.2).

Predicting the severity of complications can reveal important information for both patient and surgeon, and individualized risk assessment may help deciding the optimal extent of surgery. Recently, a nomogram was developed based on preoperative risk factors to predict the severity of complications in esophageal cancer patients who undergo surgical resection (Fig. 8.1) [12].

Table 8.2 Dindo classification

Grade	Definition
Grade I	Any deviation from the normal postoperative course without the need for treatment
Grade II	Requiring pharmacological treatment
Grade III	Requiring surgical, endoscopic or radiological intervention
IIIa	Intervention not under general anesthesia
IIIb	Intervention under general anesthesia
Grade IV	Life-threatening complication requiring ICU management
IVa	Single organ dysfunction
IVb	Multiorgan dysfunction
Grade V	Death of a patient

Adapted from Dindo et al. [11]
 ICU intensive care unit

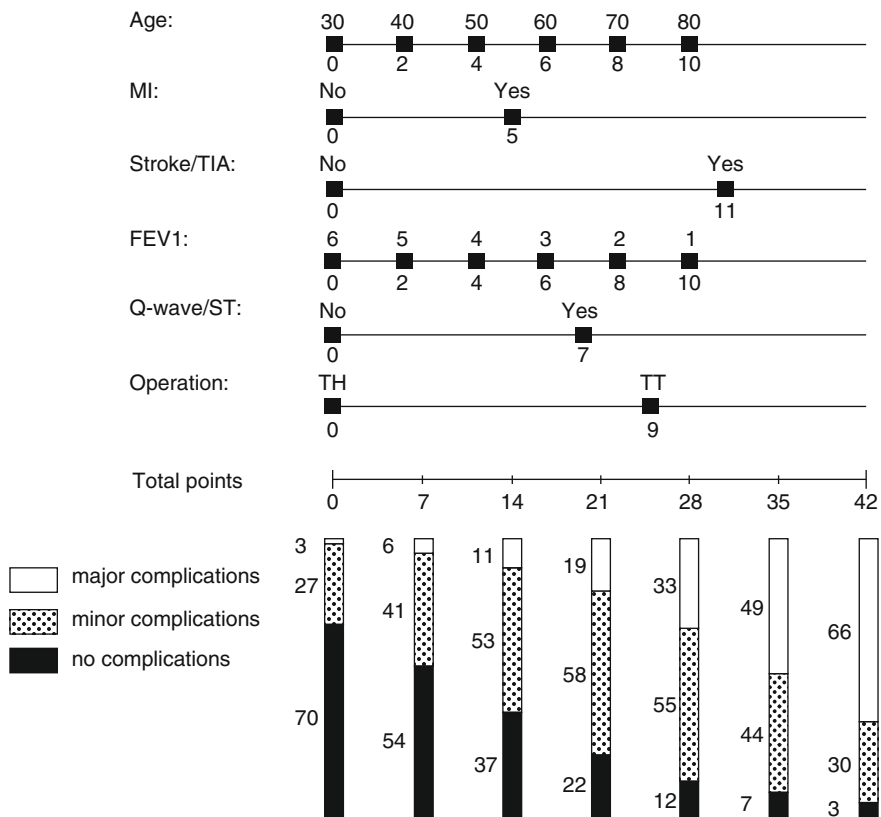


Fig. 8.1 Nomogram for the prediction of severity of complications with use of preoperative risk factors. *Instruction:* Locate the age on the axis. Determine how many point the patient receives. Repeat this for each axis. Sum the points for all predictors and locate the sum on the total points axis. Draw a line straight down to the bar graphs. Bar graphs represent the chance for an individual patient after esophagectomy for cancer to develop major, minor-to-moderate, or no complications. FEV1 forced expiratory volume in the first second, MI myocardial infarction, TIA transient ischemic attack (Adapted from Lagarde et al. [12])

Treatment and Incidence of Specific Complications

Nonsurgical Complications

Pulmonary Complications

Incidence and Definition

Surgical resection of the esophagus is considered to be one of the most extensive and traumatic gastrointestinal surgical procedures. Transthoracic resections are associated with higher postoperative complication rates compared to transhiatal esophagectomies [5]. Transthoracic esophagectomy includes a two-field lymphadenectomy that leads to pulmonary complications in a relatively large number of patients. Furthermore, one-lung ventilation can cause alveolar damage, and breathing may be impaired due to pain after thoracotomy. Risk factors for the development of pulmonary complications are advanced age, a history of smoking, and chronic obstructive pulmonary disease (COPD). Preoperative lung function test is performed to exclude patients with an inadequate lung function from surgical resection. Pulmonary complications are defined as pneumonia, acute respiratory distress syndrome (ARDS), and atelectasis [5]. ARDS is defined according to the American-European consensus conference on ARDS criteria [13]. The incidence of pulmonary complications after esophagectomy depends on the type of procedure; generally it varies between 30 % and 57 % [5, 10]. Epidural analgesia leads to less postoperative pain and is therefore associated with a lower pulmonary complication rate [14]. With the introduction of minimally invasive esophageal surgery (MIE), pulmonary complication rates have further decreased. Several large series that have compared minimally invasive to conventional open esophagectomies have shown a lower pulmonary complication rate after MIE, ranging from 10 to 30 % [15, 16].

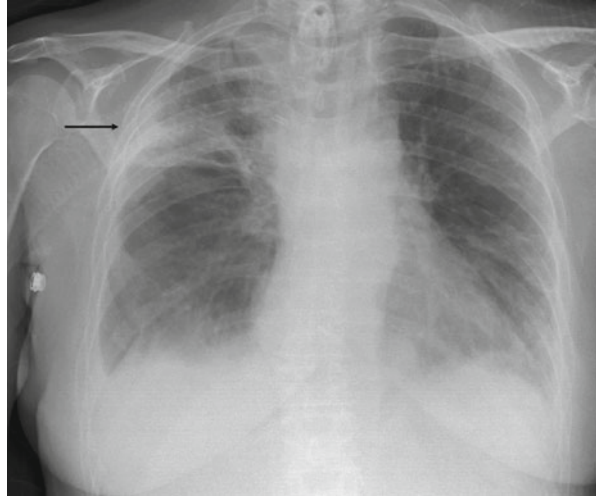
Diagnosis

Clinical signs of pneumonia include fever (<38.5 °C) and purulent sputum. Both pneumonia and atelectasis can be diagnosed on a chest X-ray. In addition, for the diagnosis of pneumonia a sputum culture is required. Pneumonia is indicated by the isolation of a pathogen from a sputum culture and a new or progressive infiltrate on a chest X-ray (Fig. 8.2). Atelectasis is indicated by lobar collapse on chest X-ray [5].

Treatment

Treatment of pneumonia consists of antibiotics and supportive care if needed. Supportive care includes oxygen and readmission to the intensive care unit with reintubation.

Fig. 8.2 X-ray of pulmonary infiltrate in the right upper lobe (*arrow*) in a patient 8 days after thoracolaparoscopic esophagectomy



Cardiac Complications

Incidence and Definition

Cardiac complications after esophagectomy include myocardial infarction and congestive heart failure but consist mainly of atrial fibrillation (AF). AF occurs most frequently after transthoracic esophagectomy with an incidence ranging from 13 to 46 % [5, 17]. It can also occur after transhiatal resections due to manipulation and blunt dissection, which inevitably compresses the atria [18]. AF is a complicated arrhythmia of incompletely understood pathogenesis. Ectopic foci, single-circuit reentry, and multiple-circuit reentry have been implicated in initiating and maintaining the condition [19]. Risk factors for the development of AF after esophagectomy include age older than 65 years, male sex, history of heart disease, and chronic obstructive pulmonary disease [17].

Diagnosis

Patients with AF suffer from shortness of breath and fatigue and can be hemodynamically compromised. Diagnosis is confirmed by means of electrocardiography [20].

Treatment

AF can be treated with medication that either reduces the heart rate or reverts the rhythm back to normal. Pharmacological therapy includes digoxin and calcium channel or β -blockers. Synchronized electrical cardioversion can also be used to convert AF to a normal rhythm [20].

Table 8.3 Univariate and multivariate analysis of potential predictors of anastomotic leakage

	Univariate logistic regression analysis		Multivariate logistic regression analysis	
	OR (95 % CI)	<i>p</i> -value	OR (95 % CI)	<i>p</i> -value
All patients (<i>n</i> =828)				
Age	1.010 (0.990–1.029)	0.332	Not in model	–
Male sex	1.797 (1.093–2.954)	0.021	1.675 (1.002–2.801)	0.049
BMI > 27 kg/m ³	1.616 (1.074–2.430)	0.021	1.548 (1.027–2.335)	0.037
Squamous cell carcinoma	0.886 (0.600–1.307)	0.540	Not in model	–
Stapled anastomosis	1.002 (0.999–1.004)	0.235	Not in model	–
Tumor stage III or IV	0.824 (0.565–1.200)	0.312	Not in model	–
Neoadjuvant chemo (radiotherapy)	0.897 (0.555–1.449)	0.656	Not in model	–
Transthoracic approach	0.964 (0.656–1.417)	0.853	Not in model	–

Adapted from van Heijl et al. [23]

CI confidence interval, BMI body mass index, OR odds ratio

Surgical Complications

Anastomotic Leakage

Incidence and Definition

Anastomotic leakage is a serious complication resulting in significant morbidity and mortality. After transhiatal esophagectomy, an anastomosis at the cervical level between the replacement conduit and the proximal esophagus is required. In case of a transthoracic procedure, cervical and intrathoracic anastomoses are possible. In general, surgeons tend to favor a cervical anastomosis, considering the hypothesis that anastomotic leakage will be confined to the neck area instead of leaking directly into the mediastinum [21, 22]. However, the performed technique seems not to be of influence on the incidence of anastomotic leakage; hand-sewn and stapled techniques show comparable leakage rates [23]. Potential predictors of anastomotic leakage were evaluated among over 800 patients who underwent esophagectomy and include male sex and a body mass index > 27 kg/m² (Table 8.3).

The incidence of anastomotic leakage after esophagectomy ranges from 1.6 to 20 %, depending on and the applied criteria [24]. In general, anastomotic leakage is defined as clinical evidence of salivary fistula or infection of the cervical wound which requires opening of the wound to objectify the leakage. Radiological anastomotic leakage is defined as extravasation of water-soluble contrast medium [21].

Diagnosis

Traditionally, anastomotic leakage can be diagnosed through X-ray with water-soluble contrast, generally 6–10 days after surgery [21, 23]. Although contrast

Fig. 8.3 CT of contrast leakage from the conduit into the right pleural cavity (*arrow*) in a patient 7 days after thoracolaparoscopic esophagectomy

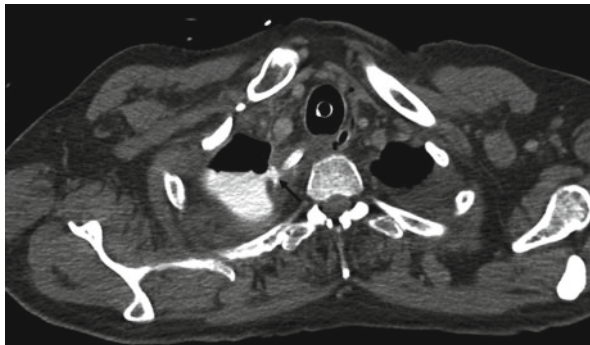
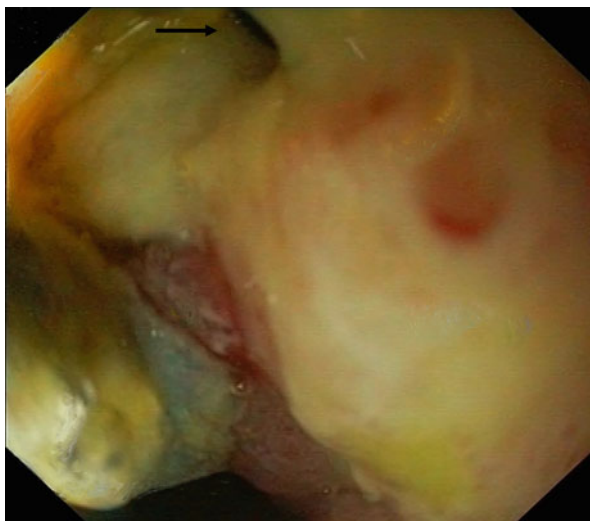


Fig. 8.4 Endoscopic view of ischemic mucosa of gastric tube with leakage site (*arrow*) in a patient 9 days after transthoracic esophagectomy



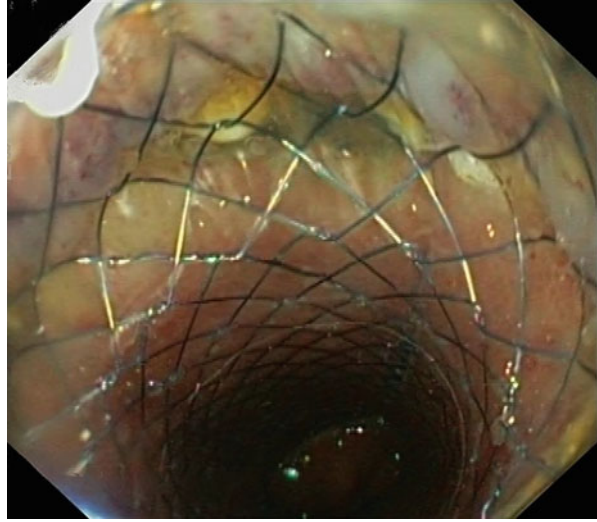
swallow examination is performed routinely in many centers throughout the world, routine examination has a low sensitivity and a low positive predictive value and therefore may not be justified in all patients after esophagectomy [25]. However, in case of clinical signs of anastomotic leakage, a swallow examination should be performed.

In patients in whom a swallow examination is not feasible, a contrast enhanced computed tomography (CT) can be performed (Figs. 8.3 and 8.4). Furthermore, upper endoscopy can be performed to rule out conduit necrosis, and moreover, during endoscopy immediate treatment is possible with stent placement [26].

Treatment

Treatment options for anastomotic leakage range from conservative treatment in case of a nonsignificant radiological leak to conduit takedown in case of severe

Fig. 8.5 Stent placement during esophagogastroduodenoscopy in a patient 9 days after transthoracic esophagectomy



conduit necrosis. Nonsurgical therapy for anastomotic leakage includes maintaining the patient nil by mouth, broad-spectrum antibiotics, stent placement (Fig. 8.5a and b), radiological drainage, and reinstating transnasal drainage of the conduit [26]. In case of larger leaks, reexploration of the cervical incision or thoracoscopic drainage can be performed. Conduit necrosis requires immediate surgical therapy and breakdown of the interponate with cervical esophagostomy. Segmental necrosis can be managed with drainage and followed up with endoscopy, but in case of extensive conduit necrosis, conduit takedown is required [26].

Chylous Leakage

Incidence and Definition

Postoperative chylous leakage results from injury to the main thoracic duct or its branches, which have a close relationship with the esophagus [27]. Chylous leakage after esophagectomy is most commonly due to perioperative injury of the thoracic duct during extensive lymph node dissection and is less frequently caused by injury to the cisterna chyli in the upper abdomen. Chyle is defined as intestinal lymphatic fluid that is enriched with fat absorbed from the intestinal lumen, which is responsible for the milky appearance of chyle after enteral feeding. Lymphatic fluid consists of lymphocytes, immunoglobulins, and enzymes [27]. The incidence of chylous leakage after extended esophagectomy ranges from 1 to 4 % and occurs more frequently after transthoracic esophagectomy [28]. Extensive loss or a long duration of chylous leakage can cause loss of calories, fluids, lymphocytes, and albumin, which may lead to immunosuppression. This can result in infection-related complications [27].

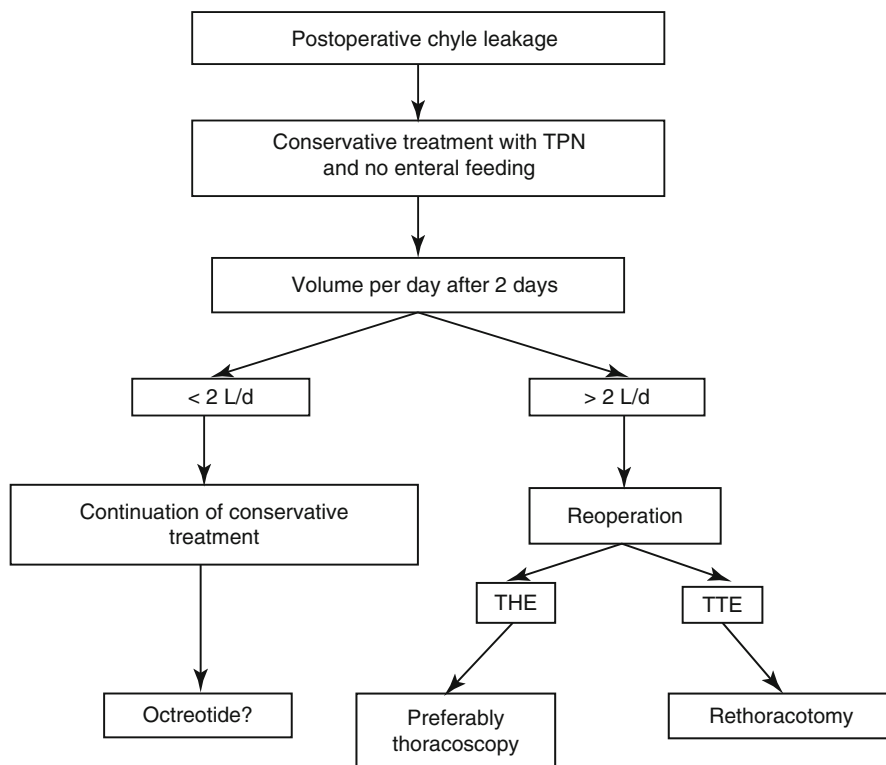


Fig. 8.6 Treatment strategy for chylous leakage after esophagectomy. This study was performed before the introduction of thoracoscopic esophagectomy at the Academic Medical Center. Currently, in most cases thoracoscopic reintervention would be performed. *THE* transhiatal esophagectomy, *TPN* total parenteral nutrition, *TTE* transthoracic esophagectomy (Adapted from Lagarde et al. [27])

Diagnosis

The diagnosis of chylous leakage is based on the appearance of the drain output, which changes from clear to milky upon enteral feeding in case of chylous leakage. After discontinuation of enteral feeding, the drain output changes back to clear. The diagnosis is confirmed if the triglyceride concentration in the drain output is greater than 1.2 mmol/L [27].

Treatment

Adequate conservative management including total parenteral nutrition instead of enteral feeding is the first step in treatment of chylous leakage. In 80 % of patients, chylous leakage can be managed solely with conservative treatment [27]. A medium-chain triglyceride diet has only a limited role in case of massive chylous leakage. Therefore, if the leakage persists for more than 2 days with a drain output of more than 2 L per day, a reoperation is indicated, preferably minimally invasive (Fig. 8.6).

Cream should be given through the feeding jejunostomy to facilitate perioperative localization of the leak, which can subsequently be ligated or clipped [27]. Fusion of intrathoracic and intra-abdominal chylous leakage should be prevented; compartmentalization is very important.

Recurrent Laryngeal Nerve Paralysis

Incidence and Definition

Esophageal surgery can result in postoperative impairment or damage of the recurrent laryngeal nerve (RLN). The mechanism of injury includes partial or complete transection, misplaced ligature, contusion, stretching, thermal damage, or a compromised blood supply [29]. Injury to the RLN leads to an incomplete closure of the vocal folds and consecutively to the inability of a successful cough since patients are unable to create sufficient pressure. Therefore, injury to the RLN is associated with an increased incidence of pulmonary complications [30]. RLN paralysis can occur uni- or bilaterally; bilateral paralysis is less common. Left-sided RLN paralysis occurs more frequently than right-sided paralysis due to the longer length of the RLN on the left side, which makes it more prone for injury. Furthermore, the left-sided RLN is at risk since the aortopulmonary window is cleared during lymphadenectomy in most centers. The incidence of recurrent laryngeal nerve paralysis ranges up to 34 % in case of a two-field lymph node dissection, but in countries where esophagectomy includes a three-field lymph node dissection, this rate can be as high as 80 %. Furthermore, RLN paralysis occurs more frequently after cervical anastomosis than intrathoracic anastomosis since the RLN is exposed during cervical dissection of the esophagus [30].

Diagnosis

The majority of RLN lesions are transient. Diagnosis of postoperative uni- or bilateral RLN paralysis is initially based on clinical symptoms such as hoarseness and a breathy voice and is proven by laryngoscopy. The patients' cough is weak, and pulmonary complications including aspiration can occur more frequently. Bilateral RLN paralysis can be a severe and life-threatening complication that manifests immediately after extubation with signs of airway obstruction such as dyspnea, tachypnea, and inspiratory stridor [29].

Treatment

Transient RLN lesions generally recover within 6–12 months after surgery [29]. Conservative therapy consists of logopedic voice and swallowing training, and in case of persistent RLN paralysis, several operative procedures can be performed depending on the position of the paralyzed vocal fold. In case of unilateral vocal fold paralysis in a lateral position with aphonia, medialization of the vocal cord allows glottal closure, which leads to an improved voice and a better swallowing

function. Medialization of the vocal cord can be achieved by a titanium implant, autologous cartilage chips, and collagen or fat implantation.

Bilateral vocal cord paralysis causes a medial position of the vocal cords with a narrow glottal opening that generally requires an emergency tracheotomy. In a later stage, lateralization of one vocal fold or a cordectomy can be performed after which the tracheotomy can be closed. Since RLN paralysis often ameliorates during the first year postoperatively, surgical interventions should be withheld during this period with the exception of cases with a poor prognosis for recovery, e.g., if the nerve was resected for oncological reasons [30].

Late Complications

Fistula from Gastric Conduit to Trachea or Bronchial Tree

Incidence and Definition

A benign fistula between the gastric conduit and trachea or bronchial tree is a rare but potentially fatal complication of esophageal surgery. Risk factors include perioperative chemoradiotherapy and extensive upper mediastinal lymph node dissection, which can cause local devascularization of the membranous trachea or mainstem bronchi [31]. Tracheo-neo-esophageal fistulas are related to tracheal trauma such as direct laceration during esophagectomy, endotracheal tube-induced trauma, or anastomotic leakage. It can also be a complication caused by dilation of an anastomotic stenosis. The incidence of fistulas between the trachea and the gastric conduit varies between 0.2 and 0.3 % after both transthoracic and transhiatal approaches [31].

Diagnosis

The clinical presentation of fistulas varies; symptoms can be relatively mild consisting of a cough associated with oral intake or more severe symptoms including recurrent bronchopneumonia, respiratory failure, and mediastinitis, which can be life threatening [32].

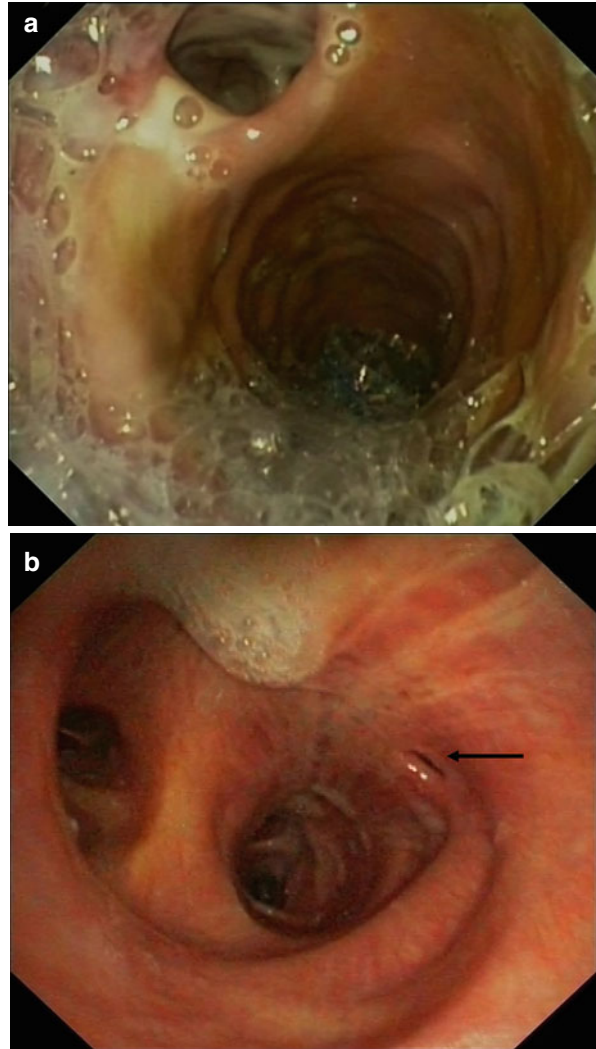
When a fistula is suspected based on clinical symptoms, radiologic contrast studies in upright and supine positions can be used to confirm diagnosis. Fistulas can be localized during endoscopy (Fig. 8.7), but because identifying a small defect in the folded neo-esophageal mucosa can be difficult, bronchoscopy can be more informative [32].

Treatment

The severity of symptoms in combination with the site and size of the fistula is most important in determining the optimal treatment strategy. The principles of management should emphasize control of sepsis and limiting ongoing soilage of the bronchial tree [31].

In the absence of severe mediastinal or pulmonary infections, a conservative treatment (nil by mouth, enteral feeding, antibiotics) can be considered.

Fig. 8.7 Mediastinal leakage in a patient 24 days after a thoracoscopic esophagectomy with a fistula to the right intermediate bronchus. **(a)** Endoscopy showing the leakage site. **(b)** Bronchoscopy showing the fistula at the right intermediate bronchus (*arrow*)



If the fistula persists for more than 4–6 weeks, endoscopic treatment with stent placement can be performed.

Surgical repair remains the mainstay of fistula treatment. Closure of the fistula can be achieved by using omentum, pleura, a pericardial graft or pericardial fat pad, or a muscle flap (sternohyoid, intercostal, latissimus dorsi, and pectoralis major, dependant on the position of the fistula and availability of vital tissue) [31]. If the gastric conduit cannot be preserved, continuity of the gastrointestinal tract can be reconstructed with a colonic interposition either in the same or in a later session if

Table 8.4 Risk factors for development of benign cervical stricture after esophagectomy

All patients (<i>n</i> =607)	Multivariate analysis	
	OR (95 % CI)	<i>p</i> -value
Transthoracic vs transhiatal	0.93 (0.58–1.49)	0.76
Colonic interposition vs gastric tube	0.11 (0.01–0.83)	0.03
Stapled vs hand sewn anastomosis	Not in model	–
Age <70 years	Not in model	–
Male vs female	Not in model	–
BMI > 25 kg/m ²	1.10 (0.77–1.57)	0.607
Smoking	Not in model	–
History of cardiovascular disease	1.78 (1.23–2.58)	0.002
Diabetes	1.82 (0.87–3.78)	0.11
% of predicted FEV1 (l/s) < 80 %	Not in model	–
Neoadjuvant chemotherapy	0.65 (0.35–1.21)	0.65
Neoadjuvant chemoradiotherapy	Not in model	–
Anastomotic leakage	2.07 (1.30–3.29)	0.002

Adapted from van Heijl et al. [33]

BMI body mass index, *FEV1* forced expiratory volume in one second

patients' condition precludes a reconstruction in the same session. The colon segment is preferably placed in the prevertebral position to reinforce the posterior wall of the trachea [32].

Strictures

Incidence and Definition

An important cause of long-term morbidity after esophagectomy is the development of benign cervical anastomotic strictures. Potential risk factors for this complication are diverse and include postoperative anastomotic leakage, neoadjuvant therapy, and a history of cardiac disease (Table 8.4). Risk factors for refractory anastomotic strictures are chemoradiotherapy, early stricture development, and anastomotic leakage [33]. End-to-side (ETS) anastomoses are associated with a lower stricture rate compared to end-to-end (ETE) anastomoses; however, anastomotic leakage occurs more frequently after ETS anastomoses [34].

Approximately 26–42 % of patients will develop strictures, which are known to be burdensome, often need frequent therapy, and lower the quality of life [35].

Diagnosis

In general, the diagnosis of benign esophageal stricture is based on clinical symptoms. Patients suffer from dysphagia and weight loss which can lead to a decreased quality of life [36].

Treatment

Several treatment modalities for benign esophageal strictures have been described including dilation with bougies or Savary dilation [36]. Endoscopic mechanical dilation is the preferred treatment of benign strictures; it is known to be a successful treatment of dysphagia [35, 37]. The majority of strictures respond well on dilation, and successful treatment in these patients is achieved in three to eight sessions. In case of refractory strictures, up to 30 dilations can be required [35, 37].

Other techniques include electrocautery incision of the stricture, intralesional steroid injections, and self-expandable metal stents (SEMS) or self-expandable plastic stents (SEPS).

Can Minimally Invasive Esophageal Surgery Decrease Short-Term Complications? Looking for Evidence-Based Surgery

Three meta-analyses comparing MIO and OO served as starting points in the quest for evidence-based surgery.

Biere et al. identified 10 studies after a comprehensive search [38]. Three comparative groups were created for analysis: (1) total MIO versus open transthoracic esophagectomy (TTE), (2) thoracoscopy and laparotomy versus open transthoracic, and (3) laparoscopy versus open transhiatal esophagectomy (THE). Our conclusion was that with MIO a faster postoperative recovery and therefore a reduction in morbidity could be achieved. Furthermore, we expect a lower mortality rate following the implementation of MIO. It was accentuated that MIO had been only investigated in case-control studies, and hence, bias may have been introduced simply by the pertaining study design.

The study of Nagpal et al. collected 12 selected studies for analysis [39]. There was no randomized study performed. They included 672 patients for MIO and hybrid MIO and 612 patients for OO. They found that MIO to be a safe alternative for use of the OO. Patients undergoing MIO may benefit from shorter hospital stay and lower respiratory complications and total morbidity as compared to OO.

In the meta-analysis of Sgourakis et al, also published in 2010, they pooled the effects of the outcomes of 1,008 patients enrolled into eight comparative studies [40]. They performed two comparisons: (1) open thoracotomy versus all MIO procedure and (2) open thoracotomy versus only MIO thoracoscopic phase. In comparison 1, both procedures report equally comparable outcomes (removed lymph nodes, 30-day mortality, 3-year survival) with the exception of overall mortality and anastomotic stricture in favor of the open thoracotomy arm. In comparison 2, no differences were noted between treatment arms concerning postoperative outcomes and survival.

These three meta-analyses generated the initiative for further prospective comparative or randomized controlled trials focusing on the short-term and oncological impact of MIO. Following this quest, we went on to assess the reduction of pulmonary infections and improved quality of life associated with MIE. We conducted a

multicenter, randomized trial comparing open with minimally invasive esophagectomy in patients with esophageal cancer.

After a long period of practicing both the transhiatal and the thoracoscopic esophagectomy for cancer, we designed a prospective randomized study for comparison of MIO and OO in 2008. The study was in the end called the TIME trial (Traditional Invasive versus Minimally invasive Esophagectomy). The TIME trial is a prospective, multicenter, randomized study comparing traditional transthoracic esophageal resection with minimally invasive resection for esophageal cancer [41]. The primary endpoint of the study concerned the respiratory complications, especially the postoperative bronchopneumonia confirmed by thorax X-ray or CT scan, and positive sputum culture.

Secondary endpoints were operation-related events, complications, ICU and hospital stay, quality of life as determined by questionnaires (SF-36 and EORTC C30-OES18), and the quality of specimen resected (length of specimen, number and location of lymph nodes resected, and circumferential resection margins). Also, hospital mortality and readmissions were recorded.

The pulmonary infection rate within the first two weeks was 29 % (16 patients) in the OO group and 9 % (5 patients) in the MIO group, $p=0.005$. The overall in-hospital incidence of pulmonary infections was 34 % (19 patients) in the OO group and 12 % (7 patients) in the MIO group, $p=0.005$. Explanation for the lower incidence of pulmonary infections may be, first of all, the used prone position in which in contrast with the lateral position the mediastinum hangs in its usual midposition; a second advantage may be the absence of total collapse of the lung during the MIO in prone position in contrast with one-lung ventilation and this permits optimal visualization of mediastinum with preserved ventilation and oxygenation; and a third factor may be the thoracotomy wound itself. All factors together could explain these advantages.

Other postoperative data included major postoperative complications (anastomotic leakage, 7 % in the OO and 12 % in the MIO, $p=0.390$) and mortality (1.8 % versus 3.4 %) that were not significantly different. Interesting is the different rate for vocal cord paralysis, 14 % in the OO group and only 2 % in the MIO, $p=0.012$. Pneumatic dissection by CO₂ from thoracic cavity into the neck can simplify the dissection in the neck and reduce the recurrent nerve lesions.

In conclusion, this randomized trial comparing open esophagectomy for cancer with minimally invasive esophagectomy shows that MIO results in a lower incidence of pulmonary infections, less rate of recurrence nerve lesions, and a better short-term quality of life without compromise of the quality of the resected specimen.

Esophageal Surgery for Benign Disease

Introduction

Benign esophageal disorders that can be treated surgically include gastroesophageal reflux disease (GERD), achalasia, and paraesophageal herniation.

GERD is a common disorder that affects 20–40 % of the Western population [42]. Frequent or long-lasting reflux of acidic gastric contents can lead to the development of GERD. The main symptoms include heartburn, retrosternal pain, regurgitation, and chronic cough. The most widely performed surgical technique for treatment of GERD is the Nissen or Toupet fundoplication during which the distal esophagus is brought into the abdominal cavity. Subsequently, the hiatus is approximated posteriorly and either a 360° (Nissen) or a 270° (Toupet) fundoplication is created [43].

Achalasia is an esophageal motor disorder that is characterized by the absence of esophageal peristalsis combined with a defective relaxation of the lower esophageal sphincter. Clinical symptoms include dysphagia, chest pain, and regurgitation of undigested food. Surgical treatment of achalasia consists of a Heller's myotomy, mainly performed laparoscopically (laparoscopic Heller's myotomy; LHM). A myotomy is performed extending from above the level of the gastroesophageal junction down to the proximal 1–1.5 cm of the stomach. To prevent reflux, an anterior fundoplication (Dor) can be performed subsequently [44].

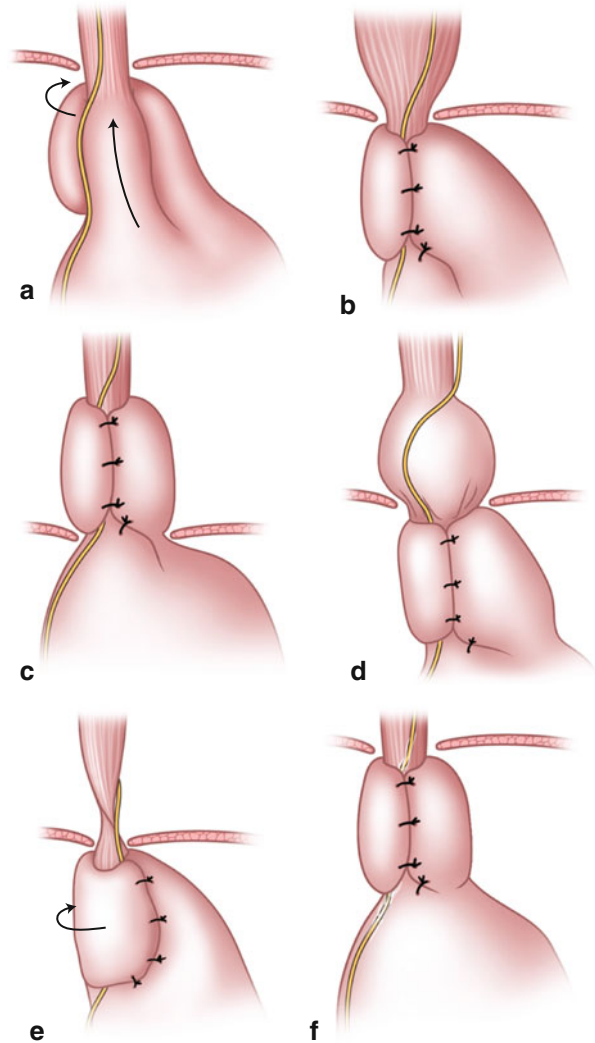
Paraesophageal or hiatal hernias are a common disorder of the digestive tract that are characterized by a protrusion of the stomach into the thoracic cavity through a widening of the right crus of the diaphragm [45]. Hiatal hernias are classified into four subtypes: type I, sliding hernias, in which the gastroesophageal junction is herniated into the thorax; type II, true paraesophageal hernias where the gastroesophageal junction maintains its position posteriorly with anterior herniation of the gastric fundus; type III, a combination of types I and II; and type IV, in which the stomach migrates completely into the thoracic cavity (upside-down stomach), sometimes accompanied by other visceral organs [45]. Type I hernias are the most common type of hiatal hernias and occur in 95 % of patients with diaphragmatic herniation. This type may predispose to gastroesophageal reflux. Only 5 % of hiatal hernias are true paraesophageal hernias (type II), but these hernias are important due to the potentially life-threatening complications such as obstruction, acute dilation, or perforation [45]. In general, no conservative treatment options are available for the treatment of type II hernias. Surgical treatment consists of complete excision of the peritoneal sac from the mediastinum and reduction of the herniated stomach and distal esophagus into the abdominal cavity and subsequent repair of the hiatus; there is still debate about the need for a fundoplication [45]. Surgery can be performed by either a conventional open procedure or a laparoscopic procedure.

Fundoplication and Its Complications

Most frequent complications after Nissen or Toupet fundoplication are depicted in Fig. 8.8. In general 90 % of fundoplications are successful. Most frequent complications are dysphagia and recurrence of reflux symptoms.

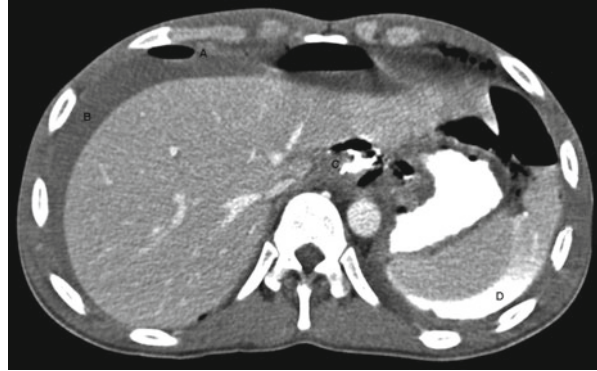
Dysphagia is a common problem early after either Nissen or Toupet fundoplication but will disappear in the majority of patients. It is persistent, however, in

Fig. 8.8 Failures after Nissen fundoplication. (a) The fundoplication has given way, leading to recurrent GERD. (b) Fundoplication is too tight (and/or too long) leading to dysphagia. (c) Intrathoracic herniation of the complete wrap. (d) Telescoping of the esophagogastric junction through the wrap. (e) Torsion due to tension of the wrap. (f) Vagus nerve lesion in combination with an otherwise intact fundoplication (Adapted from van Lanschot et al. [43])



5–10 % of patients. Recurrent reflux may occur in up to 5 % of patients. Disruption or migration, either into the chest or down the stomach, occurs in up to 7 % of patients (Fig. 8.8). Wrap disruption or migration, a too tight fundoplication, telescoping of the esophagogastric junction through the wrap, and torsion (complications A, B, D, and E in Fig. 8.8) are best treated by relaparoscopy or relaparotomy. Intrathoracic herniation is best treated by thoracotomy, but there is no surgical solution for delayed gastric emptying due to damage of the vagus nerve (Fig. 8.8f), which is probably the most severe complication after Nissen fundoplication [43].

Fig. 8.9 Esophageal perforation 5 days after esophagomyotomy and DOR fundoplication. Perforation with (A) free air around the liver, (B) free fluid around the liver, (C) extraluminal contrast and air around the distal esophagus, and (D) contrast fluid around the spleen



Esophagomyotomy and Its Complications

Intraoperative perforation is the most common complication during esophagomyotomy, and the risk of perforation ranges up to 33 % [46]. To visualize mucosal perforation immediately postoperatively, generally an X-ray with soluble contrast is performed on the first postoperative day. Diet is gradually advanced from clear liquids on day one to normal diet if the patient is doing clinically well.

In case of clinical deterioration (abdominal pain, signs of sepsis), additional diagnostic investigations have to be performed including CT with water-soluble contrast administered orally. In case of perforation, free fluid/contrast and air is visible on CT as is shown in Fig. 8.9. This image shows free contrast, fluid, and air in a patient after myotomy with a perforation on postoperative day 4.

Treatment of esophageal perforations can be performed immediately perioperatively when the perforation is identified. Delayed diagnosis of a clinically relevant perforation is a potentially fatal complication and can lead to fistula formation. Perforations can be treated by stent placement or surgically through primary closure and a tissue patch [47]. First step would be a relaparoscopy and suture repair of the perforation. Subsequently, an anterior fundoplication should be performed to seal off the repaired mucosal site which has a high risk of repeated leakage. Adequate drainage is also advised.

Paraesophageal Hernia Repair and Its Complications

Complications of paraesophageal hernia repair include visceral injury, vagal nerve injury, pneumothorax, hemorrhage, and pulmonary complications. The most important complication after hernia repair, however, is recurrent herniation [48]. Postoperative recurrence occurs in up to 44 % of patients, depending on the applied criteria (radiological versus clinical). Risk factors for the development of hiatal hernia recurrence include postoperative vomiting, obesity, coughing, and heavy lifting.

Dilation can be performed in patients with dysphagia as sole symptom of recurrent hiatal hernia. Indications for reoperation are regurgitation, dysphagia without response to dilation, and persistent chest pain [49].

References

1. Pohl H, Welch HG. The role of overdiagnosis and reclassification in the marked increase of esophageal adenocarcinoma incidence. *J Natl Cancer Inst.* 2005;97(2):142–6.
2. Kamangar F, Dores GM, Anderson WF. Patterns of cancer incidence, mortality, and prevalence across five continents: defining priorities to reduce cancer disparities in different geographic regions of the world. *J Clin Oncol.* 2006;24(14):2137–50.
3. Hulscher JB, van Sandick JW, Tijssen JG, Obertop H, van Lanschot JJ. The recurrence pattern of esophageal carcinoma after transhiatal resection. *J Am Coll Surg.* 2000;191(2):143–8.
4. Mariette C, Balon JM, Piessen G, Fabre S, Van Seuning I, Triboulet JP. Pattern of recurrence following complete resection of esophageal carcinoma and factors predictive of recurrent disease. *Cancer.* 2003;97(7):1616–23.
5. Hulscher JB, van Sandick JW, de Boer AG, Wijnhoven BP, Tijssen JG, Fockens P, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the esophagus. *N Engl J Med.* 2002;347(21):1662–9.
6. Omloo JM, Lagarde SM, Hulscher JB, Reitsma JB, Fockens P, van Dekken DH, et al. Extended transthoracic resection compared with limited transhiatal resection for adenocarcinoma of the mid/distal esophagus: five-year survival of a randomized clinical trial. *Ann Surg.* 2007;246(6):992–1000.
7. Wu PC, Posner MC. The role of surgery in the management of oesophageal cancer. *Lancet Oncol.* 2003;4(8):481–8.
8. Swisher SG, Deford L, Merriman KW, Walsh GL, Smythe R, Vaporicyan A, et al. Effect of operative volume on morbidity, mortality, and hospital use after esophagectomy for cancer. *J Thorac Cardiovasc Surg.* 2000;119(6):1126–32.
9. Wouters MW, Wijnhoven BP, Karim-Kos HE, Blaauwgeers HG, Stassen LP, Steup WH, et al. High-volume versus low-volume for esophageal resections for cancer: the essential role of case-mix adjustments based on clinical data. *Ann Surg Oncol.* 2008;15(1):80–7.
10. van Heijl M, van Lanschot JJ, Blom RL, Bergman JJ, Ten Kate FJ, Busch OR, et al. Outcomes of 16 years of oesophageal surgery: low postoperative mortality and improved long-term survival. *Ned Tijdschr Geneesk.* 2010;154:A1156.
11. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240(2):205–13.
12. Lagarde SM, Reitsma JB, Maris AK, van Berge Henegouwen MI, Busch OR, Obertop H, et al. Preoperative prediction of the occurrence and severity of complications after esophagectomy for cancer with use of a nomogram. *Ann Thorac Surg.* 2008;85(6):1938–45.
13. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *Am J Respir Crit Care Med.* 1994;149(3 Pt 1):818–24.
14. Zingg U, Smithers BM, Gotley DC, Smith G, Aly A, Clough A, et al. Factors associated with postoperative pulmonary morbidity after esophagectomy for cancer. *Ann Surg Oncol.* 2011;18(5):1460–8.
15. Schoppmann SF, Prager G, Langer FB, Riegler FM, Kabon B, Fleischmann E, et al. Open versus minimally invasive esophagectomy: a single-center case controlled study. *Surg Endosc.* 2010;24(12):3044–53.

16. Zingg U, McQuinn A, DiValentino D, Esterman AJ, Bessel JR, Thompson SK, et al. Minimally invasive versus open esophagectomy for patients with esophageal cancer. *Ann Thorac Surg.* 2009;87(3):911–9.
17. Tisdale JE, Wroblewski HA, Wall DS, Rieger KM, Hammoud ZT, Young JV, et al. A randomized, controlled study of amiodarone for prevention of atrial fibrillation after transthoracic esophagectomy. *J Thorac Cardiovasc Surg.* 2010;140(1):45–51.
18. Malhotra SK, Kaur RP, Gupta NM, Grover A, Ramprabu K, Nakra D. Incidence and types of arrhythmias after mediastinal manipulation during transhiatal esophagectomy. *Ann Thorac Surg.* 2006;82(1):298–302.
19. Nattel S. New ideas about atrial fibrillation 50 years on. *Nature.* 2002;415(6868):219–26.
20. Murthy SC, Law S, Whooley BP, Alexandrou A, Chu KM, Wong J. Atrial fibrillation after esophagectomy is a marker for postoperative morbidity and mortality. *J Thorac Cardiovasc Surg.* 2003;126(4):1162–7.
21. Walther B, Johansson J, Johnsson F, Von Holstein CS, Zilling T. Cervical or thoracic anastomosis after esophageal resection and gastric tube reconstruction: a prospective randomized trial comparing sutured neck anastomosis with stapled intrathoracic anastomosis. *Ann Surg.* 2003;238(6):803–12.
22. Boone J, Livestro DP, Elias SG, Borel Rinkes IH, Van HR. International survey on esophageal cancer: part I surgical techniques. *Dis Esophagus.* 2009;22(3):195–202.
23. van Heijl M, van Wijngaarden AK, Lagarde SM, Busch OR, van Lanschot JJ, van Berge Henegouwen MI. Intrathoracic manifestations of cervical anastomotic leaks after transhiatal and transthoracic oesophagectomy. *Br J Surg.* 2010;97(5):726–31.
24. Urschel JD, Blewett CJ, Bennett WF, Miller JD, Young JE. Handsewn or stapled esophagogastric anastomoses after esophagectomy for cancer: meta-analysis of randomized controlled trials. *Dis Esophagus.* 2001;14(3–4):212–7.
25. Boone J, Rinkes IB, van Leeuwen M, van Hillegersberg R. Diagnostic value of routine aqueous contrast swallow examination after oesophagectomy for detecting leakage of the cervical oesophagogastric anastomosis. *ANZ J Surg.* 2008;78(9):784–90.
26. Low DE. Diagnosis and management of anastomotic leaks after esophagectomy. *J Gastrointest Surg.* 2011;15:1319–22.
27. Lagarde SM, Omlou JM, de Jong K, Busch OR, Obertop H, van Lanschot JJ. Incidence and management of chyle leakage after esophagectomy. *Ann Thorac Surg.* 2005;80(2):449–54.
28. Omlou JM, Lagarde SM, Vrouwenraets BC, Busch OR, van Lanschot JJ. Compartmentalization for chylothorax originating from the abdomen after extended esophagectomy. Report of two cases and review of the literature. *Dig Surg.* 2006;23(1–2):86–92.
29. Gelpke H, Grieder F, Decurtins M, Cadosch D. Recurrent laryngeal nerve monitoring during esophagectomy and mediastinal lymph node dissection. *World J Surg.* 2010;34(10):2379–82.
30. Gockel I, Kneist W, Keilmann A, Junginger T. Recurrent laryngeal nerve paralysis (RLNP) following esophagectomy for carcinoma. *Eur J Surg Oncol.* 2005;31(3):277–81.
31. Bakhos C, Alazemi S, Michaud G, DeCamp MM. Staged repair of benign tracheo-neoesophageal fistula 12 years after esophagectomy for esophageal cancer. *Ann Thorac Surg.* 2010;90(6):e83–5.
32. Buskens CJ, Hulscher JB, Fockens P, Obertop H, van Lanschot JJ. Benign tracheo-neoesophageal fistulas after subtotal esophagectomy. *Ann Thorac Surg.* 2001;72(1):221–4.
33. van Heijl M, Gooszen JA, Fockens P, Busch OR, van Lanschot JJ, van Berge Henegouwen MI. Risk factors for development of benign cervical strictures after esophagectomy. *Ann Surg.* 2010;251(6):1064–9.
34. Nederlof N, Tilanus HW, Tran TC, Hop WC, Wijnhoven BP, de Jonge J. End-to-end versus end-to-side esophagogastrostomy after esophageal cancer resection: a prospective randomized study. *Ann Surg.* 2011.
35. Honkoop P, Siersema PD, Tilanus HW, Stassen LP, Hop WC, van Blankenstein M. Benign anastomotic strictures after transhiatal esophagectomy and cervical esophagogastrostomy: risk factors and management. *J Thorac Cardiovasc Surg.* 1996;111(6):1141–6.

36. van Hooft JE, van Berge Henegouwen MI, Rauws EA, Bergman JJ, Busch OR, Fockens P. Endoscopic treatment of benign anastomotic esophagogastric strictures with a biodegradable stent. *Gastrointest Endosc.* 2011;73(5):1043–7.
37. Pierie JP, de Graaf PW, Poen H, van der Tweel I, Obertop H. Incidence and management of benign anastomotic stricture after cervical oesophagogastronomy. *Br J Surg.* 1993;80(4):471–4.
38. Biere SS, Cuesta MA, van der Peet DL. Minimally invasive versus open esophagectomy for cancer: a systematic review and meta-analysis. *Minerva Chir.* 2009;64:121–33.
39. Nagpal K, Ahmed K, Vats A, et al. Is minimally invasive surgery beneficial in the management of esophageal cancer? A meta-analysis. *Surg Endosc.* 2010;24:1621–9.
40. Sgourakis G, Gockel I, Radtke A, et al. Minimally invasive versus open esophagectomy: meta-analysis of outcomes. *Dig Dis Sci.* 2010;55:3031–40.
41. Biere SS, van Berge Henegouwen MI, Maas KW, et al. Minimally invasive versus open oesophagectomy for patients with oesophageal cancer: a multicentre, open-label, randomised controlled trial. *Lancet.* 2012;379:1887–92.
42. Locke III GR, Talley NJ, Fett SL, Zinsmeister AR, Melton III LJ. Prevalence and clinical spectrum of gastroesophageal reflux: a population-based study in Olmsted County, Minnesota. *Gastroenterology.* 1997 May;112(5):1448–56.
43. van Lanschot JJ, Gouma DJ, Jansen PLM, Jones EA, Pinedo HM, Schouten WR, et al. Integrated medical and surgical gastroenterology. Houten: Bohn Stafleu Van Loghum; 2004.
44. Boeckxstaens GE, Annese V, des Varannes SB, Chaussade S, Costantini M, Cuttitta A, et al. Pneumatic dilation versus laparoscopic Heller's myotomy for idiopathic achalasia. *N Engl J Med.* 2011;364(19):1807–16.
45. Draaisma WA, Gooszen HG, Tournoij E, Broeders IA. Controversies in paraesophageal hernia repair: a review of literature. *Surg Endosc.* 2005;19(10):1300–8.
46. Iqbal A, Haider M, Desai K, Garg N, Kavan J, Mittal S, et al. Technique and follow-up of minimally invasive Heller myotomy for achalasia. *Surg Endosc.* 2006;20(3):394–401.
47. Erdogan A, Gurses G, Keskin H, Demircan A. The sealing effect of a fibrin tissue patch on the esophageal perforation area in primary repair. *World J Surg.* 2007;31(11):2199–203.
48. Trus TL, Bax T, Richardson WS, Branum GD, Mauren SJ, Swanstrom LL, et al. Complications of laparoscopic paraesophageal hernia repair. *J Gastrointest Surg.* 1997;1(3):221–7.
49. Haider M, Iqbal A, Salinas V, Karu A, Mittal SK, Filipi CJ. Surgical repair of recurrent hiatal hernia. *Hernia.* 2006;10(1):13–9.