Ann. N.Y. Acad. Sci. ISSN 0077-8923

ANNALS OF THE NEW YORK ACADEMY OF SCIENCES
Special Issue: *Global Perspectives on Esophageal Diseases*
REVIEW

Diagnosis, assessment, and management of surgical complications following esophagectomy

Peter P. Grimminger,[1] Lucas Goense,[2] Ines Gockel,[3] Damien Bergeat,[4] Nicolas Bertheuil,[17] Servarayan M. Chandramohan,[5] Ke-neng Chen,[6] Seung-hon Chon,[7] Collet Denis,[8] Khean-lee Goh,[9] Caroline Gronnier,[8] Jun-feng Liu,[10] Bernard Meunier,[4] Phillippe Nafteux,[11] Enrique D. Pirchi,[12] Marc Schiesser,[13] René Thieme,[3] Aaron Wu,[14] Peter C. Wu,[14] Navtej Buttar,[15] and Andrew C. Chang[16]

[1]Department of General, Visceral and Transplant Surgery, Johannes Gutenberg University, Mainz, Germany. [2]Department of Surgery, University Medical Center Utrecht, Utrecht, the Netherlands. [3]Department of Visceral, Transplant, Thoracic and Vascular Surgery, University Hospital of Leipzig, Leipzig, Germany. [4]Department Hepatobiliary and Digestive Surgery, Rennes University Hospital, Rennes, France. [5]Institute of Surgical Gastroenterology, Madras Medical College, Chennai, India. [6]Department of Thoracic Surgery I, Beijing University Cancer Hospital, Beijing, China. [7]Department of General, Visceral and Tumor Surgery, University Hospital of Cologne, Cologne, Germany. [8]Department of Digestive Surgery, University Hospital of Bordeaux, Bordeaux, France. [9]Combined Endoscopy Unit, University of Malaya Medical Center, Kuala Lumpur, Malaysia. [10]Department of Thoracic Surgery, Fourth Hospital, Hebei Medical University, Shijiazhuang, China. [11]Department of Thoracic Surgery, University Hospitals, Leuven, Belgium. [12]Department of Surgery, Hospital Britanico de Buenos Aires, Buenos Aires, Argentina. [13]Klinik St. Anna, Hirslanden, Lucerne, Switzerland. [14]Department of Surgery, University of Washington, Seattle, Washington. [15]Division of Gastroenterology and Hepatology, Department of Medicine, Mayo Clinic, Rochester, Minnesota. [16]Department of Surgery, University of Michigan, Ann Arbor, Michigan. [17]Department of Plastic, Reconstructive and Aesthetic Surgery, Rennes University Hospital, Rennes, France

Address for correspondence: Andrew C. Chang, M.D., Department of Surgery, University of Michigan, TC2120G/5344, 1500 East Medical Center Drive, Ann Arbor, MI 48109. andrwchg@med.umich.edu

Despite improvements in operative strategies for esophageal resection, anastomotic leaks, fistula, postoperative pulmonary complications, and chylothorax can occur. Our review seeks to identify potential risk factors, modalities for early diagnosis, and novel interventions that may ameliorate the potential adverse effects of these surgical complications following esophagectomy.

Keywords: complications; esophageal cancer; anastomotic leak; fistula; chylothorax

Introduction

Anastomotic leakage after esophageal resection is one of the most feared postoperative complications, occurring in 5–20% of cases,[1,2] and can result in 30-day mortality of 2.1–35.7%.[3,4] Reasons for the gravity of these complications are both the anatomy of the esophagus and the location of the anastomosis. A recent meta-analysis including nearly 3000 patients showed worse long-term prognosis in patients with severe leakage after esophagectomy.[5] According to a recent review of the experiences of 24 experienced centers worldwide, in a group of 2704 consecutive patients undergoing esophagectomy, 30-day and 90-day mortality were 2.4% and 4.5%, respectively, with an overall complication rate of 59%, including pneumonia and leak rates of 15 and 11.4%, respectively.[6]

Furthermore, this complication increases hospital stay, delays oral (but not necessarily enteral) feeding, and increases risks of both stricture formation and reoperation. Anastomotic leakage has been associated with poorer quality of life, increased cancer recurrence rates, and subsequently worsened long-term survival.[5,7–9] Despite the increasing utilization of intrathoracic anastomosis, the rate of cervical anastomosis use remains approximately 40% in a large cohort of patients treated between January 2015 and December 2016 by dedicated esophageal surgeons.[6] In view of these data, is cervical anastomosis still an important technique to master in the arsenal of esophageal surgeons?

doi: 10.1111/nyas.13920

Multiple risk factors for leakage have been proposed in the literature.[10] Treating comorbidities (malnutrition,[11] diabetes,[12] smoking cessation, and reduction of steroid use) whenever possible is obviously important. Placing the anastomosis in previously irradiated, and thus vascular-compromised, tissue[13] could also be a risk factor, but also of necessity given the importance of combined modality treatment to optimize the oncological outcomes for esophageal cancer treatment. Limiting trauma to the gastric conduit and to the vascular axis alongside the greater curvature by using gentle surgical and no-touch technique is of the utmost importance. Great care should be taken to mobilize adjacent omentum with the vascular axis consisting of the right gastroepiploic arcade, staying as far away as possible from this axis during dissection to avoid damage to collateral circulation. Increased vascularization through ischemic preconditioning has so far failed to show a significant decrease in leakage rate[14] but enhanced visualization of conduit vascularization in an attempt to define the nonischemic zone for placing the anastomosis seems promising. Several types of anastomosis have been reported and compared (hand-sewn versus stapled, circular versus triangular, and end-to-end versus end-to-side), but no single technique has been shown to be superior to others with reference to leakage, although the noncircular anastomosis (triangular or semimechanical) seems to increase the quality of life in the first postoperative year and decreases the risk of stricture and subsequent need for dilatation.[15]

Not only safe anastomoses, but also timely identification of anastomotic or other surgical complications are essential to reduce morbidity, prolonged hospitalization, mortality, and, consequently, additional medical costs.[16–18] Both surgical expertise and experience are key elements for limiting the leakage rate and managing its consequences after esophagectomy, and it is argued that centralizing surgical care may be a key determinant of lower leakage rates.[5,19] Our goal is to provide a succinct review of key principles and current knowledge relating to risk factors, modalities to identify and manage anastomotic leakage as well as associated technical complications, particularly airway fistula, respiratory failure, and chylothorax, which can affect development of a leak in patients undergoing esophagectomy.

Risk factors

Impact of anastomotic location

While there are several confounding factors, such as anastomotic technique (stapled versus hand-sewn) or minimally invasive versus open approaches, the location of the anastomosis based on tumor location, patient performance status, and functional results remains an important determinant of anastomotic leaks. Cervical anastomoses have been associated with greater leakage rates (25–45%) compared with intrathoracic anastomoses (5–15%)[20,21] and may lead to increased recurrent nerve paresis and longer hospital stays.[22] A cervical anastomosis requires a longer gastric conduit and is more likely positioned in the fundus, where vascularity is limited. Although anastomotic leaks are more frequent with cervical anastomoses, such leaks are easier to manage and are less likely to result in profound sepsis. The functional results, however, are thought to be better after an intrathoracic anastomosis despite a lack of clear evidence in the literature. More recent nonrandomized trials show similar results with an intrathoracic leakage rate between 3.5% and 23% compared with a leakage rate between 28% and 33% in the neck.[23–25] Minimally invasive surgery has been introduced to minimize surgical trauma and reduce the perioperative complication rate. Different operative techniques exist, including robotic surgery, and reports of early experiences have been published. However, a recent publication from the Netherlands, assessing a total of 866 patients, reported higher anastomotic leakage in the minimally invasive group (21.2% versus 15.5%).[2] Subgroup analysis showed a lower leakage rate in the intrathoracic anastomosis group for both the open (10% versus 17%) and the minimally invasive (21% versus 23%) procedures, with an overall complication rate of 63% and 67%. A randomized trial assessing this endpoint in minimal invasive esophagectomy is in progress.

Four randomized trials have shown lower anastomotic leakage (4–7% versus 2–39%) and less recurrent nerve palsy in favor of intrathoracic anastomosis,[26–29] although mortality rates were similar (2–17% versus 2–14%).[30] One interpretation is that cervical anastomotic leaks are easier to manage and carry a lower systemic burden for the patient, whereas intrathoracic leaks are more likely to have a detrimental impact on the patient, despite modern therapeutic options. The potential systemic burden of such complications might result in a similar mortality between the two techniques. Of note, the latest randomized trial was published in 2007 before endoluminal sponge therapy and other techniques were available. Data assessing anastomotic level in minimally invasive esophagectomy are needed and have currently been submitted for publication.

In conclusion, although cervical esophageal anastomoses are associated with higher leakage rates compared with intrathoracic anastomoses, similar perioperative mortality suggests that a cervical leak has less risk for mortality. The implementation of advanced endoscopic treatments for anastomotic leaks could modify the impact of leaks on morbidity and mortality.

Ischemic preconditioning and subsequent risk for anastomotic leak

The prevention and treatment of anastomotic leaks is important due to the associated mortality. There are several determinants of anastomotic leaks, such as (1) the intrinsic anatomic factors of the esophagus, (2) the negative pressure within the thoracic cavity, and (3) anastomotic technique, including either hand-sewn or stapled anastomoses.

Esophageal reconstruction mostly involves the stomach (more than 90% of cases). Various techniques and modalities that prevent anastomotic leakage have been introduced and assessed, including preoperative partial gastric devascularization, that is, ischemic conditioning of the stomach, and subsequent delayed esophagogastric anastomosis.[31] Kechagias and colleagues[14] summarized the experimental and clinical studies with the purpose of assessing the current role of the ischemic conditioning technique. Their report did not identify any significant reduction in the incidence of anastomotic leakage after esophagectomy despite staged ischemic conditioning.

The prevention of anastomotic leak should focus on preoperative nutritional status, intraoperative maneuvers that minimize direct trauma to the conduit, and postoperative management. The longer the gastric conduit is made, the more prone it will be to ischemia at its tip. Maintaining the conduit's blood supply and the ease of operation need to be balanced. The gastric conduit is perfused only via the right gastroepiploic artery which provides blood to 60% of the distal stomach, whereas the remaining 40% of the more proximal stomach depends on its vascular supply from a submucosal network of small vessels (Fig. 1). The stomach is tailored to form a 4-cm wide neo-esophagus to obtain a tubular-shaped conduit, with resection of the poorly vascularized fundus, permitting anastomosis closer to the right gastroepiploic artery branches.[32] Moreover, a tubular-shaped conduit promotes alignment of the anastomosis and pylorus to address the anatomical and mechanical problems of gastric retention and emptying, thereby reducing the risk of anastomotic leakage.[32] Additionally, improving perioperative management and resuming early postoperative enteral nutrition, pulmonary physiotherapy, as well as preventing hypoxemia and hypotension, are all important measures to reduce the occurrence of an anastomotic leak.[32]

Definitions and classifications of anastomotic leak

Anastomotic leaks are typically defined as the presence of contents emerging at the wound and associated systemic complications,[33] although nearly half of leaks initially are clinically silent. The Esophagectomy Complications Consensus Group (ECCG) defines anastomotic leaks as a "full-thickness gastrointestinal defect involving esophagus, anastomosis, staple line, or conduit irrespective of presentation or method of identification."[34] This same group classifies leaks into three types:

- Type I: Local defect requiring no change in therapy or treated medically
- Type II: Localized defect requiring interventional but not surgical therapy
- Type III: Localized defect requiring surgical therapy.

Lerut *et al.* used a modified classification from the Surgical Infection Study Group, dividing leaks into four grades:[35]

- Grade 1 (radiologically or endoscopically detected): without clinical signs
- Grade 2 (minor clinical): local inflammation
- Grade 3 (major clinical): severe disruption with sepsis
- Grade 4 (conduit necrosis): confirmed by endoscopy.

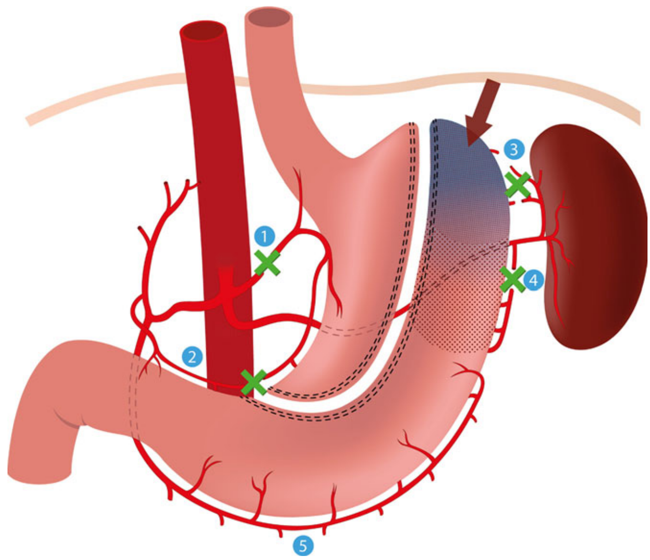

Figure 1. Illustration showing the arterial supply of the stomach after constructing the gastric tube for reconstruction in esophageal surgery. During mobilization of the stomach, ligation (green crosses) of the left (1) and right (2) gastric artery, short gastric arteries (3), and left gastroepiploic artery (4) causes the gastric tube to be supplied exclusively by the right gastroepiploic artery (5). This results in compromised blood flow in the most cranial part of the gastric tube (arrow), which is used to create the cervical anastomosis. Reprinted with permission from Ref. 135.

To properly diagnose a leak, two issues should be taken into consideration. First, that the leak should not only be confirmed but also be graded simultaneously. Second, that there is a significant difference between diagnosing suspected leaks, where the best test(s) are needed for sensitivity and specificity, and diagnosing an unsuspected leak, where the usefulness of routine tests should be evaluated.

Diagnosis of anastomotic leak and fistula

Clinical signs of a leak can vary significantly and range from no clinical signs to pleural collection to fulminant sepsis. A gold standard for diagnosing leakage has not yet been established. If this complication is suspected, it is crucial that further medical tests are administered directly as any delay can significantly affect the patient's prognosis. In contrast to a cervical leak, diagnosis of a thoracic anastomotic leak can be more difficult, and a standardized international definition does not exist.[36] If an anastomotic leak is suspected, two aspects should be considered: the clinical signs of the patient and the available diagnostic tools. The question remains as to when does one need to investigate and what tool(s) should one use. Various modalities to diagnose anastomotic leaks have been proposed:

- Clinical signs, drain fluid, and blood tests
- Upper endoscopy
- Contrast esophagogram
- Computed tomography (CT) scan (with or without oral contrast).

Clinical signs, drain fluid, and blood tests

Early signs of complications, although sometimes subtle, should be pursued. Such patients often present initially with postoperative fever or leukocytosis. The development of erythema or induration along the neck incision (if present) may alert the surgeon of an underlying leak and trigger further diagnostic studies. Changes in heart rate, often in form of atrial fibrillation, can be the first and only indicator of a leak,[37] as well as unexplained high levels of inflammation markers in the blood (white blood count and C-reactive protein).[38] The serum level of C-reactive protein can allow detection of leaks on postoperative days 3 or 4.[39] The presence of saliva or gastric contents in a drain are obvious signs of a leak, but the routine analysis of drain amylase levels on day 4 may detect leaks earlier and even more accurately than barium esophagogram.[40] In addition to clinical signs, there are several diagnostic methods that can help determine whether the patient has developed anastomotic leak: endoscopy, contrast swallow examination or CT.

Upper endoscopy

Many surgeons hesitate to perform upper endoscopy because of the risk of disrupting the anastomosis. Recent studies in an *in vivo* porcine model demonstrated that intraluminal pressure greater than 80 cm H_2O is needed to disrupt an esophagogastric anastomosis. Endoscopic air insufflation should always be gentle and progressive but even with maximum insufflation the intraluminal pressure at the anastomosis never increases beyond 9 cm H_2O, with minimal disturbance of the blood flow in the conduit.[41]

Clinical studies have confirmed that upper endoscopy performed within 1 week after esophagectomy is safe and can be performed at the bedside, even in a patient who is intubated,[12,42] without worsening an already existing leak.[20] The sensitivity of endoscopy is relatively high not only to assess the anastomosis but also to identify any degree of alteration of the integrity of the conduit, from mucosal ischemia to necrosis, and to provide information about the vitality of the gastric conduit.[7] In a prospective nonrandomized trial comparing other modalities and endoscopy to identify esophageal anastomotic leak (EAL) after esophagogastric surgery, Hogan *et al.* did not observe any complication due to endoscopy[43] and confirmed the safety and feasibility of early endoscopy in case of a suspected anastomotic leak. Endoscopy should be considered in patients with suspected anastomotic leak as it may be helpful to select those who might need surgical revision of the anastomosis.

Endoscopic evaluation must be performed carefully with low insufflation pressure[7] by an experimented gastroenterologist or surgeon in order to limit the theoretical risk of worsening the defect and/or the perianastomotic sepsis. Upper endoscopy has a few drawbacks. Its use with sedation may lead to aspiration in some patients, and is performed under general anesthesia in many centers. In addition, although its sensitivity is relatively high as a routine test for detecting intrathoracic leaks, a recent study of cervical anastomotic leaks compared the routine use of endoscopy and esophagogram and found a sensitivity of 56% and 20%, respectively.[44,45] Therefore, its routine use in patients without clinical suspicion of cervical leakage is controversial.

In summary, endoscopy is a very useful diagnostic method and can effectively complement, if not altogether replace, other diagnostic means.[12,45] In spite of the high specificity and sensitivity of endoscopy, it is still not recommended as a routine means of detecting leaks in the postoperative phase.[46]

Contrast esophagogram

The traditional approach to diagnose an esophageal leak has been to begin the study using a water-soluble contrast agent (such as Gastrografin) to prevent exacerbation of cervical sepsis by the leaked barium. While this is an inexpensive and relatively safe method, this test only fulfills its diagnostic potential when the execution of the test and the interpretation of the results are undertaken by an experienced radiologist.[47] Gastrografin can cause severe chemical pneumonitis if aspirated. Esophagectomy patients frequently have altered swallowing function and these examinations should be avoided in case of impaired consciousness because of the risk of aspiration. A normal study with a water-soluble agent should be followed by thin barium to improve sensitivity for detection of a leak by 15%.[47] Even a negative barium study does not rule out a leak because of its sensitivity of only 40% (33–52%) in patients with cervical anastomosis.[48,49] These rates are worse than those for intrathoracic leaks (93%), but specificity rates greater than 90% have been reported for such evaluation of both cervical and thoracic anastomoses.[50] Given that nearly a third of the patients diagnosed with leakage have their cervical wounds opened based upon clinical suspicion before scheduled contrast swallow, this test changes patient management in only 1.5% of the cases.[48,49] Further limitations of this method include an insufficient intake of the contrast agent or aspiration.[12,51,52] Consequently, this method should be regarded as an inadequate routine diagnostic modality when aiming to diagnose a leakage.[53] Nevertheless, its high specificity rates imply a potential ongoing role for confirming clinical suspicion of a leak, but its low sensitivity implies a less prominent role.

Computed tomography

CT with or without oral contrast is a unique modality as it allows visualization of the neck, thorax, and abdomen on a single examination. In addition to the diagnosis of an anastomotic leak, CT scan provides the location and extent of peri-anastomotic collections and covers a broader differential diagnosis than leakage alone (e.g., pulmonary complications).[43,54] The sensitivity of CT in detecting fistula, wall discontinuity, and mediastinal fluid or air is up to 80%.[55] CT imaging is noninvasive, fast, and safe in critically ill patients.

The assessment of a postoperative CT scan remains challenging because of the anatomic changes and residual air caused by esophagectomy, and lack of consensus on radiographic findings associated with leakage. This is supported by the large difference in published diagnostic values from studies that have assessed the clinical diagnostic ability of CT imaging for the detection of anastomotic leakage. Reported sensitivity and specificity by these studies range from 52% to 88% and 33% to 100%, respectively.[43,52,54–56] In most of these studies, one or two radiologists independently determined their own definition of anastomotic leakage based upon a variety of radiologic findings.[43,52,54–56]

Two studies have assessed the association of specific postoperative CT findings with anastomotic leakage after esophagectomy. In these studies, the presence of mediastinal air, mediastinal fluid, and contrast leakage was associated with anastomotic leakage.[52,56] However, these studies found that using solitary CT findings for diagnosis of anastomotic leakage resulted in lower diagnostic accuracy compared with assessment by independent radiologists who determined their own definition of leakage.[52,56] This is likely because single CT features are either too specific and not very sensitive, or vice versa. For example, contrast leakage after esophagectomy is a very specific finding for the presence of an anastomotic leak. In many patients with leakage, however, extravasation of contrast can be absent, consequently resulting in a low sensitivity.[52] On the other hand, presence of mediastinal air near the anastomosis is highly sensitive for the presence of leakage, but because this can be a frequent finding after esophagectomy this finding is not specific.[52,56]

A recent study that assessed 122 patients who underwent CT imaging for clinical suspicion of anastomotic leakage identified a risk score to overcome these limitations.[55] In this study, the potential findings of mediastinal fluid, mediastinal air, and anastomotic wall discontinuity and fistula were significantly associated with anastomotic leakage (Fig. 2). Based on these factors, an anastomotic leakage prediction score (ALP score) was developed with a sensitivity of 80% and specificity of 84% for the detection of leakage. The ALP score significantly outperformed the original clinical interpretation by radiologists (reported sensitivity of 52% and specificity of 84%, respectively).[55]

These data suggest that combining different well-recognizable CT findings in a risk score can improve the diagnostic accuracy of CT imaging for the diagnosis of anastomotic leakage after esophagectomy. In cases when the results of a CT scan remain uncertain, endoscopy could be performed, as this has proven to be an accurate test for the diagnosis of leakage.[55]

Unlike symptomatic patients, sensitivity of a CT scan performed routinely on postoperative day 7 after an intrathoracic anastomosis in asymptomatic patients was estimated in a study by Strauss *et al.* at 54.5%, compared with 45.4% for an esophagogram.[52] These rates are worse when evaluating cervical leaks only. As a consequence, rather than being performed routinely, these examinations should probably be undertaken only when a leak is suspected. Unlike upper endoscopy, CT scan does not provide information about gastric conduit viability; as with endoscopy, which includes options for therapy, CT imaging can also identify mediastinal fluid collections that might be accessible for percutaneous drainage.

Order of investigation

Typically asymptomatic patients are to be followed clinically, including measurements of serum C-reactive protein and drain amylase levels. Contrast esophagogram done routinely between days 4 and 7 has low sensitivity, but provides information on the conduit and gastric emptying. Upper gastrointestinal endoscopy has better sensitivity and specificity (100% and 100%, respectively) versus 87.5% and 90% for swallow test and 87.5% and 100% for CT scan.[43] When a leak is suspected, both endoscopy and CT scan should be considered. In addition to confirming the diagnosis of leakage, these methods provide essential information for initial treatment. Endoscopy is the only method that can assess the viability of the conduit and CT identifies peri-anastomotic collections. Even if exploration of a cervical wound is planned for confirmation of conduit viability and drainage of any fluid collection or abscess, endoscopy and CT are necessary to assess the thoracic extension of these conditions.

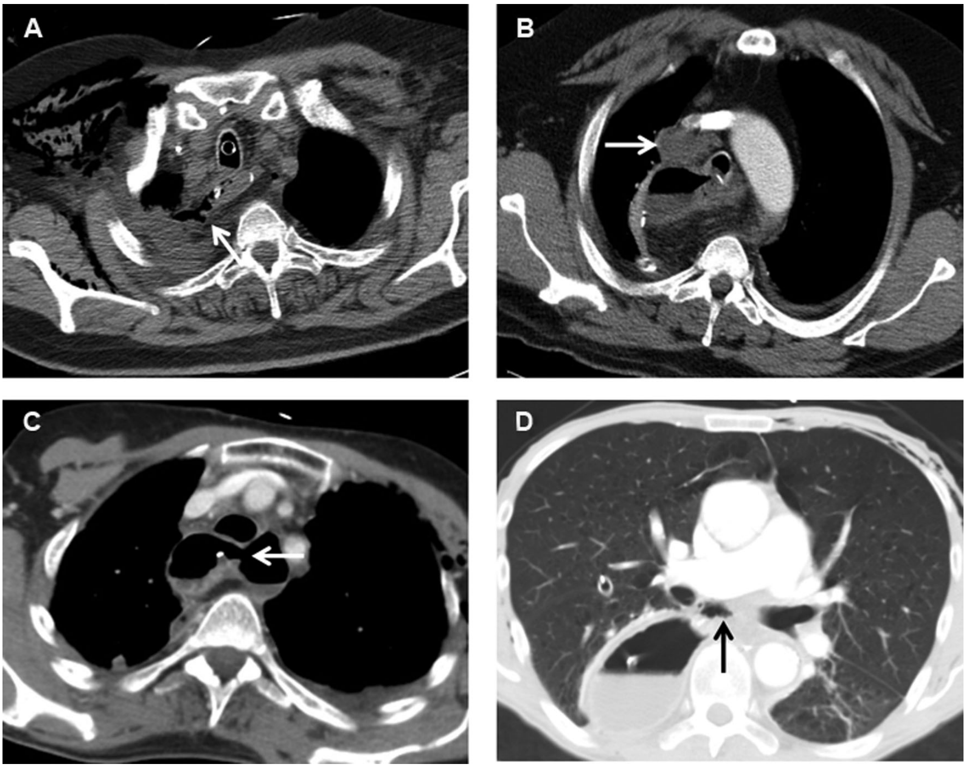

Figure 2. Examples of CT findings associated with the presence of anastomotic leakage after esophagectomy. (A) Image shows a fistula between the gastric tube and right pleural cavity (arrow). (B) Image shows a fluid collection (arrow) in the mediastinum. (C) Image shows a visible discontinuity of the esophagogastric wall (arrow). (D) Image shows a mediastinal air cavity (arrow) after esophagectomy. Reprinted with permission from Ref. 55.

Leak management

In treating a suspected or confirmed anastomotic leak, the general principles include control of sepsis (with drainage as needed), ensuring adequate nutrition, and consideration of antimicrobial therapy. The primary aim of early endoscopy is to identify a leak due to conduit ischemia. In case of severe ischemia or necrosis, emergency salvage surgery, including reversal of the anastomosis and conversion to an end esophagostomy, is mandatory. In case of mild ischemia without anastomotic leakage, endoscopy should be repeated within several days (as determined by patient stabilty). In case of an anastomotic leakage with mild ischemia, either nonoperative treatment or anastomosis revision can be considered. In case of a leak without ischemia, management includes (1) nasogastric drainage, (2) endoscopic treatment (pig tail or prosthesis) or revision of the anastomosis, or (3) administration of antiacid drugs. Early endoscopy is safe when performed cautiously, including low insufflation pressure, by an experienced endoscopist or the operating surgeon. With a very low complication rate, it is the most sensitive test for diagnosis of EAL and gastric conduit viability.

Detection of gastric conduit ischemia

One of the major factors contributing to the risk of esophagogastric anastomotic leakage following esophagectomy is the detection of gastric conduit ischemia. The native stomach has a rich blood supply derived from the right and left gastric arteries, right and left gastroepiploic arteries, and short gastric arteries. During routine esophagectomy, the stomach is fully mobilized, requiring division of at least the left gastric, left gastroepiploic, and short gastric arteries. Consequently, the fundus of the stomach becomes a watershed zone of potentially compromised blood flow. The fundus also serves as the primary target site for anastomosis to the cervical or thoracic esophageal remnant. Although complete conduit necrosis is rare, it is a devastating complication occurring in less than 2% of esophagectomies. Avoidance of conduit ischemia, defined as inadequate tissue perfusion, is one of the most important criterion for successful esophageal reconstruction.[10,57]

Several factors appear to contribute to lower risk of complications following esophagectomy for malignancy. These include participation of multidisciplinary care teams, early surgical consultation before initiation of treatment, assessment of nutritional status with enteral support via oral or feeding tube supplementation, smoking cessation, diabetes management, epidural pain management, and judicious perioperative fluid management. Intraoperative decision making should include careful assessment of the gastric blood supply, particularly in the setting of prior operations; abdominal adhesions can obscure identification and preservation of the right gastroepiploic arcade. If gastric conduit reconstruction is not available or fails, alternative esophageal replacement strategies should be considered.[58,59]

Intraoperative detection of conduit ischemia has traditionally depended on clinical judgment, with questionable reliability. A variety of other methodologies have been used clinically to assess tissue perfusion, but none have achieved widespread acceptance. Fluorescein angiography with Wood lamp is cost-efficient and widely available, but is limited to a one-time injection with >12-h half-life and dye extravasation into the extracellular space. Conventional angiography is time-consuming and difficult to perform in the operating room setting. Use of the handheld Doppler probe, optical fiber spectroscopy, and measurement of transmucosal oxygen saturation are technologies that are either limited to microvasculature assessment or unable to show variations in regional conduit perfusion. Intraoperative esophagogastroduodenoscopy risks injury to the newly created anastomosis and does not demonstrate gastric conduit vasculature.[60,61]

The reintroduction of laser-induced indocyanine green (ICG) fluorescence for both open and minimally invasive surgery has attracted new enthusiasm for the intraoperative detection of conduit ischemia. This vascular imaging technology has several advantages, including real-time assessment of both the microvasculature network and a macroscopic view of regional organ perfusion without radiation exposure. With a short plasma half-life of 3–5 min, ICG has rapid tissue clearance and can be readministered during the same operation for pre and postreconstruction evaluation. ICG is eliminated solely by bile excretion, permitting its use in patients with chronic renal disease.[61] Of note, this dye is contraindicated for patients with allergic reactions to iodinated agents. Zehetner *et al.* utilized this technology to assess regional perfusion of the gastric conduit and correlated perfusion findings with subsequent anastomotic leaks in 150 consecutive patients undergoing esophagectomy.[62] Although the overall anastomotic leakage rate was 16.7%, the leakage rate was only 2% when the anastomosis was placed in an area of robust perfusion, as determined by ICG fluorescence. In comparison, when anastomoses were constructed in an area of diminished perfusion, anastomotic leaks occurred at a rate of 45% ($P < 0.0001$), confirming a critical relationship between conduit ischemia and risk of anastomotic leak.

Intraoperative real-time assessment of gastric conduit perfusion with laser-assisted ICG fluorescence may increase the sensitivity for detecting gastric conduit ischemia compared with other methodologies or clinical judgment alone. Such information can help guide critical decision making for esophageal reconstruction and may contribute to reduced risk of anastomotic leakage and its associated morbidity following esophagectomy.

Treatment considerations

State-of-the-art management of anastomotic leakage

According to the current literature, cervical leakage is significantly higher than intrathoracic anastomotic insufficiency (32% versus 15%).[24,63–66] Possible contributing factors include the longer distance of the gastric interponat needed for cervical anastomosis, greater anastomotic tension, worse microcirculation at the tip of the esophageal substitute, and higher risk of compression at the thoracic inlet. However, cervical leaks are associated with fewer life-threatening complications, especially those with infectious presentations, such as mediastinitis, sepsis, erosion, bleeding, and aerodigestive fistulae, as compared with intrathoracic leaks.

Division of the interclavicular ligament beneath the sternum with resection of the left

Table 1. **The three pillars for managing anastomotic leaks**

Conservative measures	Endoscopic interventional treatment	Surgical revision
• Nasogastric tube/jejunostomy • Parenteral feeding • IV antibiotics (antimycotics) • Opening of the cervical wound, rinsing, possibly interventional mediastinal drainage • Early dilatation of the anastomosis/pylorus • IV anticholinergics (to reduce saliva)	• Endoscopic vacuum therapy (EVT) (intraluminal/intracavitary)/ endosponge therapy (EST) • Self-expandable metallic stents (SEMS) • Stent-over-sponge (SOS) therapy • "Bear claw"/over-the-scope-clip (OTSC) system • OverStitch • Fibrin glue, combined with vicryl plug	• Sternocleidomastoid (SCM) flap repair for complex cervical leak • Left pectoralis major muscle flap to cover complex leaks (e.g., with esophagotracheal fistula) • Resection of gastric fundic tip necrosis and refashioning of the anastomosis (local ischemia) • Diversion surgery dismantling the gastric conduit and esophagostomy (diffuse ischemia and gastric conduit necrosis)

sternoclavicular joint might prevent compression of the gastric conduit.[67] Randomized controlled trials comparing end-to-end versus end-to-side cervical anastomoses revealed increased leakage in the latter,[68] yet there were no differences in cervical anastomotic leak rates between hand-sewn versus stapled side-to-side anastomoses.[15,69] To date, no definitive technique aiming at prevention of cervical leakage can be recommended with respect to the evidence.[59] In analogy to intrathoracic anastomotic insufficiency, cervical leaks are classified clinically according to Lerut *et al.*,[35] Siewert *et al.*,[20] Veeramootoo *et al.*,[70] or Nishikawa *et al.*[71] Nishikawa *et al.* reported an endoscopic mucosal classification that considers the extent of mucosal impairment (from intact mucosa, to mild to severe mucosal degeneration) and correlates well with the occurence of postoperative anastomotic complications, offering an approach to individualized therapy.[71] State-of-the-art management of anastomotic leakage is built upon three main pillars (Table 1): (1) conservative measures to address the vast majority of these complications, (2) endoscopic interventional treatment, and (3) surgical revision. These principles depend on the extent of circumferential involvement, the control of sepsis, and the presence of ischemia/necrosis of the gastric conduit.[59,64] The treatment of cervical or intrathoracic anastomotic leakages follows the same principles, including adequate drainage. However, due to the anastomotic location, the access for drainage is different and explains the different trends for treatment, for example, opening of the cervical wound versus intrathoracic endosponge treatment.

The placement of self-expandable stents has proven to be a viable and effective treatment for anastomotic leakage.[72] While technically straightforward, stent placement requires several considerations. Anastomotic leakage or subsequent stricture within 2 cm of the cricopharyngeus muscle may not be amenable to stenting as the patient may experience an intolerable globus sensation. Angulation of the conduit or anastomosis can also affect adequate stent placement.[73] Stent migration is a common complication for which the use of large diameter stents (22–25 mm)[74] and even colonic stents with a flange diameter of up to 32 mm has been reported.[75] Others have used endoscopically deployed sutures[76] or placed a silk thread affixed to the nose or ear lobe[77,78] to prevent stent migration. A 4- to 8-week (or even shorter) period of stenting is usually adequate for healing of most anastomotic leaks.[74,79] Stenting for 2 weeks may be sufficient for management of most anastomotic leaks and also might reduce the frequency of stent-related complications, such as fistulization (to airway or vascular structures), migration with distal bowel obstruction, esophageal necrosis, and stent fracture or degradation.[79]

Among endoscopic interventions, endoscopic vacuum therapy (EVT)/endosponge therapy (EST)[80–82] seems to be more favorable and technically easier as compared with the use of self-expandable metal stents (SEMSs).[83] Current data regarding outcomes of EVT/EST versus SEMS do not differentiate between cervical and intrathoracic anastomotic insufficiency and include mixed cohorts, including Ivor Lewis (intrathoracic anastomosis) and McKeown (cervical anastomosis) esophagectomies, as well as gastrectomies.[81,83] The stent-over-sponge therapy has similar problems for cervical anastomoses as the above-mentioned drawbacks of SEMS.[84] The "bear claw" (over-the-scope-clip (OTSC®) Ovesco Endoscopy, Tübingen, Germany) system might be an option in a newly opened dehiscence with viable mucosa and strong tissue quality in both components of the anastomosis,[85] with the respective risk of injuring adherent cervical structures such as the carotid artery, the trachea, or the recurrent laryngeal nerve (RLN). Application of the OverStitch™ (Apollo Endosurgery, Inc, Austin TX) can be technically difficult when applied in the cervical esophagus but may be a better option for leaks in the middle or distal third of the esophagus, although this is described only in anecdotal reports,[86] whereas there have been reports of this approach for other types of esophageal fistulae.[87] Combined fibrin glue and vicryl plug can be applied in small defects only and usually requires multiple repetitions of the procedure.[88]

Endosponge treatment (endoscopic vacuum-assisted closure or Endo-VAC) has been used to treat esophageal anastomotic leaks successfully over 10 years.[89] The first retrospective and prospective studies including over 50 patients show that endosponge treatment is equivalent or even superior to endoscopic esophageal stent treatment.[80,90] It has also been shown that even complex anastomotic leaks can be treated using a combination of endosponge and esophageal stent treatment (Table 1).[84]

As an example of endosponge utilization, the perioperative outcomes of one referral center for gastric and esophageal cancer surgery in Mainz, Germany include an intrathoracic anastomotic leakage rate below 15% for patients undergoing minimally invasive laparoscopic/thoracoscopic and robotic-assisted Ivor Lewis resections. Of 17 cases of intrathoracic anastomotic leaks treated with endosponge at the University of Mainz, 16 patients were successfully treated using endosponge alone, while one patient required esophageal stent placement after downsizing the leak with the endosponge. In addition, EST for complex postoperative perforations, such as an acquired tracheoesophageal fistula, may be used and can avoid surgical removal of an interponat. Although the endosponge may become the first choice for management of esophageal perforations and anastomotic leaks, esophageal stents, fibrin glue injection, and other endoscopic tools remain important for second-line treatment.

Surgical options include pedicled muscle flap (such as sternocleidomastoid, pectoralis major, or, as described below, intercostal muscle) repair for complex cervical fistulas/leaks.[91,92] If gastric fundic tip necrosis (local ischemia) is present, resection of the necrotic tissue and refashioning of the anastomosis, if possible, are necessary.[59] In the face of gross or diffuse ischemia of the gastric conduit, diversion surgery, dismantling the gastric pull-up, and placing a temporary esophagostomy with staged colonic interposition is inevitable.[59,64]

Initial management for intrathoracic anastomotic leakage typically is not operative. There has been a paradigm shift in the management of intrathoracic leaks due to advances in early diagnosis, improved critical care, and endoscopic diagnostic and therapeutic strategies that has tilted the balance from aggressive surgical intervention to conservative management.

The factors that govern management include:

- Type of presentation
- Magnitude of leak
- Time of recognition
- Status of the patient
- Status of esophagus and conduit
- Operative expertise.

The presentation of an intrathoracic anastomotic leak, as defined earlier in this review, could be evident clinically or as an endoscopic diagnosis, depending upon the magnitude of the leak. The extent of leakage also dictates the general condition and status of the patient. Major determinants of outcome are the status of the remnant esophagus and gastric conduit. Compounding factors include integrity of the anastomotic or conduit staple lines and the presence of distal obstruction.

Use of systemic antimicrobial therapy, closing or occluding the defect at the earliest possible time, draining the fluid collection, preventing or relieving distal obstruction, ensuring lack of factors keeping the perforation open, and, finally, esophageal diversion or resection if sepsis is poorly controlled, are the major steps in management of an intrathoracic anastomotic leak.[93]

The surgical technique adopted depends upon the magnitude of leakage and the presence of ischemia of the esophageal remnant or gastric conduit, with the extreme being total conduit necrosis. Anastomotic disruption without conduit ischemia can be managed by revision of the anastomosis with reinforcement using a pedicled pleural, pericardial, or viable intercostal muscle flap as described below. Completion gastrectomy and end cervical esophagostomy can limit the consequences of sepsis related to a severe anastomotic leak or conduit necrosis. Reoperation for subsequent reconstruction is technically challenging and should be undertaken once the patient's functional status has been optimized and restaging evaluations confirm no evidence of recurrent or metastatic disease.

Surgical treatment of a tracheoesophageal fistula after esophagectomy using an interposition flap

Aerodigestive fistula is a rare life-threatening complication of the surgical treatment of esophageal cancer. A perioperative fistula is defined as that caused by major airway injury during esophagectomy or occurring after operation. A variety of strategies have been recommended for treatment, likely due to the differing anatomic levels of presentation. Few case reports and case series have described successful management. Hence, the optimal treatment remains elusive. Neoadjuvant radiation therapy must be taken into consideration when reoperation is necessary. Two major strategies can be adopted when the diagnosis of an aerodigestive fistula is confirmed: endoscopic treatment with a fully covered self-expanding stent or surgical treatment using an interposition flap.

Of 530 articles initially identified by systematic review,[94] nine studies (Fig. 3) described outcomes for 27 patients, 17 of whom had flaps (total, 18) placed. Of the 17 patients, 13 were alive at the time of reporting. Various tissue flaps were described, including three latissimus dorsi flaps,[95–97] five pectoralis major flaps,[92,97–99] two sternocleidomastoid muscle flaps,[100,101] one intercostal muscle flap,[97] one sternohyoid muscle flap,[102] one skin perforator pedicled by an intercostal muscle flap,[103] five pericardial flaps,[101] and one pleural flap.[102] No clear evidence supports the superiority of any one operative approach.

The institutional experience at Rennes University Hospital from June 2016 through August 2017 included six patients who developed tracheobronchoesophageal fistula after treatment for esophageal carcinoma. All six patients had received neoadjuvant chemotherapy and five had received radiation therapy (<50 Gy). One patient had sustained an intraoperative injury of the left main stem bronchus and the remaining five developed postoperative fistulae at a mean of 15.8 ± 7.8 days after surgery. At the time of diagnosis, before reoperation, five patients were in septic shock and required mechanical ventilation ($n = 4$), vasopressor or inotropic support ($n = 3$), and/or respiratory assistance via extracorporeal membrane oxygenation (ECMO; $n = 2$).

All patients were treated using an interposition flap with a skin perforator flap pedicled with intercostal muscle harvested from sites depending on the location of the perforator flap and previous operations.[103] Using an 8-MHz handheld Doppler ultrasonographic device, the cutaneous perforator vessels in the right fifth to eighth intercostal spaces were identified. An elliptical skin flap was fashioned around the vessels to allow primary closure of the donor site. The skin flap was harvested and the intercostal muscle elevated after ligating the intercostal pedicle anteriorly to the perforator vessel. The subperiosteal muscle flap was separated from the adjacent rib, maintaining continuity with the parietal pleura. The latissimus dorsi muscle was preserved, offering an alternative flap. While maintaining the epithelium in an area of the size of the fistula, the remaining skin layer was de-epithelialized to facilitate adherence to the airway mucosa (Fig. 4).

For this particular report, the gastric tract was preserved in five patients. In one patient, preparation of a second muscle flap was required when intraoperative dissection revealed that the intercostal pedicle for the planned flap had been sectioned by a suture from prior thoracotomy, despite harvesting of the initial flap from two intercostal spaces inferiorly. Of these six patients, three were alive and required reoperation for residual fistula. Three patients had died due to massive gastrointestinal bleeding, mesenteric ischemia, and multiorgan failure, respectively. These three patients required vasopressor support preoperatively, and two had also received ECMO.

Tracheobronchoesophageal fistula is a rare and life-threatening complication of the surgical treatment of esophageal cancer. Fistulae lead to microbial overgrowth, resulting in pulmonary infection, septic shock, and, ultimately, organ failure. As

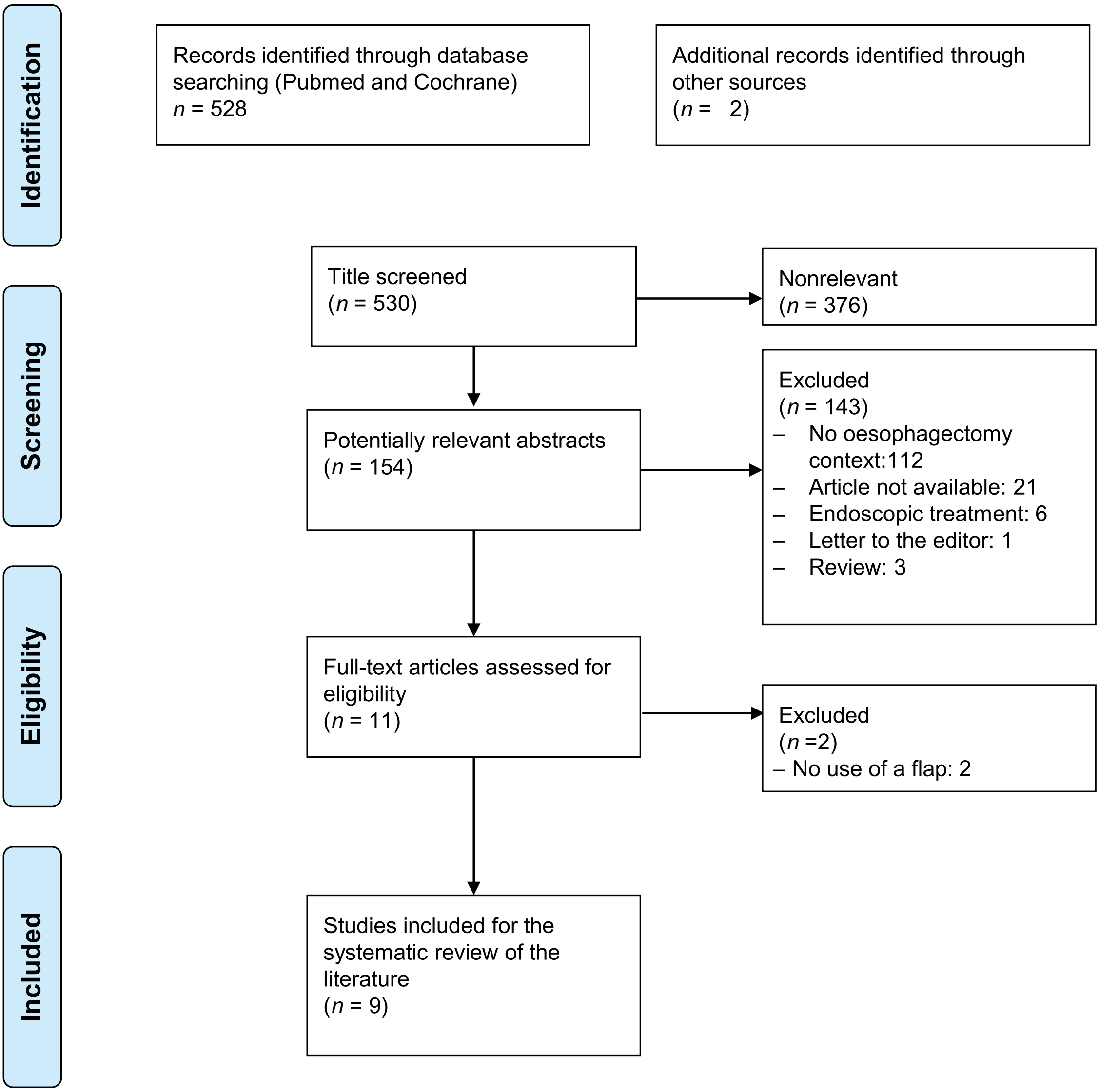

Figure 3. PRISMA flow chart for repair of acquired aerodigestive tract fistula following esophagectomy.

multiorgan failure severe enough to require vasopressor or ECMO support is associated with greater morbidity and mortality, rapid and precautionary diagnosis and surgical intervention before visceral failure are imperative. Currently, no guideline specifies the best strategy; endoprosthesis treatment is often chosen as a first-line therapy because of its availability and relative ease, although the outcome of stent coverage is poor.[104] In contrast, interposition flap repair is more complex and often deferred to a specialized team but should be considered. After initial stabilization, an intercostal pedicled flap can be prepared as an initial phase of reoperation, allowing direct closure of the donor site. The flap has a long pedicle with a pivot point close to the trachea that enables preservation of the gastric conduit and avoids tracheoesophageal compression.

Other complications that may influence the conduit or anastomosis

Pathophysiology of postoperative pulmonary complication

The reported incidence of postoperative pulmonary complication (POPC) ranges from 8% to 36%;

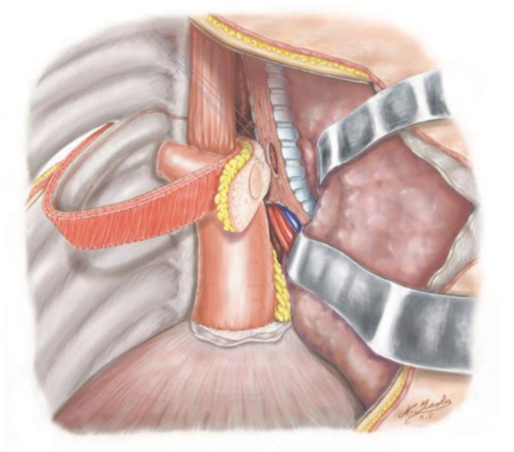

Figure 4. Skin perforator flap pedicled by intercostal muscle.

this variation may arise from the differences in definition for POPC.[105] In some reports, respiratory complications are defined by therapeutic criteria such as the use of interventions, including the need for and the duration of ventilatory assistance.[106] It is also defined as an ICU stay longer than 5 days.[107] In some reports, all abnormalities in the lungs and pleura after esophageal resection are defined as respiratory complications.[108] The lack of standardized definitions of POPC precludes valid comparisons of incidence rates across such studies. Defined grading of surgical complications, consisting of five tiers of increasing severity, has been suggested to standardize the definition of surgical complications and to increase comparability of the data from different studies.[109] This schema does not distinguish respiratory complications related to the technical aspects of the surgical procedure from respiratory complications due to other factors.

Preoperative, intraoperative, and postoperative factors have been associated with pulmonary complications after esophagectomy for cancer. Preoperative factors for POPC include age, nutritional status, use of induction therapy, baseline pulmonary function, ethanol use, smoking history, and poor performance status. Intraoperative details include stage, location of tumor, surgical approach, estimated blood loss, length of surgical procedure, entry into two separate body cavities, and disruption of bronchial innervation or lymphatic circulation. Postoperative causes include pulmonary hygiene, vocal cord paralysis, RLN palsy, and postoperative respiratory muscle dysfunction.[110]

Aged patients are more likely to have underlying, subclinical swallowing disorders, thus predisposing such patients to postoperative complications such as aspiration and pneumonia.[111] The high-risk factors for POPC in the elderly were identified as presence of comorbid diseases, such as tuberculosis, chronic obstructive pulmonary disease, pleural adhesion, or lung fibrosis. Preoperative induction chemoradiation was reported to be associated with more pneumonia, impaired pulmonary gas exchange, lower carbon dioxide diffusing capacity of the lungs, and development of acute respiratory distress syndrome. This latter complication can lead to prolonged postoperative mechanical ventilation and results in higher in-hospital mortality.[110]

Among intraoperative factors, greater blood loss and longer operation duration were reported to be associated with more POPCs and mortalities. Tumor location and the type and level of anastomosis also affect POPCs. POPC was fourfold higher for three-field incision resections for more proximal tumors than Ivor Lewis esophagectomy for distal esophageal tumors, possibly related to the greater prevalence of RLN injuries for patients whose operation included cervical dissection.[112,113]

Postoperatively, incisional pain was reported to be associated with more POPCs, which may be reduced by avoidance of thoracic incisions such as transhiatal esophagectomy, or reduced incisions such as minimally invasive esophagectomy.[114] Disorders including swallowing abnormalities, dysphagia, and poor airway protection are the most prevalent causes of respiratory complications after esophagectomy. Postoperative laryngopharyngeal dysfunction is most commonly attributed to RLN injury during surgery with resultant vocal cord dysfunction and manifests clinically by hoarseness, ineffective cough, dysphagia, and aspiration.[115] It is reported that 15.6–33.0% of patients who underwent esophagectomy had RLN injury or vocal cord paralysis by indirect laryngoscopy. Nearly 50% of patients who had vocal cord paralysis developed respiratory complications, compared with 27% of those who did not have documented RLN injury.[116]

Strategies to reduce pulmonary complications after esophagectomy should be implemented and directed to minimize the above risk factors. In

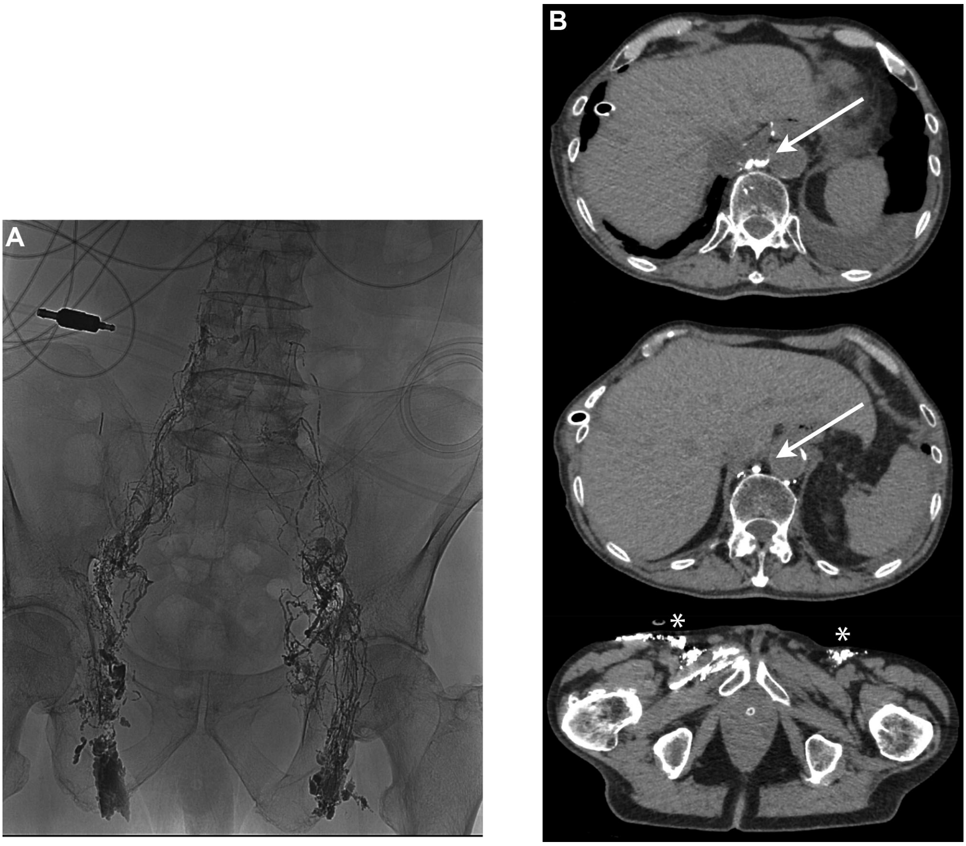

Figure 5. Percutaneous management of postoperative chylothorax. (A) Lymphangiography demonstrating opacification with lipiodol; efferent lymphatics were monitored by fluoroscopy until the lipiodol reached L3. (B) Control CT scan. Visualization of the lipiodol in the thoracic duct (arrow) several days after the procedure and in the inguinal node (asterisk).

turn, reduction of pulmonary complications may also minimize anastomotic complications.[117,118] Preoperative cardiopulmonary rehabilitation may help reduce rates of pulmonary complications for patients with poor cardiopulmonary reserve in some studies. Breathing exercises, including deep and slow abdominal breathing and coughing, can promote clearance of respiratory secretions. Cessation of smoking 4 weeks before esophagectomy has been shown to reduce rates of pulmonary complications. The use of expectorant, bronchodilator, inhaled steroids, and antimicrobial therapy as appropriate may reduce the incidence of POPCs.[119] During operation, meticulous surgical technique should be performed to avoid RLN injury and blood loss, while reducing the operating time as much as possible. Adequate postoperative analgesia utilizing epidural analgesia can reduce pulmonary complications. Vocal cord medialization after RLN injury can improve outcomes, such as hoarseness, dysphagia, dyspnea, aspiration, pneumonia, and weight loss. Vocal cord interventions should be performed as soon as possible after recognition of RLN injury.[120,121]

Indications for lymphangiography in the treatment of chylothorax after esophagectomy

In the modern era of upper gastrointestinal surgery, postoperative chylothorax is a dramatic complication that occurs between 1% and 9%[122–124] of the time after esophagectomy for cancer.[123–125] Although a rare event, chylothorax affects the postoperative morbidity by promoting the occurrence of pneumonia, with respiratory failure, malnutrition, and death in 20% of cases.[125] Currently, the debate is not completely resolved whether to perform systematic dissection of the thoracic duct, although this practice can prevent the occurrence of

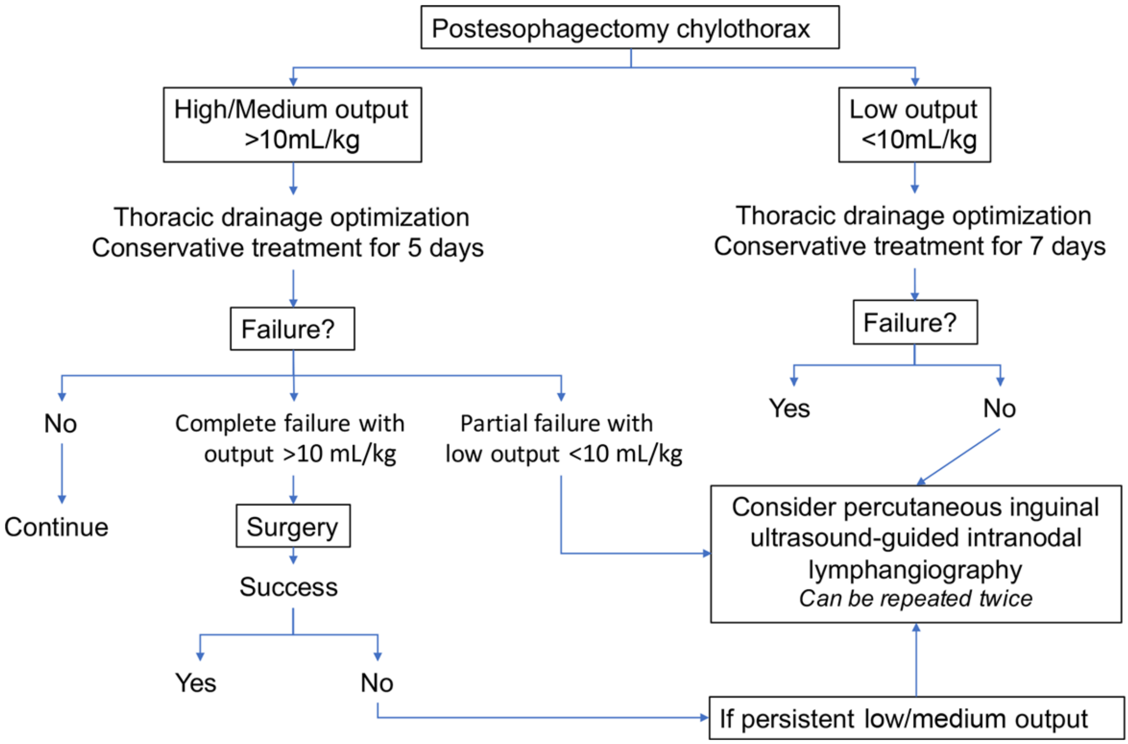

Figure 6. Treatment algorithm proposed to manage postesophagectomy chylothorax.

severe chylothorax.[126] Many therapeutic options for postoperative chylothorax, including conservative treatment, lymphangiography, and surgical revision, have been described. The optimal management is still under debate both in relation to timing and treatment modalities.

Postoperative chylothorax can be classified into three categories according to the daily output (volume/kg): low, medium, and high drain output.[124] Brinkmann *et al.* and Dugue *et al.* advocate a daily output threshold of 10 mL/kg body weight before considering thoracic duct ligation,[124,127] but the timing for surgical revision after failure of conservative treatment, which can include total parenteral nutrition or medium chain triglyceride diets, is still unclear.[128–130] Among patients with high or medium output chylothorax, high mortality rates associated with nonoperative management dictate earlier surgical revision, which has clinical success of up to 100%. The optimal management of patient with low-volume chylothorax is also more questionable, although the prolonged wait time that accompanies nonoperative treatment is not without consequences.

Lymphangiography has been considered an alternative to surgical intervention with reported success rates of pedal lymphangiography approaching 51%.[131] The technical expertise needed for this approach has limited its development and probably the success of pedal lymphangiography. Recently, percutaneous inguinal ultrasound-guided intranodal lymphangiography has been shown to be effective for management of chylothorax. The inguinal approach (Fig. 5A), contrary to pedal lymphangiography, which can be time-consuming and requires an experienced operator, is relatively easy, minimally invasive, rapid, and reliable. As described, this procedure does not require thoracic duct catheterization[132] and simplifies catheter-based management considerably. The inflammatory reaction caused by the lipiodol injectate acts as both a sclerosant as well as an embolic agent (Fig. 5B).[131] Efficacy cannot be assessed until 3 weeks, based on complete symptom regression and/or effusion regression on CT or in the chest tube. In our experience, the technical success rate is 100%, although in some cases repeat lymphangiography is needed to approach a clinical success around 80%. This technique can be easily repeated in cases of incomplete resolution but the maximum cumulative dose of lipiodol injected should be 20 mL. Above this dose, a risk of toxicity exists with symptomatic pulmonary arterial embolization of the lipiodol.[133] Lymphangiography can also be proposed in cases of repeat surgery failure.[134] This approach is an encouraging alternative to nonoperative conservative treatment and should be considered after failure of redone thoracic duct ligation or even as primary therapy for postoperative chylothorax. The consequences of postoperative chylothorax should not be discounted and this approach can be safely proposed for treatment of patients with refractory medium/low output chylothorax after esophagectomy. While the timing for such interventions should be defined by robust studies, this is limited by the low prevalence of this postoperative complication. A treatment algorithm strategy to manage chylothorax after esophagectomy is described (Fig. 6).

Acknowledgments

K.C. acknowledges funding from the Beijing Municipal Administration of Hospitals Incubating Program (PX2018044), and the Beijing Municipal Administration of Hospitals Clinical Medicine Development, Special Funding Support (ZYLX201509).

Competing interests

The authors declare no competing interests.

References

1. Kassis, E.S., A.S. Kosinski, P. Ross, Jr., *et al.* 2013. Predictors of anastomotic leak after esophagectomy: an analysis of the Society of Thoracic Surgeons General Toracic Database. *Ann. Thorac. Surg.* **96:** 1919–1926.
2. Seesing, M.F.J., S.S. Gisbertz, L. Goense, *et al.* 2017. A propensity score matched analysis of open versus minimally invasive transthoracic esophagectomy in the Netherlands. *Ann. Surg.* **266:** 839–846.
3. Junemann-Ramirez, M., M.Y. Awan, Z.M. Khan, & J.S. Rahamim. 2005. Anastomotic leakage post-esophagogastrectomy for esophageal carcinoma: retrospective analysis of predictive factors, management and influence on longterm survival in a high volume centre. *Eur. J. Cardiothorac. Surg.* **27:** 3–7.
4. van Workum, F., J. van der Maas, F.J. van den Wildenberg, *et al.* 2017. Improved functional results after minimally invasive esophagectomy: intrathoracic versus cervical anastomosis. *Ann. Thorac. Surg.* **103:** 267–273.
5. Markar, S., C. Gronnier, A. Duhamel, *et al.* 2015. The impact of severe anastomotic leak on long-term survival and cancer recurrence after surgical resection for esophageal malignancy. *Ann. Surg.* **262:** 972–980.
6. Low, D.E., M.K. Kuppusamy, D. Alderson, *et al.* 2017. Benchmarking complications associated with esophagectomy. *Ann. Surg.* https://doi.org/10.1097/SLA.0000000000002611.
7. Griffin, S.M., P.J. Lamb, S.M. Dresner, *et al.* 2001. Diagnosis and management of a mediastinal leak following radical oesophagectomy. *Br. J. Surg.* **88:** 1346–1351.
8. Lagarde, S.M., J.D. de Boer, F.J. ten Kate, *et al.* 2008. Postoperative complications after esophagectomy for adenocarcinoma of the esophagus are related to timing of death due to recurrence. *Ann. Surg.* **247:** 71–76.
9. Schaheen, L., S.H. Blackmon & K.S. Nason. 2014. Optimal approach to the management of intrathoracic esophageal leak following esophagectomy: a systematic review. *Am. J. Surg.* **208:** 536–543.
10. Jones, C.E. & T.J. Watson. 2015. Anastomotic leakage following esophagectomy. *Thorac. Surg. Clin.* **25:** 449–459.
11. Waitzberg, D.L., H. Saito, L.D. Plank, *et al.* 2006. Postsurgical infections are reduced with specialized nutrition support. *World J. Surg.* **30:** 1592–1604.
12. Page, R.D., A. Asmat, J. McShane, *et al.* 2013. Routine endoscopy to detect anastomotic leakage after esophagectomy. *Ann. Thorac. Surg.* **95:** 292–298.
13. Goense, L., P.S. van Rossum, J.P. Ruurda, *et al.* 2016. Radiation to the gastric fundus increases the risk of anastomotic leakage after esophagectomy. *Ann. Thorac. Surg.* **102:** 1798–1804.
14. Kechagias, A., P.S.N. van Rossum, J.P. Ruurda, *et al.* 2016. Ischemic conditioning of the stomach in the prevention of esophagogastric anastomotic leakage after esophagectomy. *Ann. Thorac. Surg.* **101:** 1614–1623.
15. Wang, W.P., Q. Gao, K.N. Wang, *et al.* 2013. A prospective randomized controlled trial of semimechanical versus hand-sewn or circular stapled esophagogastrostomy for prevention of anastomotic stricture. *World J. Surg.* **37:** 1043–1050.
16. Goense, L., W.A. van Dijk, J.A. Govaert, *et al.* 2017. Hospital costs of complications after esophagectomy for cancer. *Eur. J. Surg. Oncol.* **43:** 696–702.
17. Goense, L., P.S. van Rossum, M. Tromp, *et al.* 2017. Intraoperative and postoperative risk factors for anastomotic leakage and pneumonia after esophagectomy for cancer. *Dis. Esophagus* **30:** 1–10.
18. Rutegard, M., P. Lagergren, I. Rouvelas, *et al.* 2012. Intrathoracic anastomotic leakage and mortality after esophageal cancer resection: a population-based study. *Ann. Surg. Oncol.* **19:** 99–103.
19. Degisors, S., A. Pasquer, F. Renaud, *et al.* 2017. Are thoracotomy and/or intrathoracic anastomosis still predictors of postoperative mortality after esophageal cancer surgery? A nationwide study. *Ann. Surg.* **266:** 854–862.
20. Siewert, J.R., H.J. Stein & H. Bartels. 2004. [Anastomotic leaks in the upper gastrointestinal tract]. *Chirurg* **75:** 1063–1070.
21. Blewett, C.J., J.D. Miller, J.E. Young, *et al.* 2001. Anastomotic leaks after esophagectomy for esophageal cancer:

a comparison of thoracic and cervical anastomoses. *Ann. Thorac. Cardiovasc. Surg.* **7:** 75–78.

22. Gooszen, J.A.H., L. Goense, S.S. Gisbertz, *et al.* 2018. Intrathoracic versus cervical anastomosis and predictors of anastomotic leakage after oesophagectomy for cancer. *Br. J. Surg.* **105:** 552–560.
23. Daster, S., S.D. Soysal, L. Stoll, *et al.* 2014. Long-term quality of life after Ivor Lewis esophagectomy for esophageal cancer. *World J. Surg.* **38:** 2345–2351.
24. Klink, C.D., M. Binnebosel, J. Otto, *et al.* 2012. Intrathoracic versus cervical anastomosis after resection of esophageal cancer: a matched pair analysis of 72 patients in a single center study. *World J. Surg. Oncol.* **10:** 159.
25. Egberts, J.H., B. Schniewind, B. Bestmann, *et al.* 2008. Impact of the site of anastomosis after oncologic esophagectomy on quality of life—a prospective, longitudinal outcome study. *Ann. Surg. Oncol.* **15:** 566–575.
26. Chasseray, V.M., G.K. Kiroff, J.L. Buard, *et al.* 1989. Cervical or thoracic anastomosis for esophagectomy for carcinoma. *Surg. Gynecol. Obstet.* **169:** 55–62.
27. Ribet, M., B. Debrueres & M. Lecomte-Houcke. 1992. Resection for advanced cancer of the thoracic esophagus: cervical or thoracic anastomosis? Late results of a prospective randomized study. *J. Thorac. Cardiovasc. Surg.* **103:** 784–789.
28. Walther, B., J. Johansson, F. Johnsson, *et al.* 2003. 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.* **238:** 803–812; discussion 812–814.
29. Okuyama, M., S. Motoyama, H. Suzuki, *et al.* 2007. Handsewn cervical anastomosis versus stapled intrathoracic anastomosis after esophagectomy for middle or lower thoracic esophageal cancer: a prospective randomized controlled study. *Surg. Today* **37:** 947–952.
30. Biere, S.S., K.W. Maas, M.A. Cuesta, *et al.* 2011. Cervical or thoracic anastomosis after esophagectomy for cancer: a systematic review and meta-analysis. *Dig. Surg.* **28:** 29–35.
31. Holscher, A.H., P.M. Schneider, C. Gutschow, *et al.* 2007. Laparoscopic ischemic conditioning of the stomach for esophageal replacement. *Ann. Surg.* **245:** 241–246.
32. Chen, K.N. 2014. Managing complications I: leaks, strictures, emptying, reflux, chylothorax. *J. Thorac. Dis.* **6:** S355–S363.
33. Blencowe, N.S., S. Strong, A.G. McNair, *et al.* 2012. Reporting of short-term clinical outcomes after esophagectomy: a systematic review. *Ann. Surg.* **255:** 658–666.
34. Low, D.E., D. Alderson, I. Cecconello, *et al.* 2015. International consensus on standardization of data collection for complications associated with esophagectomy: Esophagectomy Complications Consensus Group (ECCG). *Ann. Surg.* **262:** 286–294.
35. Lerut, T., W. Coosemans, G. Decker, *et al.* 2002. Anastomotic complications after esophagectomy. *Dig. Surg.* **19:** 92–98.
36. Bruce, J., Z.H. Krukowski, G. Al-Khairy, *et al.* 2001. Systematic review of the definition and measurement of anastomotic leak after gastrointestinal surgery. *Br. J. Surg.* **88:** 1157–1168.
37. Stippel, D.L., C. Taylan, W. Schroder, *et al.* 2005. Supraventricular tachyarrhythmia as early indicator of a complicated course after esophagectomy. *Dis. Esophagus* **18:** 267–273.
38. Whooley, B.P., S. Law, A. Alexandrou, *et al.* 2001. Critical appraisal of the significance of intrathoracic anastomotic leakage after esophagectomy for cancer. *Am. J. Surg.* **181:** 198–203.
39. Dutta, S., G.M. Fullarton, M.J. Forshaw, *et al.* 2011. Persistent elevation of C-reactive protein following esophagogastric cancer resection as a predictor of postoperative surgical site infectious complications. *World J. Surg.* **35:** 1017–1025.
40. Baker, E.H., J.S. Hill, M.K. Reames, *et al.* 2016. Drain amylase aids detection of anastomotic leak after esophagectomy. *J. Gastrointest. Oncol.* **7:** 181–188.
41. Raman, V., K.L. Moodie, O.O. Ofoche, *et al.* 2017. Endoscopy after esophagectomy: safety demonstrated in a porcine model. *J. Thorac. Cardiovasc. Surg.* **154:** 1152–1158.
42. Maish, M.S., S.R. DeMeester, E. Choustoulakis, *et al.* 2005. The safety and usefulness of endoscopy for evaluation of the graft and anastomosis early after esophagectomy and reconstruction. *Surg. Endosc.* **19:** 1093–1102.
43. Hogan, B.A., D.C. Winter, D. Broe, *et al.* 2008. Prospective trial comparing contrast swallow, computed tomography and endoscopy to identify anastomotic leak following oesophagogastric surgery. *Surg. Endosc.* **22:** 767–771.
44. Nederlof, N., J. de Jonge, T. de Vringer, *et al.* 2017. Does routine endoscopy or contrast swallow study after esophagectomy and gastric tube reconstruction change patient management? *J. Gastrointest. Surg.* **21:** 251–258.
45. Schaible, A., P. Sauer, W. Hartwig, *et al.* 2014. Radiologic versus endoscopic evaluation of the conduit after esophageal resection: a prospective, blinded, intraindividually controlled diagnostic study. *Surg. Endosc.* **28:** 2078–2085.
46. Schaible, A., A. Ulrich, U. Hinz, *et al.* 2016. Role of endoscopy to predict a leak after esophagectomy. *Langenbecks Arch. Surg.* **401:** 805–812.
47. Tanomkiat, W. & W. Galassi. 2000. Barium sulfate as contrast medium for evaluation of postoperative anastomotic leaks. *Acta Radiol.* **41:** 482–485.
48. Jones, C.M., R. Heah, B. Clarke, *et al.* 2015. Should routine radiological assessment of anastomotic integrity be performed after oesophagectomy with cervical anastomosis? Best evidence topic (BET). *Int. J. Surg.* **15:** 90–94.
49. Solomon, D.G., C.T. Sasaki & R.R. Salem. 2012. An evaluation of the routine use of contrast radiography as a screening test for cervical anastomotic integrity after esophagectomy. *Am. J. Surg.* **203:** 467–471.
50. Hu, Z., X. Wang, X. An, *et al.* 2017. The diagnostic value of routine contrast esophagram in anastomotic leaks after esophagectomy. *World J. Surg.* **41:** 2062–2067.
51. Brams, A., P. Bulois, V. Maunoury, *et al.* 2008. [Treatment of thoracic anastomotic leaks after oesophagectomy with

self-expanding and extractible covered stent]. *Gastroenterol. Clin. Biol.* **32:** 41–45.
52. Strauss, C., F. Mal, T. Perniceni, *et al.* 2010. Computed tomography versus water-soluble contrast swallow in the detection of intrathoracic anastomotic leak complicating esophagogastrectomy (Ivor Lewis): a prospective study in 97 patients. *Ann. Surg.* **251:** 647–651.
53. Cools-Lartigue, J., A. Andalib, A. Abo-Alsaud, *et al.* 2014. Routine contrast esophagram has minimal impact on the postoperative management of patients undergoing esophagectomy for esophageal cancer. *Ann. Surg. Oncol.* **21:** 2573–2579.
54. Lantos, J.E., M.S. Levine, S.E. Rubesin, *et al.* 2013. Comparison between esophagography and chest computed tomography for evaluation of leaks after esophagectomy and gastric pull-through. *J. Thorac. Imaging* **28:** 121–128.
55. Goense, L., P.M.C. Stassen, F.J. Wessels, *et al.* 2017. Diagnostic performance of a CT-based scoring system for diagnosis of anastomotic leakage after esophagectomy: comparison with subjective CT assessment. *Eur. Radiol.* **27:** 4426–4434.
56. Upponi, S., A. Ganeshan, H. D'Costa, *et al.* 2008. Radiological detection of post-oesophagectomy anastomotic leak—a comparison between multidetector CT and fluoroscopy. *Br. J. Radiol.* **81:** 545–548.
57. Dickinson, K.J. & S.H. Blackmon. 2015. Management of conduit necrosis following esophagectomy. *Thorac. Surg. Clin.* **25:** 461–470.
58. Gockel, I., S. Niebisch, C.J. Ahlbrand, *et al.* 2016. Risk and complication management in esophageal cancer surgery: a review of the literature. *Thorac. Cardiovasc. Surg.* **64:** 596–605.
59. Messager, M., M. Warlaumont, F. Renaud, *et al.* 2017. Recent improvements in the management of esophageal anastomotic leak after surgery for cancer. *Eur. J. Surg. Oncol.* **43:** 258–269.
60. Pacheco, P.E., S.M. Hill, S.M. Henriques, *et al.* 2013. The novel use of intraoperative laser-induced fluorescence of indocyanine green tissue angiography for evaluation of the gastric conduit in esophageal reconstructive surgery. *Am. J. Surg.* **205:** 349–352; discussion 352–353.
61. Gurtner, G.C., G.E. Jones, P.C. Neligan, *et al.* 2013. Intraoperative laser angiography using the SPY system: review of the literature and recommendations for use. *Ann. Surg. Innov. Res.* **7:** 1.
62. Zehetner, J., S.R. DeMeester, E.T. Alicuben, *et al.* 2015. Intraoperative assessment of perfusion of the gastric graft and correlation with anastomotic leaks after esophagectomy. *Ann. Surg.* **262:** 74–78.
63. Haverkamp, L., M.F.J. Seesing, J.P. Ruurda, *et al.* 2017. Worldwide trends in surgical techniques in the treatment of esophageal and gastroesophageal junction cancer. *Dis. Esophagus* **30:** 1–7.
64. Turkyilmaz, A., A. Eroglu, Y. Aydin, *et al.* 2009. The management of esophagogastric anastomotic leak after esophagectomy for esophageal carcinoma. *Dis. Esophagus* **22:** 119–126.
65. van Workum, F., S.A. Bouwense, M.D. Luyer, *et al.* 2016. Intrathoracic versus cervical anastomosis after minimally invasive esophagectomy for esophageal cancer: study protocol of the ICAN randomized controlled trial. *Trials* **17:** 505.
66. Vashist, Y., G. Cataldigermen, A. König, *et al.* 2009. Management von Anastomoseninsuffizienz nach Ösophagusresektion. *Z. Gastroenterol.* **47:** P021.
67. Cassivi, S.D. 2004. Leaks, strictures, and necrosis: a review of anastomotic complications following esophagectomy. *Semin. Thorac. Cardiovasc. Surg.* **16:** 124–132.
68. Nederlof, N., H.W. Tilanus, T.C. Tran, *et al.* 2011. End-to-end versus end-to-side esophagogastrostomy after esophageal cancer resection: a prospective randomized study. *Ann. Surg.* **254:** 226–233.
69. Saluja, S.S., S. Ray, S. Pal, *et al.* 2012. Randomized trial comparing side-to-side stapled and hand-sewn esophagogastric anastomosis in neck. *J. Gastrointest. Surg.* **16:** 1287–1295.
70. Veeramootoo, D., R. Parameswaran, R. Krishnadas, *et al.* 2009. Classification and early recognition of gastric conduit failure after minimally invasive esophagectomy. *Surg. Endosc.* **23:** 2110–2116.
71. Nishikawa, K., T. Fujita, M. Yuda, *et al.* 2016. Early postoperative endoscopy for targeted management of patients at risks of anastomotic complications after esophagectomy. *Surgery* **160:** 1294–1301.
72. Dasari, B.V., D. Neely, A. Kennedy, *et al.* 2014. The role of esophageal stents in the management of esophageal anastomotic leaks and benign esophageal perforations. *Ann. Surg.* **259:** 852–860.
73. D'Cunha, J., N.M. Rueth, S.S. Groth, *et al.* 2011. Esophageal stents for anastomotic leaks and perforations. *J. Thorac. Cardiovasc. Surg.* **142:** 39–46.e1.
74. Siersema, P.D. 2005. Treatment of esophageal perforations and anastomotic leaks: the endoscopist is stepping into the arena. *Gastrointest. Endosc.* **61:** 897–900.
75. Sousa, P., A. Castanheira, D. Martins, *et al.* 2017. Treatment of postoperative leaks of the upper gastrointestinal tract with colonic self-expandable metal stents. *GE Port. J. Gastroenterol.* **24:** 169–175.
76. Ngamruengphong, S., R.Z. Sharaiha, A. Sethi, *et al.* 2016. Endoscopic suturing for the prevention of stent migration in benign upper gastrointestinal conditions: a comparative multicenter study. *Endoscopy* **48:** 802–808.
77. Shim, C.S., Y.D. Cho, J.H. Moon, *et al.* 2001. Fixation of a modified covered esophageal stent: its clinical usefulness for preventing stent migration. *Endoscopy* **33:** 843–848.
78. Choi, C.W., D.H. Kang, H.W. Kim, *et al.* 2017. Full covered self-expandable metal stents for the treatment of anastomotic leak using a silk thread. *Medicine* **96:** e7439.
79. Freeman, R.K., A.J. Ascioti, M. Dake, *et al.* 2015. An assessment of the optimal time for removal of esophageal stents used in the treatment of an esophageal anastomotic leak or perforation. *Ann. Thorac. Surg.* **100:** 422–428.
80. Laukoetter, M.G., R. Mennigen, P.A. Neumann, *et al.* 2017. Successful closure of defects in the upper gastrointestinal tract by endoscopic vacuum therapy (EVT): a prospective cohort study. *Surg. Endosc.* **31:** 2687–2696.

81. Mennigen, R., N. Senninger & M.G. Laukoetter. 2015. Endoscopic vacuum therapy of esophageal anastomotic leakage. *Gastrointest. Endosc.* **82:** 397.
82. Wedemeyer, J., M. Brangewitz, S. Kubicka, *et al.* 2010. Management of major postsurgical gastroesophageal intrathoracic leaks with an endoscopic vacuum-assisted closure system. *Gastrointest. Endosc.* **71:** 382–386.
83. Hwang, J.J., Y.S. Jeong, Y.S. Park, *et al.* 2016. Comparison of endoscopic vacuum therapy and endoscopic stent implantation with self-expandable metal stent in treating postsurgical gastroesophageal leakage. *Medicine* **95:** e3416.
84. Gubler, C., P.M. Schneider & P. Bauerfeind. 2013. Complex anastomotic leaks following esophageal resections: the new stent over sponge (SOS) approach. *Dis. Esophagus* **26:** 598–602.
85. Toshniwal, J., M. Zabielski, L.C. Fry, *et al.* 2012. Combination of the "bear claw" (over-the-scope-clip system) and fully covered stent for the treatment of post-operative anastomotic leak. *Endoscopy* **44**(Suppl. 2 UCTN): E288–E289.
86. Gaur, P., C. Lyons, T.M. Malik, *et al.* 2015. Endoluminal suturing of an anastomotic leak. *Ann. Thorac. Surg.* **99:** 1430–1432.
87. Willingham, F.F. & J.M. Buscaglia. 2015. Endoscopic management of gastrointestinal leaks and fistulae. *Clin. Gastroenterol. Hepatol.* **13:** 1714–1721.
88. Bohm, G., A. Mossdorf, C. Klink, *et al.* 2010. Treatment algorithm for postoperative upper gastrointestinal fistulas and leaks using combined vicryl plug and fibrin glue. *Endoscopy* **42:** 599–602.
89. Wedemeyer, J., A. Schneider, M.P. Manns, *et al.* 2008. Endoscopic vacuum-assisted closure of upper intestinal anastomotic leaks. *Gastrointest. Endosc.* **67:** 708–711.
90. Brangewitz, M., T. Voigtlander, F.A. Helfritz, *et al.* 2013. Endoscopic closure of esophageal intrathoracic leaks: stent versus endoscopic vacuum-assisted closure, a retrospective analysis. *Endoscopy* **45:** 433–438.
91. Nakajima, M., H. Satomura, M. Takahashi, *et al.* 2014. Effectiveness of sternocleidomastoid flap repair for cervical anastomotic leakage after esophageal reconstruction. *Dig. Surg.* **31:** 306–311.
92. Taniguchi, D., H. Saeki, Y. Nakashima, *et al.* 2016. Development of fistula between esophagogastric anastomotic site and cartilage portion of trachea after subtotal esophagectomy for cervical esophageal cancer: a case report. *Surg. Case Rep.* **2:** 107.
93. Dent, B., S.M. Griffin, R. Jones, *et al.* 2016. Management and outcomes of anastomotic leaks after oesophagectomy. *Br. J. Surg.* **103:** 1033–1038.
94. Liberati, A., D.G. Altman, J. Tetzlaff, *et al.* 2009. The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate healthcare interventions: explanation and elaboration. *BMJ* **339:** b2700.
95. Azuma, S., M. Sakuraba, S. Azumi, *et al.* 2017. Repairing bronchoesophageal tube fistula using a contralateral latissimus dorsi musculocutaneous flap. *Plast. Reconstr. Surg. Glob. Open* **5:** e1484.
96. Hayashi, K., N. Ando, S. Ozawa, *et al.* 1999. Gastric tube-to-tracheal fistula closed with a latissimus dorsi myocutaneous flap. *Ann. Thorac. Surg.* **68:** 561–562.
97. Morita, M., H. Saeki, T. Okamoto, *et al.* 2015. Tracheobronchial fistula during the perioperative period of esophagectomy for esophageal cancer. *World J. Surg.* **39:** 1119–1126.
98. Sakatoku, Y., M. Fukaya, H. Fujieda, *et al.* 2017. Tracheoesophageal fistula after total resection of gastric conduit for gastro-aortic fistula due to gastric ulcer. *Surg. Case Rep.* **3:** 90.
99. Siu, K.F., W.I. Wei, K.H. Lam, *et al.* 1985. Use of the pectoralis major muscle flap for repair of a tracheoesophageal fistula. *Am. J. Surg.* **150:** 617–619.
100. Arimoto, J., A. Hatada, M. Kawago, *et al.* 2015. Closure of esophagotracheal fistula after esophagectomy for esophageal cancer. *Gen. Thorac. Cardiovasc. Surg.* **63:** 636–639.
101. Lambertz, R., A.H. Holscher, M. Bludau, *et al.* 2016. Management of tracheo- or bronchoesophageal fistula after Ivor Lewis esophagectomy. *World J. Surg.* **40:** 1680–1687.
102. Marty-Ane, C.H., M. Prudhome, J.M. Fabre, *et al.* 1995. Tracheoesophagogastric anastomosis fistula: a rare complication of esophagectomy. *Ann. Thorac. Surg.* **60:** 690–693.
103. Bertheuil, N., C. Cusumano, C. Meal, *et al.* 2017. Skin perforator flap pedicled by intercostal muscle for repair of a tracheobronchoesophageal fistula. *Ann. Thorac. Surg.* **103:** e571–e573.
104. Shin, J.H., H.Y. Song, G.Y. Ko, *et al.* 2004. Esophagorespiratory fistula: long-term results of palliative treatment with covered expandable metallic stents in 61 patients. *Radiology* **232:** 252–259.
105. D'Journo, X.B., P. Michelet, J.P. Avaro, *et al.* 2008. [Respiratory complications after oesophagectomy for cancer]. *Rev. Mal. Respir.* **25:** 683–694.
106. Kita, T., T. Mammoto & Y. Kishi. 2002. Fluid management and postoperative respiratory disturbances in patients with transthoracic esophagectomy for carcinoma. *J. Clin. Anesth.* **14:** 252–256.
107. Karl, R.C., R. Schreiber, D. Boulware, *et al.* 2000. Factors affecting morbidity, mortality, and survival in patients undergoing Ivor Lewis esophagogastrectomy. *Ann. Surg.* **231:** 635–643.
108. Doty, J.R., J.D. Salazar, A.A. Forastiere, *et al.* 2002. Postesophagectomy morbidity, mortality, and length of hospital stay after preoperative chemoradiation therapy. *Ann. Thorac. Surg.* **74:** 227–231; discussion 231.
109. Dindo, D., N. Demartines & P.A. Clavien. 2004. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann. Surg.* **240:** 205–213.
110. Liu, J.F., Q.Z. Wang, Y.M. Ping, *et al.* 2008. Complications after esophagectomy for cancer: 53-year experience with 20,796 patients. *World J. Surg.* **32:** 395–400.
111. Sauvanet, A., C. Mariette, P. Thomas, *et al.* 2005. Mortality and morbidity after resection for adenocarcinoma of the gastroesophageal junction: predictive factors. *J. Am. Coll. Surg.* **201:** 253–262.

112. Kinugasa, S., M. Tachibana, H. Yoshimura, *et al.* 2004. Postoperative pulmonary complications are associated with worse short- and long-term outcomes after extended esophagectomy. *J. Surg. Oncol.* **88:** 71–77.
113. Adachi, W., S. Koike, Y. Nimura, *et al.* 1996. Clinicopathologic characteristics and postoperative outcome in Japanese and Chinese patients with thoracic esophageal cancer. *World J. Surg.* **20:** 332–336.
114. Rentz, J., D. Bull, D. Harpole, *et al.* 2003. Transthoracic versus transhiatal esophagectomy: a prospective study of 945 patients. *J. Thorac. Cardiovasc. Surg.* **125:** 1114–1120.
115. Aviv, J.E., H. Liu, M. Parides, *et al.* 2000. Laryngopharyngeal sensory deficits in patients with laryngopharyngeal reflux and dysphagia. *Ann. Otol. Rhinol. Laryngol.* **109:** 1000–1006.
116. Gockel, I., W. Kneist, A. Keilmann, *et al.* 2005. Recurrent laryngeal nerve paralysis (RLNP) following esophagectomy for carcinoma. *Eur. J. Surg. Oncol.* **31:** 277–281.
117. Michelet, P., X.B. D'Journo, A. Roch, *et al.* 2005. Perioperative risk factors for anastomotic leakage after esophagectomy: influence of thoracic epidural analgesia. *Chest* **128:** 3461–3466.
118. Aminian, A., N. Panahi, R. Mirsharifi, *et al.* 2011. Predictors and outcome of cervical anastomotic leakage after esophageal cancer surgery. *J. Cancer Res. Ther.* **7:** 448–453.
119. Chumillas, S., J.L. Ponce, F. Delgado, *et al.* 1998. Prevention of postoperative pulmonary complications through respiratory rehabilitation: a controlled clinical study. *Arch. Phys. Med. Rehabil.* **79:** 5–9.
120. Law, S., K.H. Wong, K.F. Kwok, *et al.* 2004. Predictive factors for postoperative pulmonary complications and mortality after esophagectomy for cancer. *Ann. Surg.* **240:** 791–800.
121. Whooley, B.P., S. Law, S.C. Murthy, *et al.* 2001. Analysis of reduced death and complication rates after esophageal resection. *Ann. Surg.* **233:** 338–344.
122. Mishra, P.K., S.S. Saluja, D. Ramaswamy, *et al.* 2013. Thoracic duct injury following esophagectomy in carcinoma of the esophagus: ligation by the abdominal approach. *World J. Surg.* **37:** 141–146.
123. Lai, F.C., L. Chen, Y.R. Tu, *et al.* 2011. Prevention of chylothorax complicating extensive esophageal resection by mass ligation of thoracic duct: a random control study. *Ann. Thorac. Surg.* **91:** 1770–1774.
124. Brinkmann, S., W. Schroeder, K. Junggeburth, *et al.* 2016. Incidence and management of chylothorax after Ivor Lewis esophagectomy for cancer of the esophagus. *J. Thorac. Cardiovasc. Surg.* **151:** 1398–1404.
125. Shah, R.D., J.D. Luketich, M.J. Schuchert, *et al.* 2012. Postesophagectomy chylothorax: incidence, risk factors, and outcomes. *Ann. Thorac. Surg.* **93:** 897–903; discussion 903–904.
126. Crucitti, P., G. Mangiameli, T. Petitti, *et al.* 2016. Does prophylactic ligation of the thoracic duct reduce chylothorax rates in patients undergoing oesophagectomy? A systematic review and meta-analysis. *Eur. J. Cardiothorac. Surg.* **50:** 1019–1024.
127. Dugue, L., A. Sauvanet, O. Farges, *et al.* 1998. Output of chyle as an indicator of treatment for chylothorax complicating oesophagectomy. *Br. J. Surg.* **85:** 1147–1149.
128. Merigliano, S., D. Molena, A. Ruol, *et al.* 2000. Chylothorax complicating esophagectomy for cancer: a plea for early thoracic duct ligation. *J. Thorac. Cardiovasc. Surg.* **119:** 453–457.
129. Mery, C.M., B.S. Moffett, M.S. Khan, *et al.* 2014. Incidence and treatment of chylothorax after cardiac surgery in children: analysis of a large multi-institution database. *J. Thorac. Cardiovasc. Surg.* **147:** 678–686.e1; discussion 685–686.
130. Alexiou, C., M. Watson, D. Beggs, *et al.* 1998. Chylothorax following oesophagogastrectomy for malignant disease. *Eur. J. Cardiothorac. Surg.* **14:** 460–466.
131. Alejandre-Lafont, E., C. Krompiec, W.S. Rau, *et al.* 2011. Effectiveness of therapeutic lymphography on lymphatic leakage. *Acta Radiol.* **52:** 305–311.
132. Nadolski, G.J. & M. Itkin. 2012. Feasibility of ultrasound-guided intranodal lymphangiogram for thoracic duct embolization. *J. Vasc. Interv. Radiol.* **23:** 613–616.
133. Guermazi, A., P. Brice, C. Hennequin, *et al.* 2003. Lymphography: an old technique retains its usefulness. *Radiographics* **23:** 1541–1558; discussion 1559–1560.
134. Chen, C.Y., Y.H. Chen, E.L. Shiau, *et al.* 2016. Therapeutic role of ultrasound-guided intranodal lymphangiography in refractory cervical chylous leakage after neck dissection: report of a case and review of the literature. *Head Neck* **38:** E54–E60.
135. van Rossum, P.S., L. Haverkamp, H.M. Verkooijen, *et al.* 2015. Calcification of arteries supplying the gastric tube: a new risk factor for anastomotic leakage after esophageal surgery. *Radiology* **274:** 124–132.