

Original Article: Anastomotic leakage after thoracic esophagectomy for esophageal cancer: Systematic review and Meta-analysis

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ABSTRACT

Introduction: The symptoms of anastomotic leak often appear only at a late stage or are nonspecific, with many different diagnoses and treatments available with no clear consensus on the underlying mechanisms. The purpose of this review is to provide a brief summary of the existing literature on the definition and classification of thoracic esophagectomy anastomotic leak, its importance and prevalence, as well as the different risk factors, diagnoses and treatments. **Material and Methods:** Scopus and PubMed electronic databases were searched to identify articles published between 1995 and 2022 on AL after esophagectomy. Terms used include: "anastomotic leak," "esophageal cancer," "cervical," "intrathoracic," "diagnosis," "management," "risk factor," combined with Boolean "OR" function study Frequent references for further research and related publications are searched. There is limited English language. **Results:** Anastomotic leak is one of the most common complications after esophagectomy and is associated with increased morbidity and mortality. Many projects range from small studies to large collaborations aimed at identifying potential preoperative and perioperative risks and improving diagnostic and management procedures. Despite the increase in available data, many aspects of anastomotic leak remain problematic and no general guidelines exist. **Conclusion:** AL after esophagectomy has many causes, is complex, and can have serious complications that will later affect the outcome. Current treatment is based on an individualized approach and reliable international evidence will help improve the prevention and treatment of AL. Treatment and patient outcomes. Higher quality evidence for such guidelines is urgently needed. The introduction of the ECGG system is a first priority to provide an up-to-date international standard for comparing the results of treatment strategies.

Introduction

In the For patients with localized cancer, radical esophagectomy offers the best chance of cure. Anastomotic leak (AL)(Fig 1) is one of the most serious complications, causing significant

morbidity, prolonged hospitalization, use of heavy medical equipment [1], and increased risk of death. AL is associated with poor quality of life and increased mortality in the long term. Cancer recurrence increases the risk of long-term survival [2-4]. The prevalence of AL ranges from

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11.4% to 21.2%, and side effects range from 7.2% to 35%. Despite increasing research, the pathophysiology and causes of leakage remain unclear [5-7]. Although AL has various etiologies, tissue perfusion appears to play an important role in the development of fluid flow. In addition, the symptoms of anastomotic leak often appear only at a late stage or are nonspecific, with many different diagnoses and

treatments available with no clear consensus on the underlying mechanisms [8-10]. The purpose of this review is to provide a brief summary of the existing literature on the definition and classification of thoracic esophagectomy anastomotic leak, its importance and prevalence, as well as the different risk factors, diagnoses and treatments [11].

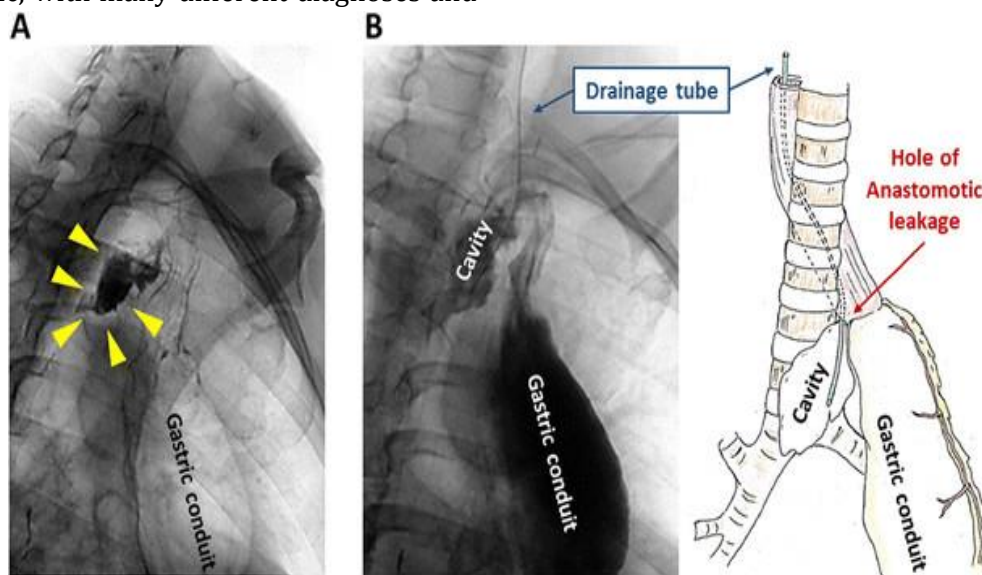


Figure 1: Anastomotic leakage after thoracic esophagectomy

Material and Methods

Scopus and PubMed electronic databases were searched to identify articles published between 1995 and 2022 on AL after esophagectomy. Terms used include: “anastomotic leak,” “esophageal cancer,” “cervical,” “intrathoracic,” “diagnosis,” “management,” “risk factor,” combined with Boolean “OR” function study. Frequent references for further research and related publications are searched. There is limited English language.

Results

The precise definition of AL after esophagectomy has been debated for a long time. In order to improve data transfer in centers, many tests have been designed to universally recognize and classify the severity of leakage and wound. The lack of a standard

procedure to define and document complications and quality measures after esophagectomy leads to some variation in the evaluation of its impact and outcome. The Clavien-Dindo classification is also included in the Standard 6 Classification and although it does not specifically mention surgery, it is recommended. Although various classifications of AL have been proposed, none has been widely accepted. Based on a review of 97 studies, Bruce et al (2001) proposed a set of definitions provided by Lerut et al (20027) and Price et al (2013). Seeking more precise definitions, the Esophagectomy Complications Consensus Group (ECCG) recently published a new grading system. 8 The ECCG criteria define AL as “the occurrence or description of lesions of the large intestine involving the esophagus, anastomoses, staple lines, or catheters” and is divided into

three types of severity. Consensus was also reached on three other postoperative complications: ductal necrosis, chyle leak, and nerve healing. The quality of the classification system is clearly demonstrated in a large study showing the results of 2704 esophagectomies and showing a reduction in the number of complications across 24 centres. Since the publication of these data, the ECGG protocol has increased to report outcomes after esophagectomy [12].

RISK FACTORS

Identifying risk factors for AL is important for prevention and treatment as well as optimization before and after treatment. Various comorbidities, use of neoadjuvant therapy, anastomosis sites, surgical procedures, and perioperative monitoring strategies and treatments are the most important and problematic risk factors for the development of AL. Some risks are modifiable and therefore can guide management of preoperative, intraoperative, and postoperative strategies for the patient. However, there is no consensus on which is the most determining factor in the development of AL, leading to a lack of reliable predictive models and risk assessment tools. First of all, good luck [13-15].

Comorbidities

Anatomical and physiological factors such as the absence of esophageal serosa in the esophageal anatomy and the presence of negative intrathoracic pressure may contribute to the development of AL. Malnutrition, such as previous malnutrition (albumin <3.0 g/dL), obesity (body mass [BMI] > 30 kg/m²) or underweight (BMI < 18.5 kg/m²), heart failure, hypertension, diabetes [16-18], kidney. Deficiency, steroids, and smoking have been associated with increased AL. Atherosclerotic calcification of the aorta and the arteries supplying the gastric tube has been identified as

an emerging risk factor in both cervical and intrathoracic ALs. The calcification scoring system may aid in patient selection, leading to earlier diagnosis of this potentially fatal complication [19-21].

Neoadjuvant treatment

Evidence about the effect of the extent and dosage of neoadjuvant chemoradiation on the occurrence of AL is conflicting, particularly regarding a 'safe' dose of radiation to the gastric fundus, the anastomotic region used in gastric tube reconstruction [22-24]. No significant association was observed in cervical anastomosis for an average radiation dose of 24.2 Gy, while exceeding a dose of 31 Gy seems to increase AL incidence [25]. In contrast, a large European multicenter study reported no impact of radiation up to 45 Gy on AL rate, as also confirmed by Nederlof, with an average of 41.1 Gy. Irrespective of AL incidence, irradiation of the upper mediastinum is associated with more severe complications [26].

Anastomotic location

A cervical anastomosis has a five times greater risk of leakage when compared to intrathoracic location. The main causes include the need for a longer gastric conduit, more likely positioned in the fundus (where the vascularity is more compromised), and increased risk of tension and/or compression at the junction between thorax and neck. The higher AL risk in the neck may also be influenced by the indication for this procedure (more proximal tumors and/or lymph node metastases, a higher radiation field and a more extended resection). However, the mortality rate is unaffected by the site of the anastomosis, although a cervical location may lead to increased recurrent laryngeal nerve paresis, wound infection, and longer hospital stay [27].

Surgical technique

The minimally invasive esophagectomy (laparoscopy and thoracoscopy) or the hybrid approach (laparoscopy and thoracotomy) have been introduced to minimize surgical trauma and reduce perioperative complications (particularly pulmonary infections) as compared to open surgery. Most studies show no difference in the incidence of AL between open and either minimally invasive or hybrid techniques [28-30]. If a value higher than AL is found, this would seem to be explained by the effect associated with the productivity increase curve, since least resistance is a complex method that requires long-term and appropriate training. b Regardless of the surgical method, precautions such as avoiding excessive traction, compression, or twisting of mechanical anastomoses and the wrong number of stitches or incomplete loops should be considered to reduce the risk of AL. Omentoplasty appears to be an important surgical procedure to prevent the formation of manual and mechanical anastomoses, as well as cervical and intrathoracic anastomoses [31-33]. The omentum will form adhesions with the underlying tissue, localizing underlying swelling and sealing small leaks.

Anastomotic technique

It is controversial which of the most commonly used esophageal anastomosis techniques has the lowest gas leakage rate. In general, cervical and intrathoracic anastomoses are usually performed using hand stitching and stitching, respectively [34-36]. Although single-layer continuous suture anastomosis is the most commonly used technique among hand sewing methods, some studies have shown that this rate is lower after two-layer anastomosis. Additionally, end-to-side anastomosis appears to have a lower incidence of leakage than the end-to-side technique, especially in cervical anastomoses [37]. Although some studies

support the superiority of manual suturing techniques over manual suturing techniques, their comparisons do not show clear differences between leaks and aftereffects. Similar AL values were obtained by comparing cords (25 mm and 29 mm) [38-40], cord and hand sewing technique. Therefore, regardless of the quality of the scientific evidence, differences in anastomosis technique do not appear to affect AL status.

Perioperative monitoring and therapy

Proper management of perioperative infections has an impact on the development of AL. In particular, hemodynamic control is important in protecting the risk of anastomosis by preventing the decrease of partial oxygen (pO_2), which is the main oxygen outlet in the abdominal cavity. Intraoperative fluid management and use of vasopressors require special attention. Although management of fluid restriction is becoming increasingly common to prevent complications after pulmonary and anastomotic surgery [41-43], excessive fluid restriction can also cause hypotension and anastomotic dehiscence. To improve fluid management, targeted therapy is planned in non-heart attack surgery based on three hemodynamic parameters (stroke volume, mean blood flow, pressure and cardiac output). This algorithm has also been used in cancer surgery, specifically focusing on the volume of blood vessels and monitoring the reduction in lung inflammation, mediastinal abscesses, and gastric tube necrosis [44-46].

Several studies have demonstrated the effectiveness of thoracic epidural analgesia (TEA) on intestinal perfusion during esophagectomy due to its improvement of microcirculation. TEA has a positive effect in reducing the incidence of AL, but general anesthesia should be avoided due to the risk of bleeding.

Administration of ephedrine during surgery appears to increase tissue perfusion in the gastric tube and aorta (thus reducing ischemia at the anastomotic site). This can be a useful tool in preventing leaks [47].

INTRAOPERATIVE INVESTIGATIONS

Gastric catheter tip ischemia (defined as graft hypoperfusion) is an important cause of esophagogastric AL. The etiology of ischemia is complex, but is mostly due to the inability of the right gastroepiploic vein alone to provide adequate blood supply to the entire canal. Despite significant advances in surgical techniques and procedures, perfusion-related complications such as ischemia and necrosis remain at very high levels of 2.5% to 20%. Complete ductal necrosis is a rare but devastating complication occurring in less than 3% of esophagectomies [48].

Intraoperative real-time monitoring of catheter perfusion status and the possibility of early catheter ischemia (which is still reversible) are important to select the best anastomosis site according to the vascular structure. If reconstruction of the gastric duct fails, another esophageal transposition (e.g., jejunal or colonic transposition) should be performed.

A variety of analytical or biochemical methods have been proposed to assess tissue perfusion, primarily including angiography, transmucosal oxygen saturation measurement, and intraoperative esophagogastric-duodenoscopy (as recently reviewed). Neither has been widely accepted.

Different optical methods such as laser Doppler flow measurement, fluorescence imaging, near-infrared imaging techniques have also been developed to evaluate perfusion performance (actual resolution of blood flow). Red spectroscopy, laser spotted contrast imaging, optical coherence tomography (OCT), and side-flow dark-field microscopy (SDF) were recently

reviewed in depth by Jansen, with the advantages and disadvantages of each.

No one can combine all the features of the best equipment, such as simplicity, contactlessness, wide view, depth resolution and many benefits. Fluorescence imaging (also known as indocyanine green fluorescein angiography) is currently the most widely used technique because it is easy to perform, non-contact, and has a wide angle of view. Fluorescence imaging based on injection of indocyanine green (ICG, a fluorescent molecule) and a near-infrared camera has many advantages, including assessment of microvascular networks and macroscopic examination of local body perfusion; The short plasma half-life of ICG allows multiplexing. Likewise, re-dosing time; It is easily removed from bile excretion, its use is allowed in patients with kidney disease. Further research has shown that it is safe, reliable and diagnostic (Figure 2).

Its biggest disadvantage is that perfusion cannot be measured directly (e.g. ml/min/g) and can only be measured with technical equipment. In fact, the use of fluorescence is associated with different beneficial effects, including microcirculation, blood flow and orientation. Additionally, the distance between the intestinal landmark and the anastomosis is associated with the risk of urine leakage (the longer the distance, the higher the risk). In addition, the initial development of ICG from the right gastroepiploic artery root to the stomach tip was used as a perfusion marker, and thus the 90-second rule was reported [49].

However, all measurements are given or subjective and cannot be translated into widely accepted and standardized methods, while attempts to determine values have not yet been accepted. Good results. Among other recently developed techniques, OCT and SDF are promising but only preliminary evidence is available in the literature. In particular, SDF not only microscopically measures intestinal

perfusion but also venous congestion, which appears to play an important role in the development of ischemia.

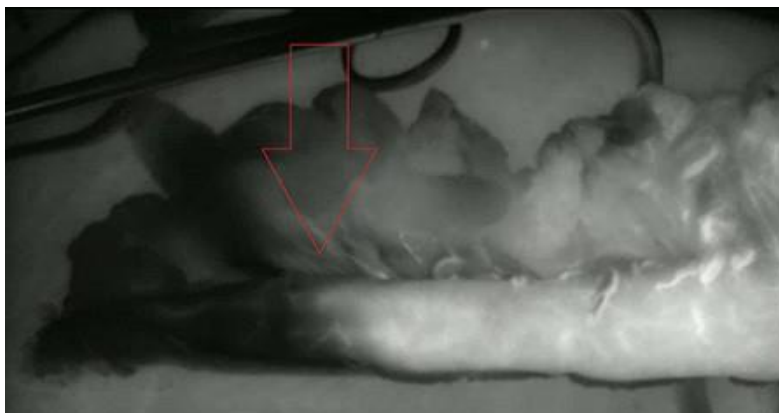


Figure 2: Gastric conduit before transfer to cervical region. This is a near infrared fluorescence view with the fluorescent signal displayed in white. A clear demarcation is noticed at the red arrow. The anastomosis was constructed within the fluorescent area.

ISCHEMIC PRECONDITIONING

Urschel has previously discussed ischemic preconditioning, which aims to improve tissue perfusion in the intestine and prevent latent ischemia.

This approach involves most or all of the gastrointestinal tract (except the gastroepiploic artery) (several days to a week before the decision and anastomosis) to allow time for the stomach to adjust to the reduced oxygenation that occurs during surgery.

Activate it to build pipelines. Vascular devascularization is achieved by preoperative arterial embolization or laparoscopic ligation. Although some positive results suggest a reduction in AL, clinical evidence regarding the effectiveness of ischemic preconditioning remains conflicting. Gastric preconditioning does not appear to reduce the overall rate of AL after esophagectomy but does appear to affect the severity of leakage [50].

This may be due to increased catheter resistance to ischemia rather than increased perfusion due to neovascularization. Ischemic preconditioning is still an active area of research, particularly due to its important role in preventing leakage.

DIAGNOSIS

There is still no consensus regarding the diagnostic criteria for AL, especially the timing and choice of diagnostic strategies. The following paragraphs summarize the general criteria for diagnosing AL, including evaluation of clinical signs and biochemical tests (e.g., blood and fluid tests), support with diagnostic equipment, and duration of the diagnostic process.

Clinical presentation

Clinical signs of leakage vary from asymptomatic to fulminant sepsis. Many factors such as location of the anastomosis, size of the defect, drainage ability and drainage management affect the clinical appearance. Common symptoms of AL include fever and abscess (if there is a cervical anastomosis); However, sometimes the first indication of an anastomotic defect may be just tachycardia, usually in the form of atrial fibrillation. A rash or induration appears at the neck incision, and there is obvious leakage of cervical salivary fluid, pus, or gas from the wound. In some cases, the infection can penetrate deep into the chest and form mediastinal abscess, pleural emphysema,

intrathoracic sepsis and tracheoesophageal fistula. Although both anastomoses are in the neck, these findings are more common after transthoracic esophagectomy than after transhiatal esophagectomy. This can be explained by differences in pleural anatomy. In transthoracic esophagectomy, the thoracic inlet is usually dissected, while in transdiaphragmatic esophagectomy the parietal pleura of the superior mediastinum is left and only the esophagus is dissected. This limits infection and prevents it from spreading into the pleural space. Additionally, negative thoracic pressure may cause continued leakage into the chest, especially in the transthoracic approach. The clinical signs of an intrathoracic leakage may vary from chest pain and dyspnea to bronchopneumonia, mediastinitis, and respiratory failure. Sepsis can progress to multi-organ failure. Other signs include the presence of saliva or gastric contents in the drain (if present) and persistent cough, especially on swallowing.

Biochemical analysis

Apart from clinical signs, some tests can raise the suspicion of a leakage. A high level of blood inflammatory biomarkers (C-reactive protein (CRP), procalcitonin, and white blood cell counts) is one of the first indicators of AL. C-reactive protein content seems to be the most informative test, both in cervical and intrathoracic anastomoses. A CRP value of approximately 17 mg/dL on postoperative day (POD) 3 has been determined to be an important determinant for the development of leakage. Amylase testing is another useful tool for early diagnosis. High amylase levels in the salivary glands are indicative of salivary glands and therefore indicate the presence of gas. Cut-off values for liquid amylase levels used in the literature to indicate potential AL range from 125 to 250 UI/L on POD 4. Although liquid amylase has comparable accuracy to Cervical

and intrathoracic anastomoses, it is not completely complete.

Diagnostic imaging

AL can be diagnosed using a variety of diagnostic methods, including swallowing imaging (esophagography), computed tomography (CT) and endoscopy.

Contrast swallow examination

Esophagography is a useful and safe method to evaluate the integrity of the anastomosis, provide information about the contour, remove spare catheters and evaluate pyloric patency. It has a special feature for the detection of AL and is indicated by the leakage of contrast material from the anastomosis or intrathoracic gastric cavity into the mediastinum, but the diagnostic results are not good. According to the review of Jones et al., sensitivity in the literature varies between 33% and 52%, with negative results for cervical anastomoses. Other disadvantages include the requirement of an electrophysiologist for reliable interpretation and the involvement of information communication (including sepsis or altered thirst or altered consciousness in humans, and adverse side effects and contraindications in sedated patients).

CT scan

CT scanning is a non-invasive, safe to use and widely used diagnostic technology. It has some advantages such as simultaneous imaging of the neck, chest and abdomen in a single examination; suitable for patients with limited mobility or serious illness; Visualization of the extent and location of extraluminal fluid that can be used percutaneously. Liquids; and the ability to cover a variety of diagnoses (such as pneumonia, abscess, pleural effusion, pneumothorax, or lung abnormalities). The main point of this diagnosis is that there are no consensus and objective criteria for detecting

radiation-induced leakage, resulting in low and inconsistent accuracy.

Diagnosis of bleeding on CT scan may be supported by the appearance of free gas or the presence of extraneous air, fluid, and/or foreign material in the mediastinum or by visualization of the walls of mediastinal blood vessels. However, since it is often seen after esophagectomy in the absence of AL, the presence of mediastinal air near the anastomosis is not clear. Oral administration of contrast material increases CT sensitivity, but this is associated with problems with sensitivity as described previously.

Incorporation of discrete, easily identifiable CT findings (e.g., mediastinal fluid and air, anastomotic wall discontinuities and fistulas) into a CT-based risk score as improved diagnosis. The validity of this method probably needs to be further validated in different locations to determine the uncertainty of the prediction model. Recently, a new screening method based on counting air bubbles (e.g., air density greater than 2 mm around the anastomosis and in the mediastinal space) has been proposed to increase the sensitivity of CT. More research is needed to find out whether this method will improve the quality of diagnosis.

Endoscopy

Upper gastrointestinal endoscopy is a safe and effective way to simultaneously diagnose and treat gas leaks. As seen in many clinical studies, intraluminal pressure generated during endoscopy does not increase the risk of anastomotic complications. Although endoscopy seems to have a lower diagnostic rate in uterine anastomosis (56% sensitivity), it is a reliable diagnostic method with a specificity and sensitivity of nearly 95%. It has many advantages: the ability to provide information about the capacity of the abdominal catheter and to detect changes in its integrity; Able to meet the criteria of intubated patients in the intensive

care environment; and avoiding verbal comparison situations.

Besides the need for an endoscopist, endoscopy also has important limitations: inability to visualize the area around the anastomosis (e.g. pleural effusions/collections, mediastinal collections associated with the aorta and trachea, etc.). In addition, patients in the ward must be sedated in order to perform this test. As a result, they often require transfer to the intensive care unit and periodic intubation, with the risk of respiratory distress.

In conclusion, every diagnosis has its pros and cons. While a CT scan is often preferred as the first test, endoscopy is often followed as a second test to confirm the CT diagnosis and begin treatment. Contrast swallowing test is still used in medicine, although it is less common than other tests, but it is gradually being replaced by other methods. The combination of CT scan and endoscopy has become the gold standard for diagnosing AL because mucosal integrity and perianastomotic conditions can be detected.

Diagnostic timing

Early and timely detection of fluid leakage is important to prevent fatal complications and reduce hospital stay and burden. Delay in diagnosis may negatively affect the patient. Since the time at which AL occurs may vary, the duration of imaging studies for early diagnosis has been a matter of debate.

While the need method is generally based on observation of the patient during postoperative surgery, supplemented by monitoring of blood inflammatory indices and, in some centers, amylase broth, studies are reserved for patients with symptoms such as: AL and/or biochemical tests higher than normal.

This approach has been subject to some criticism because its effectiveness depends on many factors that can delay diagnosis, including

the diagnosis and the surgeon's knowledge of the clinical diagnosis in the early days.

Many studies have questioned the initiation of routine examinations after esophagectomy to achieve early diagnosis in asymptomatic patients. Endoscopy is the main recommended tool because it allows direct visualization of the AL and assessment of mucosal degeneration (ischemia, necrosis) as an early prediction of fertility. Only a few studies have evaluated the effectiveness of CT scans or esophagograms for this purpose.

The main problem of traditional methods is the uncertainty of the development of AL, making it difficult to determine the exact time of diagnosis. Routine monitoring appears to have a high predictive value if performed between POD 7 and 1460; however, it develops before POD5 in some patients. Fujiwara⁶¹ recommended repeating early endoscopy (POD1 and 3) based on the observation of color changes in the proximal part of the intestinal mucosa. On the contrary, other studies report that routine measures do not provide benefit because they only lead to changes in the treatment of some patients.

The higher incidence of AL in symptomatic patients compared to asymptomatic patients (33% and 12%, respectively) also supports evaluation when necessary. Furthermore, routine examination without clear pathological findings cannot rule out the possibility of future leakage and therefore will not be useful in improving early diagnosis, as evidenced by the lack of routine imaging (endoscopy and esophagography) in asymptomatic patients.

LEAKAGE MANAGEMENT

The broad and diverse clinical spectrum associated with AL manifestations is the main reason for the lack of clinical guidelines. The principle of the management strategy is to close or contain anastomotic defects, leakage and fluid collections. However, the choice of specific

treatments depends on the location and size of the leak, the severity of symptoms, the presence of ductal ischemia or necrosis, and the time required for healing to become clear after surgery. The importance of these factors is not clearly defined, and their order in the treatment algorithm may vary depending on the subject or location. Management strategies have evolved from older protocols that monitored symptom severity, anastomosis location or size, and degree of ischemia to newer algorithms that typically consider degree of ischemia and time of diagnosis.

Despite the lack of consensus guidelines, strategies are gradually shifting from intensive surgery to more conservative, including the use of endoscopic interventions. Conservative treatment is generally recommended for patients with asymptomatic or mild symptoms, surgery for early and/or severe cases, and endoscopic procedures for all cases. However, there is a significant difference between minor surgical treatment of mild symptoms and surgical treatment of intestinal necrosis. The next section describes the different controls, with particular attention to the lessons that emerge from further research from different sources.

Conservative strategies

In general principle, care strategies include various measures for the treatment of high-grade, asymptomatic or mild cervical and intrathoracic AL. Asymptomatic or mildly symptomatic but controlled urinary incontinence (especially cervical leakage) is usually treated with zero oral therapy combined with enteral (jejunostomy) or parenteral nutrition; the average duration of treatment is 1-3 weeks; For spontaneous emptying of the cervix. AL, the neck wound should be cut and irrigated.

In a minimally symptomatic intrathoracic AL, an accurate surveillance is suggested, with the

possibility of interventional mediastinal drainage (in case of fluid collection). Systemic treatment usually consist of broad-spectrum antibiotic therapy (according to infectious parameters), by the use of anticholinergic medication (to reduce saliva), anti-acid drugs (PPI) and prokinetics (to decrease AL volume).

Endoscopic treatment

The progressive development and improvement of endoscopic techniques has provided an alternative to surgery for those cases not manageable with a conservative approach, i.e. symptomatic leakage without sepsis and/or severe conduit ischemia. Endoscopic techniques include self-expandable metallic stents (SEMS), endoscopic vacuum therapy (EVAC), stent-over-sponge (SOS) therapy, clipping with the over-the-scope-clip (OTSC) system, suturing with overstitch, and the use of a sealant.

Stent

This technique consists of positioning a prosthesis in the esophageal lumen that covers the defect waiting for tissue healing. The choice for stenting strictly depends on the possibility to also apply drainage close to the leakage, in order to drain collected fluid.²⁰ In relation to the two main complications (stent migration and tissue overgrowth), fully covered self-expanding metal stents (FSEMS) guarantee a better compromise, partially covered SEMS with uncoated terminal portions have a higher risk of tissue overgrowth, while self-expanding plastic stents have a higher risk of migration.

The low anchoring capacity of FSEMS can be overcome by fixing the prosthesis through endoscopic suturing and clipping or using stents with larger diameter or colonic stents (up to 32 mm). The median stenting time to achieve healing is 4–8 weeks (or even shorter), as also demonstrated in animal model studies. Stents are indicated when leakage continues to be less than 70% of the circumference (20); However,

in recent studies, endoscopic treatment is not recommended in cases where the circumference is >30%. The effectiveness of stent implantation can be increased by smaller lumen aperture size and shorter examination time.

The risk of failure is generally higher in the proximal neck; This is mainly due to problems in the development of the remaining arteries and its effect on stent migration. In addition, the close proximity of the esophageal sphincter may cause airway obstruction, stomach pain (at least 2 cm away from the edge of the stent and the upper sphincter can be prevented), pain, and aspiration pneumonia.

Special or custom-made stents for use in the upper esophagus are under development and have a small diameter and a short upper broad end after birth, but evidence that they work well is still limited. In addition to uterine location, other risk factors for stent failure include esophageal injury greater than 6 cm in length and stent placement more than 2 days after discharge. Complications of stent placement include erosion or ulceration, bleeding, aspiration pneumonia, perforation, fistula, and reflux.

Surgery

Surgical treatment is indicated for early leaks (within 72 hours after surgery) because these leaks are usually absent and attributed to poor performance; for ineffective drainage and/or endoscopic treatment; and for patients with severe sepsis. In the presence of nonspecific mediastinitis, empyema, systemic sepsis, or gastric duct necrosis, surgery for cervical and intrathoracic anastomoses is usually required. Initial assessment of the patient's symptoms and the viability of the intestinal mucosa is important in determining the type of intervention to be performed.

In cases of early air leakage and the absence of thoracic empyema, mediastinal debridement and drainage can be performed by thoracoscopic

method; If empyema or sepsis occurs, open surgery should be performed: a thoracotomy is performed to strip the lung and remove fluid and infiltration. integrity of the intestine.

If damage to the catheter does not occur due to ischemia and necrosis, the intestine can often be saved and the defect can be stitched, especially in early leaks. If the stomach head is necrotic (ischemic), the necrotic tissue can be removed and re-anastomosis can be performed immediately.

Sometimes reconstruction of tissue defects may require the use of pedicled flaps to improve the anastomosis; They usually include pedicled pleural, pericardial, or usable intercostal muscle flaps for the intrathoracic AL and sternocleidomastoid for the cervical AL muscle or pectoralis major muscle hip. Diffuse ischemia or necrosis of the colon causes severe pain, requiring thoracotomy or cervicotomy and removal of the anastomosis. In rare cases, gastric bypass surgery is performed with a temporary cervical esophagostomy.

However, after complete recovery, the continuity of the digestive system can be restored with colonic or jejunal intervention. Surgical treatment is usually tailored to the patient's condition, and randomized controlled trials of surgical treatment of AL are not currently available.

Conclusion

AL after esophagectomy has many causes, is complex, and can have serious complications that will later affect the outcome. Current treatment is based on an individualized approach and reliable international evidence will help improve the prevention and treatment of AL. Treatment and patient outcomes. Higher quality evidence for such guidelines is urgently needed. The introduction of the ECCG system is a first priority to provide an up-to-date international standard for comparing the results of treatment strategies. This process can be

further extended by including descriptive models of leak characteristics (e.g. leak length, perimeter, etc.) to improve comparability between studies.

Although the prognostic value of each risk is increasing, awareness of many risks is increasing. They are not clear yet. Implementation of risk stratification tools based on individual scores to predict perioperative outcomes may be the first step in clinical selection and follow-up. Significant progress has been made in the period of intraoperative monitoring of catheter perfusion, which contributes greatly to the development of AL. Indocyanine green fluorescence angiography is the most effective technique, but further development is needed to achieve a versatile technique to guide surgical planning.

Early diagnosis is an important and difficult goal of treatment to reduce complications and mortality. However, the transition from optional measurements to routine imaging does not seem feasible, especially given the low clinical costs and resources required in asymptomatic patients. Time to diagnosis is also the basis of good treatment.

The amount and severity of discharge, combined with the variety of diagnoses and treatments available, make management difficult. Recent trends in the treatment of AL show a shift towards more medical treatment than in the past, with an increase in endoscopic interventions (mainly EVAC procedures), with surgical treatment being reserved for the most severe cases.

References

- [1] R. Azhough et al., Pilonidal sinus surgery with mechanical drilling technique. *Indian Journal of Surgery*. 2020;82:824-7. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [2] N. Forghani, et al., Fulminant Guillain-Barre syndrome associated with SARS-CoV-2: A case series. *J Clin Images Med Case Rep*.

- 2022**;3(1):1626. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [3] K. Shahsavarinia, et al., Diagnostic value of red blood cell distribution width in patients with organophosphate poisoning in emergency department of Sina hospital in 2019. *J Clin Images Med Case Rep.* **2022**;3(2):1634. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [4] S. Eskandari, et al., Relationship between patent foramen ovale and COVID-19 in patients admitted to an intensive care unit. *Revista Espanola De Cardiologia (English Ed).* **2021**;74(8):725. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [5] P. Jalali, et al., GUCA2A Dysregulation as a Promising Biomarker for Accurate Diagnosis and Prognosis of Colorectal Cancer. **2023**. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [6] SM. Haghdoost, MK. Gol, The necessity of paying more attention to the neurological and psychological problems caused by the COVID-19 pandemic during pregnancy. *Health.* **2020**;3(4). [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [7] MK. Gol, D. Aghamohamadi., Effect of massage therapy with and without elastic bandaging on pain, edema, and shoulder dysfunction after modified radical mastectomy: a clinical trial. *International Journal of Women's Health and Reproduction Sciences.* **2020**;8(1):73-8. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [8] MK. Gol, et al., Design and psychometrics cultural competence questionnaire for health promotion of Iranian nurses. *Journal of education and health promotion.* **2019**;8. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [9] K. Hashemzadeh, et al., Effects of Foot Reflexology on Post-sternotomy Hemodynamic Status and Pain in Patients Undergoing Coronary Artery Bypass Graft: A Randomized Clinical Trial. *Crescent Journal of Medical & Biological Sciences.* **2019**;6(4). [[Google Scholar](#)], [[Publisher](#)]
- [10] M. Khanbabayi Gol, et al., Frequency ratio of carpal tunnel syndrome in women with breast cancer treated with lymphedema in Tabriz medical education centers; 2018-2019. *The Iranian Journal of Obstetrics, Gynecology and Infertility.* **2020**;22(12):62-8. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [11] L.H Anvar, et al., The study of rs324420 (C385A) polymorphism of the FAAH gene of the endocannabinoid system in patients with epilepsy and ADHD. *Epilepsy Research,* **2023**. 192: p. 107100. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [12] A. Mobed, et al., Biosensors technology for anti-epileptic drugs. *Clinica Chimica Acta,* **2022**. 533: p. 175-182. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [13] S. Charsouei, S., et al., Evaluation of Three- and Five-Year Disease-Free Survival in Patients With Cervical Cancer With Spinal Cord Metastasis Under Treatment With External Radiotherapy+ Brachytherapy. *International Journal of Women's Health & Reproduction Sciences,* **2022**. 10(2). [[Google Scholar](#)], [[Publisher](#)]
- [14] M. Zamani Esfahlani, et al., Oral Levothyroxine Prophylactic Administration on Bleeding and Hemoglobin Changes During and after Total Hip Arthroplasty in Patients with a History of Ischemic Heart Disease: A Randomized Clinical Trial. *Trauma Monthly,* **2023**. 28(3): p. 805-814. [[Google Scholar](#)], [[Publisher](#)]
- [15] K. Komlakh, et al., Designing a Guideline for Elective and Emergency Spinal Cord Surgeries During the COVID-19 Pandemic. *Trauma Monthly,* **2022**. 27(Especial Issue (COVID-19 and Emergency Medicine)): p. 1-7. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [16] S. Charsouei, et al., Effects of COVID-19 pandemic on perceived stress, quality of life, and coping strategies of women with breast cancer with spinal metastasis under chemotherapy. *Int. J. Women's Health Reprod.*

- Sci, **2021**: p. 55-60. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [17] S.M. Haghdoost, and M.K. Gol, The necessity of paying more attention to the neurological and psychological problems caused by the COVID-19 pandemic during pregnancy. *Health*, **2020**. 3(4). [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [18] M.K. Gol, and D. Aghamohamadi, Effect of massage therapy with and without elastic bandaging on pain, edema, and shoulder dysfunction after modified radical mastectomy: a clinical trial. *International Journal of Women's Health and Reproduction Sciences*, **2020**. 8(1): p. 73-8. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [19] M.K. Gol, A. Dorosti, and M. Montazer, Design and psychometrics cultural competence questionnaire for health promotion of Iranian nurses. *Journal of education and health promotion*, **2019**. 8. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [20] K. Hashemzadeh, M. Dehdilani, and M.K. Gol, Effects of Foot Reflexology on Post-sternotomy Hemodynamic Status and Pain in Patients Undergoing Coronary Artery Bypass Graft: A Randomized Clinical Trial. *Crescent Journal of Medical & Biological Sciences*, **2019**. 6(4). [[Google Scholar](#)], [[Publisher](#)]
- [21] M. Khanbabayi Gol, M. Eidy, and M. Zamani Eshahlani, Frequency ratio of carpal tunnel syndrome in women with breast cancer treated with lymphedema in Tabriz medical education centers; 2018-2019. *The Iranian Journal of Obstetrics, Gynecology and Infertility*, **2020**. 22(12): p. 62-68. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [22] N. Shahidi, F. Mahdavi, and M.K. Gol, Comparison of emotional intelligence, body image, and quality of life between rhinoplasty candidates and control group. *Journal of Education and Health Promotion*, **2020**. 9. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [23] S. Jiang, et al., A meta-analysis review of the effect of Zn-doped synthetic polymer materials on bone regeneration. *Journal of Drug Delivery Science and Technology*, **2022**: p. 103792. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [24] V Tajiknia, S Hassani, H Seifmanesh, A Afrasiabi, H Hosseinpour, J. *Obstetrics Gynecology and Reproductive Sciences*, **2021** 5 (9) [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [25] SM Shushtarian, M Reza soltani, MJ Namazi, *Journal of Advanced pharmacy Education & Research*. **2020**;10:(s2) [[Google Scholar](#)], [[Publisher](#)]
- [26] SM Bagheri, S Hassani, A Salmanipour, *GSC Advanced Research and Reviews*, **2022** 11 (3), 101-105 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [27] SH AH Maleki, A Gholami, M Mohammadi, A Farhiudian, *Journal of pharmaceutical Negative Results*, **2022** 13 (10), 4137-4158 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [28] SAY Ahmadi; et al, *Formerly Current Pharmacogenomics Journal*. **2020**, 17(3): 197-205 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [29] SAK AH Jalali, AH Maleki, S Hassani, E Khoshdel, *The seibold Report Journal*, **2023** 18 (05), 999-1022 [[Google Scholar](#)], [[Publisher](#)]
- [30] S Sayad; et al, *Archive of Oncology Journal*. **2020** ;26(1): 6-9 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [31] S Sayad; et al, *Annals of Research in Antioxidants Journal*. **2019**; 4(2) [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [32] S Moshar, MR Soltani, MJ Namazi, *Journal of Advanced pharmacy Education & Research*. **2020**; 10:(s2) [[Google Scholar](#)], [[Publisher](#)]
- [33] S Hassani, M Rikhtehgar, A Salmanipour, *GSC Biological and Pharmaceutical Sciences*, **2022** 19 (3), 248-252 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [34] S Habibollahi Khaled hamid, M Eghbalnejad Mofrad, SMA Alavi, MJ Namazi,

- Journal of Advanced pharmacy Education & Research. **2021**;10 185-187 [[Google Scholar](#)], [[Publisher](#)]
- [35] MR AH Jalali, S Hassani, S Albuzyad, A Moaddab, The seybold Report Journal, **2023** [[Google Scholar](#)], [[Publisher](#)]
- [36] M.E Akbari; et al, International Journal of Cancer Management.2016;9(6) [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [37] FB AH Jalali,S Hassani, A Zare,T Ziaadini, The seybold Report Journal, **2023** 18 (04), 1634-1653 [[Google Scholar](#)], [[Publisher](#)]
- [38] F Safari, H Safari, Eurasian Journal of Chemical, Medicinal and Petroleum Research, **2022** 1 (2), 150-154 [[Google Scholar](#)], [[Publisher](#)]
- [39] F Rokhtabnak, S Sayad, M Izadi, SD Motlagh, P Rahimzadeh, Anesthesiology and Pain Medicinem **2021** 11 (5) [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [40] F HYSENI; et al, The Importance of Magnetic Resonance in Detection of Cortical Dysplasia, Curr Health Sci Journal. **2021**; 47(4): 585-589 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [41] F Beiranvandi, Z Kuchaki, A Zare, E Khoshdel, A Jalali, Journal of Pharmaceutical Negative Results, **2022**, 4417-4425 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [42] E. Ghaibi, et al., Eurasian Journal of Chemical, Medicinal and Petroleum Research, **2022**, 1, 33-39. [[Google Scholar](#)], [[Publisher](#)],
- [43] E Harizi; et al, Radiology Case Reports **2022** 17 (11) 4152-4155 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [44] E Kola, A Gjata, I Kola, et al., Radiology Case Reports, **2022** 17 (3), 1032 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [45] E Kola, A Gjata, I Kola, A Guy, J Musa, et al., Radiology Case Reports, **2021** 16 (11), 3191-3195 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [46] E Ghasemi, AH Fathi, S Parvizinia., J Iran Dent Assoc **2019**; 31 (3):169-176 [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]
- [47] D Nakuci, E Kola, E Horjeti, I Kola, B Shaipi, J Musa, A Guy, M Alimehmeti, Archives of Clinical and Medical Case Reports, **2020** 4 (5), 760-765 [[Google Scholar](#)], [[Publisher](#)]
- [48] D Nakuci, E Kola, E Horjeti, I Kola, B Shaipi, J Musa, A Guy, M Alimehmeti, Archives of Clinical and Medical Case Reports, **2020** 4 (5), 760-765 [[Google Scholar](#)], [[Publisher](#)]
- [49] A. Mobed et al., Biosensors technology for anti-epileptic drugs. Clinica Chimica Acta. **2022**;533:175-82. [[Crossref](#)], [[Google Scholar](#)], [[Publisher](#)]

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