

Review of Esophagectomy Side Effects

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1. Abstract

The primary indication for an esophagectomy is esophageal cancer or Barrett's esophagus with high-grade dysplasia. Patients undergoing esophagectomy often present with dysphagia, side effects from chemotherapy, decreased appetite, and weight loss. Esophagectomy may be an operation involving the abdomen, neck, and/or chest requiring 5 to 7 days of NPO status to permit healing of the anastomosis between the upper esophagus and new esophageal conduit (usually the stomach). Esophageal cancer is that the eighth commonest cancer worldwide and therefore the sixth mostcommon explanation for cancer death. In 2011 there were 7603 deaths from esophagealcancer in the United Kingdom, accounting for 5% of all deaths from cancer. Timely diagnosis and treatment are important to manage the disease and stop comorbidities. Surgical resection of the tumor and lymph nodes is typically practiced either with or without chemo or chemo radiotherapy. Despite advancements in surgical methods and skills, complex nature of the esophagus and invasiveness of the surgery can cause serious complications in these patients [1].

2. Introduction

Esophageal Cancer (EC) is that the eight commonest cancer reported and is forth most widespread explanation for mortality worldwide where, esophageal epithelial cell carcinoma having the very best incidence [2]. Barrett's esophagus, thanks to Gastroesophageal Reflux Disease (GERD), is related to 30-40% risk of esophageal adenocarcinoma. Eventual shift of squamous epithelium to columnar epithelium, referred to as metaplasia, is seen as a results of the acidic en-

vironment within the esophagus [2]. Initially, the cancer is presented within the mid-third of the thoracic esophagus where these lesions advance into polyps and tumor, resulting in the blockage of the lumen and invading other layers of the esophagus [3]. Additionally, risk factors such as; smoking, alcohol abuse, obesity, esophageal reflux disease, viral infection, poverty, esophageal achalasia and genetic and epigenetic factors contribute chiefly to the onset of EC [4, 5]. Several markers are used for the detection of esophageal neoplastic cell lines such as; CD44, aldehyde dehydrogenase, p75NTR, CD 90 (Thy-1), NANOG, Podoplanin, CD133, SALL4 and COX2 [1]. Early detection, diagnosis and treatment are possible for esophageal cancer, due to the innovations within the medicine, however, 5-year survival rate of those patients is restricted to twenty only [5] (Figure 1).

Endoscopic resection, esophagectomy, may be a commonly performed surgery for resectable esophageal tumors [6]. Depending on the physical health of the patients and thus the stage of tumor therapeutic intervention is chosen. In Barrett-esophagus and early stage of cancer endoscopy or surgery is performed whereas, in advanced stages, with or without surgery, chemo or chemoradiotherapy is performed preoperatively [7].

Surgery usually comprises of lymph gland dissection and esophageal reconstruction. It is a particularly invasive surgery; therefore, great number of complications are related to its outcomes [8]. Recently, thoracoscopic methods became integrated with Minimally Invasive (MI) laparoscopic approaches to realize better advantages. Integration of 3D cameras have also allowed surgeons to look at histological and microanatomical organizations during the surgery. Single-port

mediastinoscopy using transmediastinal and cervical approaches has been performed during a recent few years which can cause reduction in perioperative complications [9]. Advancements in surgical techniques are likely to scale back the frequency of postoperative mortality and morbidities. Esophageal cancer surgery is taken into account among the foremost invasive cancer surgeries and is therefore related to 60-80% adverse postoperative events and corresponding reduced overall survival rate [10, 11].

Postoperative complications and morbidities are related to some common risk factors such as; smoking and alcohol consumption, advanced age, increased BMI, malnutrition, preoperative heart problem and McKeown Esophagectomy.

This review is meant to summarize a number of the foremost frequent complications reported after esophageal cancer surgery (esophagectomy), associated risk factors and therapeutic interventions which will treat or prevent these events.

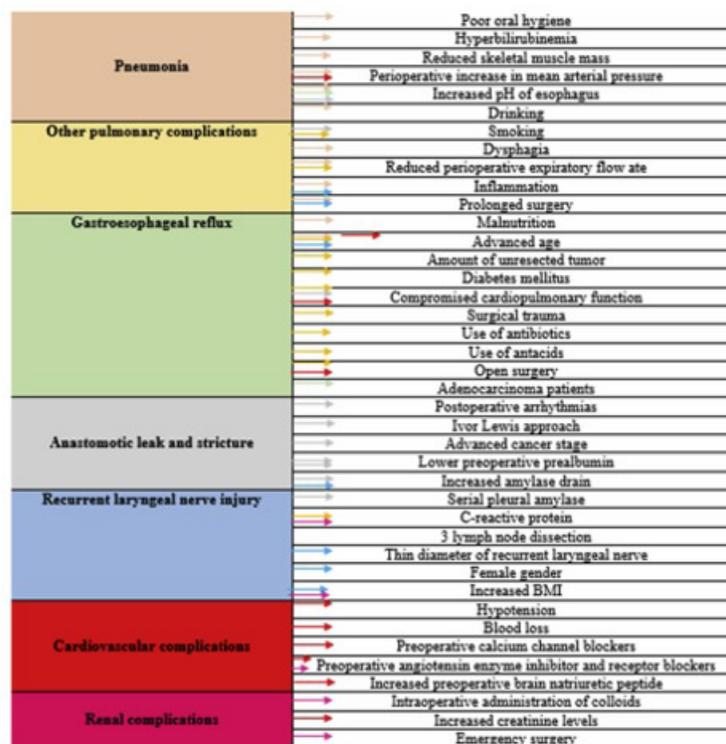


Figure 1: Highlights some of the major preoperative and intraoperative factors (on the right) that can lead to the complications (on the left)

3. Gastroesophageal Reflux (GER)

Gastroesophageal Reflux Disease (GERD) is a disorder due to the retrograde flow of refluxate into the esophagus [1].

Gastroesophageal reflux is a frequent functional complaint after Ivor Lewis esophagectomy intervention, which can affect up to 40% of patients [2]. Studies have reported that esophageal acid reflux can increase up to twenty-eight followed by heartburn and regurgitation after the surgery. Disruption of antireflux mechanism by the lower esophageal sphincter and associated anatomical structures during the surgery can cause reflux. It is also significantly related to other complications like anastomotic stricture and PP. Increased esophageal pH, pathologic bolus and acid exposure are seen in these patients. Proton pump inhibitors are often used for the treatment of GER [12]. In a recent study, Fuchs, Schmidt demonstrated that patients who underwent adenocarcinoma and squamous cell esophageal carcinoma surgeries had increased reflux-dependent mucosal damage [1], 5 years following the operation whereas, Barrett's esophagus was reported in 20% patients. These findings were common in adenocarcinoma patients. Side overlap with fundoplication has been re-

cently introduced as a surgical technique, which will be performed laparoscopically and is probably going to scale back the incidence of postoperative reflux [13]. Reconstruction of gastric tube, instead of traditional anastomosis of esophagus to the unresected gastric parts, also can reduce the frequency of GER in patients undergoing esophagectomy for adenocarcinoma. Patients presenting with postoperative gastric reflux quite once every week have reduced overall health status and are likely to possess greater incidence of fatigue, nausea, sleeplessness, vomiting and breathing problems [14].

4. Anastomotic Leakage (AL) and Anastomotic Stricture (AS)

Among the many possible postoperative complications, Anastomotic Leakage (AL) is the most common and serious [3]. Although its incidence is gradually decreasing thanks to the continual improvement of surgical methods and therefore the gradual popularization of latest technologies like video-assisted or robot-assisted thoracic surgery, AL still occurs in 8.5-25.6% of patients after esophagectomy [4-8]. AL can not only lead to mediastinitis, peritonitis and other infections, but also to anastomotic stricture, the need for re-operation and re-

currence, resulting in prolonged hospital stay and increased mortality [9-12]. Therefore, accurate prediction of the occurrence and prompt prevention of AL are essential to accelerate the recovery of patients, improve their quality of life and prolong their life survival.

5. Cardiovascular Complications

Intra and post-operative adverse cardiac events, in non-cardiac disease surgeries are one among the foremost common causes deaths. Improved technical aspects of the surgery and intraoperative monitoring of cardiovascular activity can reduce the incidence of those events. Esophagectomy is related to the best odds of asystole, Deep Vein Thrombosis (DVT) and myocardial infarction, among various other sorts of abdominal surgeries [22]. Hypotension, as a results of intraoperative fluid shift is additionally reported in some cases. Minimally invasive procedure is superior to open esophagectomy with regard with adverse cardiovascular events. The surgical apgar rating system are often exploited to successfully measure intraoperative adverse cardiac events such as; hypertension, blood loss, decreased blood pressure and pulse and predict the risk of acquiring short and future postoperative complications like, pneumonia and anastomotic leakage [23, 24]. The incidence of DVT following esophagectomy is reported as 2.9-13.7% [25].

In a retrospective review, Colwell, Encarnacion [26] reported that 32.4% patients who underwent transcervical esophagectomy developed postoperative fibrillation (AF) which was characterized by prolonged ICU and hospital stay. Another retrospective study recruiting 121 patients reported the incidence of AF as 31.4% and advanced age, chemoradiation and male gender were known risk factors. Preoperative intake of amiodarone is useful against the danger of AF after the surgery. Minimally invasive and open esophagectomy have similar incidence of AF, reported in another retrospective study. However, transthoracic approach in advanced-age patients with the history of cardiopulmonary diseases increases the danger of the event of AF, adding to days of hospitalization and other complications. In a study by Ojima, Iwahashi [27], following transthoracic esophagectomy, fibrillation was reported in 9.2% of the patients where antiarrhythmic therapy using landiolol hydrochloride was effective in 63.2% patients. Preoperative usage of calcium channel blockers, angiotensin converting enzyme inhibitors and blockers of angiotensin receptor can reduce the danger of AF, resulting in decrease in overall survival rate and subsequent mortality [56]. In a randomized clinical study, prophylactic use of landiolol hydrochloride in patients undergoing transthoracic esophagectomy was marked with the reduced frequency of AF, with the suppression within the guts rate and levels of IL-6 [28].

6. Acute Kidney Injury

Acute Kidney Injury (AKI) is a common postoperative complication [3]. postoperative AKI as defined by the AKI Network criteria occurred in 35.3% of esophageal surgeries. In the present cohort, variables independently associated with AKI were elevated BMI,

low preoperative albumin level, preoperative treatment with ACEI or ARB, large colloid infusion during surgery, and high postoperative 2 day CRP. To date, there has been little information on AKI after esophageal surgery, with risk assessment mainly focused on respiratory and cardiovascular complications [4, 5]. postoperative renal failure-defined as a doubling of the plasma creatinine levels or requirement for renal replacement therapy-occurred in 2.6% of esophagectomies for esophageal cancer [5]. The authors also identified low albumin level as an independent preoperative predictor of AKI. A recent metaanalysis demonstrated that hypoalbuminemia was a significant independent predictor both of AKI and of death after AKI development [6]. In addition, preoperative hypoalbuminemia has been shown to be a crucial risk factor for AKI after surgery. Because serum albumin levels can be influenced by several factors, including overall nutritional status, stress response, or specific disease, [7] hypoalbuminemia simply may be a marker of malnutrition or the severity of the underlying disease. However, several studies have suggested that serum albumin may have some renoprotective effects, including its ability to improve renal perfusion, preserve proximal tubular integrity and function, bind endogenous toxins and nephrotoxic drugs, and scavenge reactive oxygen species and deliver protective lysophosphatidic acid [6]. Thus, a low serum albumin level may contribute to an increased risk of AKI in patients undergoing esophageal surgery. In conclusion, AKI is a relatively common complication after esophageal cancer surgery that is associated with long hospitalization. Larger BMI, increased preoperative creatinine concentrations and cardiovascular comorbidities increase the risk of AKI. Dexamethasone appears to have a protective effect, however due the retrospective design of our study this finding should be interpreted with caution. A randomized controlled trial should be conducted to test the efficacy of dexamethasone in reducing the occurrence of AKI after esophageal cancer surgery [8].

7. Esophagectomy Side Effects Treatment

Anastomotic leakage is one of the foremost severe complications after esophagectomy and is said to increased postoperative morbidity and mortality [34]. For patients with locally advanced esophageal cancer, a radical esophageal resection offers the sole chance for cure. Anastomotic leakage (AL), one of the foremost severe complications, leads to significant morbidity, prolonged hospital stay, considerable use of healthcare resources, and increased risk of mortality.1 within the future, AL has been related to poorer quality of life, increased cancer recurrence rates, and subsequently worsened long-term survival. The incidence of AL ranges between 11.4 and 21.2%, 2-5 with an associated death rate between 7.2 and 35%. In spite of the increasing research efforts, leakage pathophysiology and causal factors remain unclear. albeit AL features a multifactorial etiology, tissue perfusion seems to play a pivotal role in leakage development. Moreover, clinical symptoms for AL often only become manifest during a later stage or are nonspecific, while an outsized variability of diagnostic and treatment options are available, without a transparent

consensus on standardized procedures [35].

8. Risk Factors

Several risk factors for AL have been identified such as age, male gender, emergency surgery, smoking, alcohol abuse, American Society of Anaesthesiologists (ASA) score, obesity, prolonged operative time, low serum albumin levels, intraoperative blood loss, diabetes, renal failure and cardiovascular disease [3-6]. Active use of corticosteroids at the time of surgery is identified both in univariable and in multivariable analyses as a big risk factor for AL, almost like the findings of Kassis, when identifying predictors of AL on the society of thoracic surgeons' general thoracic database [3] Wright, on the other hand, could not identify steroid use as a risk factor for major morbidity and mortality in univariable analysis, but he did confirm a significant causal effect in multivariable analysis [5].

9. Neoadjuvant Treatment

Neoadjuvant chemotherapy or chemo-radiation followed by surgery has become the standard of care in the treatment of esophageal cancer [3, 4]. However, a recent large retrospective European multicenter study revealed a significantly higher risk of postoperative complications including AL in cardiorespiratory comorbid patients after neoadjuvant chemo-radiation, but not after neoadjuvant chemotherapy [5, 6]. Consequently, neoadjuvant chemo-radiation should be employed with particular caution in patients with known respiratory comorbidity [7]. Numerous comorbidities are linked to increased AL risk such as obesity, heart failure, coronary artery disease, peripheral vascular disease, hypertension, steroids, diabetes mellitus, renal insufficiency, and tobacco use [8]. In addition, atrial fibrillation [9] and COPD [10] are known independent risk factors. Most comorbidities have a negative impact on microvascular perfusion, and it's been hypothesized that arteriosclerosis may play a crucial role within the etiology of AL. Consequently, several retrospective cohort studies have confirmed an association between AL and loco-regional post-coeliac [11, 12] and aortic and coeliac trunk [13] calcifications. Moreover, others have evidenced an association between AL and supra-aortic and coronary arteriosclerosis, implying that general radiological arteriosclerosis scores may be useful to estimate the risk of AL [14, 15].

10. Anastomotic Location

A cervical anastomosis features a five times greater risk of leakage in comparison to intrathoracic location. The main causes include the necessity for an extended gastric conduit, more likely positioned within the fundus (where the vascularity is more compromised), and increased risk of tension and/or compression at the junction between thorax and neck. The upper AL risk within the neck can also be influenced by the indication for this procedure (more proximal tumors and/or lymph gland metastases, a better field and a more extended resection). However, the death rate is unaffected by the location of the anastomosis, although a cervical location may cause increased recurrent laryngeal nerve paresis, wound infection, and longer hospital stay [34].

11. Surgical and Non-Surgical Technique

There are many risk factors associated with intraoperative techniques, like the whole-stomach technique, anterior mediastinal route, and cervical anastomosis, which are related to the incidence of anastomotic leakage after esophagectomy, while the location of anastomosis plays a crucial role in affecting anastomotic leakage. The better esophagectomy surgical techniques to scale back anastomotic leakage appear to be the gastric tube, posterior-mediastinal route, and stapled anastomoses. In reference to the treatment of anastomotic leakages, different treatment methods should be selected consistent with the anastomotic leakage stage and grade. As far as possible, non-surgical treatments like naso-leakage drainage, which cause less trauma and fewer complications, should be adopted [3].

12. Anastomotic Technique

Lack of consensus exists regarding the ideal anastomotic technique after esophagogastrectomy [3, 4]. The 4 most common esophageal anastomotic techniques include hand sewn (HS), circular stapled (CS), linear stapled (LS) [3, 5], and modified Collard (MC) [3, 6]. Goals of esophagogastric anastomoses include avoidance of early complications like leak and prevention of late morbidity like anastomotic stricture. Either of these early or late complications prolongs recovery and has a negative impact on quality of life [3, 7-9]. In keeping with recent reports [10-13], we have demonstrated that esophageal resection and reconstruction for primary esophageal adenocarcinoma can be achieved safely, with low mortality. However, postoperative morbidity remains relatively high (also in keeping with recent studies), with significantly prolonged hospitalization. Esophagogastric anastomotic failure was the leading cause of morbidity in this series. Dissatisfaction with a leak rate of 22.6% following hand-sewn anastomoses early in this series led to use of a semimechanical technique [14] from September 1997 onwards. Using this approach, the anastomotic leak rate fell to 7.9%, although this trend did not achieve formal statistical significance ($P=0.08$). Esophageal resection for primary esophageal adenocarcinoma may be achieved with low mortality, but postoperative morbidity remains relatively high. Objective radiographic evaluation of the esophagogastric anastomosis is essential to document anastomotic integrity, and for early intervention to minimize morbidity. Although previously reported stapled anastomotic techniques have had limited success [4], the routine use of a semimechanical side-to-side technique [14] for cervical esophagogastric anastomosis following resection of esophageal adenocarcinoma, is associated with a trend towards reduced anastomotic leak rates and warrants further careful study. However, the length of the cervical esophageal segment required for this technique may result in a more distal level of anastomosis (low cervical or upper mediastinal) than seen with hand-sewn anastomoses. Consequently, anastomotic leakage may result in mediastinal and pleural sepsis, particularly following a transthoracic resection. The gastrojejunostomy during laparoscopic Roux-en-Y gastric bypass (LRYGB) are often constructed by hand sewn (HSA), linear (LSA) and circular (CSA) stapler tech-

nique. They are all considered safe; however, it's not known which the simplest technique is. Short-term follow-up suggest no difference in weight loss or weight regain between them. A total of 385 patients with an initial body mass index of 47.1 kg/m² (35–68) were enrolled to this study. This decreased to 33.3 kg/m² (21–54 kg/m²) after 5 years [15]. There was no difference in %TWL after 3 years, $P = 0.296$, or 5 years, $P = 0.187$, between the techniques. The number of patients with weight regain wasn't different after 3 years, $P = 0.224$, or 5 years, $P = 0.795$. All techniques had similar operative time. CSA has a higher material cost. Early anastomotic stricture was more common following HSA; however, the difference was not significant. Mid-term weight loss and weight regain are not related to anastomotic technique, and there is no difference in operative time associated to them. Circular stapler technique has a higher material cost due to the additional stapler [15].

13. Discussion

This pilot study shows that it's feasible to characterize the gut-brain axis and its reference to food reward and eating behavior during a cohort post esophagectomy. Notwithstanding, 10-mg octreotide LAR was not sufficient to change guthormone response, body weight, appetitive behavior, or ad libitum food intake. Somatostatin analogues

are utilized in surgical contexts to scale back postprandial symptoms and may have beneficial nutritional effects, including the restoration of postoperative weight loss [41]. There has, however, historically been no method to systematically analyze the factors underlying their potential beneficial effects within the context of major upper gastrointestinal resection. This limits the power to appropriately target treatment to patients who are presumably to derive benefit. Recent developments in our understanding of how alterations in gut-brain axis signaling could also be implicated within the pathophysiology of postesophagectomy symptomatology and malnutrition [42] should enable a more systematic approach to therapeutic interventions. Moreover, although studies a minimum of suggest a compelling rationale for long-term nutritional benefit with the utilization of octreotide LAR through mitigation of the exaggerated postoperative gut-hormone response, this remains to be proven [36].

In this study, the primary to assess octreotide LAR during this context, the scientific thesis was that octreotide administration, shown previously to acutely inhibit GLP-1 secretion and increase ad lib food intake among patients post esophagectomy, would suppress gut hormones and potentially facilitate weight regain [36].

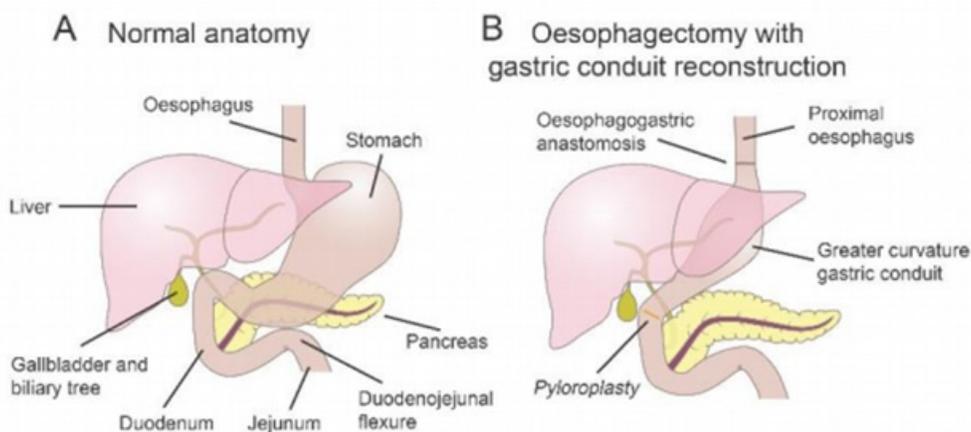


Figure 2A: Normal anatomy and **B.** oesophagectomy with gastric conduit reconstruction, with or without pyloroplasty resulting in rapid nutrient transfer to the small bowel [45, 46]

14. The Comparative Mechanisms of Weight Loss After Esophagectomy

Oesophageal cancer accounts for 27,700 deaths per annum within the European Union. Oesophagectomy is a major resection of the oesophagus and stomach and is part of the multimodal (adjuvant chemo[radio]therapy) treatment [43] (Figure 2A, B). Initially after surgery, patients may require additional chemo(radio)therapy and feeding jejunostomy. Almost 40-50% of patients remain cancer free 5 years after oesophagectomy. However, more than half of them have unintentional weight loss as they involuntarily reduce their food intake [44].

Prior to curative surgery for cancer, unintentional weight loss is common and secondary to anorexia, dysphagia, and cancer cachexia. Ini-

tially after curative surgery, the surgical stress and mucositis during chemo(radio)therapy further reduces food intake [47]. In contrast with comparable operations, restoration of normal food intake and weight gain doesn't typically occur after oesophagectomy. Weight loss after surgery increases long term morbidity and mortality even when cancer is cured and cannot be attributed to cancer cachexia, unless there is a recurrence of the cancer. Nutritional support improves morbidity, but not oncologic outcomes, while patients cannot voluntarily increase food intake after oesophagectomy [47]. The severity of pancreatic exocrine insufficiency, bacterial overgrowth and/or dumping syndrome doesn't correlate with unintentional weight loss and appropriate treatments don't consistently increase weight. Reductions in the "hunger hormone" ghrelin after oesophagectomy are also not explanatory. We do not understand exactly why these

patients experience unintentional weight loss, even when they no longer suffer from cancer cachexia and are cured of cancer. Broadly speaking, studies have shown that there are 3 known mechanisms of weight loss postoesophagectomy [48].

1) Stress response: Surgery can cause a big stress responses, which cause greater catabolism and energy consumption and decreased digestive function.

2) Poor eating function: Postoperative eating difficulties like dysphagia, trouble swallowing saliva, and choking when swallowing can worsen weight loss post-oesophagectomy. Both of those factors tend to enhance with time and can't be blamed for the unintentional weight loss seen within the future in cancer-free, post-esophagectomy patients.

3) Gut endocrine changes: The alimentary canal, the most important endocrine organ within the body, may be a complex neuroendocrine system. More than 30 known peptide hormone genes are expressed in the digestive tract, with more than 100 different hormonally active peptides produced. Patients with oesophageal cancer experience a decrease in ghrelin secretion and a significant increase in postprandial plasma glucagon-like peptide 1 (GLP-1) and peptide YY (PYY), contributing to severe appetite loss and decreased food intake after esophagectomy. There are similar mechanisms behind the intentional weight loss seen in patients post bariatric surgery. Nutritional Treatments to stop Weight Loss in Patients with Oesophageal Cancer Postoperatively.

The leading post-operative problems in patients with oesophageal cancer are dysphagia, weight loss and in some cases malnutrition, therefore adequate postoperative feeding is especially important. The exact type and timing of this feeding has been a source of much debate in recent years. In 2011, Casaer et al recommended that TPN should no longer be the preferred route of postoperative feeding for these patients, concluding that early initiation of parenteral nutrition does not improve recovery and is related to a better incidence of septic complications. It is now widely accepted that the utilization of TPN after oesophageal surgery should be administered as long as EN is contraindicated. This is supported studies by Gabor et al and Fujita et al that found a discount in severe complications and length of hospitalization in patients treated with EN rather than TPN. Within the realm of EN nutrition, there are primarily two different feeding routes used – Jejunostomy and Nasojejunal feeding. An RCT from 2007 found that Jejunostomy feeding is safe but entry site leakage, infection and occlusion might occur, with a reoperation rate of less than 2%. Nasojejunal feeding is a smaller amount invasive but dislocation occurs frequently, implying frequent replacements are needed. Currently, the choice of EN remains primarily as a result of surgeon preference with no clear data suggesting superiority of one over the other available at present [46].

15. Chylothorax After Esophagectomy

Postoperative chylothorax is a rare, but serious complication after

esophagectomy for esophageal cancer, with a reported incidence of 0.4-4% [3]. It is generally thanks to injury of the lymph vessel and/or lymphatic tributaries. The lymph fluid includes protein, lipids, and lymphocytes, and the loss of lymph fluids due to chylothorax causes hypovolemia, malnutrition, and immunosuppression [3]. Therefore, deciding on the optimal treatment for chylothorax after thoracic esophagectomy is an important issue. However, the established treatment remains controversial. Initial conservative treatments such as fasting, drugs, and pleurodesis are carried out, but some authors have argued that a planned early reoperation may significantly reduce mortality [4]. The administration of octreotide, a somatostatin analog, is understood to be highly effective in slowing lymph vessel lymph flow. The use of octreotide to control chylothorax has been reported, but there is little evidence for its efficacy [5]. Etilefrine, an α - and β -adrenergic sympathomimetic drug used in postural hypotension, causes contraction of smooth muscle fibers that are present in the thoracic duct [6]. treatment of enterocutaneous fistula after esophagectomy with scopolamine ointment

Anastomotic leakage (AL) is one among the main complications of esophageal cancer surgery, with a frequency of 13.3% consistent with the Japanese National Clinical Database [50]. In most cases, spontaneous healing is observed after conservative treatment, which can include fasting and proper drainage; however, intractable enterocutaneous fistulas sometimes develop. Large amounts of fistula discharge significantly reduce the patient's quality of life and prolong the fasting period and hospitalization. Negative Pressure Wound Therapy (NPWT) may be a relatively new treatment, which promotes healing by sealing the wound surface. The use of NPWT for enterocutaneous fistula due to postesophagectomy AL has rarely been reported. Here, we report a case of postoperative fistula successfully managed by a mixture of scopolamine ointment and NPWT [51].

Enterocutaneous fistulas complicating esophageal cancer surgery can become intractable thanks to substantial exudate, which constantly exposes the encompassing skin to strong irritation and impairs granulation. Also, an oversized amount of fistula exudate causes considerable pain [51]. For intractable enterocutaneous fistulas arising thanks to AL, a minimally invasive approach should be considered first.

NPWT may be a physiotherapy during which a negative pressure is continuously or intermittently applied to a wound during a closed environment to market the formation of granulation, adjust the wound bed, and hence facilitate wound healing. It is widely used for acute wounds, like people who can't be closed temporarily; open wounds on amputated limbs; and chronic wounds like pressure ulcers and diabetic foot ulcers [52]. Endoscopic vacuum-assisted closure treatment is increasingly used for intrathoracic leakage after esophagectomy. On the opposite hand, there are few reports of percutaneous NPWT for management of enterocutaneous fistula thanks to AL after esophagectomy. We speculated that NPWT would be fully applicable to postoperative enterocutaneous fistulas, like the one within

the present case, and would fit the criterion of a minimally invasive approach. It is also thought that a synergistic effect was obtained within the process of fistula closure by using scopolamine ointment together. The reduction within the exudate enabled protection of the wound, and granulation was promoted by the continual negative pressure. A problem with the utilization of NPWT in intestinal tract communication is that the risk of intestinal necrosis related to continuous negative pressure, possibly thanks to the negative pressure impairing the microcirculation. Therefore, the negative pressure was carefully and gradually initiated within the present case. Meanwhile, this treatment didn't require frequent gauze replacement thanks to continuous drainage and improved the condition of the encompassing skin, not only promoting wound healing but also significantly reducing patient discomfort. To our knowledge, there is no general definition of the duration of an intractable fistula. In our case, although post-esophagectomy AL was observed, the drainage and thus the overall condition were reasonably good with no serious complications. Therefore, subsequent treatment was delayed and thus the hospitalization period became quite long. We suggest that AL that doesn't improve within 1 month at the newest should be considered as intractable fistula, and in such cases, a mixture treatment with scopolamine ointment and NPWT may prove a successful treatment strategy [51].

16. Effectiveness of Jejunostomy

Esophagectomy, whether for benign or malignant disease, may be a complex operation which carries significant morbidity and mortality both for open and for minimally invasive techniques [3, 4]. Furthermore, esophageal cancer patients are prone to malnutrition due to weight loss resulting from dysphagia and side effects from neoadjuvant chemoradiation therapy [5, 6]. Jejunostomy is a means of enteral nutrition that can be accomplished via a multitude of described techniques, such as laparotomy, percutaneous, endoscopic or laparoscopy [7]. Feeding jejunostomy tubes (JT) have been commonly utilized either in the preoperative phase or at the time of an operation in patients undergoing esophagectomy [8, 9]. Due to potential complications of JT placement, the need for routine use of feeding JTs in foregut surgery has been studied [10, 11]. If morbidity and mortality from JT placement might be minimized, this is able to potentially justify its routine use in patients undergoing esophagectomy-given the substantial advantage of maintaining optimal nutrition. Among patients who underwent elective esophagectomy for cancer and received a jejunostomy tube, two-thirds didn't require the tube as a "safety valve." Tube feeding provides but half the target nutrition we wish to deliver. For certain patients, like those with substantial weight loss before surgery, a jejunostomy tube could also be reasonable. In patients unable to take oral nutrition after a week owing to a complication, many options remain [12]. Jejunostomy tubes can cause serious complications and frequent but less serious adverse events during a group of patients already at high risk for complications. We feel that it's unreasonable to subject two-thirds of patients to a

procedure that has been proven to cause harm within the absence of convincing evidence within the literature that this intervention is of clinical benefit [12]. Jejunostomy is especially utilized in complete thoracoscopic and laparoscopic minimally invasive Ivor-Lewis esophagectomy, which may significantly improve the patients' degree of comfort and portability thanks to the nutrition tube being located within the abdomen, thus improving the standard of life during indwelling and in postoperative EN support. However, some scholars believe that jejunostomy is an invasive operation, which increases surgical difficulty and trauma, with more tubule-related complications. Since January 2015, our center has routinely used laparoscopic jejunostomy for minimally invasive Ivor Lewis esophagectomy, and routine intraoperative indwelling of nasointestinal tubes for minimally invasive McKowen esophagectomy. Despite the wide application of jejunostomy, its clinical effectiveness remains undefined. Therefore, this retrospective study aimed to assess the therapeutic and undesired effects of jejunostomy in individuals administered Ivor-Lewis esophagectomy for thoracic segment esophageal carcinoma. The clinical data of 1400 patients with esophageal carcinoma were assessed, and various parameters in both EN methods were compared to research the effectiveness and reliability of jejunostomy in complete thoracoscopic and laparoscopic minimally invasive Ivor-Lewis esophagectomy [53].

17. Analysis

In this post hoc ergo propter hoc follow-up study of a randomized clinical test involving 207 patients with esophagus cancer, overall survival and disease-free survival were comparable between the HMIE and open esophagectomy procedures. No statistically significant difference in recurrence rate or location was found between groups, and major postoperative overall and pulmonary complications were identified as risk factors associated with decreased overall survival and disease-free survival [54].

This randomized clinical test may be a post hoc ergo propter hoc follow-up study that analyzes the results of the open-label Multicentre Randomized Controlled phase III clinical trial Trial, which enrolled patients from 13 different centers in France and was conducted from October 26, 2009, to April 4, 2012. Eligible patients were 18 to 75 years aged and were diagnosed with resectable cancer of the center or lower third of the esophagus. After exclusions, patients were randomized to either the HMIE group or the open esophagectomy group. Data analysis was performed on an intention-to-treat basis from November 19, 2019, to December 4, 2020 [54].

A total of 207 patients were randomized, of whom 175 were men (85%), and thus the median (range) age was 61 (23-78) years. The median follow-up duration was 58.2 (95% CI, 56.5-63.8) months. The 5-year OS was 59% (95% CI, 48%-68%) within the HMIE group and 47% (95% CI, 37%-57%) within the open esophagectomy group (hazard ratio [HR], 0.71; 95% CI, 0.48-1.06). The 5-year DFS was 52% (95% CI, 42%-61%) within the HMIE group vs 44% (95% CI,

34%-53%) within the open esophagectomy group (HR, 0.81; 95% CI, 0.55-1.17). No statistically significant difference in recurrence rate or location was found between groups. In a multivariable analysis, major intraoperative and postoperative complications (HR, 2.21; 95% CI, 1.41-3.45; $P < .001$) and major pulmonary complications (HR, 1.94; 95% CI, 1.21-3.10; $P = .005$) were identified as risk factors related to decreased OS. Similarly, multivariable analysis of DFS identified overall intraoperative and postoperative complications (HR, 1.93; 95% CI, 1.28-2.90; $P = .002$) and major pulmonary complications (HR, 1.85; 95% CI, 1.19-2.86; $P = .006$) as risk factors [54]. This study found no difference in long-term survival between the HMIE and open esophagectomy groups. Major postoperative overall complications and pulmonary complications seemed to be independent risk factors in decreased OS and DFS, providing additional evidence that HMIE could even be related to improved oncological results compared with open esophagectomy primarily due to a discount in postoperative complications [54].

After esophagectomy, the stomach is that the most ordinarily utilized reconstructive conduit. There remains debate among surgeons regarding the wants for pyloroplasty/pyloromyotomy following reconstruction. We present a series of patients having undergone near total esophagectomy and reconstruction with gastric tube without gastric emptying procedure to research critically these patients' ability to re-establish a subjectively acceptable and nutritionally adequate eating pattern without significant side effects of early satiety, dumping, or diarrhea [55].

Between 1991 and 1998, 48 patients underwent esophagectomy utilizing this system and were available for long-term follow-up and nutritional assessment. Patient weights were recorded at 2 weeks, 6 months, and 1 year and an interview conducted at a mean of 36 months postoperatively for the evaluation of eating patterns and symptoms. A subgroup of those patients (32 of 48) completed a 3-day dietary record that was assessed by a licensed nutritionist. This patient group included 10 patients (21%) who had received perioperative chemoradiotherapy [55].

Dietary intake was characterized as normal or minimally limited in 41 patients (85%). Those who had received perioperative chemoradiotherapy needed no significant increased time to return to a traditional dietary baseline (6.1 versus 5.9 months). Mean weight loss before surgery was 3 kg. Weight loss continued for the primary 6 months (mean 10 kg); however, 63% were ready to gain weight from 6 months to 1 year following surgery (mean 3 kg). Most patients were overweight before operation (mean 115% of ideal body weight) and achieved a replacement postoperative baseline (mean 104% of ideal body weight) at 1 year. Patients demonstrated a mean daily caloric intake of two ,179 kilocalories per day, which was 98% of recommended consistent with their ideal weight. Postoperative symptoms of short-term nausea (19%), occasional dysphagia with certain foods (38%), mild increased stool frequency (15%), and occasional regurgitation (25%) were noted [55].

Near-total esophagectomy with verticalized gastric tube without a gastric emptying procedure is well tolerated and allows a return to subjectively acceptable and nutritionally appropriate dietary eating pattern without significant associated side effects. © 2001 Excerpta Medica, Inc. All rights reserved [55].

The study cohort comprised 23 patients who had undergone curative resection of a primary carcinoma following esophagectomy for a primary esophageal carcinoma. Clinical characteristics and surgical outcomes were analyzed. The initial treatment for esophageal carcinoma was esophagectomy by thoracotomy in 10 patients and video assisted thoracoscopic surgery in 13. The treatments for carcinoma comprised wedge resection in three patients, segmentectomy in seven and lobectomy in 13. The pulmonary resections were performed by thoracotomy in six and video assisted thoracoscopic surgery in 17. The average operating time for the carcinoma surgeries was 202 min and average blood loss 122 ml. There were no perioperative deaths or severe complications [56]. Three- and Five-year overall survival rates were 78.0% and 68.2%. According to univariate survival analysis, age, restrictive ventilatory impairment and histology of lung cancer were significant predictors of poor prognosis (all $P < 0.05$). Significantly more of the patients with than without restrictive ventilatory impairment died of other diseases ($P = 0.0036$). Pulmonary resection for primary lung cancers following esophagectomy for esophageal carcinoma is suitable in selected patients. Such surgery requires caution concerning intrathoracic adhesions and postoperative prolonged air leakage. Patients with restrictive ventilatory impairment had a poorer prognosis, and thus the indication for surgery in these patients should be carefully considered [56].

Pyloric drainage procedures, namely pyloromyotomy or pyloroplasty, have long been considered an integral aspect of esophagectomy. However, the necessity of pyloric drainage within the age of minimally invasive esophagectomy (MIE) has been brought into question. This is partially due to the technical challenges of performing the pyloric drainage laparoscopically, leading many surgical teams to explore other options or to abandon this procedure entirely. We have developed a completely unique, technically facile, endoscopic approach to pyloromyotomy, and sought to assess the efficacy of this new approach compared to the quality surgical pyloromyotomy [57]. Methods Patients who underwent MIE for cancer from 01/2010 to 12/2019 were identified from a prospectively maintained institutional database and were divided into two groups according to the pyloric drainage procedure: endoscopic or surgical pyloric drainage. 30-day outcomes (complications, length of stay, readmissions) and pyloric drainage-related outcomes [conduit distension/width, nasogastric tube (NGT) duration and re-insertion, gastric stasis] were compared between groups [57]. Results 94 patients were identified of those 52 patients underwent endoscopic PM and 42 patients underwent surgical PM. The groups were similar with reference to age, gender and comorbidities. There were more Ivor-Lewis esophagectomies in the endoscopic PM group than the surgical PM group [45 (86%), 15

(36%) $p < 0.001$]. There was no significant difference within the rate of complications and readmissions. Gastric stasis requiring NGT re-insertion was rare within the endoscopic PM group and didn't differ significantly from the surgical PM group (1.9-4.7% $p = 0.58$) [57].

18. Conclusions

Esophagus may be a complex organ with limited abilities of self-repair. Esophageal malignancies suffer from limited treatment options. Surgical interventions and chemoradiotherapy are most generally practiced during this aspect. However, invasiveness of the surgical procedure is associated with the number of peril and post-operative complications including, mortality. Efficient management of these adverse event contributes to the success of overall therapeutic procedure. Patients' history, detailed examination and preoperative preventive measures can improve surgical outcomes. Early diagnosis of the cancer can be treated by lesser non-invasive therapies such as endoscopic radiofrequency ablation for Barrett's esophagus and end mucosal re-section for nodular conditions. Moreover, tissue engineering has opened great diversity of therapeutic alternatives such as; stem cell therapy, bio-scaffolds and biomaterial, which are under animal-based, pre-clinical and clinical investigations for esophageal reconstruction [5]. A number of animal studies have reported successful outcomes in this regard, such as the use of tubelized acellular matrix autologous skeletal myoblasts, enclosed by human amniotic membrane and seeded with autologous epithelial cells for esophageal stenosis and extracellular matrix scaffolds made of porcine urinary bladder extracellular matrix [105, 106]. Multidisciplinary approach is available of esophageal cancer, nonetheless, detailed studies regarding side-effects of these therapies can improve the outcomes of the procedures and hasten recovery. Endoscopic pyloromyotomy employing a novel approach may be a safe, quick and reproducible technique with comparable results to a surgical PM within the setting of MIE [57].

The combination of scopolamine ointment and NPWT could also be considered one effective treatment option for intractable enterocutaneous fistula thanks to AL after esophagectomy [51].

In conclusion, this pilot study outlines, during a postesophagectomy cohort with significant weight loss, the parallel characterization of multiple levels of the gut-brain axis and eating behavior, which can benefit future work aiming to better elucidate the role of these processes in the etiology of postoperative malnutrition. Moreover, it provides insight into the impact of a 4-week 10-mg octreotide LAR treatment course on the postprandial gut hormone response, food reward, and eating behavior. Although gut-hormone suppression was suboptimal, patients didn't exhibit altered weight or appetitive behavior. These findings could also be went to inform the planning of future studies investigating the worth of gut-hormone attenuation as a therapy for malnutrition and weight loss, while also improving our mechanistic understanding to facilitate the development of more targeted therapeutic strategies [36].

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