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Factors that Impact Outcome in Patients Post-Esophagectomy

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Abstract

Background: Esophageal malignancy and severe benign esophageal disorders are now treated by esophagectomy. Although mortality rates after esophagectomy have progressively decreased, many patients continue to suffer from increasing problems despite advances in patient selection, surgical techniques, and postoperative care. The purpose of this research is to determine the perioperative variables that affect morbidity and mortality after esophagectomy.

Methods: A thorough search of Google Scholar, UpToDate, and the Lindell Library was conducted to find previously published papers describing the different outcomes related to esophagectomy. This research consulted a total of 30 reviews and two publications. The esophagus's architecture, perioperative evaluations, surgical methods, and anastomoses that reduce morbidity and mortality after esophagectomy were all investigated.

Discussion: Patient selection was risk stratified using ERAS criteria and the Charlson score. A recent study has shown that minimally invasive access is linked with better results than more intrusive approaches. According to further research, hospital duration of stay and surgery volume are related in an inverse manner. In the postoperative period, the ERAS protocol had a significant impact on postoperative care.

Conclusion: In recent decades, surgical and medical advances have improved the post-esophageal resection results, although overall morbidity and death rates remain high. Perioperative factors that influence postoperative outcomes have been discovered and are the subject of this review. Centralization of preoperative and postoperative care, less invasive esophagectomy techniques, and surgical care in high-volume facilities should enhance post-esophagectomy outcomes.

Introduction

Since Czerny's 1870s introduction of esophagectomy, surgically removing a portion of the esophagus has been feared for its catastrophic postoperative outcomes[1]. The esophagus is removed, and the remainder of the stomach is formed into a tube (-the conduit). The stomach is drawn up into the chest, thus completing the esophagus and linking it to the conduit. The cross-connection creates an anastomosis, which results in a continuous functioning digestive system[2]. Surgical techniques differ depending on the surgeon's degree of comfort and patient-specific variables. Surgical methods include thoracotomy, minimally invasive, robotic, Ivor-Lewis, Transhiatal, and McKeown 3-Field. Despite efforts to standardize surgical techniques and improve preoperative risk assessments, esophagectomy remains technically challenging and is associated with a 30-60% postoperative morbidity rate[3].

Understanding esophageal anatomy is critical to better differentiate the right surgical technique. The esophagus is divided into four layers: the innermost mucosa, submucosa, muscularis propria, and adventitia. Unlike the remainder of the gastrointestinal system, the esophagus lacks a serosal layer. A stratified squamous epithelium protects the lining[4]. It is situated in the posterior mediastinum and spans the seventh cervical to the eleventh thoracic vertebrae. The trachea and pericardium surround the esophagus ventrally, the azygos vein and thoracic duct dorsally, and the aorta and pleura laterally[5]. The esophagus is classified anatomically into four segments: cervical, thoracic, lower thoracic (esophagogastric junction), and abdominal. The cricopharyngeus muscle, bronchoaortic constriction, and esophagogastric convergence are shown in Figures 1 and 2. These anatomical landmarks are critical for avoiding anastomotic leaks, strictures, and perforations during surgery[6].

The arterial blood supply is received from branches of the inferior thyroid arteries and vessels from the thoracic aorta, bronchial arteries, inferior phrenic arteries, and the left gastric artery. Blood drains into the inferior thyroid, hemiazygos, azygos, and left gastric vein[6]. The stomach is often utilized as a conduit in an esophagectomy. It receives blood from the right gastroepiploic artery and supplies both the esophagus and stomach remnants. Due to the esophageal and stomach requirements for abundant vascular supply, a shortfall may result in tissue ischemia and necrosis, resulting in an anastomotic leak[1]. In the lymphatic system, the esophagus forms a submucosal plexus, and the regional lymph nodes stretch from the periesophageal cervical nodes to the celiac nodes[5]. The recurrent laryngeal nerve runs through the thoracic region and is critical to consider during surgery due to its increased risk of injury during lymph node dissection.

The unique features of the esophagus, its surrounding organs, resection, and reconstruction methods make intraoperative and postoperative phases more difficult. The Esophageal Complications Consensus Group (ECCG) reports national results after esophagectomy and compares them to the Dutch Upper Gastrointestinal Cancer Audit (DUCA). Table 1 presents DUCA surgical complications, 30-day hospital mortality, and readmissions[7]. The outcomes vary based on the surgical resection and method utilized. To evaluate perioperative outcomes between surgical procedures, Meredith et al. highlight the importance of operational results in Tables 2 and 3[8]. Pulmonary complications are the most frequent post-esophagectomy issues and the main cause of surgery-related death. Pulmonary problems may occur because of faulty anastomoses that allow saliva, swallowed debris, or leaky gastric secretions to enter the esophagus, staple line, or conduit[9]. Postoperative conduit necrosis, diaphragmatic hernia, atrial arrhythmias, and deep vein thrombosis are possible. Additional perioperative complications and symptoms include hemorrhages, vocal cord paralysis, tracheobronchial tree damage, chyle leaks, dysphagia, reflux, and reoperation[8].

The main objective of this article is to conduct a review of the literature on the variables that influence patient outcomes after esophagectomy. The goal is to use risk stratification to reduce the occurrence of anastomotic leaks and pulmonary complications, to identify surgical techniques that reduce morbidity rates, to recognize the relationship between hospital volume and surgical outcomes, and to link specific postoperative management to improve patient quality of life following esophagectomy.

Background

The esophagus is generally unsalvageable or inferior to the quality of life after an esophagectomy[10]. In other words, esophageal resection is reserved for individuals with resistant illnesses or diseases that are unaffected by previous therapy for benign diseases to esophageal neoplasms. Esophageal cancer is a disease in which an esophagectomy is required for an incentive cure. In terms of mortality, esophageal cancer ranks sixth among all malignancies and eight among cancer causes worldwide[11]. Squamous cell carcinoma and adenocarcinoma are the two forms of esophageal cancer. The majority of esophageal adenocarcinomas (EAC) arise as a result of Barrett metaplasia in persistent gastroesophageal reflux. The cardia's precancerous metaplastic columnar cells replace the esophageal squamous epithelium. Helicobacter pylori (H. pylori) has been found to exacerbate gastroesophageal reflux by lowering the lower esophageal sphincter pressure as a result of its enhanced acid secretions and higher incidence rate of EAC[12]. Alcohol and tobacco usage, poor socioeconomic position, human papillomavirus (HPV), Epstein-Barr virus, and polyomaviruses are all potential risk factors for esophageal squamous cell carcinoma (ESCC)[12]. The epidemiology and biology of HPV-associated ESCC are largely unknown; however, investigations have shown that 5% of carcinomas are double-positive (HPV-positive and p 16-overexpressing)[12]. Esophagectomy plus perioperative therapy is the gold standard treatment for resectable esophageal cancer. Squamous cell cancer may be treated with just chemoradiotherapy[11]. In general, the therapy and surgical approach to esophagectomy are determined by the stage and location of the tumor. The gastroenterologist, surgeon, and oncologist all contribute to the therapy strategy.

Esophagectomy is often indicated for benign diseases including blockage, perforation, or dysmotility of the esophagus. Conservative treatment is first-line therapy for many minor diseases; however, if repeated therapies fail or the esophagus becomes non-functional, resulting in a poor quality of life, an esophagectomy is necessary[10]. Caustic intake, severe gastroesophageal reflux disease (GERD), and benign neoplasms are all risk factors that may contribute to esophageal blockage. Angulated, 2 cm or longer, or irregularly formed strictures are more than likely to fail dilation and commonly require resection[10]. Alkalotic ingestion may also induce strictures and is usually treated surgically, while acidic injuries are typically treated medically[10]. Patients with GERD who have severe dysmotility symptoms, refractory strictures, perforations, or malignancy progression need an esophagectomy. The most common benign neoplasms that need an esophagectomy are leiomyomas[10].

Boerhaave's syndrome, iatrogenic injuries, and external trauma are the most common causes of perforations. Esophagectomy is urgently advised for major perforations greater than 5 cm with contamination in the mediastinum or abdomen, pre-existing strictures, and uncontrolled leaks lasting more than 24 hours[10]. Achalasia is a condition in which the lower esophageal sphincter is unable to relax, resulting in dysmotility symptoms. It progresses to solid and liquid dysphagia and results in considerable esophageal dilatation, thus decreasing reflux. Food retention and regurgitation of undigested food occur as a result of a damaged esophagus, reducing nutrient intake. Achalasia is considered to be end-stage when the tortuous, sigmoid esophagus is involved, and the esophagus is dilated by more than 6 cm[10].

Preoperative Management and Risk Stratification

Individual complications have an amorphous connection with esophagectomy mortality. Numerous studies have used an enhanced recovery after surgery (ERAS) program. ERAS is a well-established multimodal technique that has been shown to reduce hospital stays, decrease surgical stress response, decrease morbidity, and accelerate recover[13]. As illustrated in Table 4, ERAS comprises of preoperative, intraoperative, and postoperative components. The goal of preoperative measures is to improve and prepare the patient for surgery. Preoperative nutrition, fasting and carbohydrate loading, prehabilitation, patient education, smoking and alcohol cessation, multidisciplinary route, cardiac evaluation, and venous thromboprophylaxis are among the variables[13].

Malnutrition is common in patients with esophageal disorders due to dysphagia-related symptoms. Significant weight loss and dietary deficits may increase the risk of surgical complications, readmission rates, and hospital length of stay[13]. Assume that the prevalence and associated variables of underweight patients are related to a lack of nutrition. In such a situation, several studies suggest perioperative immune nutrition in addition to enteral nutrition. Overall, immunonutrition is more beneficial than standard nutrition and preoperative immunonutrition alone[11, 13]. Chronic obstructive pulmonary disease (COPD) is more prevalent in underweight individuals (BMI < 18.5 kg/m^2), which results in a reduction in diffusion capacity and forced expiratory volume in one second (FEV_1). Patients with a FEV_1 less than 60% of the predicted average value are three times more likely to suffer a pulmonary complication after surgery[1]. The significant prevalence of COPD, along with decreased spirometry and diffusing capacities, results in poor respiratory performance status post-esophagectomy[14]. Nutritional status is a significant perioperative prognostic factor that should be addressed prior to esophageal resection.

In contrast to underweight individuals, studies have demonstrated that obese patients have a significantly longer operational duration and contribute to a more difficult operation[14]. Comorbid diseases such as hypertension, type 2 diabetes, and cardiovascular disease are more likely to occur when BMI rises. Cardiovascular illness raises the likelihood of an abrupt cardiac episode under anesthesia, resulting in a more difficult operation and a longer hospital stay. Mitzman et al. use the Society of Thoracic Surgeons (STS) database to demonstrate that patients who are extremely obese (BMI > 40 kg/m^2) require lengthier surgery durations. Obese individuals spend 45 minutes longer in the operating room, one day longer in the hospital, and are 50% more likely to be readmitted within 30 days after surgery than normal BMI patients (18.5-24.9 kg/m^2) [14]. As a result, patient education, risk assessment, and prehabilitation regimens of exercise and dietary treatments are recommended prior to surgery to minimize unfavorable prognostic risk factors in overall survival rates.

Prehabilitation programs encompass nutritional supplementation, psychological counseling, medical optimization, and respiratory rehabilitation[13, 15]. Preoperative respiratory therapy has been shown to substantially reduce postoperative pulmonary morbidities[13, 15]. Deep breathing exercises, spirometry, and inspiratory muscle training are all part of the therapy. The prehabilitation process has also been proven to decrease anxiety and depression, as well as enhance the quality of life in studies[13]. Furthermore, a meta-analysis found that combining steroids and neutrophil elastase inhibitors lowers pulmonary morbidity, organ failure, and cardiovascular complications[15]. Prehabilitation regimens, however, may be impractical for many patients since some individuals with operable esophageal disorders only have hours to days to complete the recommended therapy.

Tobacco use is a major risk factor for pulmonary morbidities[15]. Many studies have reported that preoperative smoking cessation should last longer than 30 days to minimize post-esophagectomy respiratory complications, including pneumonia and wound infections[13,15]. Exhaled carbon monoxide levels may confirm and evaluate smoking status, ensuring that the patient has genuinely quit smoking before surgery. Alcohol cessation should also be advised since it may lead to cardiac and hemorrhagic complications[13].

Several reviews have revealed the Charlson Comorbidity Index (CCI), which includes 19 strictures that predict ten-year mortality for patients with a variety of comorbid illnesses. The parameters include diabetes, congestive heart failure, peripheral vascular disease, chronic lung illness, liver disease, hemiplegia, renal disease, leukemia, lymphoma, metastatic tumors, and acquired immunodeficiency syndrome. Each variable is evaluated based on its probable impact on mortality, in this instance, post-esophageal resection. A Charlson score of 2 or greater has been linked to an increase in postoperative complications and long-term mortality[11]. To minimize postoperative problems, patients with a Charlson score of 2 should have cardiac and pulmonary testing prior to surgery. To evaluate the cardiac and pulmonary state, echocardiography, spirometry, pulmonary function testing (PFT), and cardiopulmonary exercise testing (CPET) should be performed[13]. Furthermore, venous thromboembolism develops in 5% to 7% of individuals following esophagectomy. Studies have suggested that high-risk patients be treated prophylactically with low-molecular weight heparin (LMWH) and mechanical methods before and after surgery[13].

From December 2010 to June 2017, Baranov et al. compared the association between age and postoperative outcomes in a database created by Dutch high-volume esophageal cancer hospitals. 357 individuals under the age of 75 were compared to 89 patients who were 75 years or older. There were many components that were evaluated for comparison: surgical complications; inpatient mortality; 30-day mortality; and survival after the minimally invasive Ivor Lewis Total Esophagectomy. Age, BMI, sex, hospital volume, American Society of Anesthesiologists (ASA) physical status classification, a Charlson Co-morbidity index score, tumor type, location, and stage were the most common patient variables[16]. Regarding general and severe complications, age did not seem to make a difference. Notably, the older group had greater rates of cardiac problems and delirium, as well as a longer hospital stay. Overall, the research indicates that esophagectomy should not be delayed due to age alone[16].

Operative Procedures

There are many surgical techniques for esophageal excision. As a result of its dependable blood supply and ability to reach into the thoracic or neck, the stomach is the ideal conduit. The right gastroepiploic artery, which feeds the distal end of the anastomosis, provides the primary blood supply to the gastric conduit[3]. Each surgical method includes an abdominal incision to provide access to the creation of the gastric conduit[3]. The cervical excision is performed on the left side. The upper, middle, and lower thoracic (EGJ) excisions are performed on the right, whereas the abdominal excision is performed on the left. It is possible to reach all parts of the esophagus using the right approach; however, only the distal esophagus can be reached using the left approach[5]. Numerous studies compare surgical techniques based on postoperative complications, morbidity and mortality rates, and overall survival rates.

The Ivor Lewis esophagectomy (ILE), commonly known as the transthoracic surgical technique, is addressed via an abdominal incision, a right posterolateral thoracotomy, and a right chest anastomosis. The chest anastomosis reduces conduit assembly tension, resulting in a shorter pull distance. The incidence of anastomotic leak and stricture has decreased to 4.8% compared to 7.6% in the Transhiatal (THE) approach[8]. The stated median operation time is 366 minutes[17]. The ILE is strongly recommended for malignancies of the lower third of the esophagus because it enables en bloc excision of the esophagus and mediastinal lymph nodes. Nonetheless, it is not optimal for tumors located in the center third due to the inability to establish adequate proximal margins[6]. Numerous studies have recommended the ILE with a right thoracic anastomosis given its benefits and favorable postoperative results. It has been the preferred technique during the past decade, accounting for 62.4% of esophagectomies, compared to 21.5% done through THE[8, 11]. McKeown remained consistent throughout the decade, fluctuating between 13.2% and 19.4%[18]. Patients using the ILE technique had substantially better oncologic results, with 679 R0 resections (95.6%) and a mean lymph node harvest of 13, compared to 122 R0 resections (93.1%) and nine lymph nodes harvested with the THE approach[8]. Additionally, patients experienced fewer wound infections, recurrent laryngeal nerve damage, and a shorter hospital stay, although their operation duration was much longer than that of the THE[3, 8]. The ILE has a drawback in that it increases the risk of pulmonary complications. The anastomotic leak in the mediastinum is not usually readily accessible, increasing the risk of mediastinitis and severe pneumonia[3, 18].

Transhiatal esophagectomy (THE) is performed via incisions in the abdomen and left neck. The technique entails mobilizing the stomach laparoscopically, dissecting the thoracic esophagus, and forming a cervical esophagogastric anastomosis through a left cervical incision[8].

The median operation time resulted in the shortest duration of 278 minute**s**[17]. Individuals with impaired pulmonary function, severe pulmonary fibrosis, or borderline fitness are chosen for this appraoch[13]. Additionally, the neck anastomosis results in an accessible neck incision in the event of a proximal anastomotic leak. If the anastomosis is distal to the neck incision, access to the leak is difficult due to the lack of a chest incision. Assume that the esophagus is not dissected openly; blind dissection may exacerbate lymph node harvest[3]. Blind dissection may also pierce the pleura, resulting in frequent pleural effusions, atelectasis, and pneumonia, as well as the greatest pulmonary consequences as compared to the transthoracic approach[8]. On the downside, THE is associated with the greatest rates of anastomotic leaks, anastomotic strictures, wound infections, intrathoracic hemorrhages, recurrent laryngeal nerves, chylothorax, urinary tract infections, and sepsis[6, 8, 18].

McKeown's approach is referred to as the three-field incision. It is performed via a left-sided neck incision, a right-sided chest incision, and an abdominal incision with a left-sided neck anastomosis. Neck anastomoses feature controllable and accessible anastomotic leaks, reduced reflux rates, and extensive proximal resection margins[6]. As a limitation, once the anastomosis or tip of the gastric conduit is ischemic, the McKeown method becomes susceptible to gastric conduit failure and may eventually result in an anastomotic leak[19]. Another retrospective research established the importance of recurrent laryngeal nerve palsy (RLNP) in McKeown's method, which significantly increased hospital length of stay due to an inability to properly protect the airway[1]. Considerably, many patients with RLNP injuries recover in approximately 18 months with conservative management[1]. The surgical technique is the most time-consuming, taking 414 minutes to complete. Complication rates are often greater with this technique and do not seem to alter as the operational duration increases[17].

Principles of Surgical Approach

Esophagectomy may be performed using one of three surgical techniques: minimally invasive esophagectomy (MIE), open transthoracic esophagectomy (OTE), or robot-assisted esophagectomy (RAE). Hospital and surgeon preferences are given for surgical operations. Numerous studies have been conducted to further enhance esophageal resection outcomes by comparing mortality, safety, efficacy, and quality of life among surgical methods.

MIE is conducted using a variety of video-assisted thoracoscopic and laparoscopic procedures, while OTE is performed using a thoracotomy and laparotomy. Total Minimally Invasive Ivor Lewis esophagectomy, Hybrid Ivor-Lewis esophagectomy, and Laparoscopic Transhiatal esophagectomy are the three most often used MIE techniques. MIE is now the recommended surgical technique across the globe, since many studies have proven that it substantially reduces the incidence of respiratory complications formerly linked with OTE. Additionally, a MIE through a transthoracic route is the best approach for esophageal resection in patients who have already undergone neoadjuvant therapy[8,20]. Minimal invasive technique have been shown to substantially reduce pulmonary and wound complications, decrease estimated blood loss, and increase R0 resection rates and lymph node harvesting[8, 9]. Takahasi et al. reviewed the TIME trial and concluded that MIE enhanced global health, physical component, and quality of life more than the OTE approach[3]. Takahasi et al. also examined the Society of Thoracic Surgeons' National Database to compare the results of MIE with open esophagectomy. The database showed that although morbidity and mortality rates were comparable, MIE was linked with longer surgical times, shorter hospital stays, and higher rates of empyema and reoperations[3]. In contrast, patients who underwent open esophagectomy had an increased rate of postoperative transfusions, ileus, and wound infections[3]. Research has confirmed these findings and demonstrated evidence to support the use of a minimally invasive approach as the standard of care for esophagectomy to improve further pulmonary complications, hospital length of stay, and quality of life.

Robot-assisted esophagectomy (RAE) has a lower risk of postoperative complications and a higher quality of life than open esophagectomy (OTE)[9]. Robotic surgery allows for more accurate dissection of lymph nodes in the upper mediastinum. Yang et al. found that RAE, rather than MIE, increased the surgeon's confidence in completing bilateral recurrent laryngeal nerve (RLN) lymph node dissection in resectable ESCC. Additionally, it has been shown that RAE substantially reduces the incidence of RLN damage associated with vocal cord palsy and hoarseness[21]. The favorable capabilities of the robotic system are anticipated by its three-dimensional vision, tenfold magnification, tremor control, and ambidexterity[9]. The limitations of the surgical technique were a longer operation time, particularly the robotic-assisted Ivor Lewis (RAIL) procedure, which took 409 minutes[8]. While prolonged operation times may raise the risk of postoperative respiratory problems, many studies have shown no evidence of an increased risk of respiratory complications[8,9]. Significantly, RAIL had the lowest rate of wound infections (0.7%) and the lowest rate of pulmonary sequelae (pleural effusion, pneumonia, or pulmonary embolism) (9.7%)[8]. Overall, the 5-year overall survival rates (OS) for the two comparison groups were not statistically significant; RAE resulted in a 69% OS and MIE resulted in a 59% OS[9].

In 2003, the robot-assisted minimally invasive thoracolaparoscopic esophagectomy (RAMIE) was created to aid in overcoming the technological limitations of the MIE[20]. With its stable three-dimensional precise dissection, mobility, and vision enhancements, robot-assisted surgery offers many advantages[3]. Many studies have shown that the RAMIE, as compared to an OTE, has a substantial reduction in postoperative complications, blood loss, pulmonary and cardiac issues, postoperative discomfort, and improved functional recovery and short-term quality of life[20]. However, the overall oncologic outcomes of radical resections (R0), the number of resected lymph nodes, and overall survival rates did not vary significantly from an OTE[20].

Reconnection Location

Following an esophageal resection, the gastric pull-up is inserted cervically or intrathoracically, forming an esophagogastric anastomosis. The location and kind of anastomosis may result in anastomotic leakage, which can have lethal implications. Despite MIE's better surgical methods and improved patient selection, studies indicate that the morbidity and mortality linked with anastomotic leaks remain significant[22]. Merritt et al. reviewed research that found that following an open esophagectomy, cervical anastomosis resulted in a greater incidence of anastomotic leakage than intrathoracic anastomosis. A total of 262 patients were randomized and received a complete MIE with either a cervical or intrathoracic anastomosis in another comprehensive review. Consequently, 12.3% of patients had an intrathoracic anastomotic leak, while 31.7% developed a cervical anastomotic leak[22]. The higher leak rate in a cervical anastomosis may be attributed to increased strain and location in the stomach fundus, as well as potentially decreased vascular supply. Simultaneously, distal intrathoracic esophagogastrostomies are performed in less severe longitudinal stress regions with improved stomach perfusion[23]. The management of an anastomotic leak varies depending on where the anastomosis is located. Cervical anastomotic leaking may be less dangerous than intrathoracic anastomotic leaks. The cervical leak has the potential to reduce leak-associated morbidity due to its quick and accessible surgical neck incision[23].

The diameter, length, and direction of the gastric conduits all influence the function of the upper gastrointestinal tract. Inadequate conduit repair may result in complications due to ingested food and fluids accumulating in the esophagogastric anastomosis, stomach body, and gastric outlet[24]. Thus, esophageal and gastric reconstruction are just as crucial as resection since leakages of luminal contents are evidently frequent. To prevent excessive esophageal devascularization during gastric tube construction, it is critical not to dissect the intrathoracic esophagus higher than the tip of the conduit can safely reach[24]. Numerous studies provide contradictory data about the rates of anastomotic leakage after narrow and wide gastric tubes or complete stomach reconstruction. According to some accounts, eliminating the lesser curvature may result in ischemia of the stomach's top portion and an increased risk of anastomotic leakage. In comparison, one research concluded that eliminating the top portion of the greater curvature and repositioning the staple line closer to the lesser curvature maintains the maximum amount of intramural vascular network feasible[23]. In contrast, another revision highlighted that vascular and lymphatic stripping of the lesser curvature had no effect on the intramural vascular network and recommended complete stomach rebuilding, which resulted in decreased anastomotic leakage rates[23]. It's worth noting that most providers and facilities now use a wide (4-5 cm) gastric tube reconstruction[23]. When the gap between the pylorus and the hiatus is too large after gastric mobilization, the Kocher's maneuver may be performed. The gastric tube is extended by splitting the hepatoduodenal ligament's peritoneal reflection and performing Kocher's procedure through duodenal mobilization[23]. If a very high cervical anastomosis is accomplished and extra length is required, a longitudinal or circular incision of the gastric serosa may be done as well[23].

Many surgeons have practiced and refined different anastomotic methods to reduce complications associated with anastomotic leakages. Techniques include hand-sewn, stapled (linear-stapled, circular-stapled, and double-stapled), end-to-end, side-to-side, single-row, and double-row techniques[23]. Vetter et al. conducted a meta-analysis and discovered that the side-to-side line-on-staple line (STS) esophagogastrostomy method results in lower anastomotic leakage rates than the end-to-side hand-sewn technique in cervical anastomosis[23]. The leakage rates were considerably greater in the intrathoracic end-to-side double-stapling and cervical end-to-side hand-sewn methods than in the intrathoracic side-to-side linear, end-to-side purse-string, and cervical side-to-side linear stapled esophagogastrostomy techniques[23]. Another study demonstrated improved outcomes with the linear-stapled technique; however, the various anastomotic stapled or hand-sewn methods had no effect on anastomotic leakage rates or postoperative outcomes[25]. In contrast, a study reviewed by Kesler et al. confirmed a 5.6% intrathoracic leak rate using the STS method in 177 patients, compared to an 8.3% leak rate in 48 patients undergoing anastomosis using an end-to-end anastomotic (EEA) stapler [24]. Rather than strong scientific confirmation, the anastomotic method remains a surgeon's decision and personal experience[23].

Additional surgical procedures have been utilized to decrease anastomotic leakage and stricture rates, thus lowering esophagectomy morbidity and death. Numerous studies have emphasized the benefit of pedicled omental flaps in promoting esophagogastric reconstruction healing[23]. The top portion of the omentum along the gastric fundus is wrapped and stapled to the esophagogastric anastomosis. The gastroepiploic artery adequately perfuses the fatty tissue, providing an ample supply of nutrients and oxygen to the anastomotic region, thus boosting angiogenesis and oxygenation of the healing process. Additionally, the omental flap protects against leakage by covering the defect and forming a protective barrier that prevents infection or free leakage into the mediastinum[23].

Postoperative Management

The ERAS program has been established with the goal of improving short- and long-term surgical outcomes and mortality. Table 4 illustrates the postoperative components which include early mobility and rain removal, early enteral feeding, perioperative pain management, postoperative nausea, and vomiting, and postoperative glycemic control[13, 26]. Early mobilization is critical in decreasing the risk of muscle loss, pulmonary complications, and venous thromboembolism development. Patients are encouraged to ambulate on the day after surgery, if possible, and to utilize the incentive spirometry[13, 26]. Thoracic epidural analgesia (TEA) with local anesthetic and opioids, as well as systemic acetaminophen and diclofenac, is frequently used to manage perioperative pain. TEA has indicated that it may help reduce anastomotic leak rates by perhaps improving microcirculation[13].

A thorough barium swallow exam (esophagram) is performed during the first few days after surgery to further analyze the anastomosis for leak detection and to monitor the emptying of the gastric conduit. The first study used a water-soluble contrast medium that is ideally nonionic and low in osmolarity. The use of a hyperosmolar contrast medium may lower the risk of aspiration pneumonia and mediastinal inflammation caused by erupted barium[27]. To minimize the risk of pneumonia, the swallow study is performed prior to the start of enteral and oral feedings.

Many patients undergoing an esophagectomy are often maintained nil-by-mouth (NPO) postoperatively due to the substantially higher rates of anastomotic leakage and pulmonary complications[28]. Optimizing the patient’s nutritional condition, on the other hand, is important for enhancing functional and healthy outcomes with lower infection rates. Many institutions have changed their nutritional assistance in terms of optimum time (early versus delayed) and nutrition delivery route. Table 5 depicts and compares clinical studies on oral feeding following esophagectomy using various surgical techniques[29]. Artificial nutritional supplements (tube feeds) or direct oral feeding may be used to give feedings. TPN, nasoduodenal/nasojejunal tubes, and a jejunostomy tube are all methods of artificial enteral nutrition. On postoperative day one (POD1), enteral nutrition is recommended to be started through a feeding jejunostomy tube (j-tube) [13, 29]. In terms of malnutrition, complication rate, and functional recovery, early artificial enteral feeding following esophagectomy has been shown to be superior to complete parenteral nutrition[29]. Parenteral nutrition should be used only when enteral feeding is not possible, since it is linked with an increased risk of metabolic abnormalities, elevated liver enzymes, and sepsis[13].

Zheng et al. define early enteral nutrition as occurring within 48 hours after surgery as opposed to delayed feeding lasting more than 72 hours[29]. Patients who began j-tube feedings within 48 hours after surgery had the lowest thoracic drainage volume, the earliest initial fecal passage, the shortest duration of a systemic inflammatory reaction, and the shortest hospital length of stay. The incidence of pneumonia was greatest in the late feeding group, indicating that enteral feeding early in the first 48 hours is correlated with improved outcomes[29]. Conversely, a retrospective analysis of transthoracic esophagectomies from 1996 to 2010 found no significant difference in infectious complications such as pneumonia, wound infection, and sepsis when compared to j-tube feeding after the third postoperative day[29].

A meta-analysis examined the effect of home enteral nutrition (HEN) following surgery on individuals who choose to continue enteral feeding at home rather than have the feeding tube removed upon discharge. Overall, it may take patients up to nine months following surgery to adjust to a new diet, since many patients have gastrointestinal adverse effects within a year after surgery[30]. The systemic evaluation, which was based on randomized controlled trials, was the first to assess the effect of HEN after an esophagectomy. It was proven that HEN enhanced nutrition status, physical and role function, and decreased nausea, appetite loss, diarrhea, and sleep disruptions in post-surgery patients when compared to an oral diet, without increasing gastrointestinal side effects[30].

Traditionally, a feeding tube is inserted prior to or during the procedure to give enteral access to patients undergoing esophagectomy since the anastomosis requires 5-7 days of nil by mouth to heal post-surgery[31]. Due to the significant danger of anastomotic leakage once liquids or solids are introduced, there is no consensus on the timing and safety of oral consumption following surgery. Early oral feeding on POD1 versus POD3-POD7 in patients with a stable esophagram post-surgery has been found to have a substantial advantage in terms of hospital duration of stay and restoration of bowel function[29]. Table 5 summarizes the outcomes of the oral feeding experiment. In contrast, recent research assessing the early implementation of oral intake as liquids on POD1 and semi-solids on POD2 found no increase in complications and no advantage in terms of regaining bowel function and quality of life[13]. Another randomized trial compared the duration and functional recovery to a standard of care (NPO for five days) in direct oral feeding following a MIE with an intrathoracic anastomosis. Anastomotic leakages and pneumonia rates were also assessed. Direct oral feeding had no effect on functional recovery and was not associated with an increased incidence or severity of postoperative consequences[28].

Morbidity and Mortality

The surgeons' and institutions' expertise and volume of esophagectomies are equally as important as the surgical technique in minimizing morbidity and mortality rates. Many studies show that patients who had esophagectomy performed by high-volume surgeons had improved results in terms of morbidity and mortality outcomes, with a confirmed 23% decrease in mortality rates[3]. A systemic study revealed a current examination of the empirical connection between hospital esophagectomy volume and postoperative duration of stay. Figure 3 displays an inverse-dose response connection between hospital duration of stay and surgery volume. Centers with four cases per year had an average hospital stay of approximately 15-20 days, while hospitals with more than 17 cases per year had an average hospital stay of less than 15 days[32]. The study shows that an esophagectomy is a volume-sensitive operation, and patients who have esophagectomies at hospitals that conduct more than 17 cases per year may have a substantially shorter hospital stay. The type of facility, the patient's insurance, surgical complications, and medical morbidities had no effect on outcomes. In a 13-year observational cohort analysis of open esophagectomy operations, the effect of hospital size on national trends and in-hospital outcomes was examined throughout the United States. Across small, medium, and big hospitals, no significant variations were found in patient mortality or hospital mortality. However, from 2002 to 2014, all hospitals' in-hospital mortality rates declined[33].

Methods

A search is conducted using Google Scholar, UpToDate, and the Lindell Library to find previously published peer-reviewed publications reporting on the results of esophagectomy. The research focuses on surgical methods, anastomosis types, and different strategies for reducing morbidity and mortality after esophagectomy. The search term "esophagectomy" was used in conjunction with terms "complications," "esophageal cancer," "risk factors for esophageal cancer," "enteral feeding," "surgical methods," "anastomotic leaking," "minimally invasive esophagectomy," "morbidity," and "mortality." Throughout the literature study, a total of 30 reviews were consulted. Additionally, literature such as Evidence-Based Gastroenterology and Hepatology and Lange 2020 Current Medical Diagnosis and Treatment were used. The study was restricted to the period from 2018 to 2021. The inclusion criteria required concise summaries of the study's major results and proof of the study's internal validity. Each study was independently evaluated, and data was gathered to better enhance the different outcomes of esophageal resection.

Discussion

Interpretation

Esophagectomy is a complex operation associated with high morbidity and mortality rates. Patients with esophageal cancer and severe benign esophageal diseases are the most frequent candidates for esophagectomy. Common risk factors for esophageal cancer include alcohol and tobacco use, HPV infection, chronic GERD, H. pylori infection, and severe Barrett's esophagus. The most often seen complications after an esophagectomy include pulmonary, anastomotic leakages and strictures, cardiac arrhythmias, chyle leaks, and reoperations. Due to high rates of operational and surgical complications, numerous studies recommend that surgery be reserved for patients with refractory illness, esophageal cancer, or severe end-stage benign disorders that have not been improved by previous therapy[10, 11, 12].

The studies included in this review all have a common objective: to reduce morbidity and mortality, postoperative complications, and to improve patients' quality of life after esophagectomy. To promote early recovery, preoperative treatment and risk stratification in patient selection are conducted in accordance with ERAS recommendations. Prior to surgery, exercise and nutritional therapies are advised since malnourished and very obese patients have a greater risk of regression, readmission rates, infectious, pulmonary, and cardiovascular complications[1, 14].

The impact of surgical techniques has been examined in terms of operation duration, overall morbidity and anastomotic leakage rates, number of resected lymph nodes, and proportion of textbook and researched results. Numerous studies have shown that ILE has become the most frequently used surgical method for esophageal resection. ILE has been proven to significantly reduce the risk of pulmonary and wound complications while also shortening hospital stays. THE is no longer widely utilized and has mostly been replaced by ILE over the last decade due to its association with the highest frequency of anastomotic leakages, anastomotic strictures, wound infections, and RLNPs. Additionally, less invasive esophagectomies have become the favored technique. MIE is associated with the fewest postoperative complications, the least estimated blood loss during surgery, and the highest rates of R0 resection and lymph node harvest. Advanced methods, such as the RAIL and RAMIE, have been linked to lower rates of RLN injuries, wound infections and pulmonary complications, blood loss, and improved short-term quality of life with greater functional recovery.

Anastomotic leaks are a common consequence of esophagectomy, and they are linked with a high risk of mortality. The placement of the anastomosis is most effective when it is tension-free and well-nourished with nutrients and blood flow. Numerous studies have shown that, as compared to cervical anastomoses, intrathoracic anastomoses substantially lower anastomotic leak rates. To further avoid anastomotic leaks and strictures, the majority of providers and centers choose a thin and wide gastric tube or whole stomach reconstruction. The desired conduit restoration technique was not accomplished since many studies disagreed on whether the intramural vascular network is impacted by removing the smaller curvature or reconstructing the whole stomach. Additionally, the anastomotic method remains a matter of surgeon preference and personal experience, rather than a rigid solitary practice. The STS method, in conjunction with the linear-stapled anastomotic approach, is preferred for decreasing intrathoracic leak rates, resulting in improved results.

Postoperative management is best carried out in accordance with ERAS recommendations, which include criteria such as early mobilization, the use of a nonionic and low osmolar contrast media in the esophagram, early enteral feeding, and perioperative pain control. A number of studies have validated that early enteral feeding (within 48 hours) results in a quicker restoration of bowel function and a shorter hospital stay as compared to delayed enteral feeding (more than 72 hours). The research on early direct oral feeding is sparse since many trials have not standardized oral intake time. Typically, oral feeding is started on POD5-POD7; however, several studies have established a POD1 oral feeding and found no increase in complications or improvement in bowel function or quality of life[13, 29, 31].

Implications and Recommendations

Historically, esophagectomy has been linked with high rates of postoperative complications, morbidity, and mortality. Many studies on the ERAS protocol have used risk variables and recommendations to enhance surgical results. Patients with significant symptoms and a low quality of life should be prioritized in terms of criteria and patient selection for surgery. Symptoms may include dysphagia of solids and liquids, food retention and regurgitation, or repeated aspirations. Surgery volume is critical to consider, as many studies indicate that patients should seek out institutions that do more than 17 esophagectomies each year, since this results in a much shorter hospital stay.

To minimize the surgical stress response, patients and their families should be counseled preoperatively with a focus on postoperative goals. Nutritional evaluation should be performed on all patients before surgery to identify postoperative prognostic variables. If the predominance of underweight patients and related variables contribute to the lack of nutrition, perioperative immune nutrition, in addition to enteral nutrition, is suggested. Although prehabilitation programs benefit most patients, they are opportunistic for individuals with limited preoperative windows. Tobacco users should be compelled to quit smoking four weeks before surgery, since smoking increases the risk of pulmonary problems. In addition, patients with a Charlson score of 2 or greater should complete a pulmonary and cardiac function test prior to surgery.

Minimally invasive access is linked with more favorable results, such as less perioperative blood loss, a lower incidence of pulmonary complications, and a shorter hospital length of stay. Furthermore, minimally invasive transthoracic esophagectomy is regarded as the best technique for optimizing overall results. Throughout the years, methods such as RAIL and RAMIE have been developed to shorten the recovery period and blood loss associated with surgery. The conduit reconstruction is determined by its perfusion supply. A narrow or wide conduit is recommended as the initial choice for improving vascular and nutritional supply, coupled with an STS linear-stapled method to minimize the chance of an anastomotic leak.

Early mobilization should be promoted as soon as possible to minimize the risk of muscle mass loss. Patients experiencing postoperative pain should get thoracic epidural analgesia in addition to acetaminophen and NSAIDs. Within the first few days after surgery, an esophagram with a water-soluble, nonionic, and low osmolar contrast agent should be completed. The degree of risk should be used to determine nutritional intervention. While the optimal method and time of oral feeding delivery remain unknown, early enteral feeding (within 48 hours after surgery) through a j-tube is still helpful and highly recommended. Finally, HEN should be explored for patients who want to continue feeding through an enteral tube at home.

Limitations

Several limitations identified in the extensive literature review include the aim of treating all patients who had surgery, varied clinical research, a lack of defined definitions and standards, and many studies with small cohort sizes. Since most of the research aimed to treat all patients who had surgery, patient classification and functional assessment were inconsistent throughout the literature. Many evaluations also included clinical research, and the quality of clinical studies is extremely varied, with just a few treatments backed by strong evidence. In high-volume facilities, prevention and management of anastomotic leaks are guided mostly by observation and personal experience rather than scientific evidence. Numerous studies found that standardized definitions of anastomotic leakage, surgical methods, and patient functional assessment differed. Due to the absence of conventional descriptions, there is a potential for misunderstandings, which may obstruct impartial research on surgical results. Lastly, research on early oral feeding is deficient in studies with high sample numbers, restricting our capacity to make strong recommendations regarding oral feeding practice.

Conclusion

Although post-esophagectomy results have improved significantly over the last several decades as a result of surgical and medical advancements, overall morbidity and mortality rates remain high. Esophagectomy outcomes have traditionally focused on the surgical team and on postoperative complications, length of stay, morbidity, and mortality rates. Clinical routes that are more standardized are being explored to improve outcomes in esophageal cancer and benign esophageal diseases.

ERAS criteria and the Charlson score were used to stratify patients for risk. Given the uneven patient classification observed in the literature, further research is required to develop reliable and consistent prediction techniques for patient selection. Patients who were underweight or very obese were categorized as high-risk, suggesting a higher chance of postoperative complications. Further research is needed to offer a comprehensive preoperative nutritional assessment for malnourished and obese individuals in order to enhance surgical outcomes. This covers long-term nutritional effects as well as the safety of scheduling direct oral feedings.

Mobilization and early enteral feedings have been shown to enhance bowel function and quality of life sooner. According to recent studies, less invasive access through a transthoracic route allows for full esophageal dissection and mobilization of the gastric conduit. The MIE technique produced more remarkable outcomes, including less expected blood loss during surgery, fewer pulmonary and wound infections, a shorter hospital stay, and a higher percentage of lymph node excision. Additionally, new techniques such as the RAIL and RAMIE significantly decrease the time required for recuperation and blood loss connected with surgery. However, further research is required to fully compare RAIL and MIE and their related consequences. Additionally, evidence demonstrated that hospital length of stay and surgery volume had inverse dose response correlations.

Despite advancements in perioperative care and minimally invasive methods, more research is needed to standardize postoperative complications treatment and terminology. Initiating this study has been hampered by a lack of resources (hospital volume), opposition to change, and staff training. There is also a need for further research that specifically concentrates on the ERAS recommendations in the context of various esophagectomy procedures, as well as the long-term morbidity and mortality rates.

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Appendices

Figure 1.[6]

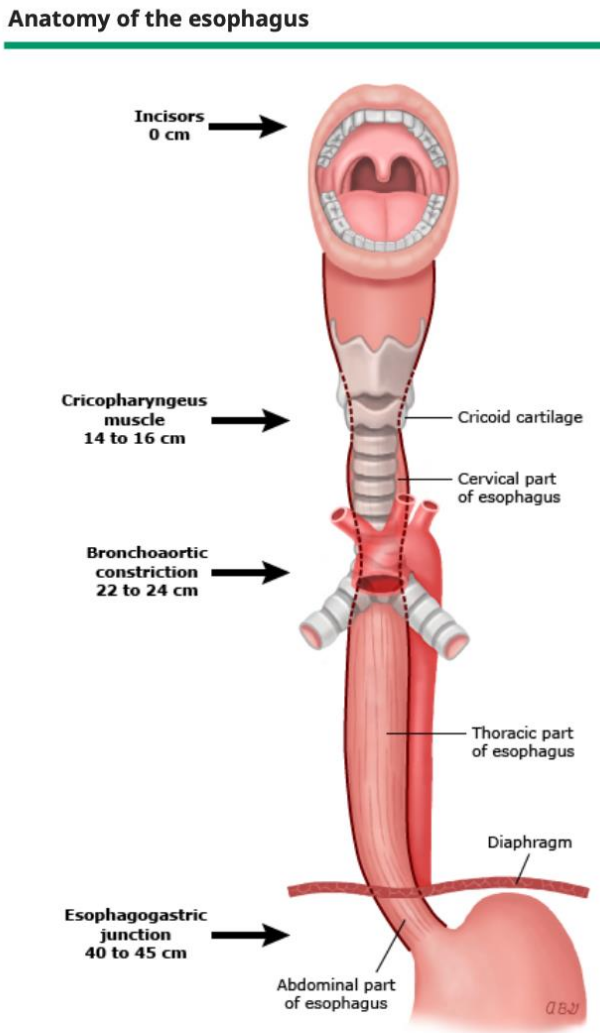
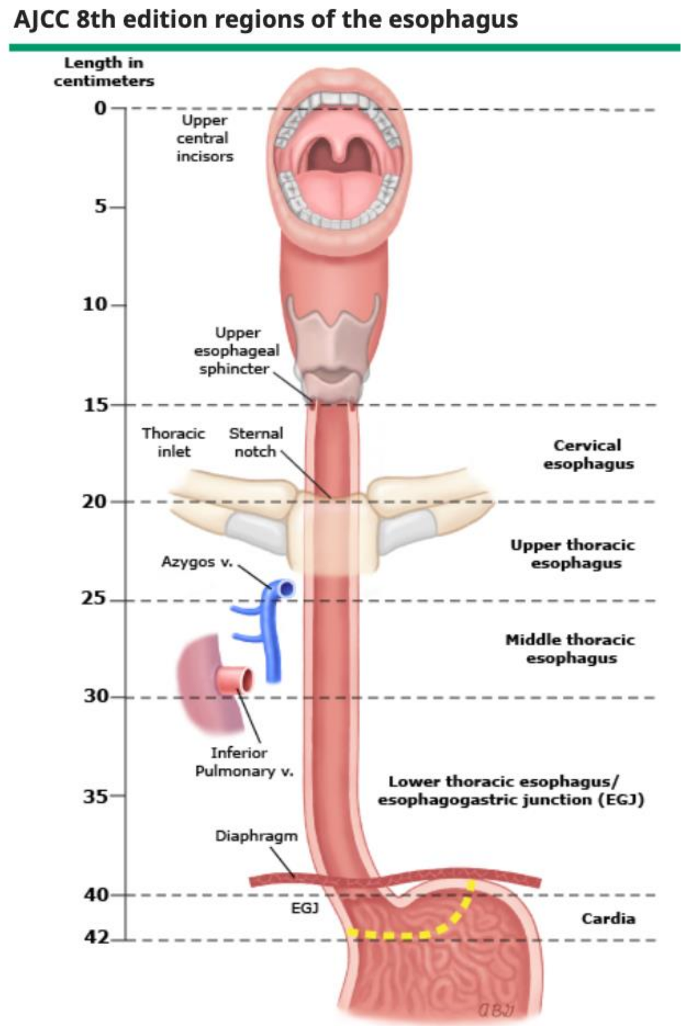


Figure 2.[6]



AJCC: American Joint Committee on Cancer

Figure 3. Relationship between hospital surgical volume and length of stay (LOS) in days versus Hospital Surgical Volume per year[32].

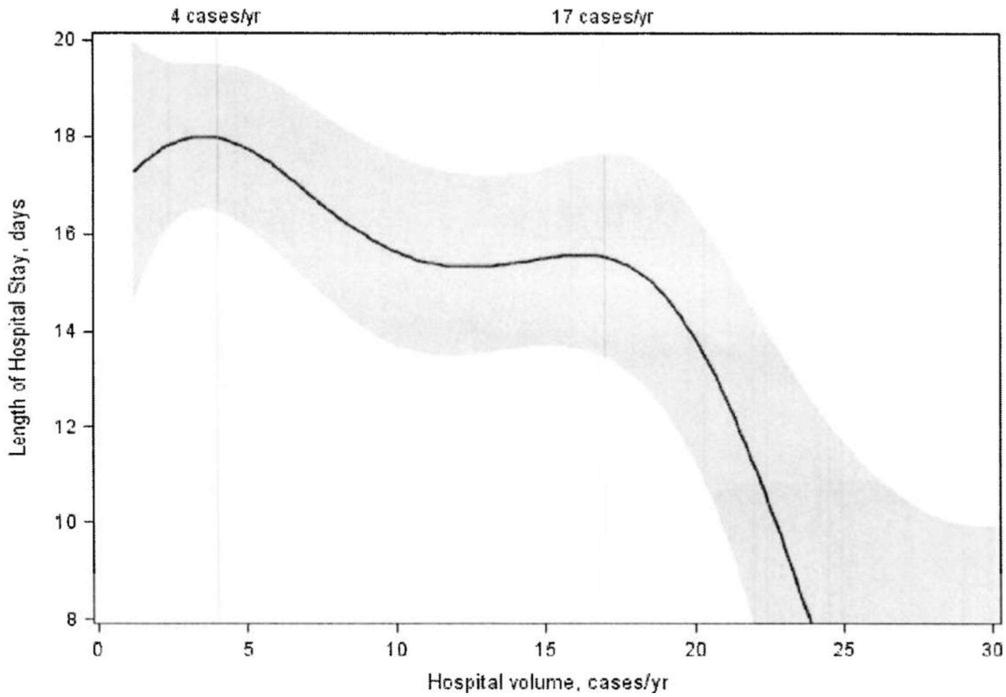


Table 1. Outcomes of the DUCA (Dutch Upper Gastrointestinal Cancer Audit) to Type of Resection[7].

	Esophagectomy	
Total (n =)	**1617**	
	Median	**[IQR]**
Hospital stay (d)	11	[9–18]
ICU stay (d)	2	[1–4]
	n	%
Intraoperative complication	89	5.5%
Postoperative complication	1046	65%
Reintervention	420	26%
Radiological	170	
Endoscopic	187	
Reoperation	208	
In-hospital/30-d mortality	38	2.4%
30-d mortality	27	1.7%
Readmission	233	15%
Postoperative complication Clavien Dindo grade III or more	468	29%

ICU indicates intensive care unit.

Table 2. Operative Outcomes[8].

	OIL $N = 475$ N (%)	RAIL $N = 144$ N (%)	MIE TT $N = 95$ N (%)	OTH $N = 69$ N (%)	MIE TH $N = 63$ N (%)	P value
Preoperative stage						
0-I	55 (14.8)	33 (24.3)	13 (15.5)	14 (27.5)	10 (18.9)	0.05
II-IV	317 (85.2)	103 (75.7)	71 (84.5)	37 (72.5)	43 (81.1)	
Neoadjuvant therapy	274 (57.7)	112 (77.8)	73 (76.8)	35 (50.7)	43 (68.3)	0.001
Estimated blood loss (ml, mean ± SD)	289 ± 354	156 ± 107	189 ± 188	275 ± 226	251 ± 383	< 0.001
Length of hospitalization (days, median, range)	10 (1–115)	10 (4–66)	9 (6–60)	10 (7–63)	10 (7–43)	0.2
Length of operation (min, mean ± SD)	286 ± 69	409 ± 104	299 ± 87	273 ± 89	231 ± 65	< 0.001
Resection						
R0	449 (94.7)	144 (100)	86 (93.5)	62 (89.9)	60 (96.8)	0.04
R1	18 (3.8)	0	6 (6.5)	5 (7.2)	1 (1.6)	
R2	7 (1.5)	0	0	2 (2.9)	1 (1.6)	
Lymph node harvest (mean ± SD)	10 ± 6	20 ± 9	14 ± 7	9 ± 5	9 ± 6	< 0.001

Table 3. Surgical Complications[8].

	OIL $N = 475$ N (%)	RAIL $N = 144$ N (%)	MIE TT $N = 95$ N (%)	OTH $N = 69$ N (%)	MIE TH $N = 63$ N (%)	P value
Anastomotic leak	23 (4.8)	4 (2.8)	4 (4.2)	9 (13.0)	4 (6.3)	0.03
Chyle leak	5 (1.1)	1 (0.7)	1 (1.1)	0	0	0.8
Anastomotic stricture	36 (7.6)	11 (7.6)	3 (3.2)	19 (27.5)	16 (25.4)	0.001
Wound infection	25 (5.3)	1 (0.7)	6 (6.3)	4 (5.8)	10 (15.9)	0.001
Myocardial infarction	6 (1.3)	1 (0.7)	3 (3.2)	1 (1.4)	0	0.4
Cardiac arrhythmias (includes A-fib)	55 (11.6)	25 (17.4)	17 (17.9)	9 (13.0)	10 (15.9)	0.3
Any complication[a]	145 (30.5)	34 (23.6)	28 (29.5)	28 (40.6)	31 (49.2)	0.003
Pulmonary complication[b]	81 (17.1)	14 (9.7)	18 (18.9)	17 (24.6)	24 (38.1)	0.001
Pneumonia	72 (15.2)	10 (6.9)	8 (8.4)	12 (17.4)	18 (28.6)	0.001
Aspiration	7 (1.5)	3 (2.1)	2 (2.1)	10 (14.5)	11 (17.5)	0.001
Pulmonary embolus	9 (1.9)	3 (2.1)	3 (3.2)	0	2 (3.2)	0.6
Pleural effusion	12 (2.5)	2 (1.4)	9 (9.5)	8 (11.6)	7 (11.1)	0.001
Re-operation	12 (2.5)	0	2 (2.1)	7 (10.1)	4 (6.3)	0.001
Mortality	7 (1.5)	2 (1.4)	2 (2.1)	0	2 (3.2)	0.6

[a] Defined as the presence of one or more complication in a single patient

[b] Defined as the presence of pleural effusion, pneumonia, or pulmonary embolus in a single patient

Table 4. Components of the enhanced recovery after surgery (ERAS) protocol[13].

Preoperative	Intraoperative	Postoperative
Preoperative nutrition	Surgical approach	Early mobilization
Prehabilitation	Anaesthetic management	Early removal of drains
Patient education and counselling	Perioperative fluid management	Early enteral feeding
Smoking and alcohol cessation	Prevention of hypothermia	Perioperative pain control
Multidisciplinary team		Postoperative nausea and vomiting
Cardiopulmonary assessment		Postoperative glycemic control
Venous thrombo-prophylaxis		
Preoperative fasting and carbohydrate-rich loading		

Table 5. Literature review of comparative trials on oral feeding after esophagectomy[18].

Authors/year	Design	Procedures	*n*	Diets	POD PO started	Results
Mahmoodzadeh 2015[20]	RCT	Open Ivor-Lewis, gastrectomy	109	EOF *vs* DOF	1 *vs* ROBF	Fewer rehospitalizations and decreased ROBF with EOF
Sun 2015[22]	RCT	MIE McKeown	68	EOF *vs* DJF	1 *vs* 7	Faster gastric emptying, ROBF with EOF
Lassen 2008[19]	RCT	Gastrectomy, pancreatectomy, hepatectomy, esophagectomy	447	EOF *vs* DJF	1 *vs* 6	No difference in morbidity between EOF, DJF
Giacopuzzi 2017[50]	Prospective cohort	Open or MIE Ivor-Lewis, McKeown	52	ETF *vs* DTF	1 *vs* 6	Earlier mobilization and removal of drains with ETF pathway
Weijs 2015[25]	Prospective cohort	MIE Ivor-Lewis	100	EJF, ETF *vs* DJF, DTF	0 *vs* 4-7	No difference in complications
Lopes 2018[21]	Retrospective	Open esophagectomy, gastrectomy	161	EOF *vs* DJF	2 *vs* 5-7	No difference in complications
Speicher 2018[30]	Retrospective	Open transhiatal	203	EOF *vs* DJF	3 *vs* 15	Decreased cervical leak rate with DJF
Eberhard 2017[28]	Retrospective	Open or MIE Ivor-Lewis	359	ETF *vs* DTF	2 *vs* 7	Fewer severe complications and leaks with DTF
Bolton 2014[29]	Retrospective	Open or MIE transhiatal	120	EJF *vs* DJF	7 *vs* 12	Decreased cervical leak rate with DJF

MIE: Minimally invasive esophagectomy; EOF: Early oral feeding alone; ETF: Early oral feeding with supplemental total parenteral nutrition; EJF: Early oral feeding with supplemental tube feeding; DOF: Delayed oral feeding alone; DTF: Delayed oral feeding with supplemental total parenteral nutrition; DJF: Delayed oral feeding with supplemental tube feeding; TPN: Total parenteral nutrition; RCT: Randomized controlled trial; ROBF: Return of bowel function.

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