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Esophageal Cancer: Basic Surgical Treatment Methods

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Abstract. Esophageal cancer is a prevalent malignant tumor in China, which is one of the highest-incidence areas for this disease globally. The treatment methods are diverse, with radical surgical resection being the preferred treatment plan. Depending on the different stages of the disease and the medical conditions of the region, the choice of surgical methods includes endoscopic resection, traditional open radical surgery, minimally invasive surgery, and palliative surgery. This article focuses on the applicable conditions and advantages and disadvantages of various types of surgery, and makes a horizontal comparison: for early-stage esophageal cancer, radical surgery is mostly used, and minimally invasive surgery has the advantages of less trauma, less intraoperative bleeding, and higher short-term life quality after surgery compared with traditional open surgery; for locally advanced and progressive esophageal cancer, a multidisciplinary comprehensive assessment is recommended, and then preoperative neoadjuvant therapy around surgery should be carried out; for patients who are not suitable or cannot tolerate radical surgery, palliative surgery can be adopted to alleviate esophageal obstruction. Lymph node dissection is usually carried out together with radical surgery, and two-field lymph node dissection is currently the mainstream standard for the scope of dissection, but it has limitations depending on the surgical method and the tumor metastasis, and three-field lymph node dissection has not yet been widely recognized. The treatment of esophageal cancer surgery is developing towards minimally invasive and multidisciplinary comprehensive directions, and how to improve the resection rate of esophageal cancer and the postoperative quality of life of patients has always been the focus of research.

Keywords: Esophageal cancer, surgical treatment, minimally invasive surgery, neoadjuvant therapy, lymph node dissection.

1. Introduction

According to Global cancer statistics 2022: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries [1], in 2022, there were 224,000 new cases of esophageal cancer and 187,000 deaths in China, accounting for more than 40% of the global total, making it a high-incidence area for esophageal cancer. Over the past few decades, the treatment of esophageal cancer in China has developed rapidly, with a comprehensive treatment approach that combines surgery with radiotherapy and chemotherapy, and the introduction of advanced technology and equipment. This has led to an increase in diagnostic accuracy, a reduction in surgical time, and a decrease in postoperative mortality and the incidence of complications. This article mainly focuses on the current state of surgical treatment for esophageal cancer, introduces and compares the commonly

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used surgical methods, and aims to explore the direction of development of esophageal cancer surgery from the advantages and disadvantages of various surgical methods.

2. Introduction of esophageal cancer

Esophageal cancer is a common malignant tumor in the digestive system, originating from the epithelium of the esophageal mucosa and occurring between the lower pharynx and the esophagogastric junction (GEJ). The main clinical manifestations include dysphagia or difficulty swallowing, pain behind the sternum, reflux, and vomiting. Esophageal cancer can be divided into esophageal squamous carcinoma (ESCC) and esophageal adenocarcinoma (EAC) in terms of pathological histology. There are significant geographical differences in the incidence of these types, with more than 90% of esophageal cancer cases in China being ESCC, predominantly affecting men over 40 years old. It is generally believed that these cancers are related to dietary habits, living environment, fungal infections, and genetic factors [2]. With the support of endoscopic technology, esophageal cancer can be screened in the early stages and treated promptly, effectively reducing the incidence and mortality rates [3]. However, esophageal cancer in its early stages may have no obvious symptoms or only mild symptoms, and in fact, most patients are diagnosed when the disease has already progressed to the middle or advanced stages [4]. The possibility of lymph node metastasis (regional, upper abdominal, and cervical) is relatively high, which makes the treatment incomplete or increases the difficulty and risk of surgery. This is an important reason for the poor prognosis of esophageal cancer. For patients who can tolerate surgery, the preferred treatment for esophageal cancer is radical surgery combined with mediastinal lymph node dissection. Surgery alone may not achieve the desired effect, so a multidisciplinary approach combined with surgical treatment is usually adopted to improve the survival rate and quality of life for patients.

3. Current status of surgical treatment methods

Before selecting a specific surgical plan, it is essential to first ensure that the patient meets the indications for surgical treatment and to exclude contraindications. Indications include: good overall condition, the ability of major organs to tolerate surgery, no distant metastasis; the local lesion is expected to be resectable; no persistent chest and back pain; no hoarseness and no irritating cough. Contraindications include: obvious tumor invasion, signs of penetration into adjacent organs and distant metastasis; severe cardiopulmonary insufficiency, unable to withstand surgery; cachexia [5]. Generally, the earlier the lesion, the higher the possibility of resection. Comprehensive information, such as the phenotype of the tumor and relevant imaging findings, can effectively determine whether the tumor can be resected.

3.1. Endoscopic resection

This includes Endoscopic Mucosal Resection (EMR) and Endoscopic Submucosal Dissection (ESD). These techniques are suitable for early-stage esophageal cancer, especially when the tumor is limited to the mucosal layer. Taking ESD as an example, the patient undergoes routine full anesthesia for gastroscopy preparation. Under gastroscopy, the condition of the esophageal mucosa is observed to identify the location of the lesion. The argon plasma coagulation probe is used for marking, and a mixed solution is injected into the surrounding tissue of the lesion to cause local elevation. After cutting the mucosa around the lesion, dissection is carried out along the submucosal layer, and the lesion tissue is completely resected and removed using a snare device.

The advantage of endoscopic mucosal resection lies in the time and effort saved in surgical operations, and it reduces the damage of thoracotomy, preserving the structure of the original digestive tract, etc. The shortcomings are the relatively limited depth and range of resection, and the inability to accurately assess the lymph node situation during surgery, thus, there is a higher possibility of recurrence. High-risk factors for recurrence after ESD include: positive resection margins, low differentiation in pathological grading, tumor thrombus in the vessels, extensive range (lesion length $\geq$ 2 cm), and deep infiltration (involving the submucosal layer > 200 μm). Patients with the above

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high-risk factors are recommended to have radical surgical treatment or supplementary radiotherapy [6]. A recent analysis of superficial esophageal squamous cell carcinoma in Asian patients suggests that ESD can be considered curative if the following clinical pathological factors are met postoperatively: ① The length of the lesion is ≤ 20 mm; ② The tumor's macroscopic pathological Paris classification is type 0 to II; ③ The tumor is limited to the mucosal layer (pT1a stage); ④ No tumor thrombus in the vessels [7].

3.2. Traditional open radical surgery

Traditional open-radical surgery is the main method for treating esophageal cancer, with the goal of completely resecting the tumor and its surrounding lymph nodes. Surgeons select the surgical approach individually based on the location of the tumor, the degree of tumor invasion, the length of the tumor, the status of lymph node metastasis, the patient's surgical tolerance (such as cardiopulmonary function), and the surgeon's personal habits and experience. The conventional surgical approaches are generally divided into transthoracic esophagectomy (TTE) and transhiatal esophagectomy (THE).

3.3. Transthoracic esophagectomy

There are three main types of transthoracic esophagectomy: the Sweet procedure, the Ivor-Lewis procedure, and the McKeown procedure.

Sweet Procedure: The esophageal cancer is resected through a posterior lateral incision in the left chest, and the stomach is used to replace the esophagus. This procedure is suitable for most patients with lower thoracic esophageal cancer at the cardia and most middle thoracic lesions. Its advantage lies in the fact that the surgery can be completed through a single incision, without the need to change the patient's surgical position during the operation, resulting in less trauma and a relatively shorter operation time [8]. However, in recent years, some scholars have argued that the Sweet procedure makes it difficult to expose the opposite azygos vein arch when mobilizing the esophagus, and the exposure of the upper mediastinum is poor, which may easily lead to residual lesions and incomplete lymph node dissection [9].

Ivor-Lewis Procedure: During the surgery, the patient first lies supine, and the surgeon mobilizes the stomach and creates a tubular stomach through a median incision in the upper abdomen; then the patient is placed in a left lateral position, and a right posterior lateral incision is made through the intercostal space between the 4th and 5th ribs to enter the thoracic cavity, mobilize the thoracic esophagus and tumor, and bring the tubular stomach through the esophageal hiatus into the right thoracic cavity for intrathoracic esophagogastric anastomosis. Compared with the Sweet procedure, this procedure can fully expose the lymph nodes beside the recurrent laryngeal nerve and the apex of the lung for thorough dissection. Although the operation time is significantly increased, there is no significant difference from the former in terms of intraoperative bleeding and average hospital stay [8]. In the long run, patients who have undergone a right thoracic approach have a non-significant increase in 5-year survival rate compared to those who have undergone a left thoracic approach, which needs further statistical research to confirm [10].

McKeown Procedure: During the surgery, the patient first takes a semi-prone position, and the surgeon enters the thoracic cavity through a posterior lateral incision at the 5th intercostal space in the right chest, cuts the azygos vein arch, and mobilizes the esophagus; then the patient is turned to a supine position, and the stomach is mobilized through a median incision in the upper abdomen, the esophagus is cut at the esophagogastric junction, a tubular stomach is made, and a suture is used to pull at the bottom of the stomach; an oblique incision is made along the anterior edge of the left sternocleidomastoid muscle in the neck, the esophagus is mobilized, and the thoracic esophagus is pulled out through the neck, the tubular stomach is pulled out from the esophageal bed, and an end-to-side circular stapler anastomosis is performed. This procedure has a long operation time, but it is more convenient for anastomosis of upper esophageal cancer.

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3.4. Transhiatal esophagectomy

This includes non-thoracotomy transhiatal esophagectomy and esophageal inversion stripping. Traditional thoracic approach surgery causes significant trauma to patients, especially for those with poor cardiopulmonary function, the burden of surgery is excessive, and the incidence of postoperative complications and unexpected mortality rates is high. This procedure avoids thoracotomy, has minimal surgical trauma, and the use of stapling devices shortens the operation time, reduces intraoperative bleeding, and also achieves the purpose of radical treatment [11]. Some scholars compared 50 studies on transthoracic and transhiatal esophageal surgery published from 1990 to 1999 [12] and found that the perioperative mortality rate for transhiatal esophageal surgery was 5.7%, while that for transthoracic surgery was 9.2%. At the same time, the postoperative pulmonary complications for transhiatal esophageal surgery were 6% lower (18.7% vs. 12.7%), but there was a significant increase in cardiac complications (6.6% vs. 19.5%), and the outcomes of vocal cord paralysis and anastomotic leakage were also not ideal. It can be seen that a notable feature of THE surgery is that, due to the absence of thoracic surgery, the control of pulmonary complications is more satisfactory. However, due to the blind operation during surgery, the trauma to the adjacent structures of the esophagus during mobilization is significantly increased [13]. It is worth noting that THE is almost impossible to complete the mediastinal lymph node dissection above the carina, and if there is lymph node metastasis in this part, there is a high probability of residual tumor.

3.5. Minimally invasive esophagectomy (MIE)

In recent years, minimally invasive surgeries, including video-assisted thoracoscopic MIE (VAMIE) and robotic-assisted MIE (RAMIE), have gradually been promoted and applied in esophageal cancer surgery. The short-term advantages of minimally invasive surgery are evident [14], and it has gradually taken precedence over traditional TTE. It is recommended for use when equipment conditions and the patient's physical condition permit, but its long-term efficacy still needs to be verified.

A study that included 21 studies with 9,355 patients showed that there were no significant differences between the VAMIE and RAMIE groups in terms of intraoperative blood loss, the number of lymph nodes dissected, postoperative anastomotic fistula, recurrent laryngeal nerve injury, overall complication rate, and mortality within 90 days after surgery. However, in terms of intraoperative blood loss, postoperative pulmonary complications, and overall complications, the minimally invasive groups were significantly better than the open surgery group [15]. Another study indicated that the McKeown minimally invasive procedure, compared to open surgery, had shorter operation time, less intraoperative bleeding, and a shorter hospital stay, but there was no significant difference in long-term outcomes between the two [16].

Regarding the approach selection for VAMIE, Su Pengfei et al. [17] concluded from a retrospective study of 99 patients who underwent laparoscopic surgery that, compared to the traditional radical surgery under thoracoscopy, the transhiatal esophagectomy through laparoscopy had advantages in shortening the operation time and ICU monitoring time for esophageal cancer patients, reducing intraoperative blood loss, and was more conducive to postoperative recovery, with comparable long-term prognosis.

3.6. Neoadjuvant therapy before surgery

Although surgery is the primary treatment for esophageal cancer, many cases are diagnosed late when the disease has already advanced to a stage where surgery alone is not enough to achieve a radical cure or effective treatment. For any locally advanced or locally progressive esophageal cancer, a preoperative multidisciplinary comprehensive assessment is recommended, and a comprehensive treatment plan should be designed around surgical treatment [6]. Neoadjuvant therapy before surgery has the following advantages [18]:① The tumor's blood supply is intact, which is beneficial for maintaining the local intensity and oxygen concentration of the targeted lesion's chemotherapy drugs;② Patients have better tolerance before surgery; ③ It can reduce the tumor stage and increase

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the R0 resection rate; ④ Early elimination of subclinical distant metastatic lesions; ⑤ Reduction of intraoperative tumor seeding and metastasis; ⑥ Preoperative chemoradiation also has a synergistic effect of mutual sensitization; ⑦ It can be used to evaluate the sensitivity of the tumor to chemotherapy drugs in the body.

Studies have shown that the timing of surgery after preoperative chemoradiation (CRT) may affect the possibility of tumor resection and surgery-related complications. The optimal timing for surgery is usually 7 to 8 weeks after neoadjuvant chemoradiation [19], but prolonging the interval between surgeries due to neoadjuvant chemoradiation can also have an adverse effect on the patient's long-term survival rate [20].

3.7. Palliative surgery

Some patients have contraindications to surgery or do not meet the criteria for surgical treatment. Their conditions have progressed to an advanced stage where surgical resection is not possible, or the lesion cannot be radically removed upon exploration. Esophageal cancer causes stenosis, obstruction, and dysphagia, making it difficult for patients to eat autonomously. To improve the nutritional status of patients and solve the problem of eating, palliative surgery can be used clinically. Common surgical methods include gastrostomy (or jejunostomy), esophagogastric bypass anastomosis, and intubation of the esophageal lumen, etc. [21].

Gastrostomy (or jejunostomy) is suitable for patients with severe obstruction where no other method can solve the problem of nutritional intake. This surgical procedure is simple, causes little damage to the patient, and is basically tolerable except for patients with severe cardiopulmonary dysfunction, but some patients are unwilling to accept it on a psychological level. If the method of creating a fistula is unreasonable or the care is not good, it can cause digestive juices to overflow, resulting in skin ulceration and pain around the fistula, as well as indigestion and diarrhea.

Esophagogastric bypass anastomosis is suitable for patients who have undergone exploration and cannot completely remove the tumor, and who also have severe difficulty swallowing food. This method allows patients to obtain nutrition orally, improve the overall condition of the body, and provide conditions for subsequent radiotherapy and chemotherapy. When mobilizing the esophagus, attention should be paid to protecting the vagus nerves on both sides. If there is a large diverticulum at the lower end of the esophagus or a tumor is found during the operation, the cardia of the esophagus should be resected, and the method is the same as the intrathoracic esophagogastric anastomosis for the resection of lower esophageal cancer.

Intubation of the esophageal lumen refers to placing a rubber tube or plastic tube of appropriate length and thickness at the stenosis caused by the esophageal cancer lesion to allow food to pass through and improve the obstruction condition. However, with the development and advancement of medical imaging technology and metal materials, esophageal stents have been widely used in clinical practice, making this surgical method rarely used nowadays.

3.8. Lymph node dissection

Lymph node dissection during surgery is an essential component of esophageal cancer surgery, contributing to the accuracy of pathological staging and extending disease-free survival [22]. The esophagus extends through the neck, chest, and abdomen, involving a wide range and a large number of lymph nodes, making lymph node dissection challenging and significantly impacting the efficacy of esophageal cancer surgery. Studies have found that esophageal cancer may have lymph node metastasis at an early stage [23], which significantly increases the difficulty of lymph node dissection in radical surgery.

The extent of lymph node dissection in esophageal cancer surgery has always been a matter of debate. The currently widely accepted approach is the two-field lymph node dissection [24], which is divided into standard, extended, and complete types. The standard two-field lymph node dissection includes not only the extensive local resection of the primary tumor but also the entire posterior mediastinal lymph node dissection from the diaphragm to below the carina and the main pulmonary

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artery window; in the abdomen, it includes the celiac artery lymph nodes, common hepatic artery lymph nodes, splenic artery lymph nodes, lesser curvature of the stomach lymph nodes, and lymph nodes of the lesser omentum. The extended two-field lymph node dissection, in addition to the standard two-field lymph node dissection, also includes the lymph node dissection along the right tracheal groove up to the right recurrent laryngeal nerve and the lymph nodes beside the brachiocephalic trunk. The complete two-field lymph node dissection, based on the extended two-field lymph node dissection, also includes the lymph node dissection in the left tracheal groove, including the lymph nodes beside the left recurrent laryngeal nerve.

Lymph node metastasis of esophageal cancer may involve the neck. Due to the limitations of the surgical approach, THE is almost impossible to complete the dissection of mediastinal lymph nodes above the carina. A study by D'Journo et al. [25] clearly showed that standard two-field lymph node dissection would lead to insufficient staging and incomplete resection in 25% of patients and over 35% of lymph node-positive patients. In the same study, researchers found that extended lymph node dissection significantly reduced the proportion of false-negative patients with N status, but it does not necessarily improve overall prognosis. Conversely, for patients who ultimately have occult residual lesions after surgery and are unlikely to be treated with adjuvant therapy, standard two-field lymph node dissection will cause patients to miss the opportunity for radical treatment.

Since middle and lower esophageal cancer can also have lymph node metastasis in the neck and upper mediastinum, in addition to the already mentioned thoracic and abdominal lymph node dissections, the three-field lymph node dissection includes the lymph node dissection around the esophagus in the neck, the lateral side of the internal jugular artery, and the supraclavicular lymph nodes. Studies have shown that the one-year survival rate of the three-field group is significantly higher than that of the two-field group [26], but the relevant literature on three-field lymph node dissection mostly comes from East Asia, and the research results are scarce, so it has not yet been adopted as the standard method for lymph node dissection in esophageal cancer surgery.

4. Conclusion

The conventional surgical approaches for treating esophageal cancer, such as TTE and THE, often result in significant trauma and high rates of postoperative complications, leading to generally poor quality of life after surgery for patients. With the widespread adoption of minimally invasive procedures like ESD, VAMIE, and RAMIE as preferred options over traditional open surgery, there has been a notable improvement in the short-term quality of life for patients. Reducing surgical trauma for patients, increasing the resection rate of cancer, and improving patient survival rates continue to be key areas of research focus.

Currently, the primary method of assessing whether the tumor has been completely resected during surgery is intraoperative frozen section diagnosis. If the resection margins are negative and no lymph node metastasis is observed, it can be preliminarily determined that there is no residual tumor. However, this also leads to an extension of the surgery duration. If the endoscopy, thoracoscopy, laparoscopy, and robotic tools can be used to quickly confirm the extent of resection needed during surgery, it would effectively shorten the surgery time and thus alleviate the burden on patients.

The application of neoadjuvant therapy before surgery has made it possible to radically resect tumors that were previously difficult to remove and has reduced the likelihood of early tumors metastasizing and becoming difficult to cure. In addition to radiotherapy and chemotherapy, emerging treatment modalities such as immunotherapy and targeted therapy also hold great potential and may become new breakthroughs for the radical cure of cancer.

For patients who cannot undergo radical tumor resection, palliative surgery can be chosen to achieve the goal of self-feeding and nutrition, thereby improving the patient's physical condition to prepare for subsequent treatments. There is still controversy over the choice between two-field and three-field lymph node dissection, with the two-field approach currently being more widely accepted. More research is needed to prove the necessity and effectiveness of three-field lymph node dissection in specific surgical contexts.

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This article mainly focuses on preoperative preparation and the surgery itself during the perioperative period, lacking an in-depth analysis of postoperative care and complications management for patients. It is necessary to refer to more follow-up information and case studies of postoperative complications to improve the response plans for problems encountered throughout the entire treatment process.

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