International Journal of Healthcare Sciences ISSN 2348-5728 (Online)
Vol. 5, Issue 2, pp: (542-547), Month: October 2017 - March 2018, Available at: www.researchpublish.com

Surgical Esophagectomy Management of Esophageal Cancer: A Review

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Abstract: **This review discusses staging, etiology, prognostic factor and surgical treatment modalities available for esophageal cancer. We searched for articles published through December, 2017 in the following five electronic databases: PubMed, Science Direct, Embase, Web of Science, and Scopus, for both English and non-English language articles with the following keywords: "esophageal cancer", "amputations", "esophagectomy", "surgical management". Esophageal cancer is a severe malignancy with regards to mortality and prognosis. Esophageal cancer is staged according to the widely accepted TNM system. Surgical resection continues to be the major therapy for potentially treatable esophageal cancer. Neoadjuvant treatment can improve longterm end result after esophagectomy. Additionally, MIE could improve temporary end result, and 3-field lymph node dissection could reduce the risk of recurrence. Staging plays an integral part in directing stage specific therapy protocols and has a good influence on total survival. Usual imaging modalities utilized in staging consist of CT, EUS and PET scans. Present treatment choices consist of multimodality treatment mainstays of present therapy include surgery, radiation and chemotherapy. The progress made in surgery lead surgeons to consider minimal techniques to reduce morbidity and mortality of such high-risk procedures. New techniques of MIE and robotic surgery in a close to future will certainly offer chance to push the boundary of the indications in very selected group of patients.**

Keywords: **MIE, "esophageal cancer", "amputations", "esophagectomy", "surgical management".**

1. INTRODUCTION

Esophageal cancer is taken into consideration a significant malignancy relative to prognosis and mortality rate. Accounting for more compared to 400000 deaths worldwide in 2005 [1].Esophageal cancer is the 8th most common cancer, and the sixth most usual source of cancer related fatalities worldwide with developing nations comprising greater than 80% of overall situations and deaths [2].Over 490000 new instances of esophageal cancer were reported in 2005. While numerous various other sorts of cancer are expected to reduce in occurrence over the following 10 years by 2025 the frequency of esophageal cancer is anticipated to increase by 140% [1].According to the National Cancer Institute, in the United States there will certainly be roughly 17990 new cases and 15210 fatalities in 2013 [3].Regardless of lots of developments in medical diagnosis and treatment, the 5-year survival rate for all patients detected with esophageal cancer varies from 15% to 20% [4].The epidemiology of esophageal cancer in established nations has drastically transformed over the past forty years. Forty years ago squamous cell carcinoma (SCC) was responsible for above 90% of the cases of esophageal carcinoma in the United States. Substantial differences of occurrence of esophageal cancer feed on the basis of geographic and racial distinctions, which could be connected to differences in exposure to run the risk of elements.

This review discusses staging, etiology, prognostic factor and surgical treatment modalities available for esophageal cancer.

2. METHODOLOGY

We searched for articles published through December, 2017 in the following five electronic databases: PubMed, Science Direct, Embase, Web of Science, and Scopus, for both English and non-English language articles with the following keywords: "esophageal cancer", "amputations", "esophagectomy", "surgical management", "therapy", as the medical subject heading (MeSH). Study designs that were included were randomized controlled trials (RCTs), case-control studies, cohort studies, prospective and retrospective uncontrolled studies, cross-sectional studies, and review studies. Case reports and case series were excluded. We searched bibliographies for all retrieved and relevant publications to identify other studies.

3. DISCUSSION

- **Staging of esophageal cancer:**

The clinical staging of esophageal cancer is analyzed with the widely approved TNM system established by the American Joint Committee on Cancer (AJCC). Pretreatment staging of esophageal cancer will directly affect overall therapy alternatives readily available to each patient and their prognosis, so exact hosting is important.

T staging of esophageal cancer concentrates on determining the deepness of invasion of the primary tumor. A crucial facet of T staging concentrates on developing if the primary tumor has invaded the bordering mediastinal frameworks, given that these patients would no much longer be considered surgical candidates. (Table 1) explains the TNM system, particularly describing depth of invasion in T staging [5].This aspect of hosting is crucial in determining stage-specific methods for therapy. For example, for T3 or T4 tumors the oncology group will certainly utilize preoperative chemotherapy or combination radiation and chemotherapy in order to make the primary tumor resectable by surgical excision. On the other hand, T1 or T2 tumors are treated mostly with surgical resection [6].Offered the value of T Staging in therapy options and general diagnosis, many methods have been utilized to precisely establish T Stage. These choices consist of computer tomography (CT), endoscopic ultrasound (EUS) and 18F-fluorodeoxyglucose positron emission tomography (FDG-PET scan) [7].

Table 1.TNM system, specifically referring to depth of invasion in T staging

Category	Description
Tis	Carcinoma *in situ*
T1	Tumors invade lamina propria or submucosa
T2	Tumors invade muscularis propria
T3	Tumors invade adventitia
T4	Tumors invade adjacent structures
N0	No regional lymph node metastases
N1	Regional lymph node metastases
M0	No distant metastasis
M1a, M1b	Distant metastasis

- **Prognostic factor:**

Platelet count has been utilized to help determine the prognosis of other cancers because platelets are an essential element of the inflammation procedures. Platelet matter is vice versa relevant to the cancer prognosis, as in a greater platelet matter correlates to a poorer prognosis. The absolute cut off for platelet count as a prognostic variable has been questioned. In one study of ESCC, platelet matters were higher in patients with huge tumors. It was figured out that those patients with platelet counts ≤ 205000 had a better 5-year survival rate than patients with platelets > 205000 particularly when nodes were involved [8].

Tumor length is used as a prognostic factor in ESCC but the length cutoff factor in predicting survival has been objected to. Researchers in China took a look at tumor length in the senior population (over 70 years of ages) and the cutoff point was calculated to be 4.0 centimeters. Patients with a tumor length of ≤ 4.0 cm had a much better 5-year survival than those with a tumor length of > 4.0 centimeters, specifically with a T3-4 quality or nodal-negative patients [9].

Cancer triggers a hypercoagulable state and this setting urges tumors to grow and produce more pro-coagulants. D-dimers are completion product of fibrin and fibrinolysis and have been reported to be connected with tumor prognosis, tumor phase, lymph node participation, and overall survival. One research took a look at the plasma D-dimer levels in patients with esophageal cancer before and after surgery along with patients without cancer. Their study revealed that high levels of D-dimers in the pre-operative state correlated with a greater tumor stage and surgery triggered more patients to have a hypercoagulable state which shortened their survival time [10].

Nourishment is an essential aspect that influences patients with esophageal cancer during their perioperative period. Early enteral nutrition was kept in mind to safeguard the digestive tract mucosa, improved the nutritional condition, and boosted the immune standing patients undertaking esophagectomy. Enteral nutrition secured the intestinal mucosa by keeping the intestinal tract obstacle versus plasma endotoxins [11].One more research study considered immunonutrition in patients with head and neck cancer and esophageal cancer undertaking chemoradiotherapy. Plasma levels of arginine, eicosapentaenoic acid, docosahexaenoic acid, and nucleotides were gauged in patients undergoing chemoradiotherapy, that

got either an Immune regulating Enteral Nutrition formula (IEN) or an isocaloric, isonitrogenous formula, Standard Enteral Nutrition (SEN). IEN patients had less weight management, boosted anti-oxidants, and kept their functional abilities compared to those with the SEN formula [12].

- **Treatment strategy for esophageal cancer:**

The National Comprehensive Cancer Network (NCCN) in the United States [13], the European Society for Medical Oncology (ESMO) [14], and the Japan Esophageal Society (JES) [15] has separately recorded standards for esophageal cancer therapy. The NCCN and ESMO standards are based upon the UICC/AJCC classification, while the JES standards are based on the Japanese Classification of Esophageal Cancer. Surgical resection remains the pillar of potentially curable esophageal cancer. Nevertheless, trials of adjuvant chemotherapy or radiotherapy have been performed to boost survival since the long-term results of patients treated with surgery alone are unsuitable. To this day, no study has confirmed that postoperative adjuvant therapy has a survival benefit [16]; hence, recent tests have concentrated on neoadjuvant therapy. Meta-analyses on neoadjuvant therapy for esophageal cancer have offered strong proof that neoadjuvant chemoradiotherapy gives a better survival advantage than surgery alone for both squamous cell carcinoma and adenocarcinoma [16].Also, neoadjuvant chemotherapy offered an evident survival benefit for adenocarcinoma, yet its advantage for squamous cell carcinoma is still debatable [17].According to these findings, the NCCN guidelines advise preoperative chemoradiotherapy for T2 or greater tumors. Neoadjuvant chemotherapy is also advised for adenocarcinoma in this group. Definitive chemoradiotherapy is a choice, particularly for cervical esophageal cancer. The ESMO standards also suggest preoperative chemoradiotherapy for T3-- 4 cases. Relating to the reaction to neoadjuvant chemo(radio)treatment, further chemoradiation caused a general survival that amounted surgery in patients with squamous cell cancer, in spite of a boost in local recurrence (French and German Phase III research) [18].Therefore, definitive chemoradiotherapy is an alternative for neoadjuvant therapy responders. A European study hall showed that perioperative (both preoperative and postoperative) chemotherapy substantially boosted the survival of patients with reduced esophageal or esophagogastric adenocarcinoma (MAGIC trial) [19].Appropriately, the ESMO guidelines advise perioperative radiation treatment for patients with adenocarcinoma. In Japan, surgeons attempted to enhance the survival of patients with sophisticated esophageal cancer by extended radical lymphadenectomy [20].Positive long-lasting outcomes have been achieved in Japan because of enhancements to surgical procedures. Therefore, attention has been concentrated on adjuvant radiation treatment to control micrometastasis. A clinical study in Japan exposed that adjuvant chemotherapy enhanced the disease-free survival of patients with node-positive clinical stage II/III squamous cell carcinoma (JCOG 9204). A current followup research study made clear that the total survival of patients treated with neoadjuvant chemotherapy complied with by surgery was considerably better compared to that of patients treated with surgery adhered to by radiation treatment (JCOG 9907). Based upon these searchings for, the current common therapy for resectable sophisticated squamous cell carcinoma of the esophagus is neoadjuvant chemotherapy adhered to by esophagectomy in Japan.

- **Surgical approaches:**

Several different approaches exist for esophagectomy (Table 2). Conventionally, the standard procedures have been thoracoabdominal or transhiatal open esophagectomy. Recently, Minimally Invasive Esophagectomy (MIE) using thoracoscopy and/or laparoscopy has been developed to reduce the surgical stress of esophagectomy.

Table 2: Surgical approaches for esophageal cancer

Open esophagectomy (OE) : Cervical esophagectomy
McKeownesophagectomy (3-phase esophagectomy) : Ivor-Lewis esophagectomy (through laparotomy and right thoracotomy) Transhiatalesophagectomy without thoracotomy Left thoracoabdominalesophagectomy
Minimally invasive esophagectomy (MIE) : Total MIE (thoracoscopic and laparoscopic esophagectomy) Hybrid MIE (either thoracoscopic or laparoscopic esophagectomy) Laparoscopic-assisted transhiatalesophagectomy Video-assisted mediastinoscopictranshiatalesophagectomy Robot-assisted MIE

McKeown esophagectomy (3-phase esophagectomy): This technique consists of subtotal esophagectomy with right thoracotomy with anastomosis of the cervical esophagus to the stomach offered the neck. This strategy enables the biggest

longitudinal and radical margins, allows full lymphadenectomy, and minimizes the danger of intrathoracic leak. Cervico-thoraco-abdominal 3-field lymph node dissection could be performed with this approach.

Ivor-Lewis esophagectomy (with laparotomy and appropriate thoracotomy): Ivor-Lewis esophagectomy includes middle and lower esophagectomy through appropriate thoracotomy with anastomosis of the intrathoracic esophagus to the belly at the level of the azygosarch. This approach is used commonly for patients with tumors of the middle or lower 3rd of the esophagus. This technique enables total resection of the tumor with a prolonged thoracoabdominal lymphadenectomy, protects against problems with a risk-free and straightforward technique, and gives excellent digestion comfort with a high intrathoracic anastomosis.

Transhiatal esophagectomy: Transhiatales ophagectomy is a subtotal esophagectomy by transhiatal breakdown combined with transcervical dissection without thoracotomy. Reconstruction is executed with a gastric tube via the esophageal bed with cervical esophagogastric anastomosis. The advantages of this strategy consist of limited surgical trauma, reduced operative time, and less regular respiratory system difficulties and mortality. Because the oncological quality of resection is endangered by not enough mediastinal clearance, this strategy is often carried out for onset tumors or tumors situated in the esophagogastric junction. Both a large-scale cohort and a meta-analysis contrasting transthoracic with transhiatales ophagectomy showed that transhiatal esophagectomy was related to considerably decreased operative time, length of hospital stay, postoperative breathing problems, and very early mortality [21].

Minimally invasive esophagectomy (MIE): Minimally invasive strategies have been incorporated into esophageal cancer surgeryin order to boost the postoperative end results of esophagectomy [22].A number of writers have shown that overall MIE making use of a mixed thoracoscopic and laparoscopic method could be carried out securely, but the temporary end result advantages of this strategy stay questionable [23].Oncologic end results agree with, and MIE may have an advantage over open esophagectomy in terms of lymph node breakdown [24].The benefits of MIE must be verified by randomized control studies.

Salvage esophagectomy:

Salvage esophagectomy is defined as esophagectomy for remnant or slipped back tumors after conclusive chemoradiotherapy. Although definitive chemoradiotherapy is a therapy with medicinal potential, locoregional failing remains a significant problem and 40% to 60% of patients have recurrent locoregional condition [25].Although salvage esophagectomy has the possible to heal these patients, the significant issues of this method are high morbidity and mortality rates [26].Anastomotic leakage and pulmonary insufficiency are observed often after salvage esophagectomy, and the reported hospital death ranges from 3% to 22.2% [27].Consequently, salvage esophagectomy should be taken into consideration for thoroughly selected patients at specialized centers.

- **Short-term result of esophagectomy:**

Esophagectomy is an extremely intrusive surgery for which high morbidity and death rates have been reported. A massive possible cohort at multiple Veterans Administration health centers between 1991 and 2001 demonstrated a 9.8% mortality rate and a 49.5% morbidity rate [28].In this record, the most frequent postoperative difficulties were pneumonia (21%), respiratory failure (16%), and ventilator support for even more compared to 48 hours (22%). Cervico-thoraco-abdominal 3-field lymph node dissection is the most radical lymphadenectomy treatment for esophageal cancer. It has come to be a basic surgery in Japan, and has been embraced in some Western high-volume centers [29]. The reported death and morbidity rates of esophagectomy with 3-field lymphadenectomy are received Table 2 [29].Although the frequency of frequent laryngeal nerve paralysis was high after 3-field dissection, the mortality rates of this procedure show up to be comparable to those of standard esophagectomy when it is done in high-volume centers.

The possible benefits of streamlining esophageal and various other highrisk cancer surgeries are recent topics of discussionin lots of healthcare systems. Numerous meta-analyses demonstrated that esophagectomy at low-volume health centers was related to a substantial boost in the incidence of in-hospital and 30-day mortality [30] In order to boost short-term outcomes after esophagectomy, centralization to specialized health centers is important. Whether MIE boosts temporary end results after esophagectomy remains a controversial topic. Among the anticipated advantages of MIE is improved temporary outcomes, specifically minimized pulmonary difficulties. Some authors reported that compared with open up esophagectomy, MIE considerably reduced pulmonary issues [31], while other authors demonstrated similar pulmonary morbidity rates between MIE and open esophagectomy. Current randomized control trial which contrasted MIE with open esophagectomy exposed that pulmonary infection within 2 weeks after surgery was less in the MIE group than in the open group [32].Further tests are required to validate the outcome.

Long-lasting outcome of esophagectomy Long-term end result after esophagectomy differs amongst nations or institutes. Although the tumor phase and history factors differed among patients, long-term results were better in Japanese research studies and in the Japanese computer system registry as compared to the other research studies. The finding that results were much better in Japan might arise from distinctions in the quality of lymph node breakdown due to the fact that 3-field lymphadenectomy is a guideline in Japan. Large-scale potential randomized trials are needed to offer definitive proof that differences in result are due to differences in the top quality of lymph node dissection. The influence of hospital volume on lasting outcomes after esophagectomy stays a subject of dispute [30].More analysis is needed to provide conclusive evidence of this impact.

4. CONCLUSION

Esophageal cancer is a severe malignancy with regards to mortality and prognosis. Esophageal cancer is staged according to the widely accepted TNM system. Surgical resection continues to be the major therapy for potentially treatable esophageal cancer. Neoadjuvant treatment can improve longterm end result after esophagectomy. Additionally, MIE could improve temporary end result, and 3-field lymph node dissection could reduce the risk of recurrence. Staging plays an integral part in directing stage specific therapy protocols and has a good influence on total survival. Usual imaging modalities utilized in staging consist of CT, EUS and PET scans. Present treatment choices consist of multimodality treatment mainstays of present therapy include surgery, radiation and chemotherapy. The progress made in surgery lead surgeons to consider minimal techniques to reduce morbidity and mortality of such high-risk procedures. New techniques of MIE and robotic surgery in a close to future will certainly offer chance to push the boundary of the indications in very selected group of patients.

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