Update Management Of Esophageal Cancer

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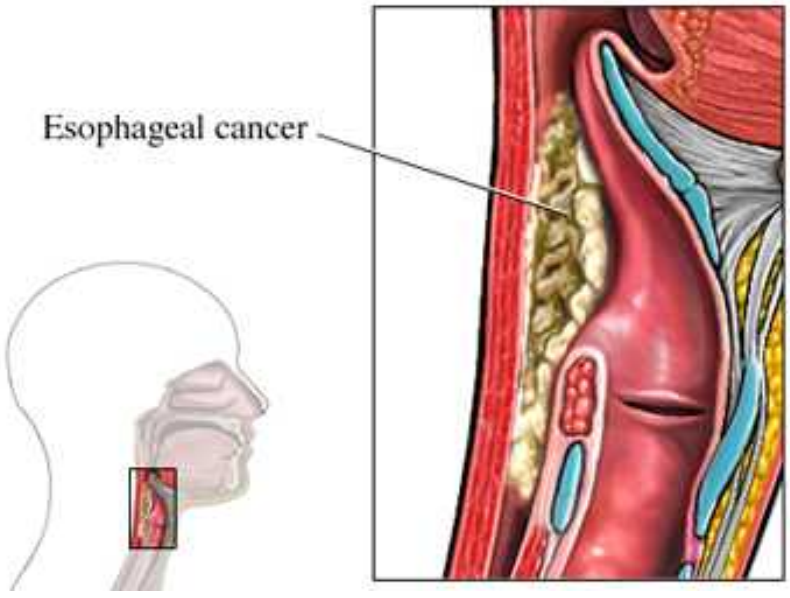


INTRODUCTION

Esophageal cancer is a devastating disease. It is the 6th most common cause of cancer deaths worldwide. Although some patients can be cured, the treatment for esophageal cancer is protracted, diminishes quality of life, and is lethal in a significant number of cases. The principal histologic types of esophageal cancer are squamous cell carcinoma (SCC) and adenocarcinoma. Both are common in men. SCC is the most common histology in Eastern Europe and Asia, while adenocarcinoma is most common in North America and Western European countries.

Squamous cells line the entire esophagus, so SCC can occur in any part of the esophagus, but it often arises in the upper half.

Adenocarcinoma typically develops in specialized intestinal metaplasia (Barrett metaplasia) that develops as a result of gastroesophageal reflux disease (GERD); thus, adenocarcinoma typically arises in the lower half of the distal esophagus and often involves the esophagogastric junction.

•*Etiology:-*

exposure of the esophageal mucosa to noxious or toxic stimuli, resulting in a sequence of dysplasia to carcinoma in situ to carcinoma.

● Predisposing Factors:-

Squamous Cell carcinoma	*Adenocarcinoma*
1.cigarette smoking 2.chronic alcohol exposure	1-High body mass index 2- GERD

SCHEME

1) Pathophysiology
2) Clinical picture
3) Differential Diagnosis
4) Classification,Staging
5) Investigations
6) Management
7) Prognosis

1) Pathophysiology

Major risk factors for SCC include alcohol consumption and tobacco use. Most studies have shown that alcohol is the primary risk factor .

Alcohol damages the cellular DNA by decreasing metabolic activity within the cell and therefore inhibits detoxification and promotes oxidation. Alcohol is a solvent, specifically of fat-soluble compounds. Therefore, the carcinogens within tobacco are able to penetrate the esophageal epithelium more easily.

Some of the carcinogens in tobacco

include the following:

Aromatic amines

Nitrosamines

Polycyclic aromatic hydrocarbons

Aldehydes

Phenols

Other carcinogens, such as nitrosamines found in certain salted vegetables and preserved fish, have also been implicated in esophageal SCC. The pathogenesis appears to be linked to inflammation of the squamous epithelium that leads to dysplasia and in situ malignant transformation.

Adenocarcinoma of the esophagus most

commonly occurs in the distal esophagus and has a distinct relationship to GERD. Untreated GERD can progress to Barrett esophagus (BE), in which the stratified squamous epithelium that normally lines the esophagus is replaced by a columnar epithelium.

The chronic reflux of gastric acid and bile at the gastroesophageal junction and the subsequent damage to the esophagus has been implicated in the pathogenesis of Barrett metaplasia. Diagnosis of Barrett esophagus can be

confirmed by biopsies of the columnar mucosa during an upper endoscopy

2) Clinical Picture:-

✧ Symptoms:-

1-Dysphagia, the most common presenting symptom of esophageal cancer, is initially experienced for solids but eventually progresses to include liquids.

2-Weight loss - This is the second most common symptom, occurring in more than 50% of people with esophageal carcinoma. It is caused by dysphagia and tumor-related anorexia.

3-Bleeding - Patients may experience bleeding from the tumor leading to iron

deficiency anemia.

4-Pain - Pain may be felt in the epigastric or retrosternal area; pain over bony structures indicates metastatic disease.

5-Hoarseness - This is caused by invasion of the recurrent laryngeal nerve.

6-Persistent cough

7-Respiratory symptoms (persistent cough and recurrent pneumonia) - These can be caused by aspiration of undigested food or by direct invasion of the tracheobronchial tree by the tumor (tracheobronchial fistula).

✧ Signs:-

Physical examination findings in patients with esophageal cancer are typically normal, unless the cancer has metastasized to neck nodes or the liver. Lymphadenopathy in the supraclavicular area or the presence of hepatomegaly often indicates unresectable disease.

3)Differential Diagnosis

a) Achalasia

b) Esophageal Leiomyoma

c) Esophageal Stricture

d) Gastric Cancer

4)Classification,Staging:-

TNM Classification:-

T1 - Tumor invades lamina propria or submucosa

T1a - Lamina propria

T1b - Submucosa

T2 - muscularis mucosa

T3 - adventitia

T4 - adjacent structures

T4a - Resectable tumor invading into pleura, pericardium, diaphragm, or adjacent peritoneum

T4b - Unresectable tumor invading other adjacent structures (eg, aorta,

vertebral body, trachea)

N0 - No regional lymph node metastasis

N1 - 1-2 regional lymph nodes

N2 - 3-6 regional lymph nodes

N3 - More than 6 regional lymph nodes

M0 - No distant metastasis

M1 - Distant metastasis

●***Staging:-***

Stage1A	T1	N0	M0
Stage1B	T2	N0	M0
Stage2A	T2,3	N0	M0
Stage2B	T1,2	N1	M0
	T2,3	N0	M0

Stage3A	T1,2	N2	M0
	T3	N1	M0
	T4a	N0	M0
Stage3B	T3	N2	M0
Stage3C	T4a	N1,2	M0
	T4b	Any N	M0
	Any T	N3	M0
Stage 4	Any T	Any N	M1

5)Investigations:-

i. **Esophagogastroduodenoscopy** (EGD; allows direct visualization and biopsies of the tumor)

ii. **Endoscopic ultrasonography** (EUS; most sensitive test for T and N staging ;

used when no evidence of M1 disease)

iii. **Computed tomography (CT**) of the abdomen and chest with contrast (for assessing lung and liver metastasis and invasion of adjacent structures)

iv. **Pelvic CT scan** with contrast if clinically indicated

v. **Bronchoscopy** (, to help exclude invasion of the trachea or bronchi)

vi. Laparoscopy and thoracoscopy (for staging regional nodes)

vii. **Barium swallow** (very sensitive for detecting strictures and intraluminal masses, but now rarely used)

6)Management:-

Treatment of esophageal cancer varies according to stage— (stages I-III) versus metastatic cancer(stageIV)—and histologic subtype—squamous cell carcinoma (SCC) versus adenocarcinoma.

1)Adenocarcinoma:-

Endoscopic therapy (endoscopic mucosal resection, endoscopic submucosal dissection and/or ablation) is preferred for high-grade dysplasia (HGD) or T1a tumors ≤2 cm;

Esophagectomy is indicated for patients with extensive HGD or T1a

adenocarcinoma with nodular disease that is not adequately controlled by ER

For patients with adenocarcinoma T1b, N+ tumors and locally advanced resectable tumors (T2-T4a, any regional N) preoperative chemoradiation is preferred then Esophagectomy.

For patients with adenocarcinoma who have not received preoperative therapy, postoperative fluoropyrimidine-based chemoradiation is indicated.

2)Squamous Cell Carcinoma:-

Primary treatment options for patients with SCC T1b, N+ tumors and locally advanced resectable tumors (T2-T4a, any regional N) include preoperative

chemoradiation and esophagectomy

no postoperative treatment is indicated if no residual disease is present at surgical margins (R0 resection).

Surgical Indications and Contraindications:-

Surgery remains the cornerstone of treatment for esophageal cancer.

Indications for surgery :-

1-Esophageal cancer in a patient who is a candidate for surgery

2-High-grade dysplasia in a patient with Barrett esophagus that cannot be adequately treated endoscopically .

Contraindications to surgery:-

1-Metastasis to N2 nodes (ie, cervical or supraclavicular lymph nodes) or solid organs (eg, liver, lungs); the treatment of patients with celiac lymph node involvement remains controversial

2-Invasion of adjacent structures (eg, the recurrent laryngeal nerve, tracheobronchial tree, aorta, pericardium)

3- the presence of severe, associated comorbid conditions (eg, cardiovascular disease, respiratory disease)

Esophagectomy:-

Esophageal resection (esophagectomy) remains a critical component of multimodality therapy for patients with tumors of any stage. Endoscopic mucosal resection is an experimental approach to patients with T1a disease or high-grade dysplasia that is limited to certain centers and performed only under protocol. Esophagectomy is no longer is used for palliation of symptoms because other treatment modalities have become available for relieving dysphagia.

An esophagectomy can be performed by using an abdominal and a cervical incision with blunt mediastinal dissection

through the esophageal hiatus (ie, transhiatalesophagectomy [THE]) or by using an abdominal and a right thoracic incision (ie, transthoracic esophagectomy [TTE]).

THE offers the advantage of avoiding a chest incision, which can cause prolonged discomfort and can further aggravate the condition of patients with compromised respiratory function. After removal of the esophagus, continuity of the gastrointestinal tract is usually reestablished using the stomach.

COMPLICATIONS:-

1-Respiratory complications (15-20%) - Include atelectasis, pleural effusion, and pneumonia

2-Cardiac complications (15-20%) - Include cardiac arrhythmias and myocardial infarction

3-Septic complications (10%) - Include wound infection, anastomotic leak (breakdown of the new connection between the stomach and esophagus), and pneumonia

4-Anastomotic leaks and stricture may require dilatation (20%). Leaks may be treated with endoscopic placement of self-expanding, removable plastic stents.

Chemoradiotherapy:-

Chemotherapy and radiotherapy for esophageal cancer are delivered preoperatively. No survival benefit is obtained when radiation and chemotherapy are administered postoperatively; however, postoperative continuance of chemotherapy started preoperatively may be beneficial. [97] The aims of preoperative (neoadjuvant) chemotherapy and radiotherapy are to reduce the bulk of the primary tumor before surgery to facilitate higher

curative resection rates and to eliminate or delay the appearance of distant metastases.

Palliative Care:-

In patients who are not candidates for surgery, because of their clinical condition or advanced disease, treatment focuses on control of dysphagia. The goal of palliative care is to prevent and relieve suffering and improve quality of life for patients and their caregivers regardless of the disease stage. In patients with unresectable or

locally advanced cancer, palliative interventions provide symptomatic relief and may result in significant prolongation of life, improvement in nutritional status, the sensation of well-being, and overall quality of life.

Postoperative Care and Follow-up:-

The average length of postoperative hospital stay for patients with esophageal cancer is 9-14 days. Patients usually spend the first postoperative night in the intensive care unit (ICU).

Patients can be extubated immediately after the operation, but mechanical ventilation should be continued if any concerns about the respiratory status are

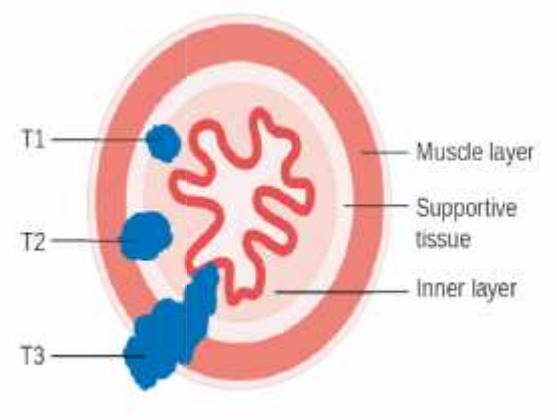
present. Feeding through the feeding jejunostomy begins on postoperative day 1. On postoperative day 6, a swallow study is performed to check for anastomotic leakage. If no leak is present, patients start oral feedings.

7)Prognosis:-

Survival in patients with esophageal cancer depends on the stage of the disease. Squamous cell carcinoma and adenocarcinoma, stage-by-stage, appear to have equivalent survival rates.

Lymph node or solid organ metastases are associated with low survival rates. In 2007-2013, the overall 5-year survival rate for esophageal cancer was 18.8%.

Stage	Survival Rate
Localized	42.9 %
Regional	23.4%
Distant	4.6%
All Stages	18.8%



CONCLUSION

Treatment of esophageal cancer varies by disease stage, as follows:

Stage I-III (locoregional disease) - Available modalities are endoscopic therapies (eg, mucosal resection or ablation), esophagectomy, preoperative chemoradiation, and definitive chemoradiation.

Stage IV – Systemic chemotherapy with palliative/supportive care for patients with ECOG performance score of 2 or less and palliative/supportive care only for patients with ECOG performance score of 3 or more.

Surgical options include the following:

1) Ivor Lewis esophagogastrectomy (laparotomy plus right thoracotomy)
2) McKeown esophagogastrectomy (right thoracotomy plus laparotomy plus cervical anastomosis)
3) Minimally invasive Ivor Lewis esophagogastrectomy (laparoscopic approach)
4) Minimallyinvasive McKeown esophagoga strectomy (laparoscopic approach)
5) Robotic minimally invasive esophagogastrectomy
6) Transhiatalesophagectomy (THE)

7) Transthoracic/transabdominalesophage ctomy with anastomosis in chest or neck

Palliative care options for patients who are not candidates for surgery are as follows:

1. Chemotherapy
2. Radiotherapy
3. Laser therapy
4. Stents

Refernces:-

1-Edwards MJ, Gable DR, Lentsch AB, et al. The rationale for esophagectomy as the optimal therapy for Barrett's esophagus with high-grade dysplasia.
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3-Torre LA, Bray F, Siegel RL, Ferlay J, Lortet-Tieulent J, Jemal A. Global cancer statistics, 2012. CA Cancer J Clin.
4-Brown LM, Devesa SS, Chow WH. Incidence of adenocarcinoma of the esophagus among white Americans by sex, stage, and age. J Natl Cancer Inst.