

Management of Oesophageal Carcinoma

Meenakshi Yeola^{1*}, Shiven Nayyar², Akshaya Iyengar³

Dept. Of Surgery, Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences, Sawangi(M), Wardha, Maharashtra, India

Short Communication

Please cite this paper as: Meenakshi Yeola, Shiven Nayyar, Akshaya Iyengar. Management of Oesophageal Carcinoma. AMJ 2023;16(2):

<https://doi.org/10.21767/AMJ.2023.3932>

Corresponding Author:

Dr. Meenakshi Yeola

Dept. Of Surgery,

Jawaharlal Nehru Medical College, Datta Meghe Institute of Medical Sciences,

Sawangi(M), Wardha, Maharashtra, India

meenakshi@gmail.com

ABSTRACT

Oesophageal cancer is a cancer the majority of which is poorly understood and deadly diseases in the world, owing to its extreme aggressiveness and low survival rate. Round the world, the commonest type according to the histology is the squamous cell carcinoma, with a higher incidence in progressing nations. Adenocarcinoma is the most common histologic subtype in Europe and the United States. In developed countries, the most common type of oesophageal cancer is adenocarcinoma, and important risk factors include long lasting gastro-oesophageal reflux disorder (GERD), obesity and cigarette smoking. Most common type of oesophageal cancer in India is squamous cell carcinoma. TNM and Siewert are two classifications used to classify the oesophageal tumors. Because esophagectomy is highly invasive and likely to impair quality of life, less invasive strategies are expected to emerge. Endoscopic mucosal resection can be used to treat localised tumours, whereas esophagectomy, neoadjuvant chemotherapy, chemo radiotherapy, or a combination of modalities can be used to treat regional tumours. At present, esophagectomy is considered the surgery of choice in conjunction with chemo-radiotherapy. These novel endoscopic techniques can provide comparable survival outcomes without the morbidity of a large operation. Gastric malignancies that are difficult to resect endoscopically can be treated laparoscopically with similar success

Key Words

Oesophageal Carcinoma, Treatment, Squamous Cell Carcinoma, Endoscopic Management Esophagectomy, Chemotherapy.

Introduction

Epidemiology

Oesophageal carcinoma is the eighth most common cause of cancer in the planet. It is the world's sixth most frequently diagnosed and the world's sixth leading cause of cancer-related mortality. By 2025, the incidence rate for oesophageal cancer is anticipated to grow by 140 percent, compared to many other cancer forms¹. According to the National Cancer Institute, there will be 17990 new cases and 15210 deaths in the United States in 2013². After 5 years of therapy, the five-year chance of survival for all individuals with oesophageal cancer disease is between 15% and 20%³. In advanced nations, the epidemiology of oesophageal cancer has altered significantly during the past 40-50 years. 40 years ago, more than 90 percent of total of oesophageal cancer cases in the United States were caused by squamous cell carcinoma (SCC). Eighty percent of oesophageal cancer cases in the U.S. are caused by adenocarcinoma⁴.

Types

Both SCC and adenocarcinoma are histologically the most common types of esophageal cancer, respectively. Incidence rate of squamous cell carcinoma range from 11.8 to 16.3 per 1 million person-years among persons 65 and older, with men at an eight times higher risk than women. Esophageal adenocarcinoma is the most widespread kind of esophageal cancer in North Americans and Europeans. It is more common in South Americans and Asians.

Risk Factors

Risk factors for squamous cell carcinoma(SCC) and adenocarcinoma type are given as follows:

B.E. is associated with cancer, even though the probability of cancer transformation in Europeans and Americans is small, raising doubt on monitoring initiatives and the quest for an earlier detection of adenocarcinomas among B.E. patients⁵.

Esophageal adenocarcinoma is associated with gastroesophageal reflux disease (GERD), Barrett's esophagus, obese, smoking, alcoholism, nutritional deficiencies, and the use of nonsteroidal anti-inflammatory medicines (NSAIDs), proton pump inhibitors (PPIs), and drugs used for lowering cholesterol levels (statin).

Fat distribution around the abdomen (central obesity) is another risk factor for EAC. Elevated adipocytes and inflammatory cells in fat deposits experience reduced inflammation and promote cancer progression by expressing adipokines and other pro-tumor substances. Tumor microenvironment adipocytes are involved in energy generation as well as promoting cancer progression⁶

Clinical features

Generally patients present with the earliest symptom of dysphagia which is progressive in nature.

They have difficulty in swallowing solid more than liquids. Consequently this leads to loss of appetite and excessive weight loss. Also sometimes due to involvement of left recurrent laryngeal nerve, patient may present with hoarseness of voice. Patients have chronic cough in cases of malignant tracheo-esophageal fistula.

Tnm Staging

The staging of oesophageal carcinoma is as follows, according to the TNM staging

Siewert Classification of Gastro-Esophageal Junction Tumors

It is divided into 3 types

TYPE I : from 5 cm proximal to 1 cm proximal to the gastro-oesophageal junction.

TYPE II : 1 cm proximal to 2 cm distal to the gastro-oesophageal junction.

TYPE III : 2 cm distal to 5 cm distal to the gastro-oesophageal junction.

According to the 8th AJCC update, type I and II are considered as esophageal cancer and type III as gastric cancer.

TI is now subcategorized as T1a and T1b

T1a is tumor is invading the lamina propria or muscularis mucosa but are above submucosa. So, amenable to endoscopic resection.

T1b is tumor is invading the submucosa.

Diagnosis and screening

Screening

Unsedated transnasal endoscopy

Unsedated transnasal endoscopy (uTNE) is a technique in which an ultra thin endoscope is inserted through the nose after application of topical anaesthetics. It is beautifully tolerated in patients and is an extremely safe procedure providing good compliance among patients. It provides an

assessment of the oesophagus of a quality as good as that of OGD (Oesophageo-gastro-duodenoscopy).⁽⁷⁾

Cytosponge TM

Cytosponge TM is a novel non-endoscopic cell collecting gadget which is used through the mouth. It comprises of a gelatine made capsule attached on a string which is intentionally swallowed into the stomach, where it expands to about 3 cm in about 5–10 minutes. When taken out, the gadget collect cells from the oesophageal layer and then the sample goes through cytological analysis for the biomarker Trefoil Factor III (TFFIII), a key component of Barrett's diagnosis⁷.

Balloon cytology

Balloon cytology is another non-endoscopic screening modality which has a capability to obtain a DNA from the distal oesophageal lining with the use of a specially designed textured balloon which is then sent for molecular cytology analysis.

Dye-based chromo endoscopy

Dye-based chromoendoscopy was utilized to address the shortcomings of white light endoscopy. Methylene blue, indigo carmine and acetic acid are some of the tints being studied.

Virtual chromo endoscopy

This technique uses digital post-processing to recreate endoscopic pictures in real time without the use of dyes.

Confocal laser end microscopy

A blue laser light and intravenous fluorescein are used for 1,000x magnification in Confocal Laser Endomicroscopy (CLE). A histological analysis is equivalent to the high-quality visuals that are produced.

Diagnosis

Endoscopic biopsy is the investigation of choice. For staging purposes PET-CT (Positron Emission Tomography CT scan) is the investigation which is employed and for TNM staging, investigation of choice is EUS (endoscopic ultrasound). In PET-CT the isotope used is 18-FDG.

To rule out esophageal cancer, the Society of Thoracic Surgeons and the National Comprehensive Cancer Network suggest upper endoscopy as the standard imaging examination for individuals with the previously noted complaints. It is routine trend to utilize chromoendoscopy and narrow band imaging during an endoscopy in order to boost the screening of dangerous lesions. Chromoendoscopy entails surface application of staining for better visibility of mucosal tissue cells. In conjunction with biopsies, brush cytologicals can also be performed if oesophageal strictures prohibit proper biopsies.

Chromoendoscopy (dyes are topically applied in order to better see the mucosal tissue cells.) and restricted band imaging (blue light and green light is used to visualise blood

streams and mucosa) are often employed during endoscopy for better identification and therefore diagnosis of suspected wounds. Biopsies of suspect lesions should be attempted, although if oesophageal stricture limits good biopsies, brush cytologicals can also be utilised. It should only be used in individuals who are unable to undergo top endoscopic procedures⁸.

Other Investigations

Barium studies: barium swallow shows Rat tail appearance or Apple core appearance (also seen in colon cancer on barium enema) and shouldering effect. Process of patient with symptoms of oesophageal carcinoma:

According to several researchers, using proton pump inhibitors (PPIs) or nonsteroidal anti-inflammatory medications, aspirin, or statin decreases the chance of acquiring an esophageal cancer. Other studies, on the other hand, have not found any impact from the approach. For the main objective of preventing carcinoma, there have been no guidelines for the use of these medication.

The main aim of this research is to discuss the different treatment modalities and propose the best modality.

Results

Squamous cell carcinoma and adenocarcinoma of the oesophagus have a variety of therapeutic options based on the stage at diagnosis-surgical, medical and radiological treatment.

Surgical Treatment

Surgery is the mainstay treatment for Tinsitu, T1 as well as for some of the TII stage carcinoma of the esophagus. There are different surgical techniques for oesophagectomy but the main surgical interventions included are trans-hiatal oesophagectomy (THE) and trans-thoracic oesophagectomy. In THE the stomach is dislodged from its nearby structures and blood streams by carrying out a midway in-line supra-umbilical cut during surgery of abdomen. A small cervical cut is employed on the left hand side of throat during surgery of neck. The Ivor Lewis method, the McKeown Modification (3 hole approach), or the left transthoracic approach are the three main approaches in trans-thoracic esophagectomy. Lymph node dissection is yet another important component of these surgeries. Every surgical method has a wholenew lymph node reclamation rate which is based on the degree of exposure during the surgery of open, laparoscopy or laparoscopic supported surgery. Laparoscopic surgeries offer very minimal amount of bleed and better patient compliance but lymph nodes can be better taken out in open surgeries as compared to the laproscopic surgeries. Oesophagectomy is considered now the surgery of choice with margin status proximally as 10cm and distally 5 cm. Oesophagectomy is of 3 types:

- transhiatal
- ivor lewis type
- mckeown (3 field esophagectomy)

Transhiatal Oesophagectomy

The image represents the steps followed during the transhiatal type of esophagectomy. Two incisions are given, one at midline and other on left lateral aspect of the neck. The site of anastomosis is the neck. This type of esophagectomy is carried out if the tumor is in lower 1/3rd or in the mid 1/3rd of esophagus.

Ivor-Lewis Oesophagectomy

The above image depicts Ivor-Lewis type of esophagectomy. It is most commonly performed type of surgery is Ivor-Lewis type of esophagectomy. Two incisions are given, in the abdomen and in right thorax., site of anastomoses being the thorax. Most common complication seen in ivor lewis type is atelactasis and the most common cause for mortality is anastomotic leak eventually leading to mediastinitis. Most common long term complication is stricture formation at anastomotic site.

Mckweon Oesophagectomy

It is a 3-incision operation which is usually done for patients with Siewert class I and II and any tumor involving oesophagus above the GE junction. Mckweon type involves tranfer of the oesophagus; thoracic tube ligation; laproscopy of the abdomen; lymphoid nodal removal; jejunostomy for nutrition of the patient and a left-sided incision is given on the neck for doing anastomosis. Mckweon type is considered advantageous over Ivor-Lewis type since it has a lower risk of cancer developing again, easy leak repairs, and a smaller incision may work since site for anastomosis is in the neck^{9,10}.

Another therapeutic option for advanced staging cancer is esophageal mucosa resection (EMR) or esophageal mucosa dissection. In EMR, the oesophageal mucosa and submucosa are dissected done for better visualization and subsequently then can be staged accordingly. It has been suggested the EMR should be carried out on lesions with a 'd' less than 2 centimetres and in those where less than 1/3rd of the esophageal layer circumference is involved. It is used in conjugation with radio-frequency ablating therapy and cryo-therapy burning method to eradicate BE.

Minimally Invasive Oesophagectomy

Newer strategies have been evolving in order to lessen the number of mortalities after surgery and this also increases the patient tolerance. A study among patients undergoing oesophagectomy was carried out on 222 patients, in which it was found that only 1.4% was the mortality rate and it also decreased the number of post-surgical days in the hospital. Clearly this method had increased patient compliance^{11,12}.

Medical Treatment

Chemotherapy and radiotherapy are used in conjunction with surgery for better outcomes. This is related to better patient compliance, currently being used for patients of stages TIII and N1. Patients with TIII or N1 stage carcinoma will be receiving new upcoming chemotherapy along with radiotherapy. Chemotherapy and radiation, in addition to surgery, are important therapeutic modalities that are utilised in either a neoadjuvant or adjuvant context. Patients with T3 or N1 stage cancer will undergo neoadjuvant chemo radiotherapy. The triple treatment medication regimen for esophageal cancer, according to the 2013 National Comprehensive Cancer Network recommendations, includes paclitaxel or carboplatin, cisplatin or fluoropyrimidine, and oxaliplatin or fluorouracil. Radiation doses of 41.4-50.4 Gray are indicated.

It is assessed that the chance of lymph nodal metastasis in tumors bound to the mucosa (T1a), predominantly adenocarcinomas in clinical practice, is 1%-2%, subsequently, an endoscopic nearby treatment might be viewed as adequate as conclusive treatment. In tumors attacking the submucosa (T1b), the jeopardy of nodal metastases surpasses 10%, thusly an authoritative endoscopic treatment isn't achievable in principle. In such kind of tumor staging (high-grade dysplasia, T1a) the most well-known remedial methodology is the blend of endoscopic resection strategies through mucosal resection (EMR) to eliminate the neoplastic/metaplastic cells related with ablative procedures, for example, radiofrequency to eliminate the excess metaplastic/dysplastic lingering tissue. MIE (minimally invasive esophagectomy) employing thoracoscopy and/or laparoscopy has become more popular in recent years all over the world.(2)

Patients' survival rates and health-related quality of life have all been proven to improve with curative surgical treatment, chemotherapy, and chemoradiotherapy.(1) Esophageal carcinoma is a challenging disease and requires multidisciplinary approach to improve the prognosis.

Preoperative chemotherapy or chemoradiotherapy improves outcomes compared to surgery alone, although the role of radiation therapy in conjunction with preoperative chemotherapy is still debated¹³. Esophageal cancer usually manifests late, when the illness has progressed to the point that curative therapy is no longer viable. Identification of at-risk persons, particularly those with BO, is a critical issue, and new improvements in screening technologies, including non-invasive procedures, may help with cancer diagnosis and detection at an earlier stage.

Multimodality therapy is one of the current therapeutic choices. Surgery, radiation, and chemotherapy are the cornerstones of contemporary treatment.(3)

Therapeutic choices and subsequent chance of survival for oesophageal Cancer is as follows:

Mckweon type of oesophagectomy has many advantages over the other types and should be considered for surgical procedures. But the sole decision of the type of surgery rests with the surgeon¹⁴. Studies on different carcinoma of gastrointestinal tract were reported¹⁵⁻¹⁷.

Conclusion

It may differ according to the surgeon experience and also on the exact site of the tumour. Minimally invasive surgeries are coming up in the recent days and may become the surgery if choice in the coming future. Robot assisted surgeries like robot-assisted minimally invasive esophagectomy (RAMIE) and video-assisted thoracic surgery esophagectomy (VATS-E) are in development

References

1. Short MW, Burgers K, Fry V. [Esophageal cancer. American family physician.](#) 2017; 95(1):22-8.
2. Watanabe M, Otake R, Kozuki R, et al. [Recent progress in multidisciplinary treatment for patients with esophageal cancer.](#) *Surgery today.* 2020; 50:12-20. Doi: <https://doi.org/10.1007/s00595-019-01878-7>
3. Napier KJ, Scheerer M, Misra S. [Esophageal cancer: A Review of epidemiology, pathogenesis, staging workup and treatment modalities.](#) *World J Gastrointest Oncol.* 2014;6(5):112. Doi: <https://doi.org/10.4251/wjgo.v6.i5.112>
4. Arnal MJ, Arenas AF, Arbeloa AL. [Esophageal cancer: Risk factors, screening and endoscopic treatment in Western and Eastern countries.](#) *World J Gastroenterol.* 2015;21(26):7933. Doi: <https://doi.org/10.3748/wjg.v21.i26.7933>
5. Sinh P, Sharma P. [Gastric cardia cancer: how much is it from fat?.](#) *Dig Dis Sci.* 2012;57:2493-6. Doi: <https://doi.org/10.1007/s10620-012-2324-z>
6. Brown AM, Giugliano DN, Berger AC, et al. [Surgical approaches to adenocarcinoma of the gastroesophageal junction: the Siewert II conundrum.](#) *Langenbeck's Arch Surg.* 2017;402:115-3-8. Doi : <https://doi.org/10.1007/s00423-017-1610-9>
7. Franklin J, Jankowski J. [Recent advances in understanding and preventing oesophageal cancer.](#) *F1000Research.* 2020;9. Doi: <https://doi.org/10.12688/f1000research.21971.1>

8. Kim TJ, Lee KH, Kim YH, et al. [Postoperative imaging of esophageal cancer: What chest radiologists need to know](#). *Radiographics*. 2007;27(2):409-29.
Doi: <https://doi.org/10.1148/rg.272065034>
9. Flanagan JC, Batz R, Saboo SS, et al. [Esophagectomy and gastric pull-through procedures: surgical techniques, imaging features, and potential complications](#). *Radiographics*. 2016;36(1):107-21.
Doi: <https://doi.org/10.1148/rg.2016150126>
10. D'Amico TA. [Mckeown esophagogastrectomy](#). *J Thorac Dis*. 2014; 6(Suppl 3):S322.
Doi:<https://doi.org/10.3978/j.issn.2072-1439.2014.03.28>
11. Laura SF, Warsingih W, Kusuma MI, et al. [Fifty five years old male with gastrointestinal stromal tumor: a case report](#). *Int J Res Med Sci*. 2019;7(7):2823.
Doi:<http://dx.doi.org/10.18203/23206012.ijrms20192927>
12. Luketich JD, Alvelo-Rivera M, Buenaventura PO, et al. [Minimally invasive esophagectomy: outcomes in 222 patients](#). *Ann Surg*. 2003;238(4):486.
Doi: <https://doi.org/10.1097/01.sla.0000089858.40725.68>
13. Ilson DH. [Adenocarcinoma of the esophagus: controversies and consensus](#). *Chin Clin Oncol*. 2017;6(5):52.
Doi: <https://doi.org/10.21037/cco.2017.09.02>
14. Park BJ, Kim DJ. [Robot-Assisted Thoracoscopic Esophagectomy with Total Mediastinal Lymphadenectomy: A Guide to a Systematic Approach Using the Concept of Fascial Plane Dissection](#). In *Techniques in Minimally Invasive Thoracic Surgery*. 2022;95-104.
Doi: <https://doi.org/10.5090/jcs.21.065>
15. Marfani GM, Kashikar SV, Singhanian S. [Double Barrel Oesophagus-A Case Report](#). *J Clin Diagnostic Res*. 2018;12(8).
16. Khanna S, Talwar D, Kumar S, et al. [Bulimia nervosa leading to squamous cell carcinoma of the esophagus in a young adult](#). *Cureus*. 2021;13(6).
Doi : <https://doi.org/10.7759/cureus.15536>
17. Ambad RS, Koundal P, Singh A, Jha RK. [Association between Glutathione-S-Transferase and Gastric Carcinoma: A Case Control Study](#). *Evolution Med. Dent. Sci*. 2020;9(39):2783-6.

Figures & Tables

Table 1: Squamous cell carcinoma(SCC) and Adenocarcinoma

Risk factor	SCC	Adenocarcinoma
Geography	Southeastern Africans, Asians, South Americans Most common overall most common in India	Western Europeans, North Americans, Australians
Race	Blacks > Whites	Whites > Blacks
Gender	M > F	M > F
Alcohol	++++	-
Tobacco	++++	++
Obesity	-	+++
GERD	-	++++
CREST syndrome	-	++
Barrett's esophagus	+	+++
Dietary regime: salad containing legumes and fruits	+++	+
Social class	+++	-
Role of genetics	+++	+
MC site	Middle 1/3rd	Lower 1/3rd

Table 2: The staging of oesophageal carcinoma

Category	Description
Tis	Carcinoma <i>in situ</i>
T1	Cancer invades lamina propria or submucosa

Category	Description
TII	cancer involve the muscularis propria
TIII	cancer invade adventitia
TIV	Cancer invade adjacent structures
NO	No lymphoid nodal metastasis
NI	Regional node metastasis ++
NII	distant metastasis not present
M1a, M1b	Distant metastasis ++

Table 3: Therapeutic choices and subsequent chance of survival for oesophageal Cancer.

STAGE	AJCC STAGING	TREATMENT OF CHOICE	FIVE-YEAR SURVIVAL (%)
Localized	Stage I (T1, N0, M0) through stage IIB (TIII, N0, M0)	Endoscopic mucosa resecting has become the surgery of choice.	42%
		Esophagectomy is done if the tumor has invaded the submucosa but there is no lymphoid nodal involvement	
Region	Stage IIB (T1-II, N1, M0) through stage IIIC (any T classification, NIII, M0)	Esophagectomy along with lymph node removal	22%
		Neoadjuvant/adjvant chemo-therapy or chemo-therapy along with radio-therapy	
Distant	Stage IV	Brachytherapy	6%
		Oesophageal bypass surgery	
		Jejunal stoma surgery	
		Palliation	
		Self-enlarging mucosal stenting	
		Trastuzumab(HER2 + cancers)	

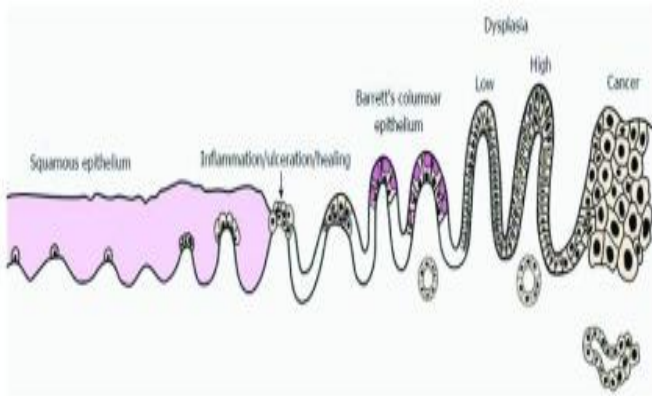


Figure 1: Selection of articles satisfying the inclusion criteria

Siewert classification type	Description
Type I	Adenocarcinoma of the distal esophagus, which usually arises from an area with specialized metaplasia of the esophagus (i.e. Barrett's esophagus) and may infiltrate the esophagogastric junction from above
Type II	True carcinoma of the cardia arising immediately at the esophagogastric junction
Type III	Subcardinal gastric carcinoma that infiltrates the esophagogastric junction and distal esophagus from below

Figure 2: Siewert classification of gastro-esophageal junction tumors

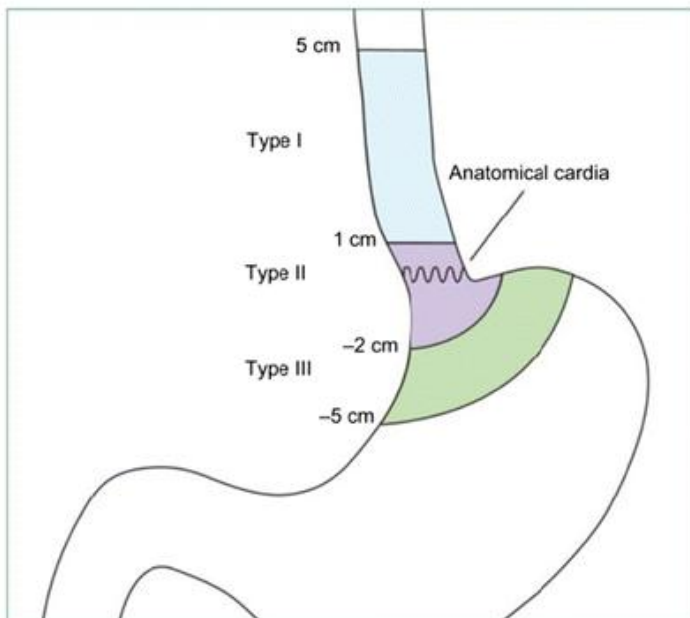


Figure 3: Gastro-Esophageal Junction Tumors

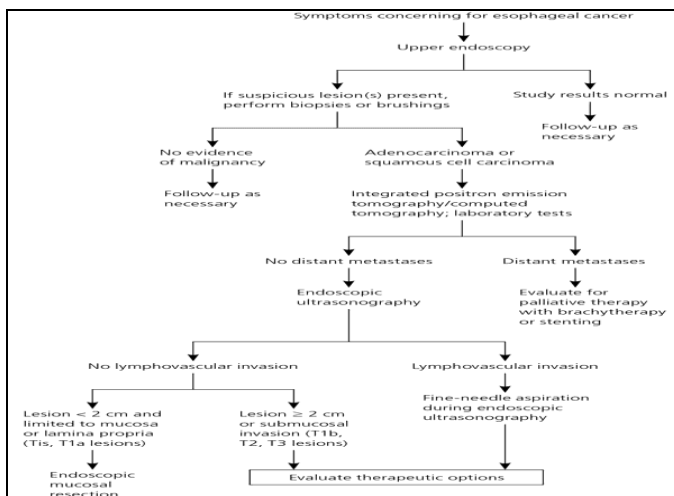


Figure 4: symptoms of oesophageal carcinoma.