OPEN ACCESS TEXTBOOK OF GENERAL SURGERY

OESOPHAGEAL CANCER

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DEFINITION

Oesophageal cancer has long been considered one of the deadliest malignancies. The most common histologic types are squamous cell carcinoma and adenocarcinoma, which together constitute more than 97% of oesophageal malignancies. Squamous cell cancer arises from the cells that line the upper part of the oesophagus. Adenocarcinoma arises from glandular cells that are present at the junction of the oesophagus and stomach. Although squamous carcinoma is more evenly distributed throughout the length of the oesophagus, adenocarcinoma is predominantly a disease of the distal oesophagus and gastrooesophageal junction, and is rarely found in the upper oesophagus. Rarely, melanoma, sarcoma, small cell carcinoma, or lymphoma may arise in the oesophagus.

PREVALENCE AND RISK FACTORS

In the year 2002, 462,000 new cases of oesophageal carcinoma were diagnosed globally, accounting for 4.2% of all cancer diagnoses and was the sixth most common cause of cancer-related death worldwide. The incidence of oesophageal carcinoma is characterized by a large geographical variation and the disease is on average seven-times more common in men than in women. Squamous cell carcinoma is still the dominant histological type in Europe, Asia and Africa but the incidence of adenocarcinoma has been on the increase and today accounts for approximately 30% of all cancer cases.

There are considerable geographic and racial variations in the incidence of this cancer, which is mostly explained by varying exposure to risk factors, although genetic susceptibility may play a partial role. South Africa is considered a zone of high endemic occurrence for the squamous variant. Many of the causative and risk factors for adenocarcinoma and squamous carcinoma have been well established.

For squamous cell carcinomas, exceptionally high incidence rates are observed in the Eastern Cape region of South Africa, and throughout an oesophageal cancer belt that extends from the shores of the Caspian Sea (in Iran and the former Soviet Union) across northern China. Paradoxically, high-incidence areas often are located near low-incidence areas. Within China itself, for example, incidence rates for oesophageal cancer can vary between provinces by a factor of more than 100

Race

In the United States, where statistics are well kept, the black-to-white age-adjusted incidence rate ratio was 5.6 for squamous cell carcinoma. This is notable as it appears to be controlled for diet, socio-economic class and regional bias. This bias does not appear to hold true for adenocarcinoma of the oesophagus.

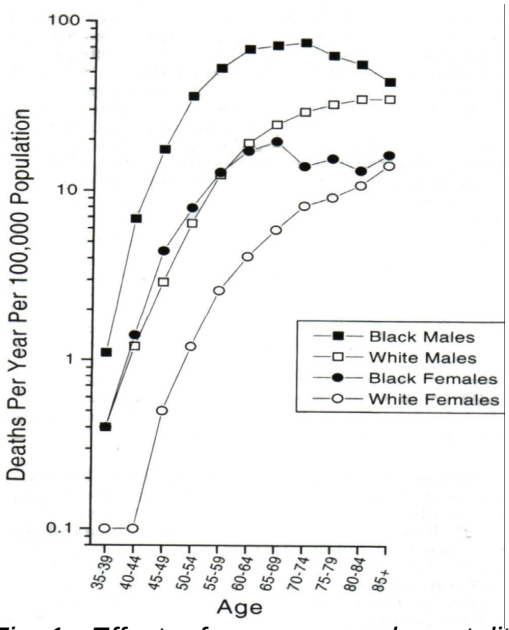


Fig 1: Effect of race on and mortality for squamous carcinoma of the oesophagus in an American population matched for diet and socio-economic status

This increased risk extends to both males and female (Fig 1).

Sex

Male sex is a risk factor for squamous carcinoma. Male to female ratios ranges from 20:1 in France to 2:1 in local series and Western Studies. This may relate to increase smoking and drinking rates. Our local experience is illustrated in Fig 2. Notably, this bias extends over all racial grouping.

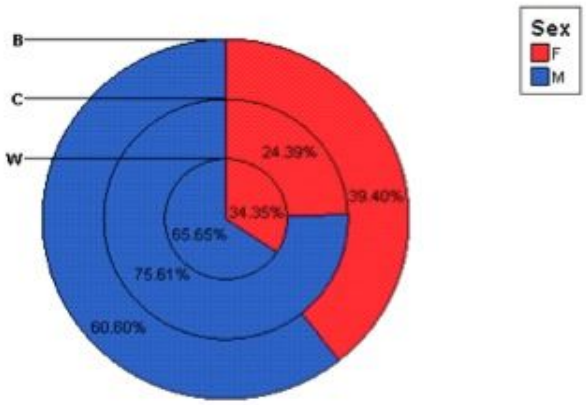


Fig 2: Local racial distribution of oesophageal carcinoma at Groote Schuur Hospital 1990 – 2000 (n = 1470)

Age

Squamous cancer occurs most commonly during the sixth and seventh decades of life. The disease becomes more common with advancing age; it is about 20 times more common in those older than 65 years than in persons younger than 65 years. Alarmingly, adenocarcinoma appears to be occurring in younger age groups.

Smoking

In Western cultures, retrospective evidence has implicated cigarette smoking and chronic alcohol exposure as the most common etiological factors for squamous cell carcinoma. Epidemiologic studies conducted in many countries have established that the risks of oral cavity, pharyngeal, laryngeal, lung, and oesophageal cancers are significantly increased among cigarette smokers. The degree of exposure, as measured by the average number of cigarettes smoked per day, is associated with substantially increasing levels of risk. The American Cancer Society Cancer Prevention Study II concluded, after 4 years of follow-up (1982-1986), that the age-standardized relative risks in current smokers at baseline of dying of oesophageal cancer was 7.6 when compared to those of individuals who have never smoked.

Ethanol

Neither smoking nor drinking alone has nearly the same effect than as used in synergy (Fig 3). Smoking has a synergistic effect with heavy alcohol consumption, and heavy exposure to both increases the risk of squamous carcinoma by a factor of more than 100. This is further complicated by the increased risk of other aerodigestive tract cancers in a person who smokes and drinks alcohol.

	TOBACCO (gm/day)			
ALCOHOL (gm/day)	0–9	10–19	20–29	30+
0–40	1.0*	3.4	3.2	7.8
41–80	7.3	8.4	8.8	35.0
81–120	11.8	13.6	12.6	83.0
121+	49.6	65.9	137.6	155.6

Fig 3: Combined effect of smoking and ethanol ingestion of squamous carcinoma (Vizcaino et al)

Ethanol is not a carcinogen but may act as a cofactor by helping carcinogens diffuse across the mucosal barrier. It appears to enhance the carcinogenic effects of N-nitrosodimethylamine in tissues of the nasal cavity, upper digestive tract, and lung, when administered orally to mice. Induction by ethanol of the cytochrome P-450-dependent microsomal oxidizing system, derived from the liver, lung, and upper digestive tract, may serve to enhance susceptibility to and activation of

chemical procarcinogens. Chemicals such as ethanol may accelerate the microsomal degradation of vitamin A, resulting in hepatic depletion of retinol.

Gastro-Oesophageal Reflux

As a consequence of the irritation caused by the reflux of acid and bile, 10-15% of patients who undergo endoscopy for evaluation of gastro-oesophageal reflux disease (GORD) symptoms are found to have Barrett epithelium. Adenocarcinoma may develop in these patients, representing the last event of a sequence that starts with the development of GORD and progresses to (Barrett) metaplasia, low-grade dysplasia, high-grade dysplasia, and adenocarcinoma. The risk of adenocarcinoma among patients with Barrett metaplasia has been estimated to be 3060 times that of the general population.

In 1952, Morson and Belcher first described a patient with adenocarcinoma of the oesophagus arising in a columnar epithelium with goblet cells. In 1975, Naef et al emphasized the malignant potential of Barrett oesophagus. A nationwide population-based case-control study performed in Sweden found an odds ratio of 7.7 (95% confidence interval, 5.3-11.4) for adenocarcinoma among persons with recurrent symptoms of reflux, as compared with persons without such symptoms, and an odds ratio of 43.5 (95% confidence interval, 18.3-103.5) among patients with long-standing and severe symptoms of reflux.

Other Factors

Vitamin or nutritional deficiencies have been recognized as contributing factors. In a high-risk country such as China, deficiencies in vitamin or microelement levels may play a role in causation. Riboflavin deficiency in China may contribute to a high incidence of oesophageal cancer.

Human papillomavirus infection has been recognized as a contributing factor. It is believed that the infection results in loss of function of the tumour suppressor genes p53 and Rb. The importance of this mechanism is not well established. *Helicobacter pylori* infection which is associated with gastric ulcer formation has not been found to be associated with oesophageal cancer.

In 1919 Paterson and Kelley described a syndrome consisting of dysphagia from an oesophageal web, iron-deficiency anaemia, and glossitis. The association of oesophageal webs with iron-deficiency anaemia, glossitis, cheilosis, koilonychia, brittle fingernails, and splenomegaly is referred to as the Plummer-Vinson or Paterson-Kelly syndrome. The condition is premalignant: approximately 10% of individuals will develop neoplasms of the oesophagus or hypo pharynx. Tylosis palmaris et plantaris is a rare autosomal dominant syndrome associated with hyperkeratosis of the palms and soles and a high rate of oesophageal squamous carcinoma.

Squamous carcinomas arising in lye strictures are responsible for 1-4% of oesophageal carcinomas. Fortunately caustic burns to the oesophagus are increasingly rare however, squamous cell carcinoma may develop in such patients 40 to 50 years after injury. Three quarters of all these tumours are located in the middle third of the oesophagus. Because of the increased risk, patients with prior history of caustic ingestion should be routinely screened, particularly when the time from injury exceeds 20 years.

Achalasia has been recognised as an inciting condition since 1872. The risk for developing oesophageal carcinoma may be 14% to 16% greater than the normal population risk. Patients often present in late stages of disease due to confusion of symptoms and the fact that it takes more tumour to obstruct widened oesophagus. The median age of occurrence about 10 years younger

than average. Cancers can occur in the middle and lower third of the oesophagus but are more common in the middle third, which frequently corresponds to the air-fluid interface of retained food and liquids.

Adenocarcinoma

- Barrett's oesophagus
- Gastro-oesophageal reflux disease (GORD)
- Obesity (by increasing the risk of GORD)

Squamous Cell Carcinoma

- Smoking
- Alcohol
- Tylosis
- Acalasia
- Oesophageal Diverticulae
- Plummer-Vinson Syndrome
- Human Papillomavirus infection

Table 1: Causative and Risk Factors for Adenocarcinoma and Squamous Cell Carcinoma

PATHOPHYSIOLOGY AND NATURAL HISTORY

The oesophagus itself has several unique properties that distinguish the behaviour of cancer in this organ from those of other gastrointestinal malignancies. In contrast to the rest of the gastrointestinal tract, the oesophagus has no serosa, thus reducing the resistance against local spread of invasive cancer cells. Furthermore, the oesophagus has an extensive network of lymphatics, allowing for early regional tumour advancement. The end result is local spread and invasion into surrounding tissue, with early metastatic disease developing in most patients.

SIGNS AND SYMPTOMS

The clinical presentation of patients with oesophageal cancer can be attributed to the direct effects of the local tumour, regional or distant complications of the disease, or paraneoplastic syndromes. Adenocarcinoma and squamous carcinoma have similar clinical manifestations, which reflect the extent of local oesophageal involvement.

Dysphagia, the most common manifesting symptom, usually develops in response to dense solid food, and progresses gradually to interfere with the intake of softer foods and, finally, liquids. This can sometimes be accompanied by vomiting or regurgitation of saliva or food uncontaminated by gastric secretions, particularly in patients with advanced local disease. Pain is frequent and can occur in the absence of dysphagia. It can be related to swallowing itself (odynophagia) or to the local extension of the tumour into adjacent structures, such as the pleura, mediastinum, or vertebral bodies. Constant pain is a serious sign and frequently indicates mediastinal invasion. Hoarseness caused by invasion of the recurrent laryngeal nerve is a sign of unresectability. Cough with swallowing frequently indicated the presence of a malignant oesophago-airway fistula. Stridor is an infrequent presenting sign and usually correlated with a large upper third carcinoma that is displacing or directly invading the airway.

Weight loss is common and correlates with dysphagia, dietary changes, and tumour-related anorexia. Weight loss is noted in more than 70% of patients. If loss is greater that 10% of baseline weight this carries a worse prognosis.

Hypercalcemia is the most common paraneoplastic syndrome. In the absence of bone metastases, it is most common in patients with squamous carcinoma and is believed to be caused by the production of a parathyroid hormone–related protein.

Symptoms Caused by Local Tumour Effects

- Dysphagia
- Cough and regurgitation
- Odynophagia
- Weight loss
- Upper gastrointestinal bleeding

Symptoms Related to Invasion of Surrounding Structures

- Respiratory fistula
- Hoarseness from recurrent laryngeal nerve invasion
- Hiccups from phrenic nerve invasion
- Pain caused by local spread

Symptoms Related to Distant Disease

- Metastatic disease to the lungs, liver, and central nervous system
- Hypercalcemia

Table: 2 Symptoms of Oesophageal Cancer

DIAGNOSIS

The goals of the workup are to establish the diagnosis and to stage the cancer. This combines a thorough history, examination, laboratory investigation and imaging.

Physical

The examination findings are often normal. Hepatomegaly may result from hepatic metastases.
Lymphadenopathy in the lateral cervical or supraclavicular areas represents metastasis and, if confirmed by needle aspiration or biopsy findings, is a contraindication to surgery.

Endoscopy

Endoscopy will allow the direct visualization of any tumour mass and histological confirmation with a biopsy or brush cytology. Occasionally, obstruction by the tumour mass may make the harvesting of an adequate biopsy difficult. Under these circumstances, dilation of the patient at the same sitting may provide for an adequate biopsy as well as ameliorating symptoms. Flexible endoscopy is currently the standard as it can general be performed under minimal sedation. In difficult cases, or where rigid endoscopy is required, a general anaesthetic may be necessary.
In case where the tumour involves the upper half of the oesophagus, a bronchoscopy is necessary to examine the trachea and bronchi to rule out airway invasion. The presence of such rules out the patient form resection and may alert the medical staff to the potential of an airway fistula. The application of radiotherapy may also be contraindicated, as it will promulgate the fistula formation. Under these circumstances, a stent is usually the treatment of choice.

Radiological Examinations

Contrast Studies

Contrast swallows are often the mainstay of screening for oesophageal carcinoma. Typical early lesions are characterised as defects in the smooth lining of the oesophagus. (Fig 4) More advance tumours are annular and constrictive. (Fig 5) Confusion can occurs with benign, often reflux associated strictures or with achalasia in the lower oesophagus. Malignancies often have ‘shouldering’ where benign lesions are smooth, however the burden of proof lies in endoscopic examination and histology. Ulceration and fistulisation can occur into the airway, mediastinum and pleura. If this is suspected pre-examination, caution needs to be extended on the selection of contrast agents.

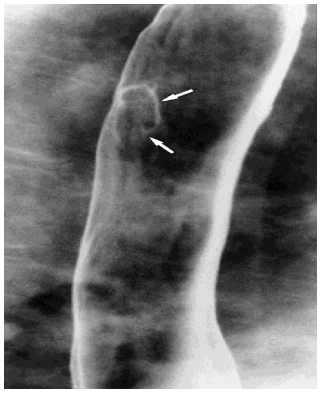


Fig 4: Contrast swallow – early carcinoma of the mid-oesophagus

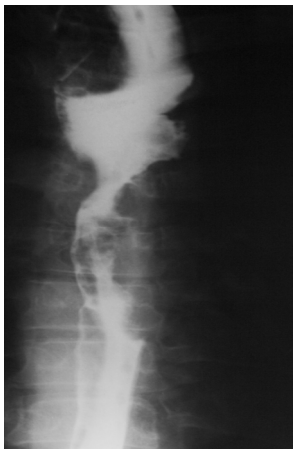


Fig 5: Contrast swallow – large obstructing tumour of the mid-oesophagus

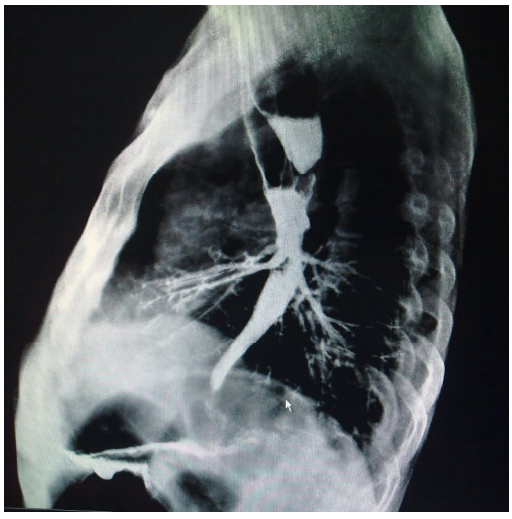


Fig 6: Contrast swallow – oesophageal tumour causing malignant tracheo-oesophageal fistula

Computed Tomography

Computed tomography (CT) of the chest, abdomen and pelvis, can evaluate whether the cancer has spread to adjacent tissues or distant organs (especially liver and lymph nodes). (Fig 7) The importance of CT stems from its ability to assess the presence of metastatic disease and the extent of direct invasion of local structures, such as the aorta or major airways, any of which will preclude surgical intervention. The technique should use both oral and intravenous contrast media and should include cuts from the thoracic inlet down to the mid-abdomen. It must be noted, however, that CT is not very accurate in assessing the histologic depth of the tumour (T), nor is it sensitive in assigning lymph node status (N). In fact, the overall accuracy of CT in nodal detection is less than 60%.

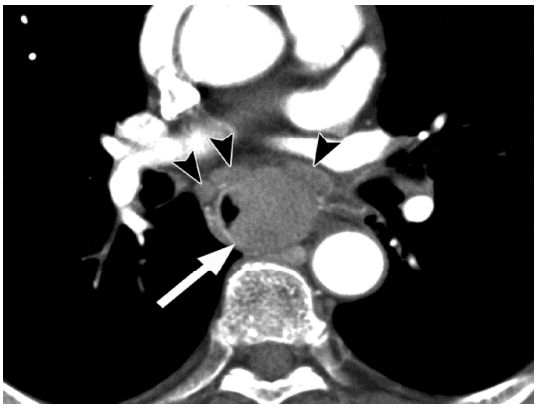


Fig 7: Computed tomography – large mid oesophageal lesion at the level of the mid-oesophagus with multiple large metastatic lymph nodes

PET Scan

PET scanning with 18-fluorodeoxyglucose has been recently incorporated into the staging evaluation of oesophageal cancer (Fig 8). It accentuates masses are metabolically active, indicating faster-growing cells that might be expected in cancer. This non-invasive test is more sensitive than CT for detecting distant metastases. Recent studies have suggested that PET scanning can detect metastatic disease in 15% of

patients who were believed, based on conventional diagnostic techniques, to have localized oesophageal cancer. The superimposition of CT and PET scans is even more sensitive in identifying patients with occult metastases.

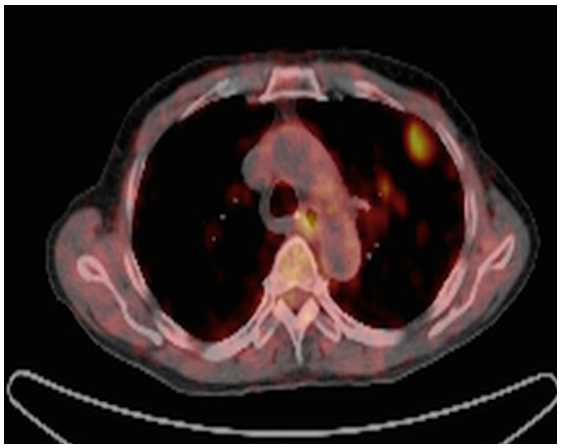


Fig 8: CT-PET scan of mid oesophageal malignancy with lung metastasis

Oesophageal Ultrasound

Endoscopic ultrasonography has proven very useful in assessing the local depth of the tumour (T), lymph node involvement (N) and, with increased clinical experience, involvement of non-regional (M1a) lymph nodes. The overall accuracy of endoscopic ultrasonography in tumour depth assignment is about 80% and improves with more advanced stages of disease. With stringent criteria, the accuracy of detecting lymph node involvement approaches almost 75%. This accuracy can be improved further by endoscopic fine-needle aspiration of suspicious lymph nodes, which allows pathologic confirmation of involvement(Fig 9). This exam is equipment and operator intense and is not widely available at this time.

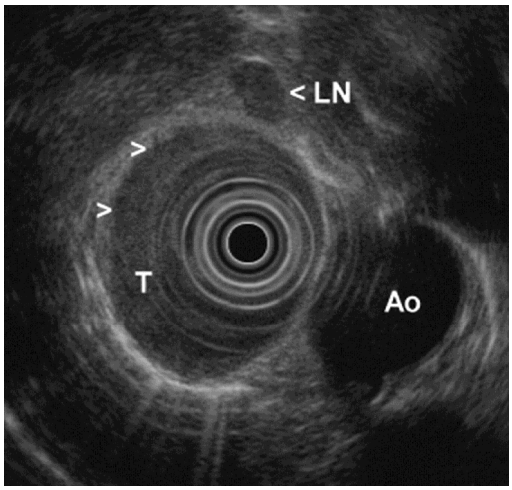


Fig 9: Oesophageal ultrasound showing tumour (T) and surrounding adenopathy (LN) in relation to the Aorta (Ao)

STAGING

TNM			Stage
Tis	N0	M0	0
T1	N0	M0	I
T2	N0	M0	IIA
T3	N0	M0	
T1	N1	M0	IIB
T2	N1	M0	
T3	N1	M0	III
T4	Any N	M0	
Any T	Any N	M1	IV

Table 2: American Joint Committee on Cancer tumour-node-metastasis (cTNM) classification

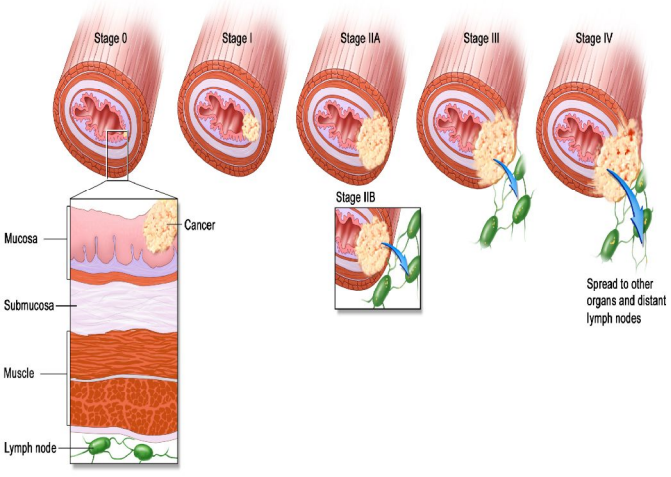


Fig 10: TNM Staging of oesophageal carcinoma

After establishing a diagnosis of oesophageal cancer, adequate staging is required, because staging is the most important step in choosing appropriate therapy. More than 50% of patients have unresectable or metastatic disease at the time of presentation. For the others, survival is closely related to the stage of the disease. The staging evaluation allows patients to be assigned a clinical stage according to the American Joint Committee on Cancer tumour-node-metastasis (cTNM) classification. (Fig 10a-b) Informed recommendations about therapy and appropriate information regarding prognosis depends on this clinical staging, an assessment that can, however, only approximate the true disease stage

The pathologic extent of disease (pTNM) cannot truly be determined without an oesophagectomy, and survival is closely linked to this pathologic stage. The ability of the clinical (cTNM) stage to predict the pTNM accurately has improved with the development of more modern staging modalities. Optimal clinical staging for this disease should include at least computed tomography (CT) scanning of the chest and abdomen. If available endoscopic ultrasonography and, if appropriate, a positron emission tomography (PET) scan should be considered to avoid inappropriate intervention.

TREATMENT

The most appropriate method to prolong life and control dysphagia should be tailored for each patient individually, depending on tumour characteristics, patient preference, and the specific expertise of the physician. The following treatment modalities are available to help achieve this goal:

Surgery

Historically, oesophageal cancer has carried a dismal prognosis. This has been attributed to the late presentation of patients with this disease and the technical difficulty of an adequate surgical resection in the presence of advanced local and regional involvement. Oesophageal resection (oesophagectomy) remains an integral part of the treatment of oesophageal cancer. It is used in patients who are considered candidates for surgery. It no longer is used for palliation of symptoms because other treatment modalities such as radiotherapy or intubation are more successful for relieving dysphagia at a much lower risk. An oesophagectomy can be performed by using an abdominal and a cervical incision with blunt mediastinal dissection through the oesophageal hiatus (ie, transhiatal oesophagectomy (Fig 11)) or by using an abdominal and a right or left thoracic incision (ie, transthoracic oesophagectomy).

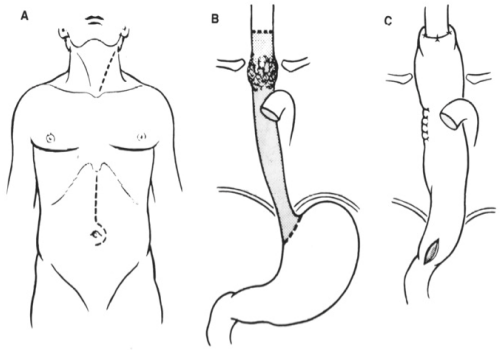


Fig 11: Incisions for a transhiatal oesophagectomy with removal of tumour and interposition of stomach

Transhiatal oesophagectomy offers the advantages of avoiding a chest incision, which can be a prolonged cause of discomfort and can further aggravate the condition of patients with compromised respiratory function. After removal of the oesophagus, continuity of the gastrointestinal tract is usually re-established using the stomach. Some authors have questioned the validity of transhiatal oesophagectomy as a cancer operation because part of the operation is not performed under direct vision and fewer lymph nodes are removed compared to transthoracic

oesophagectomy. However, many retrospective and prospective studies have shown no difference in survival between the operations, suggesting that the type of operation is not the factor influencing survival but, rather, the stage of the cancer at the time the operation is performed.

Surgical results have improved significantly over recent years, however. Multiple surgical series from major medical centres now report that patients undergoing surgery alone have median survival rates between 13 and 19 months, 2-year survival rates between 35% and 42%, and 5-year survival rates of 15% to 24%. Although these numbers are certainly more promising, they can hardly be characterized as a medical success story, especially when we keep in mind that much of this improvement is the result of better clinical staging and better patient selection.

Contraindications to surgery include metastasis to N2 nodes (ie, celiac, cervical, or supraclavicular lymph nodes) or solid organs (eg, liver, lungs) are a contraindication. Invasion of adjacent structures (eg, recurrent laryngeal nerve, tracheobronchial tree, aorta, pericardium) is a contraindication. Severe associated co-morbid conditions (eg, cardiovascular disease, respiratory disease) can decrease a patient's chances of surviving an oesophageal resection. Cardiac function and respiratory function are carefully evaluated preoperatively. A forced expiratory volume in 1 second of less than 1.2 L and a left ventricular ejection fraction of less than 0.4 are relative contraindications to the operation.

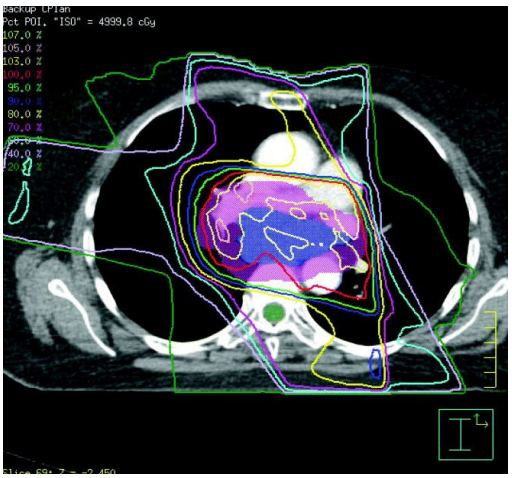
Complications occur in Complications occur in approximately 40% of patients. Respiratory complications (15-20%) include atelectasis, pleural effusion, and pneumonia. Cardiac complications (15-20%) include cardiac arrhythmias and myocardial infarction. Septic complications (10%) include wound infection, anastomotic leak, and pneumonia. Anastomotic stricture may require dilatation (20%).

The mortality rate depends on the functional status of the patient and the experience of the surgeon and the team taking care of the patient. A mortality rate of less than 5% should be the goal for oesophagectomy for cancer. With rare exceptions, this mortality rate is usually achieved only in tertiary care centres.

Radiotherapy

Radiation therapy is successful in relieving dysphagia in approximately 50% of patients. In patients with advanced oesophageal cancer, the preoperative combination of chemotherapy and radiotherapy has shown good results. In a large multicenter study, Herskovic and colleagues reported a 2-year survival rate of 38%, with a median survival of 12.5 months.

High-dose definitive radiation therapy, as an alternative to surgical resection, is challenging because of the anatomic location of the oesophagus. Any radiation therapy portal encompassing the oesophagus will also include other vital structures, such as major blood vessels, major airways, the heart, and lungs (Fig 12a-b). Although modern radiation techniques have fewer adverse side effects, toxicity is still common with the radiation doses required.



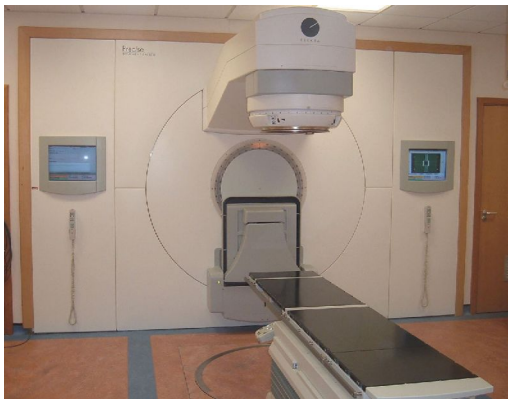


Fig 12a and 12b: Therapeutic plan and machine for external beam radiotherapy

Radiation therapy has been used in the past as a single-modality approach with curative intent. However, except for those with very early-stage disease, radiation has had little impact on long-term survival. For more advanced disease, single-modality radiation therapy should, in general, be considered a palliative intervention in patients whose underlying medical co-morbidities preclude surgical resection or aggressive multimodality treatment.

Brachytherapy is the internal application of radiotherapy, usually in the form of 'afterloading' with radioactive wire or pellets (Fig 13). This has the advantage of low total body does and seldom affects other viscera. In addition, it allows treatment to be given over a short period of time. It can be given in conjunction with external beam radiotherapy or as a 'boost' for difficult or refractory patients. Disadvantages are the low depth of penetration, which makes it inappropriate for large tumour, and the expense of equipment and need for expertise.

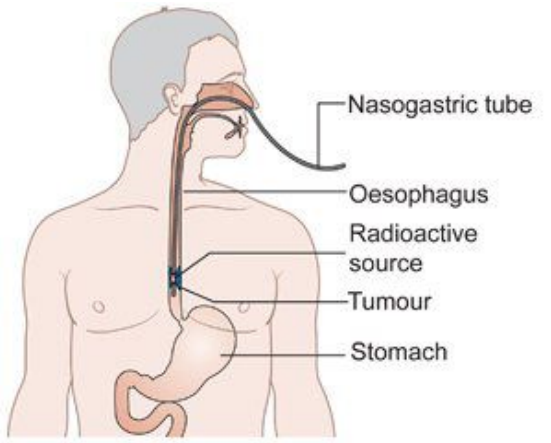


Fig 13: Endo-oesophageal radiotherapy (brachytherapy) of oesophageal cancer

Intubation

For patients who are not candidate for surgery or radiotherapy, intubation may provide a quick amelioration of the dysphagia. Optimally they may be intubated with expandable metallic stents, which can be deployed by endoscopy under fluoroscopic guidance and can keep the oesophageal lumen patent (Fig 14). They are particularly useful when a tracheoesophageal fistula is present. The cost and availability of the stents may relegate the patient to be intubated via a 'pulsion' technique which carries a much higher complication rate.

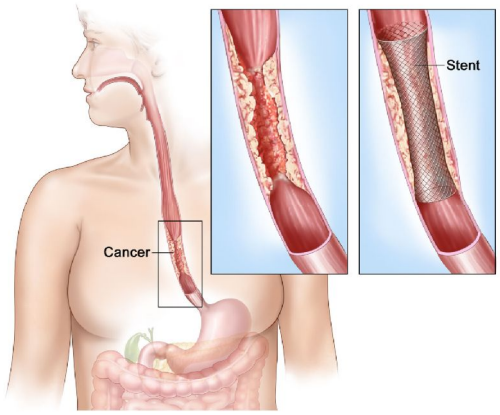


Fig 14: Placement of oesophageal stent for palliation of obstruction from oesophageal carcinoma

Chemotherapy

In 2006, a Cochrane review tried to assess the effectiveness of chemotherapy versus best supportive care or different chemotherapy regimens against each other, in metastatic oesophageal carcinoma. The authors found that there was no consistent benefit of any specific chemotherapy regimen. Chemotherapy agents with promising response rates and tolerable toxicity are cisplatin, 5-fluorouracil (5-FU), paclitaxel, and anthracyclines. Future trials comparing palliative treatment modalities should assess quality of life with validated quality of life measures. Chemotherapy as a single modality has limited use and only a few patients achieve a modest and short-lived response.

Other Modalities of Treatment

Laser therapy (Nd:YAG laser) can help achieve temporary relief of dysphagia in as many as 70% of patients. Multiple sessions are usually required to keep the oesophageal lumen patent. This treatment often requires multiple sessions with specialised and expensive equipment. Results are also limited by the experience of the operator

Photodynamic therapy (PDT) offers an interesting nonsurgical form of therapy. PDT refers to the administration of photosensitising chromophores, which are selectively retained by dysplastic malignant tissue. Light is delivered in the area where the photons are absorbed by the photosensitiser. The photosensitiser becomes photoexcited and transfers its energy to a chemical substrate that causes biologic damage to the abnormal tissue. A drawback of PDT is the formation of oesophageal strictures in 34% of patients. Therefore, even though the initial results are encouraging, this form of treatment is still considered experimental and is not widely available.

Multimodality Treatment

Multimodality treatment approaches have evolved over recent years in response to the frequent locoregional and distant recurrences identified after surgery or radiation therapy alone. Several different combinations and sequences of treatment modalities have been tried, with mixed results. Chemotherapy has been given preoperatively, postoperatively, or both. A cisplatin-based regimen is often used. Preoperative chemotherapy has been studied in several randomized clinical trials that compared surgery alone with chemotherapy followed by surgery. These studies have demonstrated that induction chemotherapy can produce up to a 50% clinical response rate but less than a 10% pathologic complete response rate, and that the 2-year survival rate after subsequent surgery is approximately 35%. However, the results of these studies have been mixed, and no clear survival advantage has been identified with the induction regimens.

More intensive multimodality approaches have attempted to exploit the radiosensitizing properties of chemotherapy by using concurrent cisplatin-based chemotherapy and radiation as definitive treatment or as a preoperative adjuvant. In 1992, Herskovic reported that compared chemotherapy given concurrently with radiation with radiation therapy alone. A clear survival benefit for the combined approach was identified, with a 5-year survival rate of 25% compared with radiation therapy alone [18]. How this approach can be integrated with surgery has remained unclear. Currently, in many major referral centres, trimodality therapy is used for suitable patients who have at least T3 lesions, any nodal involvement with oesophageal cancer, or both.

PROGNOSIS

Survival depends on the stage of the disease. Lymph node metastases or solid organ metastases are associated with low survival rates. A recent report of 1085 patients who underwent transhiatal oesophagectomy for cancer showed that the operation was associated with a 4% operative mortality rate and a 23% 5-year survival rate. A subgroup of patients with a better 5-year survival rate (48%) was identified. These patients received preoperative radiation and chemotherapy (ie, neoadjuvant therapy), with complete response (ie, disappearance of the tumour).

The overall 5-year survival rate for oesophageal cancer remains approximately 20-25% for all stages. Patients without lymph node involvement have a significantly better prognosis and 5-year survival rate compared to patients with involved lymph nodes. Stage IV lesions are associated with a 5-year survival rate of less than 5%. Most approaches of surgery have similar survival rates. Squamous cell carcinoma and adenocarcinoma, stage-by-stage, have equivalent survival rates.

PREVENSION AND SCREENING

More recently, there has been an effort to discover early, asymptomatic, oesophageal adenocarcinoma by screening patients with Barrett's oesophagus. The identification of high-grade dysplasia (i.e., carcinoma in situ) is considered an indication for oesophagectomy, because occult invasive cancer is frequently identified at the time of resection, and because invasive cancer will develop in almost 50% of patients with high-grade dysplasia who do not undergo oesophageal resection.