Carcinoma of the oesophagus

Cancer of the oesophagus is a distressingly common cancer in men and women.

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Cancer of the oesophagus is the third leading cancer in males, comprising about 5.6% of all cases in males and 4th common in females, comprising 3% of all cancers. The age-adjusted incidence rates are 61/100 000 population in males and 36.8/100 000 in females for the age group 70 - 74 years, steadily increasing from 50 - 54 years. The majority of patients (33%) present in the age group of 65 and above.

The condition is 3.8 times more likely in smokers and the incidence increases if there is alcohol intake in addition to smoking. The age-standardised rates are 37.5/100 000 population in Transkei, Eastern Cape (3 times more) than in other geographical areas, due mainly to consumption of maize, which contains low levels of niacin, riboflavin, vitamin C, zinc, cadmium and magnesium. The incidence is also very high in the black population and forms 13% of all cancers in black males.

Evaluation and investigation

A detailed history of complaints of difficulty in swallowing, cough associated with swallowing, loss of weight, and backache is essential to diagnosis. Weight loss of > 10% in the 6 months preceding treatment has an adverse impact on survival. Investigations include a general physical examination for performance status, including body weight and regional and distant spread, investigations such as barium swallow, endoscopy for histological diagnosis, the length of the lesion and the type of the lesion, a CT scan of the chest and upper abdomen for local extent, extra-oesophageal spread, nodal disease and liver involvement. PET CT has a better sensitivity and specificity than CT alone and changes the management decision in about 20% of cases. Endoscopic ultrasound is optimal for loco regional staging to determine the depth of invasion and loco regional lymph nodes.

The criteria for curative versus palliative treatment should be:

- lesion length of 5 cm or less
- no metastatic disease
- ECOG performance status 0 - 1.

Curative therapy

Only approximately 20% of patients are suitable for curative therapy. Options for curative therapy include surgical resection, definitive chemoradiation, and chemoradiation followed by surgical resection (trimodality therapy). Postoperative chemotherapy and radiation is only recommended for gastro-oesophageal cancers.

Surgery alone

The aim is to achieve a wide resection with 5 cm margins and a regional lymphadenectomy. The approach may be transthoracic or transhiatal. High lesions (above the aortic arch) require the additional resection of the pharynx and larynx, and are not treated primarily with surgery. About half the patients taken to surgery can be resected, with a 5-year survival of 20 - 35%. The surgery should be performed in a high-volume tertiary referral centre.

Definitive chemoradiation

Chemoradiation has been shown to be superior to radiation alone in an intergroup study.[2] The 2-year survival was 38% versus 10% ($p < 0.001$), 5-year survival 27% versus nil ($p < 0.001$).

However, chemoradiation is associated with significant morbidity. Good results have been reported for the rare T1N0M0 lesions with radiation alone.[3] Dose escalation is controversial. The Intergroup randomised patients receiving chemo-radiation to 64.8 or 50.4 Gy with concurrent 5-FU and cisplatin showed no statistically significant difference in recurrence patterns with the higher dose.[4] However, a large proportion of the recurrences are local (about half) so there is a rationale for adding a brachytherapy boost. Hishikawa *et al.*[5] report 27.9% overall survival at 2 years with high-dose-rate brachytherapy following external beam radiation in comparison to 19.6% with external beam radiation alone. Sharma *et al.*[6] have reported 22% 5-year survival in a select group of patients with a combination of external beam radiation followed by low-dose-rate brachytherapy along with 5FU radio-sensitisation.

Preoperative chemoradiation

Complete response rates after chemoradiation are approximately 20%. This led to trials comparing preoperative chemoradiation versus oesophagectomy alone. Many of these trials do not report an improvement in overall survival for trimodality therapy. Stahl *et al.*[7] report no survival benefit with the addition of surgery following chemoradiation although local tumour control (64% versus 41% at 2 years) and the quality of swallowing were improved. A meta-analysis of 9 trials[8] has shown that neo-adjuvant chemoradiation improved the 3-year loco regional control (odds ratio 0.88, $p = 0.6$) and survival

Table I. AJCC staging of cancer of the oesophagus

AJCC Staging (2002)

Primary tumour (T)

TX: Primary tumour cannot be assessed

T0: No evidence of primary tumour

Tis: Carcinoma *in situ*

T1: Tumour invades lamina propria or submucosa

T2: Tumour invades muscularis propria

T3: Tumour invades adventitia

T4: Tumour invades adjacent structures

Regional lymph nodes (N)

NX: Regional lymph nodes cannot be assessed

N0: No regional lymph node metastasis

N1: Regional lymph node metastasis

Distant metastasis (M)

MX: Distant metastasis cannot be assessed

M0: No distant metastasis

M1: Distant metastasis

Tumours of the lower thoracic oesophagus:

M1a: Metastasis in celiac lymph nodes

M1b: Other distant metastasis

Tumours of the midthoracic oesophagus:

M1a: Not applicable

M1b: Non-regional lymph nodes and/or other distant metastasis

Tumours of the upper thoracic oesophagus:

M1a: Metastasis in cervical nodes

M1b: Other distant metastasis

AJCC stage groupings

Stage 0	Tis, N0, M0
Stage I	T1, N0, M0
Stage IIA	T2, N0, M0
	T3, N0, M0
Stage IIB	T1, N1, M0
	T2, N1, M0
Stage III	T3, N1, M0
	T4, any N, M0
Stage IV	Any T, any N, M1
Stage IVA	Any T, any N, M1a
Stage IVB	Any T, any N, M1b

As the above staging can be done using EUS or, SURGERY, the AJCC 1978 staging should be applied until facilities for EUS are available everywhere and patients come in a stage where surgical staging is possible

AJCC Staging (1978)

Primary tumour (T)

TX: Primary tumour cannot be assessed

T0: No evidence of primary tumour

Tis: Carcinoma *in situ*

T1: Tumour 5 cm or less, no obstruction, no circumferential involvement, no extra-oesophageal spread

T2: Tumour more than 5 cm, any size with obstruction, circumferential involvement and no extra-oesophageal spread

T3: any tumour with extra-oesophageal spread

Regional lymph nodes (N)

NX: Regional lymph nodes cannot be assessed

N0: No regional lymph node metastasis

N1: Movable unilateral palpable lymph nodes

N2: Movable bilateral palpable nodes

N3: Fixed nodes

Distant metastasis (M)

MX: Distant metastasis cannot be assessed

M0: No distant metastasis

M1: Distant metastasis

PET CT has a better sensitivity and specificity than CT alone and changes the management decision in about 20% of cases.

(odds ratio 0.66, $p = 0.038$) at the expense of increased treatment-related mortality.

Palliative therapy

Advanced oesophageal cancer carries a very poor prognosis, with a median survival time that ranges from 2.5 to 6.2 months.[9] Most patients present with an advanced stage of disease and in a poor general condition, where palliation of symptoms is the main aim of treatment. The main symptoms requiring palliation are dysphagia, odynophagia, regurgitation and pain.

Dysphagia appears when the oesophageal lumen is less than 15 mm in diameter. The options for relieving dysphagia include serial dilatations, stenting, external beam radiation, chemotherapy, brachytherapy (low-dose-rate and high-dose-rate), photo-dynamic therapy or a combination of modalities.

Brachytherapy and stenting

High-dose-rate brachytherapy has an advantage over the low-dose-rate or medium-dose-rate because treatment is quick and therefore the discomfort the patient suffers from having the oesophageal applicator in place for a long period is avoided. Sur *et al.*[10] have compared brachytherapy schedules of 6 Gy x 3 fractions and 8 Gy x 2 fractions in a multi-centre IAEA study and reported similar results for overall survival and dysphagia-free survival. The overall survival was 7.9 months for the whole group (9.1 months for 6 Gy x 3 fractions and 6.9 months for 8 Gy x 2 fractions, $p = > 0.05$). The dysphagia-free survival for the whole group was 7.1 months (7.8 months for 6 Gy x 3 fractions and 6.3 months for 8 Gy x 2 fractions, $p = > 0.05$). Due to limited resources, more use of brachytherapy needs to be considered, as this could reduce the waiting period for the patients needing external beam radiation.

A multicentre Dutch study compared a single 12 Gy dose of intraluminal brachytherapy with placement of a stent in 209 patients.[11] Dysphagia improved more rapidly and completely after stent placement but long-term relief of dysphagia (after 3 months) was better after brachytherapy. Stent placement resulted in a higher complication rate than brachytherapy (33% versus 21%) mainly due to increased late haemorrhage. There was no difference in survival between the two groups.

External beam radiation

This is usually given in 5 - 10 daily fractions (compared with 1 or 2 of brachytherapy), and can achieve palliation of dyphagia in about 66% of patients for 2 months or longer.

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Weight loss of > 10% in the 6 months preceding treatment has an adverse impact on survival.

In a nutshell

- Cancer of the oesophagus is the third leading cancer in males, comprising about 5.6% of all cases in males, and 4th most common in females, comprising 3% of all cancers.
- Patients present with difficulty in swallowing, loss of weight, and backache.
- Essential investigations should include a barium swallow, endoscopy and a CT scan of the chest and upper abdomen for local extent, extra-oesophageal spread, nodal disease and liver involvement.
- Early referral to a specialist centre by the general physician would help in proper treatment selection.
- Treatment can be palliative (80%) or curative (20%). Treatment should be individualised for each patient.
- The choice of treatment depends on expertise and facilities available, tumour and patient factors and local economics.