

Oesophageal Carcinoma A Review of Current Practice in the United Kingdom

Philip Camilleri

Oesophageal carcinoma is on the rise in all western countries, currently with an incidence of 10/100, 000 in the UK. As the numbers of gastric carcinoma cases fall worldwide, the incidence of gastro-oesophageal junction tumours is increasing.¹

Aetiology and classification

The main risk factors for development of carcinoma of the oesophagus are listed in Table 1. In particular, Barretts oesophagus represents metaplastic change from the usual stratified flat epithelium to an intestinal type columnar epithelium. It is a pre-malignant condition although the rate of conversion to malignancy is thought to be low, between 0.5-1.0% of cases. Patients with Barretts change require life long endoscopic follow up with regular biopsies to assess for dysplastic change.²

Classification of Oesophageal Cancers

There are two main histological types of primary carcinoma at this site, namely squamous cell carcinoma and adenocarcinoma. A number of rarer types have also been identified (Table 2). Twenty years ago, squamous cancers far outnumbered any other histological type seen but now they comprise 20-30% of all new cases, arising mainly in the upper two thirds of the oesophagus.

In contrast adenocarcinoma in contrast now makes up 70 – 80 % of oesophageal cancers, mainly in the lower third and with background of Barretts metaplasia usually present .

Both arise as locally infiltrating tumours that spread submucosally and radially through the muscular layers of the oesophagus and beyond. Local and regional lymph node spread is very common and is present in up to 80% of all cancers at time of diagnosis. Routes of spread may be to nodes above as well as below the diaphragm. Haematogenous spread occurs to the liver, lungs and bones.

Keywords

Oesophageal cancer, current practice

Philip Camilleri MRCP FRCR
Department of Clinical Oncology,
Oxford Radcliffe Hospitals, Oxford, UK
Email: Philip.camilleri@btinternet.com

Clinical features

The survival rates of patients treated for oesophageal carcinoma are poor, around 25 % at 3 years, mainly because of the extent of disease at time of presentation with most patients presenting late.³ Between 30 and 40 % of all patients diagnosed with oesophageal disease have localised malignancy and are fit enough for surgery.

Increased awareness and regular endoscopic follow up of Barretts oesophagus have begun to change the stage at which diagnosis occurs although it is still too early to make any confident statements about this. The symptoms leading up to presentation vary as can be seen in Table 3.

Table 1: Risk factors

Alcohol
Tobacco
Diet - high in nitrosamines e.g. dried or smoked fish
Aflatoxin
Achalasia
Barretts oesophagus
Tylosis Palmaris
Plummer Vincent Syndrome
Caustic burns
Previous radiotherapy to the chest or neck
Male sex

Table 2: Less common histological types of oesophageal cancers

Small cell carcinoma
Sarcoma
Melanoma
Mucoepidermoid carcinoma
Adenoid cystic carcinoma
Lymphoma

Table 3: Symptoms

Painless dysphagia, initially to solids, progressing to complete dysphagia to all fluids including saliva.
Weight loss
Pain either local or distal
Early satiety
Dyspepsia
Hoarseness from recurrent laryngeal nerve palsy

Table 4: Palliative measures for local control⁷

External beam radiotherapy
Brachytherapy
Endoscopic Photodynamic therapy
YAG laser endoscopic ablation
Expandable metal stent

Management of early disease

Surgical resection is the modality of choice for curative treatment of early oesophageal carcinoma. The surgery is complex, requiring a total oesophagectomy with gastric pull-up and lymphadenectomy.

Once the diagnosis is obtained by endoscopic biopsy, work up should include prone contrast-enhanced CT scan to assess the degree of contact between the tumour and the aorta, and to detect metastatic disease to the liver and lungs. Laparoscopy and biopsy of affected nodes that may preclude resection is undertaken.

Surgery alone will provide a 35% 3 year survival rate for early disease. Most patients who relapse have distal metastases, suggesting that micro-metastatic disease was present at the outset.

In the late 1990s, practice changed to include pre-operative chemotherapy following the completion of the Medical Research Council's (MRC) OE – 02 randomised controlled trial. This paper compared two cycles of chemotherapy pre-operatively with surgery alone in 802 patients. Patients had to be deemed eligible for radical surgery by the surgical team.

It showed that giving two cycles of chemotherapy (Cisplatin and 5 Fluorouracil) prior to surgery improves the 3-year survival by 9% increasing it to 44% (95% Confidence interval [CI] 3-16%). Overall survival improved significantly in the chemosurgery group (Hazard Ratio 0.79, CI 0.67-0.93, p=0.004).

The rationale behind chemotherapy is to deal with micro-metastatic disease as early as possible, giving the patient a better chance at long term survival following successful surgery. Indeed, complete resection rates were higher for those on chemo (60% vs. 54%). The response rate to chemotherapy was high, with only 17% showing progressive growth.

Side effects of treatment are mild and post-operative complications were similar in both groups. Furthermore chemotherapy often results in symptomatic improvement within days of the first cycle of chemotherapy.⁴

Although this study has its detractors and critics, it has been embraced by surgical and oncological teams across the UK. Current practice involves discussion of each new oesophageal carcinoma patient in a multi-disciplinary meeting attended by the radiologists, pathologists, surgeons, oncologists and clinical nurse specialists.

All patients thought to be surgically resectable will be referred to the oncologists, who assess the patient's fitness for chemotherapy, with most patients deemed fit. Of course, close

co-operation between the teams is vital for the smooth co-ordination of the various aspects of management. Surgery is scheduled for the third week after the second cycle of chemotherapy has been delivered.

Combining chemotherapy and radiotherapy pre-operatively is also gaining popularity following the publication of a number of papers worldwide. The morbidity of combining three toxic treatments (chemotherapy, radiotherapy and surgery) is however considerable⁵ and as a result, it has not yet been adopted as the gold standard. Carefully selected fit patients may, however, benefit from this combined modality treatment.

For those patients who are deemed inoperable for medical reasons, combined chemoradiotherapy is an alternative to surgery. A landmark paper by Herskovic in 1992 showed that with combined chemoradiation using Cisplatin and 5 Fluorouracil concurrently with radiation to 50Gy, the 5-year survival rate could be as high as 27% which is comparable to many series of surgical survival.⁶ However, there are no randomised controlled studies of radical chemoradiotherapy compared with surgery.

Palliative treatment

Sadly, for the many patients who relapse, or who have metastatic disease at diagnosis there are no curative options.

Measures aimed at symptomatic control are effective and varied (Table 4). These provide some improvement in swallowing for a limited amount of time and sometimes the benefit may be measured in months rather than weeks. The choice of palliation depends on local availability as well as the patient's level of fitness.

Chemotherapy may be offered to those who are still relatively fit and well despite metastatic disease. This prolongs the median survival of those with metastases to about 9 months, which is an improvement of around 3 months. Early involvement of the palliative care team is essential to ensure maximal benefit and prolong survival

References

1. Powell J, McConkey CC, Gillison EW, Spychal RT; Continuing rising trend in oesophageal adenocarcinoma. *Int J. Cancer.* 2002 Dec 1; 102(4): 422-7.
2. Shepherd N, LR Biddlestone; CPD Bulletin Cellular Pathology. 1999 Vol.1 (2): 39-43.
3. Muller JM, Erasmi H, Stelzner M, Zieren U, Pichlmaier H; Surgical therapy of oesophageal carcinoma. *Br J Surg.* 1990 Aug; 77(8):845-57.
4. Medical Research Council Oesophageal Cancer Working Party; Surgical resection with or without preoperative chemotherapy in oesophageal cancer: a randomised controlled trial. *Lancet.* 2002 May 18;359(9319):1727-33.
5. Fiorica F, Di Bona D, Schepis F, Licata A, Shahied L, Venturi A, Falchi AM, Craxi A, Camma C; Preoperative chemoradiotherapy for oesophageal cancer: a systematic review and meta-analysis. *Gut.* 2004 Jul; 53(7):925-30
6. Herskovic A., Martz K., al-Sarraf M., Leichman L., Brindle J., Vaitkevicius V., Cooper J., Byhardt R., Davis L., Emami B. Combined chemotherapy and radiotherapy compared with radiotherapy alone in patients with cancer of the esophagus. *N Engl J Med* 1992; 326:1593-1598.
7. Tytgat GN, Bartelink H, Bernards R, Giaccone G, van Lanschot JJ, Offerhaus GJ, Peters GJ; Cancer of the esophagus and gastric cardia: recent advances. *Dis Esophagus.* 2004; 17(1):10-26.