

Squamous cell carcinoma of the oesophagus: 10 years on

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The outlook for patients with squamous cell carcinoma of the oesophagus has steadily improved over the last 10 years. Operative mortality for resection within 10% is now attainable and, in many specialist centres worldwide, it is considerably less (1-8). This is largely attributed to surgical technique and better peri-operative care (9). The improvement in operative mortality is also reflected in the overall 5-year survival rate after curative resection which is consistently of the order of 20-40% (1-6, 9-12). For early lesions ($T_1-T_3N_0$) 5-year survivals of between 40% and 80% are often quoted (1,4,12,13). These outstanding achievements, though not universal, place surgery once more firmly in the forefront in the management of oesophageal cancer. This article examines current trends and highlights the relevant contributions made in this field in the last ten years.

Regrettably, the above results have not been matched by similar advances in radiotherapy, and the survival rate of 22% reported by Pearson (14) has not been repeated. Indeed, updated studies (15) from the same institution in Edinburgh in 1982, revealed 5-year survival of only 9%. Most recent reports indicate survivals of between 5% and 10% following radical radiotherapy (16-19), but the outcome is inevitably influenced by the diverse criteria used in patient selection. There have been no large clinical trials comparing radical radiotherapy with surgery. The recent significant fall in operative mortality has, however, diminished the quest for such trials and debate is currently focused on adjuvant—intracavitary or external—radiotherapy, particularly before surgery. The aim of preoperative irradiation is that of 'down staging' or even complete tumour 'sterilisation' (4). Recent studies of preoperative radiotherapy revealed significant improvement of both the resectability rate and long-term survival (2,20-22), notably in advanced lesions.

However, two large, randomised clinical trials (11,23) of preoperative radiotherapy *versus* surgery alone failed to show any improvement in overall survival, and in other series radiotherapy was associated with a significant increase in operative mortality (11) and morbidity (21). A multicentre, prospective, randomised study in Japan (24) aimed at evaluating the position further, particularly in relation to 'sandwich' radiation techniques, failed in its objectives. Of a total of 364 patients entered in the trial only 207 completed treatment because of extensive disease or operative complications. Meaningful evaluation was therefore not possible. This highlights some of the difficulties associated with clinical trials concerning this condition.

The number of deaths from carcinoma of the oesophagus in England and Wales has risen substantially over the last 10 years, primarily in men. There were 3621 deaths (25) in 1977 compared with 4770 deaths (26) registered in 1987; a 32% increase. Early detection of oesophageal cancer is essential, but screening of those at risk can only be justified in areas where the incidence is high as was demonstrated in the Linxian and Henan provinces in China. It is clear that late presentation, which accounts for over 80% of patients, even in China (2) is now the main limiting factor in improving prognosis. Huang (13) established that nearly 90% of patients with early carcinoma had mild but genuine symptoms in the absence of overt dysphagia. A recent survey (27) of 6719 cases from all over Europe also revealed that the majority of patients (85%) with oesophageal carcinoma confined to the mucosa and submucosa were symptomatic. Once dysphagia has developed, the lesion is often well advanced and the prognosis poor, especially when lymph nodes are involved. The family doctor has much to contribute to the eventual outcome by being vigilant in those at greatest risk. Prompt outpatient endoscopy is evidently important, and staining methods with Lugol's iodine (1) or toluidine blue (13,28) further enhance detection and

accurate assessment of superficial and early squamous cell carcinomas.

Until recently, many took the view that all surgical treatment was essentially palliative. Patients can now be offered treatment in some specialist centres which aims at 'cure', or at the very least adequate palliation. There is still, however, disagreement as to the correct surgical approach. Blunt transhiatal or abdominocervical oesophagectomy modified for oesophageal carcinoma by Kirk (29) in 1974, was performed in over 100 patients by Orringer (30) with a 6% postoperative mortality rate and a 5-year survival of 17%. This technique is rapidly gaining popularity and is suitable particularly in those with early lesions and elderly patients who may not otherwise tolerate a transthoracic approach (31). The procedure cannot, however, be regarded as truly radical since it leaves behind potentially involved lymph nodes. Whether mediastinal lymphadenectomy significantly increases the survival rate is still a matter for debate, but microscopic residual tumour within the oesophageal bed is likely to invade and obstruct the conduit, and Kirk (32) recently stressed that wide bypass without resection is infinitely preferable to inadequate resection. The alternative in this situation is to irradiate any residual tumour. The lymph nodes in question are not, however, amenable to effective irradiation because of their position within the posterior mediastinum, which is the site commonly used for placement of the conduit. A further drawback to the transhiatal approach is that for lesions of the lower third of the oesophagus, control of local disease may not be possible since virtually the entire stomach is required for oesophageal replacement and adequate distal clearance cannot be guaranteed. Moreover, careful pre-operative staging is essential to exclude patients with advanced tumours in whom the procedure is not only hazardous but also inappropriate.

The results for a three-phase (McKeown) subtotal oesophagectomy with radical *en bloc* resection of lymph nodes are particularly impressive. Extensive radical surgery of this type is performed in only a few centres. In Akiyama's large series (1) of over 400 patients with squamous cell carcinoma, the overall actuarial 5-year survival was 36%, and for patients with early lesions this approached 80%. Skinner's (33) 5-year survival rate following *en bloc* resection of a less radical nature, was 20%. DeMeester *et al.* (34) reported a survival of 53% for both adeno and squamous cell carcinoma. The 30-day mortality in the above series being 1.7%, 10% and 7%, respectively. It is now well-established that lymphatic infiltration is often widespread irrespective of the level of the primary lesion (1,35). For instance, nodes associated with the right recurrent laryngeal nerve are involved in 31% of cases and those around the coeliac vessels in 30–66% (1). This forms the rationale of undertaking extensive nodal dissection with the aim of cure. This is based on the premise that clearance of metastatic lymph nodes in this condition would yield better survival according to basic oncological principles. Akiyama, a strong advocate of this procedure, reiterates the need for adjuvant therapy in patients with positive nodes in the superior

mediastinum and neck, since these regions are virtually impossible to clear completely by surgery alone (1). Indeed, a case can be made for routine irradiation to these areas in all patients. By the same token it is important to define clearly what is meant by radical radiotherapy in treating patients with the intent of cure. The entire oesophagus and its lymphatics may need to be included in the radiation field (23) for it to be considered truly radical. This necessarily entails tailoring of the target volume by using new techniques (16) in order to allow a high tumoricidal radiation dose to be more widely prescribed. In almost all recent reports (16,18,19) of radical radiotherapy given with the intent of cure, the standard longitudinal margin used was only 3–5 cm away from the tumour and no serious attempt was made at treating any of the distant draining lymphatics. The outcome in terms of survival was dismal. Any future trial involving surgery and radiotherapy should address this question carefully and clearly define treatment methods so that they are comparable.

The two-phase Lewis–Tanner operation continues to be the most popular method for resection. It is, however, only suitable for middle and lower third carcinomas. It does not permit extensive nodal dissection, nor can a subtotal oesophagectomy be achieved with the added security of a clear surgical margin. An intrathoracic anastomotic leak is also more hazardous than a similar dehiscence after anastomosis in the neck, and symptoms of reflux are common after a two-phase procedure (36). Nonetheless, Wong (3) achieved a 3.5-year survival rate of 41% in 107 patients after curative resection using this method. The 30-day mortality was 6.9% and normal swallowing function was obtained in over 80% of patients.

A single approach for carcinoma of the oesophagus is clearly not tenable, and flexibility is called for rather than adherence to strict criteria for surgery. Embarking on radical surgery in all patients is a futile exercise, since in many the poor prognosis is already determined at the outset. For instance, tumours of the endophytic or protuberant endophytic type are highly malignant and few patients survive for long (1). Similarly, radical surgery is unnecessary in patients with very early superficial lesions, in whom a lesser procedure (transhiatal oesophagectomy) is more appropriate. Each patient merits individual consideration and accurate evaluation before surgery is sensible and expedient. This should ideally include the following: endoscopy, barium swallow, endoscopic luminal ultrasound (37), abdominal and cervical ultrasound, bone scan, CT scan (38), bronchoscopy (1), laparoscopy, and lung function tests. Alone, none of these can be relied upon in determining the extent of the disease. DNA content or ploidy determination (39) and oestrogen receptor studies (40) are also important prognostic indicators. Careful selection of patients would lessen the operative risk and avoid unnecessary operation. Surgery should not, however, be denied to patients on the basis of age alone (31, 41–43), particularly since the majority of patients are aged over 60 years. Nor should tumours with a length in excess of 5 cm be considered inoperable (1,12,44).

Although most surgeons agree that surgery provides the best palliation for patients with advanced disease, there are other techniques which are firmly established in the palliation of oesophageal tumours, particularly those associated with malignant oesophagorespiratory fistulas. These include radiotherapy (45), pulsion or traction intubation (46–49) and YAG laser recanalizations (50), or a combination of these complementary techniques. Permanent relief of dysphagia, however, is only achieved in a minority of patients, and this often requiring several hospital admissions at close intervals. The procedures are not without significant morbidity (51) or mortality (4).

There have been many attempts at combined modality therapy using surgery, adjuvant chemotherapy and/or radiotherapy, but none has made any major impact on the disease even though results to date are encouraging (52–56). Until new markers emerge for early detection of oesophageal cancer, the outcome is only likely to be improved by early referral and the creation of specialist units where the concentration of numbers and resources will allow expertise to develop and trials to take place (49, 57). Most now agree that surgeons who operate frequently for this condition achieve the best results (58–61). The successes previously mentioned from leading centres further endorse this opinion, but there is also a need for a multidisciplinary approach and funds for new technology to achieve accurate staging. The importance of precise documentation cannot be overemphasised, and the recently introduced new TNM classification by the Japanese Committee for Registration of Oesophageal Carcinoma (12) provides an accurate and simple basis for comparing results between units and countries.

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