

## Difficult Decisions

# Surgery for carcinoma of the oesophagus

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### Introduction

Carcinoma of the oesophagus is a relatively uncommon malignancy in the United Kingdom, with a mean incidence of approximately 7.5 per 100,000 population. However, this translates into some 4,000 deaths per annum, and management of oesophageal cancer presents a major therapeutic challenge. The reasons for this are the magnitude of surgery involved in resection of oesophageal tumours, and the poor general condition and nutritional status of patients at the time of presentation. As a consequence of these factors, the potential for morbidity and mortality following resectional surgery is high.

Dysphagia is the commonest presentation of oesophageal cancer in the Western World, and by the time this symptom is manifest, some two-thirds of the circumference of the oesophagus is involved by tumour.<sup>1</sup> It is hardly surprising therefore that even in those tumours considered resectable, over 90% have penetrated the full thickness of the oesophageal wall and 72% have metastasized to lymph nodes.<sup>2</sup> In these circumstances, it is hardly surprising that resectability rates as high as 30% have been reported, in those patients initially considered suitable for surgery.<sup>3</sup> This review article by Earlam and Cunha-Melo did little to enhance the reputation of surgical treatment of oesophageal carcinoma by also reporting an overall operative mortality of 29% and five year survival of 4%. The clinician's dilemma of how to best manage these unfortunate patients was compounded by the increasing availability of palliative modalities such as endoscopic intubation and laser therapy at the time of publication of this rather depressing review. This review has, however, been criticized on the grounds of being historical and retrospective, and unrepresentative of the current level of achievement in specialist units. Indeed, more recent reports from such units are more optimistic, with operative mortality around 10% or less and five year survival

between 10 and 20%.<sup>4-8</sup> The principal reasons for improved outcome in such circumstances include better staging techniques, enabling more appropriate patient selection, and a greater understanding of factors influencing morbidity and mortality in relation to pre-operative preparation, operative and anaesthetic technique and postoperative management.

### Therapeutic objectives and options

The objectives of treatment in oesophageal cancer are firstly to restore the ability to swallow and avoid an unpleasant demise due to starvation and secondly to prolong useful survival, the ultimate ambition being cure of the disease. A caveat to these objectives must be that the therapeutic modality employed in their achievement should have an acceptably low mortality. Whilst many forms of therapy have had their vogue, only surgical resection has stood the test of time in producing the best quality and durability of palliation, with the bonus of cure in a proportion of patients. In a study of the quality of swallowing following resection, endoscopic intubation and surgical intubation, we found over 90% of patients were able to swallow entirely normally following resection, compared to 33% following fiberoptic endoscopic intubation and 15% after surgical intubation.<sup>9</sup> Preliminary studies suggest that endoscopic laser therapy may produce better palliation than intubation, although multiple treatments are necessary in order to achieve this.<sup>10,11</sup> It should be remembered that neither endoscopic intubation nor laser therapy is without its risks, principally associated with perforation, the reported mortality of endoscopic intubation being 11%.<sup>12</sup> Mean survival following both intubation and laser therapy is 6-8 months,<sup>11,13</sup> no five year survivors having been reported. Radiotherapy has the theoretical advantage of avoidance of operative mortality but in the series of Cederquist,<sup>14</sup> radical radiotherapy carried a mortality of 9%, emphasiz-

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ing that a radical course of radiotherapy in a debilitated patient is not without its risks. Only Pearson<sup>15</sup> has reported encouraging survival data comparable to surgery in those patients who were able to complete the course of radiotherapy. However, such results have never been repeated and even in this series, continued dysphagia was a major problem, necessitating dilatation or intubation in 50% of patients.

### Selection for surgical treatment

Careful surgical management begins with accurate selection of patients and the avoidance of inappropriate surgical intervention. Whilst staging may be academic in patients presenting with widely disseminated disease, and those whose age and general health obviously preclude consideration of aggressive therapy, it is necessary in the majority of patients in order to plan a therapeutic strategy. The relative inaccessibility of oesophageal tumours makes staging more difficult than in other sites, but incurability can be inferred from the presence of recurrent laryngeal nerve paresis, tracheo-oesophageal fistula or the presence of distant metastases in palpable lymph nodes. Metastatic disease in the lungs or liver may be apparent on chest X-ray and ultrasound. Computed tomographic (CT) scanning, which is helpful in other contexts, may detect these with increased accuracy. Invasion of contiguous structures such as the aorta and bronchial tree can be elicited by CT scanning, and extensive transmediastinal spread invariably denotes unresectability. CT scanning is, however, least accurate in the prediction of involvement of mediastinal lymph nodes. It is unable to distinguish between regional nodes involved by tumour or the seat of reactive hyperplasia. In our experience, patients with nodal metastases from squamous lesions have a 10% five year survival rate, and therefore the mere detection of enlarged lymph nodes by CT scanning is by no means in itself a contra-indication to surgery.

If tumour staging indicates likely operability, the fitness of the patient to undergo resection needs to be investigated. Age is an important factor in this context, one important series having shown operative mortality in the over 70 age group to be double that of the 40–60 group,<sup>16</sup> the presence of serious intercurrent disease is also prognostically important, and as most problems following resection are cardio-respiratory in nature, pre-existing disease in these systems has also been shown to increase operative risk. The presence of cardiac disease

requires full cardiological assessment before a decision to resect can be taken and evidence of pulmonary disease likewise requires assessment by a chest physician, as patients with more than 30% loss of functional reserve will experience problems if subjected to thoracotomy. Diabetes and chronic renal or hepatic disease also require careful assessment, as severe degrees of these militate against an aggressive surgical approach.

On the basis of these assessments of tumour staging and patient fitness, the majority of clinical situations will resolve themselves into two groups, namely where an aggressive and potentially curable surgical approach is justified, and a group in whom palliation should be the prime objective. Our unit in Lancaster treats all patients referred to hospital with a diagnosis of oesophageal carcinoma from a well defined catchment population in an area of high incidence. By applying the above staging and selection criteria, using 75 as an arbitrary upper age limit, although relying more on biological than chronological age, we have found that approximately 40% of referred patients fulfil the criteria for a radical surgical approach. In this group of patients, a 97% resectability rate of those submitted to surgery has been achieved, with an overall hospital mortality of 8.6%.<sup>17</sup> The literature shows clearly that attempts to be less selective and more aggressive result in a reduction of the resectability rate and an increase in operative mortality. In the review of Earlam and Cunha-Melo,<sup>3</sup> 58% of patients were submitted to surgery, but only 39% underwent resection. In a large series from the Mayo Clinic, 67% were subjected to surgery, but only 45% underwent resection.<sup>18</sup> Ong *et al.*<sup>19</sup> showed that as resection rate increased from 45% to 58%, mortality increased from 18% to 44%. Thus, the proportion of patients in the various series actually undergoing resection is relatively constant, and the aim of accurate staging should be to ensure that as far as possible, only those patients who are likely to have resectable tumours are submitted to surgery.

### Reducing the risks of resectional surgery

Once a decision to operate has been taken, it is important to take all necessary precautions to reduce morbidity and mortality, and this begins with pre-operative preparation. As many patients with oesophageal carcinoma are malnourished, anaemic and occasionally dehydrated, it is important to spend a few days correcting these deficiencies. Hyperalimentation, providing approximately 3,000 calories per 24 hours of appropriate compo-

sition and with vitamin supplements is usually advisable if more than 10% of body weight has been lost. The method of delivery of nutritional support depends on the degree of oesophageal obstruction present. If the patient is able to swallow liquids, a fluid diet of appropriate composition is the simplest. If a liquid diet cannot be tolerated, a fine bore feeding tube may be passed at endoscopy, or the neoplastic stricture dilated. Where enteral nutrition is not feasible, intravenous hyper-alimentation should be used. The pre-operative cardiac and respiratory assessment referred to should be combined with optimal treatment of any abnormalities identified. Chest physiotherapy should be commenced pre-operatively, and prophylactic antibiotics as well as thrombo-embolism prophylaxis should be instituted.

In regard to the operation itself, oesophago-gastrectomy with oesophago-gastric anastomosis is the safest procedure for resection of oesophageal tumours. We prefer the Ivor-Lewis technique, with a preliminary laparotomy at which the stomach and cardia are mobilized and a subsequent right thoracotomy, which gives excellent access for wide excision and conduct of the oesophago-gastric anastomosis. A cervical phase as described by McKeown<sup>20</sup> may be added for proximally situated tumours. Greater longitudinal clearance than is normally practised in cancer surgery is necessary because of the well documented propensity for both squamous and adenocarcinomata to extend sub-mucosally for a considerable distance from the apparent macroscopic tumour limits, although there is recent evidence to suggest that this is primarily associated with distal oesophageal tumours.<sup>21</sup> Oesophageal anastomoses are less likely to heal than upper portions of the alimentary tract because of the relatively poor blood supply of the oesophagus, the absence of a serous coat and high intra-luminal pressures associated with swallowing. As a result, anastomotic dehiscence is the greatest single cause of mortality in many series, and this risk appears to be increased by the presence of microscopic tumour at the anastomosed ends, emphasizing the importance of adequate clearance. However, fortunately, clinically relevant anastomotic leakage is no longer a major problem, with recently reported rates of 1.5 and 2.3%.<sup>2, 21</sup>

Various modifications in operative technique have been suggested as means of reducing morbidity and mortality associated with oesophagectomy. It has been suggested that cervical anastomoses are better than intra-thoracic anastomoses on the basis that if leakage occurs, it is of less significance than a mediastinal leak. However, a large international multi-centre study has shown that mediastinal leaks occur just as frequently from cervical anastomoses

as from intra-thoracic anastomoses, as the former frequently come to lie in the upper mediastinal after surgery.<sup>22</sup> Many would consider it of greater importance to minimize the risk of leakage occurring at all, rather than contemplating the most favourable site for this to occur.

A second technique which has received much attention latterly, on account of its potential of reducing morbidity and mortality of resection, is trans-hiatal oesophagectomy without thoracotomy. Orringer in the United States has by far the greatest experience, and in his hands, morbidity and mortality are low.<sup>23</sup> However, in the international multi-centre study previously referred to,<sup>22</sup> peri-operative mortality associated with trans-hiatal oesophagectomy was 19% compared to 13% using the Ivor-Lewis technique. The incidence of pulmonary complications was similar to that following thoracotomy, as was the requirement for temporary postoperative ventilatory support. The incidence of non-pulmonary complications was higher than after thoracotomy, with such complications as tracheo-bronchial injuries, damage to the recurrent laryngeal nerve and thoracic duct and significant haemorrhage, which are seen much less frequently during thoracotomy under direct vision. A third technique which has also attracted attention latterly is the use of stapled anastomoses with a view to reducing mortality associated with anastomotic leakage. The few trials that have been conducted have shown that stapled anastomoses only appear to reduce anastomotic leakage where the incidence of this complication from sutured anastomoses is high.<sup>25</sup> However those authors obtaining low leakage rates with sutured anastomoses have found no benefit with the use of staples, and indeed a higher incidence of anastomotic stricture was observed in both series.<sup>21, 25</sup>

Advances in post-operative management have also helped to improve results of surgery for oesophageal carcinoma. Most patients are now routinely nursed in the intensive care unit, at least for the first few days post-operatively, with careful monitoring of cardio-respiratory parameters. The decreased incidence of anastomotic leakage as a major complication of oesophageal resection has enabled attention to be focused on prevention of respiratory complications. The administration of analgesics via a thoracic epidural catheter has been a significant advance, allowing adequate pain relief and co-operation with intensive physiotherapy, without the need for systemic therapy and the risk of respiratory depression. While elective temporary ventilatory support should be available if required, careful selection, pre-operative preparation and the measures outlined above, have considerably diminished its necessity in our practice.

## Results of resectional surgery

Attention to these various factors in patient selection, pre-operative preparation, operative technique and postoperative management have all played their part in improving results following resection. A hospital mortality of 10% or less should be attainable in specialist units treating significant numbers of patients. As oesophageal carcinoma is a relatively uncommon disease, it is only centralization of care of such patients in specialist units that enables a multi-disciplinary approach between surgeons, physicians and anaesthetists, backed-up by a skilled nursing team. In these circumstances, management policies can be defined and modified based on a continuing review of results, and Matthews has clearly shown how improvement in results parallels experience in the management of this condition.<sup>26</sup> With regard to survival, none of these improvements have brought overall five year survival anywhere near those of Eastern series treating early lesions. Akiyama *et al.* have reported five year survival of 34% in early lesions treated in Japan,<sup>27</sup> and Huang has reported a five year survival rate of 96% in the treatment of superficial lesions detected by screening in a high incidence area of China.<sup>28</sup> In the Western World, where tumours are advanced at the time of presentation, the overall five year survival rate is 10–20%. However, stratification of 49 patients undergoing resection followed in excess of five years from our unit has revealed interesting results. While the overall five year survival rate was 14.3%, that for node negative cases was close to 50%, and for superficial lesions was 75%. Unfortunately, however, node negative cases comprised only 29% of those undergoing resection, and superficial lesions only 10%.<sup>29</sup> Thus, in the small proportion of tumours presenting early, survival figures are not dissimilar from Eastern series, and from equivalent stages of other tumours such as colorectal carcinoma, the problem being that in the Western World, such a small proportion of oesophageal tumours are detected early. Attempts to compensate for this by the use of adjuvant radioth-

erapy or chemotherapy to improve survival have regrettably been unsuccessful to date.<sup>30,31</sup> As survival is inversely proportional to tumour staging,<sup>32</sup> the overwhelming quest for the future must be the pursuit of means to secure earlier diagnosis of oesophageal carcinoma.

## Conclusion

Carcinoma of the oesophagus remains a formidable disease because of its late presentation in the Western World, by which time over 70% have metastasized to lymph nodes. Improved staging techniques have facilitated the selection process of the 40% of patients in whom an active surgical approach is justified, and minimize the frequency of inappropriate surgical intervention in the remainder. Advances in pre-operative preparation, operative technique and post-operative management have enabled resection to be performed in specialized centres with an operative mortality of 10% or less and the prospect of cure in 10–20% of patients, with restoration of normal swallowing in the majority. There is, as yet, no conclusive evidence that these results can be improved by performing ultra-radical resectional surgery or by using radiotherapy or chemotherapy as adjuncts to surgery.

In the current situation, a palliative procedure to improve swallowing and prevent an unpleasant demise from starvation will be the objective in approximately 60% of patients. Palliative bypass surgery has been superseded by less invasive means of palliation including fiberoptic endoscopic intubation and endoscopic laser therapy. The higher operability rate and more favourable results obtained from the Far East in the management of early lesions, together with similar results obtained in the West in the small proportion of patients who present early, emphasize the need to direct our attention towards earlier diagnosis, to which careful surveillance of high risk groups, notably those with high grade dysplasia in Barrett's oesophagus may contribute.

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