An audit of the treatment of cancer of the oesophagus

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Abstract
The treatment of cancer of the oesophagus in The General Infirmary at Leeds between the years 1975 and 1988 was reviewed. All cases with histologically proved cancer of the oesophagus were included, data being obtained from case notes, theatre operation books, endoscopy records, pathology records, and the Yorkshire Cancer Registry. Three hundred and sixteen patients were identified. Demographic details, mode of presentation, preoperative investigations, surgical management, methods of palliation, and survival data were entered into a database. The male to female ratio was 3:2 and the median age at presentation was 69 years (range 35-96). Surgical exploration was carried out in 134 of 316 patients (42%). Resection of the tumour, whether curative or palliative, was possible in 106 of 134 patients (79%). Operative (30 day) mortality was 27%. In 22 of 134 patients (16%), only intubation of the tumour was possible, while six patients (5%) had a thoracotomy or laparotomy alone. Median survival of the 106 patients after surgical resection was 292 days (range 0-142 years) and seven of them (7%) were still alive five years later. Of the remaining 182 patients (58%) who were not operated upon, 36 patients (11%) had a radical course of radiotherapy with a median survival of 175 days (range 80-453) and 146 patients (46%) either had endoscopic intubation (n=64) or received no specific treatment (n=82) with a median survival of 106 days (1-725) and 91 days (1-358) respectively. None of the 182 patients who did not have surgical treatment was alive at five years.

(Gut 1994; 35: 941-945)

The outlook for patients with cancer of the oesophagus is bleak. Although encouraging results have recently been reported from specialist centres,1-3 five year survival figures for all cases remain at about 5%.4 The poor results of surgery for cancer of the oesophagus have led many surgeons to question its value5 or to look at adjuvant treatment.6 Although good results have been reported in selected series of patients who received radical surgery or radiotherapy, there have been no randomised trials of surgery v radiotherapy.

Almost all published reports of series of patients with oesophageal cancer have concentrated on the outcome of those who have received treatment.7 The aim of this study was to determine the outcome of all patients who presented to our hospital with oesophageal cancer and to compare the results of surgical treatment with those of non-surgical treatment.

Patients and methods
Patients who presented to The General Infirmary at Leeds between 1975 and 1988 were identified retrospectively from a number of sources: (a) histopathology records, (b) endoscopy records, (c) theatre operation books, (d) Yorkshire Cancer Registry. A proforma was devised and the hospital notes were reviewed by two of the authors (PMS and TG). Information recorded included demographic details, mode of presentation, preoperative investigations and staging, risk factors, operative details, histological examination, postoperative course, and subsequent adjuvant or palliative treatment.

Preoperative investigations used to stage the disease included barium swallow, flexible oesophagoscopy and biopsy, bronchoscopy, chest radiography, abdominal ultrasonography, and computed tomography of chest and abdomen. Metastatic disease was said to be present if a tumour was identified in the liver, lung, distant lymph nodes or at other sites distant from the oesophagus and regional lymph nodes.

Patients were excluded from the study if the tumour originated in the hypopharynx or stomach, if the hospital records were unobtainable or if the eventual outcome was unknown. A total of 28 patients were excluded.

STATISTICAL ANALYSIS
All grouped data are expressed as median (interquartile range). Intergroup comparisons were made by means of the Mann-Whitney U test and χ² test.8 Life tables were drawn up by the Kaplan-Meier method and differences in survival assessed by the log rank test.9

Results
Adequate data were obtained in 316 patients (192 male: 124 female; median age 69 years (range 35-96). Forty eight of the 316 tumours (15-2%) were located in the upper third, 148 (46-8%) in the middle third, and 120 (38%) in the lower third of the oesophagus, as defined by the revised UICC TNM classification of 1987.10

HISTOLOGICAL TYPE
Histological type was squamous in 174 (55-1%), adenocarcinoma in 131 (41-5%), malignant melanoma in three (0-9%), mixed
TABLE I Operative procedures used in 106 patients who had oesophagectomy

<table>
<thead>
<tr>
<th>Operative procedure</th>
<th>Number of patients (n=106)</th>
<th>Operative mortality (30 day) n (%)</th>
</tr>
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<tbody>
<tr>
<td>Left thoracalabdominal</td>
<td>28 (26-4)</td>
<td>6 (21-4)</td>
</tr>
<tr>
<td>Laparotomy - R thoracotomy, thoracic anastomosis ('Ivor-lewis')</td>
<td>45 (42-5)</td>
<td>12 (26-7)</td>
</tr>
<tr>
<td>Laparotomy - R thoracotomy, cervical anastomosis ('Three-stage')</td>
<td>15 (14-2)</td>
<td>5 (33-3)</td>
</tr>
<tr>
<td>Transhiatal oesophagectomy (Orringer procedure)</td>
<td>15 (13-2)</td>
<td>5 (35-7)</td>
</tr>
<tr>
<td>Oesophagectomy and pharyngolaryngectomy</td>
<td>4 (3-8)</td>
<td>1 (25)</td>
</tr>
<tr>
<td>Anastomosis stapled</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Left thoracotomy</td>
<td>24</td>
<td></td>
</tr>
<tr>
<td>Oesophagectomy and cervical anastomosis</td>
<td>28</td>
<td></td>
</tr>
</tbody>
</table>

Complication       | Number of patients (n=106) | Operative mortality (30 day) n (%) |
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>Anastomotic leak*</td>
<td>21 (21)</td>
<td></td>
</tr>
<tr>
<td>Septicaemia</td>
<td>18 (17)</td>
<td></td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>23 (21-7)</td>
<td></td>
</tr>
<tr>
<td>Respiratory</td>
<td>42 (39-6)</td>
<td></td>
</tr>
<tr>
<td>Gastric retention</td>
<td>12 (11-3)</td>
<td></td>
</tr>
<tr>
<td>Thromboembolic</td>
<td>5 (4-7)</td>
<td></td>
</tr>
<tr>
<td>Chylothorax</td>
<td>4 (3-8)</td>
<td></td>
</tr>
<tr>
<td>Vocal cord palsy</td>
<td>3 (2-8)</td>
<td></td>
</tr>
<tr>
<td>Haemorrhage</td>
<td>10 (9-4)</td>
<td></td>
</tr>
<tr>
<td>Anastomotic stricture</td>
<td>27 (25-5)</td>
<td></td>
</tr>
</tbody>
</table>

*Radiologically confirmed and clinically significant.

was necessary in 14 patients (13%): for haemorrhage (7), anastomotic dehiscence (6), and chylothorax (1). No statistically significant differences in anastomotic leakage were apparent between hand sewn and stapled anastomoses (12 of 78 hand sewn (15%) vs 9 of 28 stapled (32%) \( \chi^2=2.66, 1 \text{ df}, \text{NS} \) but anastomotic stricture, which required dilatation on at least one occasion occurred more often after stapled anastomosis (12 of 28 stapled (43%) vs 15 of 78 (19%) \( \chi^2=4.87, 1 \text{ df}, \text{p}<0.05 \)).

Gastric retention was more common among patients with an intact pylorus (8 of 43 (19%) than in patients who had had pyloroplasty or pyloromyotomy (1 of 63 (2%) \( \chi^2=7.46, 1 \text{ df}, \text{p}<0.01 \)).

**Surgical treatment**

Surgical exploration was carried out in 134 of 316 patients (42%). Resection of the tumour was possible in 106 of 134 patients (79%). Thus, only 34% of the 316 patients had oesophageal resection. Splenectomy was carried out at the time of oesophageal resection in 14 of 106 patients (13-2%). Twenty two patients (7%) had oesophageal intubation at the time of surgical exploration and six patients (2%) had thoracotomy or laparotomy alone because of the extent of tumour or metastatic disease. Table I shows the operative procedures used.

Mortality

Twenty nine patients (27%) died within 30 days of oesophagectomy and 31 (29%) within three months of operation. No evidence was found that anastomosis in the neck (mortality=35%) was any safer than anastomosis in the chest (mortality=25%) (Table I).

Morbidity

Postoperative complications occurred in 78 of 106 patients (74%) (Table II). Reoperation

**Non-surgical treatment**

Thirty six patients (11%) received radical radiotherapy, 64 (20%) had endoscopic intubation, and 82 (26%) received no specific treatment.

**Radiotherapy**

The course of radical radiotherapy (55 Gy in 20 fractions with intensity correction given over four weeks) was completed in 29 of 36 patients (81%). Of these 36 patients, the tumour was situated in the upper third in 27 patients (all squamous cell carcinoma) and in the middle third in nine patients (six squamous cell carcinoma, six adenocarcinoma). Median length of survival from diagnosis in patients who completed the course of radical radiotherapy was 175 days (range 80–453).

Preoperative radiotherapy was used in one patient but, in that patient, endoscopic perforation of the oesophagus occurred for which emergency oesophagectomy was carried out.

**Adenocarcinoma cases**

Adenocarcinoma was found in nine (seven patients, 12-2%) of the 71 adenocarcinoma cases. Of these patients, 77% were male and the median age at diagnosis was 62 years (range 42–76 years). Median survival was 32 months (range 6–104 months).

**Clinical features**

Dysphagia was the most common mode of presentation: 267 of 316 patients complained of this symptom (85%). Symptoms of gastro-oesophageal reflux were reported by 122 of 316 patients (39%), epigastric or retrosternal pain by 108 patients (34%), weight loss by 144 patients (46%), and symptoms of anaemia by 49 patients (16%).

**Survival**

Forty two of 106 patients (40%) who had surgical resection survived for one year, 21 patients (20%) survived for two years, and seven patients (7%) survived for more than five years and were free of recurrence. In the group of 77 patients who survived for more than one month after operation, the median duration of survival from diagnosis was 1-06 years (IQ range 0-67–2-10 years). Analysis of survival rate according to histological type showed no significant difference (squamous cell carcinoma 1-0-10 years (0-71–2-12), adenocarcinoma 1-02 years (0-58–2-04)).
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Intubation or no treatment
No fewer than 146 of 316 patients (46%) either had no specific treatment (n=82) or had endoscopic intubation (n=64). Although these patients were significantly older than patients who had an operation or received radiotherapy (p<0.01), a large proportion of them (94 patients, 64.4%) seemed to have had no surgical input into their management despite the apparent absence both of metastatic disease and of contraindications to surgery.

Of the 64 patients who had endoscopic intubation, six (9%) died in hospital, two after perforation of the oesophagus, three with aspiration pneumonia, and one from carcinomatosis. Blockage of the tube with food occurred in 12 patients (19%) and overgrowth of the tube with tumour occurred in 11 patients (17.2%). The median duration of survival among patients who had endoscopic intubation was 106 days (1–725). The median survival of patients who received no specific treatment was 91 days (1–358).

Metastatic disease was present in 15 of 134 patients who had surgical exploration (11%), five of 36 patients who received radiotherapy (14%), 19 of 82 patients who had endoscopic intubation (23%), 11 of 64 patients who received no specific treatment (17%), and overall in 50 of 316 patients (16%).

The median length of survival for all patients from time of histological diagnosis was 77 days (range 1 day–14·2 years). Survival was significantly longer in patients who had had surgical treatment than in patients who had received radiotherapy (log rank $\chi^2$, p<0.01), than in those who were treated by intubation (p<0.005) and than in patients who received no specific treatment (p<0.001).

The Figure shows the influence of primary treatment on survival.

Discussion
A nihilistic tendency still pervades the treatment of cancer of the oesophagus. Much of this attitude stems from a review of the surgical treatment of about 84,000 patients who had received treatment between 1953 and 1979. It suggested that of every 100 patients with oesophageal cancer, only 39 would have the tumour resected, of whom 26 would leave hospital and only four would survive for five years. Much has changed, however, since that era. Surgical and anaesthetic techniques have improved, preoperative staging has permitted more precise selection of patients for operation, and more radical surgical procedures with en bloc resection and extensive lymphadenectomy have been developed, which are associated with improved local control of disease and better chance of cure. Nevertheless, despite these advances, the results of this study, which encompasses the years 1975–88, show no improvement on the data summarised by Earlam and Cunho-Melo. Thus, the prevailing pessimism seems amply justified.

There are a number of criticisms of the study. Retrospective reviews of case notes inevitably suffer from inadequate collection or recording of appropriate data at the time of presentation, with consequent gaps in the data. Statistical comparisons between various treatment groups may not be scientifically valid as, older, frailer patients and those with more advanced tumours are more likely to be treated by non-surgical means. Analysis of subgroups within a study is notorious for leading to bias, while comparisons of groups may prove to be ‘not statistically significant’ simply because the study does not have the power to show such differences, even if they did exist. Accurate TNM staging of the tumours was not possible and identification of the patients who had received potentially curative rather than merely palliative resection was also not possible because of inadequate information recorded in the case notes. Hence, the results after strictly ‘curative’ resections would have been better than the overall results reported here. For example, reports of consecutive series of patients suggest that curative resection is carried out in about 60% of cases. If this was the case in our series then the five year survival after curative resection would be about 7/64 (11%).

Changes in surgical technique that occurred in the period of the study were reflected in the operative procedures used. The latter part of the study included patients who had transhiatal blunt oesophagectomy and patients in whom somewhat more extensive lymphadenectomies were carried out than had been the custom in the 1970s. None the less, few, if
any, patients received truly radical thoracic lymphadenectomy as described by Skinner and Lerut. Critics of the transhiatal Orringer blunt oesophagectomy have suggested that it is an inadequate cancer operation, which should be reserved for patients who have impaired respiratory function. Its proponents, however, argue that operative mortality and longterm survival rates are similar or even better than after standard techniques of resection. The philosophy behind the approach is that palliation of pain and dysphagia is the main goal, while cure, if it occurs, is by accident. Advocates of en bloc resection with extensive lymphadenectomy, on the other hand, argue that improved survival can only be achieved by meticulous wide excision of the tumour and its lymphatic field as is commonplace in the treatment of colorectal cancer and is increasingly being used in the treatment of gastric cancer (R2/3 resection). The numbers in this study do not permit adequate comparison of small subgroups, but there has certainly been a noticeable trend towards the use of en bloc resection in carefully selected patients.

The incidence of postoperative complications in this series was 74%. This may have been related in part to the large number of surgeons who carried out the resections. A review of 46,692 patients reported an overall incidence of postoperative complications in 36%. Many authors, however, report only the more serious complications, or the complications that are a specific consequence of a particular operative technique. Gastric stasis was more likely to occur if the pylorus was left intact. Similar findings have been shown previously in randomised studies. Vagal denervation of the pylorus and antrum results in decreased myoelectric activity and the movement of gastric contents may lead to vomiting and possible aspiration and death from bronchopneumonia. It would seem, therefore, that pyloroplasty or pyloromyotomy should be carried out routinely.

The incidence of benign anastomotic stricture was similar to that reported by others but the incidence of anastomotic leakage was excessive. Development of strictures is inversely related to the size of the stapling device but this is limited by the diameter of the oesophageal lumen. Failure to achieve mucosa to mucosa apposition may result in fibrosis and the mucosal rent may prevent natural dilatation of the oesophagus in response to boluses of food. Anastomotic leakage may be the result of a number of factors but vascular insufficiency, anastomotic tension, and poor surgical technique are the most likely causes. The incidence of leakage was similar for anastomoses in the neck and in the chest and we did not find that leakage from cervical anastomoses carried a lower mortality than leakage from anastomoses in the chest. The cervical anastomoses in our series were confined to the transhiatal and McKeown techniques, however, and it may be that other techniques such as the left sided, two part approach are associated with improved morbidity. To reduce postoperative morbidity, at least on the basis of our results, we would suggest using hand sewn anastomosis, not leaving the pylorus intact, concentrating cases into the hands of a few experienced surgeons, and perhaps avoiding transhiatal and three stage procedures unless absolutely necessary.

The proportion of patients in whom the histological diagnosis was adenocarcinoma was higher than we had anticipated but seems to be in line with recent series from the United Kingdom. Although it is difficult to be certain of the precise site of origin of a tumour, we took great care to exclude cases in which the gastric cardia seemed to be the primary site. A number of reports have suggested that the incidence of adenocarcinoma of the oesophagus has increased, perhaps as a result of greater cigarette consumption in women particularly in the lower socioeconomic classes of our ageing society. Gastro-oesophageal reflux of long duration was a common symptom and this raises the possibility that some of the tumours may have arisen in oesophageal mucosa of Barrett’s type. The median duration of survival in patients treated with radiotherapy was significantly less than in patients who had surgical resection. The two groups of patients are not comparable, however, because the patients given radiotherapy tended to have a poorer prognosis, a greater number of risk factors, and were considered less fit than those in whom resection was carried out. Comparison of palliation between the two groups was also not possible because of the retrospective nature of the study and the absence of careful assessment of quality of life in such palliation at the time of follow up. Similarly, it was not possible to assess the comparative success of palliation with either surgical or endoscopic intubation.

Perhaps the finding of most concern in this study was the apparent undertreatment of a large proportion of patients. Almost 30% of patients did not seem to have been referred for a surgical opinion despite the fact that many seemed to have been good candidates for surgical intervention. The incidence of resection in this series compares poorly with resectability rates from specialised centres. Admittedly, retrospective analysis of case notes can give a misleading impression and makes it difficult to define accurately selection criteria for a specific treatment, but the paucity of risk factors recorded and the absence of investigations to stage the disease suggest that some of these patients were denied potentially curative resection.

The prognosis for patients with cancer of the oesophagus remains poor. Instead of a large number of surgeons each operating on a few patients and achieving death rates of about 30% at three months after operation, as in this and other studies, a few surgeons each of whom operates on a comparatively large number of cases are needed. Also needed are a few expert anaesthetists working with one or two physiotherapists and an experienced nursing and intensive care team who have a
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positive outlook and are dedicated to the survival of the patient. This team approach can be extended to the use of multimodality treatment with, in appropriate cases, adjuvant radiotherapy, chemotherapy, and perhaps immunomodulation. While the precise role of these methods of treatment has yet to be defined, effort needs to be directed at achieving earlier diagnosis by means of endoscopy – repeated if necessary, increasing surgical resection rates, more widespread use of en bloc resection in patients who undergo potentially curative resection, reducing postoperative mortality and morbidity, and substantially enhancing palliation of this grim disease.

This paper was presented to the Association of Surgeons of Great Britain and Ireland, April 1993.