# OESOPHAGOGASTRIC CARCINOMA: AN EIGHT-YEAR EXPERIENCE IN A DISTRICT GENERAL HOSPITAL

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In this era of cancer guidelines it is important that achievable targets are not based on the selected patient population seen at tertiary referral centres. Guidelines must reflect the entire cancer population both in terms of the stage of the disease and the physiological status of patients. The Royal Lancaster Infirmary (RLI) serves a population of 220,000. Since January 1996 all patients with oesophageal or gastric cancer have received 'curative' and palliative surgical or endoscopic therapy under one surgeon (TL). This has facilitated accurate prospective audit of these cancers in our population.

This study includes two groups: a retrospective audit of patients undergoing resections for oesophagogastric cancer between 1990 and 1995 (N = 76) by one general surgeon with an interest in upper gastrointestinal surgery, and a prospective audit of all patients diagnosed with oesophagogastric cancer from 1st January 1996 to the end of 1997 (N = 138).

The overall hospital mortality following surgical resection was 13% and the overall leak rate was 4%. Crude five-year survival in the retrospective group was 20%. In the prospective group the incidence of oesophagogastric cancer was 31.4 per 100,000 population per year. The overall resection rate was 39% and was higher for gastric cancer (57%) compared to oesophageal cancer (18%) or cancers around the gastroesophageal junction (29%). Despite the availability of direct access endoscopy with short waiting times, most patients undergoing resection had advanced disease – either stage III (54%) or stage IV (19%).

## INTRODUCTION

Cancers of the oesophagus and stomach are diseases for which only surgery offers a real chance of cure at present, and an aggressive approach has been adopted by most surgeons managing these patients. This surgery is technically demanding and is a significant physiological insult for the patient to overcome. Operative results and long-term outcomes vary significantly in published series, most of which come from academic institutions which deal with a referred population often already superselected both in terms of the stage of disease and the physiological status of the patient. It does not necessarily represent the true picture of the disease within an entire community. For example, quoted resection rates for patients with oesophageal carcinoma referred to an academic centre will obviously be higher than a resection rate calculated using all patients in the community diagnosed with the disease as the denominator.

As oesophageal and gastric tumours are usually treated by the same surgeon, and with a significant increase in the number of adenocarcinomas presenting at the junction between the stomach and oesophagus[1,2], it is becoming more appropriate to evaluate results inclusive of oesophageal, gastric and oesophagogastric carcinomas. Furthermore, tumours in these three zones are treated primarily by surgery and are subject to a similar debate about how aggressive the lymph node dissection should be.

This study evaluates our results in treating patients with oesophagogastric carcinoma over an eight-year period within a relatively isolated community of 220,000 people. Patients with a diagnosis of oesophagogastric cancer, with only one exception, underwent surgery or palliative care at the RLI during this period.

## METHODS

The study is divided into two groups:

1 a retrospective audit of patients who underwent resection for oesophagogastric carcinoma between 1990 and the end of 1995 by one of the five general surgeons.

2 a prospective two-year audit of all patients with an oesophagogastric carcinoma in the community served by the Royal Lancaster Infirmary. The validity of the prospective data collection was checked by cross-reference to cancer and histopathology records. All but one patient with oesophagogastric cancer had their surgery or endoscopic palliation under one of the authors (TL) during the study period, which facilitated accurate prospective data collection.

Both groups underwent assessment of tumour pathology, staging, hospital mortality and leak rates. In the retrospective group we evaluated longterm outcome. In the prospective group we evaluated cancer incidence, resection rates and how patients were palliated.

Patients were grouped in zones according to the site of the tumour

- oesophageal zone – upper and middle third of the oesophagus
- oesophagogastric zone – lower third of the oesophagus, oesophagogastric junction and cardia
- gastric zone – body and antrum.

Preoperative staging usually involved chest X-ray and CT scanning. Endoscopic ultrasonography and staging laparoscopy were not employed. Oesophageal and oesophagogastric carcinomas were usually resected by a two stage Ivor Lewis-type oesophagectomy. Gastrectomy, either distal or total, was essentially a D1 resection but included lesser and greater omentectomy and all nodes removed by taking the left gastric artery flush with the coeliac axis (D1 plus group 7 nodes).

The TNM classification was used to stage the patients pathologically[3]. Statistical analysis was with the Chi-squared test.

## RESULTS

The retrospective group comprised those treated by resection only and included 76 patients for analysis. The prospective group, which included all patients irrespective of treatment offered, numbered 138 patients. The demographics of the two study populations stratified into the three zones (oesophageal, oesophagogastric and gastric) are shown in Table 1.

| | | RETROSPECTIVE Resection Only | | | | |
|---|---|---|---|---|---|---|
| **Zone** | | *N* | *Age* | | *M:F* | |
| **Oesophageal** | | 5 | 67 (46-75) | | 2:3 | |
| **Oesoph-gastric** | | 34 | 68 (26-75) | | 27:7 | |
| **Gastric** | | 37 | 71 (54-83) | | 22:15 | |
| **Total** | | 76 | 70 (26-83) | | 51:25 | |
| | | | PROSPECTIVE | | | |
| | | **Resection** | | | **Palliation** | |
| **Zone** | *N* | *Age* | *M:F* | *N* | *Age* | *M:F* |
| **Oesophageal** | 4 | 70 (62-73) | 3:1 | 18 | 77 (64-95) | 7:11 |
| **Oesoph-gastric** | 17 | 60 (38-72) | 14:3 | 41 | 78 (43-91) | 26:15 |
| **Gastric** | 33 | 71 (23-86) | 14:19 | 25 | 74 (38-95) | 12:13 |
| **Total** | 54 | 69 (23-86) | 31:23 | 84 | 74 (38-95) | 45:39 |

*Table 1 Demographic details of the two study populations. Ages are given as medians (range)*

Most of the tumours were adenocarcinomas as expected: 90% in the retrospective group and 81% in the prospective group. In the oesophageal zone, however, 44% of the tumours were squamous in cell type (Table 2).

| **Zone** | N | Adeno | Squamous | Lymphoma | Other |
|---|---|---|---|---|---|
| **Oesophageal** | 27 | 13 | 12 | | 2 |
| **Oesoph-gastric** | 92 | 82 | 6 | | 4 |
| **Gastric** | 95 | 86 | | 8 | 1 |
| **Total** | 21 | 181 (84%) | 18 (8%) | 8 (4%) | 7 (4%) |

*Table 2 Pathological subtypes in the two groups combined*

*Staging:* In the retrospective resected group only 9% were stage I, 37% were stage II, 38% were stage III and 16% were stage IV. When evaluating stage of disease according to the three zones, an increase in stage IV (palliative) resections was noted in the gastric zone (33%), compared to 0% in the oesophageal group and 12% in the oesophagogastric group (Figure 1A). In the prospective series accurate staging was performed in those patients who underwent resection (N = 54). Overall, 6% were stage I, 22% were stage II, 54% were stage III and 19% were stage IV disease. A breakdown of the stage of disease in each of the three zones is shown in Figure 1B.

*Hospital mortality (Table 3)* In all instances a true hospital mortality is quoted rather than a 30-day mortality. This includes deaths following palliative resections and late deaths in patients transferred to the medical wards or hospice but never getting home. In the retrospective series of 76 patients there was an overall hospital mortality of 13.2% (10/76). Four of these deaths occurred late in patients undergoing palliative resections. In the prospective group (N = 54) the overall hospital mortality was 13% (7/54). This includes one late death in a patient undergoing palliative resection.

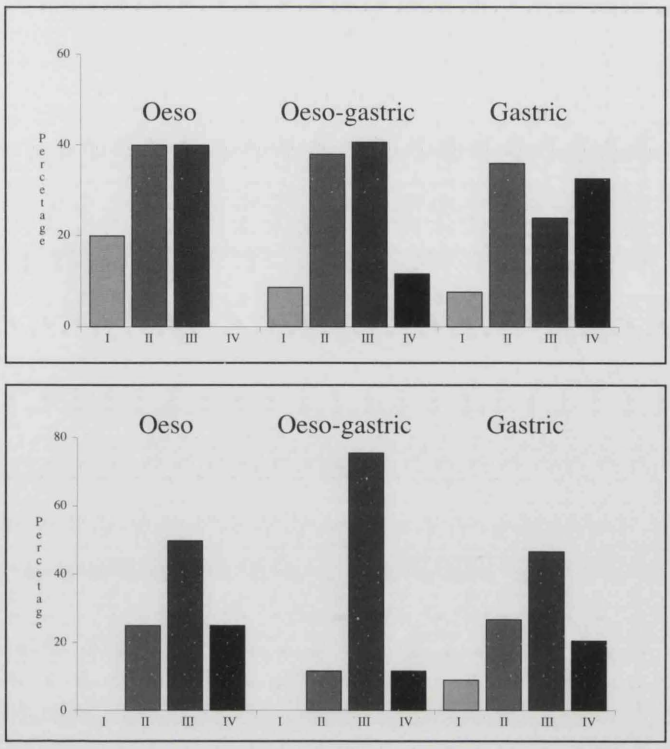





*Fig 1 – Stage of disease in each of the three anatomical zones in resected patients. A: retrospective data, n = 76; B: prospective data, n = 54*

| RETROSPECTIVE | PROSPECTIVE | COMBINED |
|---|---|---|
| **Oesophageal** | | |
| 0/5 0% | 1/4 25% Respiratory – 1 | 1/9 11% |
| **Oesophagogastric** | | |
| 6/34 17.6% | 3/17 18% | 9/51 18% |
| Leak – 2 | Respiratory – 2 | |
| Respiratory – 1 | Duodenal Stump – 1 | |
| Myocardial Infarction –1 | | |
| Palliative –2 | | |
| **Gastric** | | |
| 4/37 10.8% | 3/33 9% | 7/70 10% |
| Leak – 1 | Leak – 1 | |
| Respiratory –1 | Respiratory –1 | |
| Palliative – 2 | Palliative – 1 | **TOTAL 17/130 13%** |

*Table 3 Hospital mortality in both the retrospective and prospective series of patients who underwent resections*

The mortality following resection for both series combined was thus 13% (17/133).

*Leak rates* In the retrospective group there were two oesophagogastric anastomotic leaks following oesophagectomy that resulted in mortalities. One further patient had a leak but was salvaged and eventually reconstructed with a colon interposition. There was one patient who had an anastomotic leak following total gastrectomy which was fatal. In the prospective group there was one anastomotic leak following a total gastrectomy that lead to death. When combining the prospective and retrospective groups (oesophagectomy, n = 60; gastrectomy, n = 70) the overall anastomotic leak rate was 4% (5/130). There was also one patient who died as a result of a duodenal stump dehiscence following a prolonged ileus.

*Longterm outcome* Using data from the retrospective group, overall median survival was 16 months with 19.7% of patients alive at the end of the six year audit (oesophageal, 20%; oesophagogastric, 14.7%; gastric, 24.3%) (Figure 2A). There were obvious differences in survival by stage when plotting the Kaplan-Meier graphs (Figure 2B) but no differences in survival by zone.

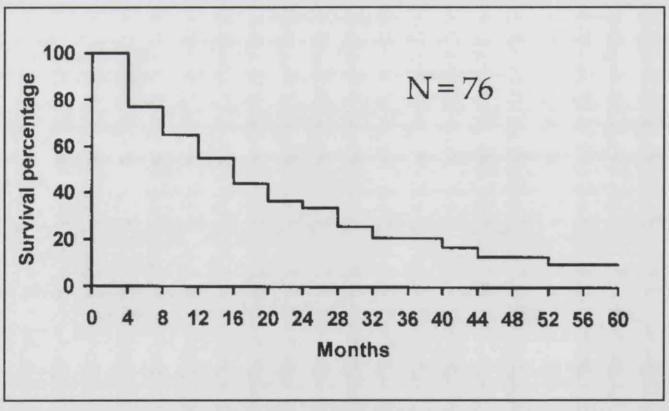


*Figure 2A Overall survival following resection. The median survival was 16 months.*

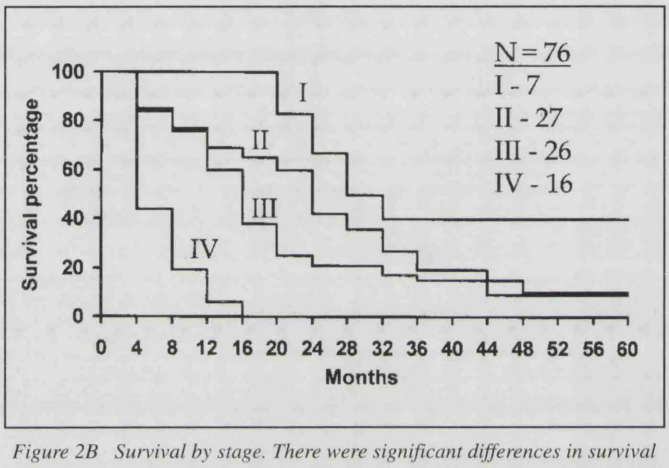


*Figure 2B Survival by stage. There were significant differences in survival noted dependant on the stage of the disease.*

*Palliation versus resection* The prospective group of 138 patients included all patients with oesophageal or gastric carcinoma known to the RLI, which serves a population of 220,000 people. The annual incidence of oesophagogastric cancer in our population was thus 31.4 per 100,000. Only one of these patients was referred outside our hospital for treatment. Overall 39% (54/138) of patients were respectable and 61% (84/138) of patients formed the palliation group. By zone, 18% (4/22) of patients with oesophageal carcinoma, 29% (17/58) of patients with oesophagogastric carcinoma and 57% (33/58) of patients with gastric carcinoma were resected.

Overall 51% of patients were palliated by placement of a plastic oesophageal prosthesis. In 27% of patients, mainly those with gastric carcinoma, no form of palliation was possible (Table 4).

*Retrospective versus prospective* Age and pathology was similar in both resection groups (retrospective, n = 76; prospective n = 54). There was a definite increase in the number of gastrectomies performed in the prospective period (retrospective 37/76, 48.7%; prospective 33/54, 61%; $p<0.01$). There was also an increase in the proportion of stage III disease offered resection (retrospective, 25/76, 33%; prospective 29/54,54%; $p<0.01$).

| | N | Palliation |
|---|---|---|
| **Oesophageal** | 18 | Radiotherapy/Alcohol injection – 5 |
| | | Oesophageal prosthesis – 11 |
| | | Nil – 2 |
| **Oesophagogastric** | 41 | Oesophageal prosthesis – 32 |
| | | Radiotherapy – 2 |
| | | Chemotheraphy – 1 |
| | | Nil – 6 |
| **Gastric** | 25 | Nil – 15 |
| | | Bypass surgery – 5 |
| | | Chemotherapy – 2 |
| | | Laparotomy only – 3 |

*Table 4 Methods of palliation*

## DISCUSSION

This series looks at a demographically well-defined population of patients with oesophagogastric carcinoma. Since 1996 all carcinomas for resection have come to the RLI and are managed by the senior author (TL), who also performs all oesophageal stenting, dilations and alcohol injections. Thus an accurate assessment of the number of patients with these cancers is possible. The prospective database still requires periodic validation by cross-reference to cancer and histopathology records to ensure completeness. This includes carcinomas diagnosed for the first time at *post mortem* examination. Our population incidence of 31.4 per 100,000 per year closely matches national figures for the incidence of oesophageal and gastric cancer combined[4] – supportive evidence that we are picking up all patients with these diagnoses in our population. Thus the prospective data in this series accurately depicts oesophageal and gastric carcinoma in a community rather than the selected population of patients referred to an academic institution for possible resection.

It is recognised that the pattern of cancers in the stomach and oesophagus has changed dramatically over the last twenty years. The overall incidence of gastric cancer has fallen slightly but there has been a marked change in the distribution of cancer within the stomach with a reduction in antral cancer nearly matched by an increase in cancer of the cardia and gastroesophageal junction[2,5,6]. In the oesophagus there has been a marked increase in adenocarcinoma of the lower oesophagus so that squamous carcinoma is no longer the dominant oesophageal malignancy[1] and many standard pathology textbooks need to be rewritten. Overall there has been a significant increase in the proportion of adenocarcinoma around the gastroesophageal junction (cancers of the cardia, gastroesophageal junction and lower one-third oesophagus). Although attempts have been made to separate these tumours anatomically, in practice it is increasingly accepted that these 'junctional' tumours should be grouped together.

Oesophageal and gastric cancers can then be subdivided into three zones: upper two-thirds of oesophagus (where squamous carcinoma is still common), oesophagogastric cancers from the 'junctional' area and gastric cancers of the body/antrum. We have used this three-zone analysis in this paper and we suspect that it will be used increasingly for these cancers.

In our series two cavity Ivor Lewis-type procedure was the usual operation for oesophageal and 'junctional' tumours although three stage and transhiatal procedures with cervical anastomoses were employed on occasion. Our D1 gastrectomy includes lesser and greater omentectomy and removal of all the lymph nodes along the left gastric artery right down to its origin from the coeliac axis. The more radical D2 gastrectomy has been reported to have better longterm survival, particularly in the Japanese literature[7,8]. But in two recently-published prospective randomised trials comparing D1 and D2 gastrectomy in European patients, the increased hospital mortality associated with D2 resection was prohibitive and is expected to prevent any longterm benefit[9,10]. There were weaknesses in both these trials but unless the case for D2 gastrectomy is proven in further well-run multicentre prospective randomised trials we intend to continue with our present surgical approach to these cancers.

It is important to recognise that most distinct general hospitals (DGHs) around the UK have responded to the Calman report into cancer services[11] by increasing specialisation among the general surgeons. Often one or two surgeons with a particular interest in upper gastrointestinal surgery have taken on all the oesophageal and gastric cancers. This is well-demonstrated in our hospital where until January 1996 all the general surgeons performed gastrectomy for cancer while most of the oesophageal and 'junctional' cancers were treated by two surgeons with a special interest in the foregut. Since January 1996 increased specialisation has resulted in all oesophageal and gastric cancer surgery coming under one surgeon. It is important that this shift in work pattern is acknowledged by tertiary referral centres who must stop using historical data from the pre-Calman era when comparing their results with those of the DGHs. It is increasingly accepted that results were poor when all general surgeons performed these operations[2]. It is also important to avoid direct comparison of the results in selected tertiary referral populations with those achieved at the "coal face" in unselected populations. Corrections must be made for age, comorbidity and disease stage.

Oesophagogastric cancer still presents late. In our data only 9% of patients in the retrospective series and 6% of patients in the prospective series had stage I disease. Other series – particularly in the Japanese literature – report an increased incidence of early carcinoma[12,13]. This may be due to their screening programme and meticulous technique whilst performing endoscopy. It may also be related to their patient population and different histological interpretation of early cancer. In our prospective series 54% of all patients had stage III disease. In the oesophagogastric zone this was up to 76%. Late presentation remains the principle reason for the poor results from oesophagogastric cancer in the western world and direct access endoscopy seems to have had little impact on this.

Overall hospital mortality in this series for patients undergoing resection for oesophagogastric cancer was 13%. Bonavina *et al* reported on 4663 oesophagectomies and had a 12.9% mortality[14]. Data from Skinner *et al* report a mortality of 3% in a carefully-selected population group[15]. Our mortality and leak rates for gastrectomy are similar to many reported series[9,10,16]. Bonekamp *et al* in 380 patients undergoing D1 gastrectomy had 4% mortality and 4% leak rate[10]. Cushieri in 200 patients undergoing D1 gastrectomy reported a 6.5% mortality and 5.5% leak rate[9]. Our clinical leak rate of 4% is low compared to other series (7-11%)[14,15,17,18,19]. The higher mortality is mainly due to respiratory causes and to reporting of true hospital mortality, including late deaths in patients with advanced disease who were transferred to the medical wards or hospice. Better postoperative pain relief with thoracic epidural analgesia has now been introduced, which, with more aggressive pulmonary toilet, may help to reduce mortality. Other contributing factors include a population of elderly patients with other diseases and advanced tumours, and an aggressive approach in offering surgery. Many series still report 30-day mortality which is no longer appropriate, a view supported by Cushieri *et al*[9]. All hospital deaths must be reported.

The results we have presented reflect what is now happening in many DGHs in the post-Calman era. Despite an aggressive 'intention to resect' approach, only 39% of patients presenting with oesophagogastric cancer are resected. This figure is higher for gastric cancer (57%), where palliative resections are more often undertaken than in oesophageal cancer. In the majority of patients, advanced age and poor general condition prevent resection rather than advanced stage of the disease. Resection rates of up to 40% for oesophageal cancer and 70% for gastric cancer were being advocated as targets during discussion at a recent meeting of the new Association of Upper Gastrointestinal Surgeons of Great Britain and Ireland, but these figures are unrealistic in the context of the entire population of patients and generally refer to the selected group of patients seen at tertiary referral centres.

The overall five-year survival for oesophagogastric cancer remains abysmal. In our retrospective series only 20% of patients were alive at five years following resection. If this is extrapolated to the prospective series in which only 39% of patients are undergoing resection of their cancers then the cure rate for oesophagogastric cancer is only 8%. Series quoting overall higher survival figures are often highly selected, excluding patients with stage IV and even stage III disease[15,18] and ignoring the majority of patients who are unsuitable for resection. The Norwegian multicentre study demonstrated an overall survival for gastric carcinoma of 40%, but 40% of the patients had stage I disease[13]. The jury is still out as far as improving results by more aggressive surgery in western patents is concerned. Effective adjuvant and neoadjuvant therapy is desperately needed and at last worthwhile multicentre trials such as the Medical Research Council (MRC) trials are underway. It is pleasing to note that the MRC gastric and oesophageal cancer sections have recently merged, reflecting the new concept of oesophagogastric cancer as an entity rather than trying to preserve the artificial separation of the two organs as far as cancer is concerned.

We hope that this paper will help to document what is happening in DGHs in the post-Calman era and ensure that we do not try to compare apples with oranges – especially when it comes to writing national guidelines for the management of these cancers.

***Acknowledgments***

*The authors would like to express their thanks to their physician gastroenterologist colleagues, Drs Anthony Adamson and Colin Brown, for their excellent support and teamwork as well as Drs Miles Rucklidge and Sue Harding for anaesthetising this high-risk group of patients with such skill. We would also like to thank Dr Margaret Stewart for regular histology feedback and Drs Margaret Ellam and Caroline Watt and the CancerCare services for regular patient feedback facilitating prospective audit and for general support and treatment of these patients with oesophagogastric cancer.*

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