Original Article

Gastro-Oesophagectomy With Two Field Lymphadenectomy- An Optimal Treatment For Resectible Carcinoma Of The Oesophagus And Gastric Cardia

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ABSTRACT

Background: The aim of the study was to examine the outcome of surgical treatment for carcinoma of the oesophagus and gastric cardia with two-field lymph node dissection at a high volume centre by a single surgeon over 7 years period. **Methods**: From January 1992 to March 1999, 316 patients underwent oesophagectomy with two field lymph node clearance for cancer of the oesophagus at our unit by a single consultant surgeon. Once the data collection at the base hospital was complete, it was sent to The Cancer Intelligence Unit Information Centre at Bristol for verification of data. The data analysis was then undertaken using SPSSv9. The main technique utilized was the Kaplan-Meier survival estimate. Kaplan-Meier survival functions were produced and compared, using the log rank test, for a number of pre-specified variables and their associated levels. Multivariate analysis was performed using Cox's proportional hazards modelling. **Results:** The average age at the time of surgery was 63.5 years, with a male to female ratio of 2:1. 86% of patients had dysphagia at the time of presentation. 88%(277) Patients had Ivor Lewis oesophagectomy, while 6%(20) had McKeown`s and 1%(4) had left thoracolaparotomy. 5% (14) of the patients underwent total laryngo-pharyngo-oesophagectomy. In total 62% (197) of patients had adenocarcinoma and 31% (99) had squamous cell carcinoma. 68% (215) of patients had lymph node metastasis while 32% (101) had no lymphatic involvement at resection. 80% had pyloroplasty or pyloromyotomy. 8% had anastomotic leak. 30-day mortality was 7%. Overall 5-year survival was 33%, with a very significant survival difference between lymph node negative and positive patients (25%vs 49%; $p<0.01$). There was no statistically significant difference in survival on the basis of gender ($p=0.47$), histology ($p=0.48$) or age ($p=0.299$). In total 72 patients received adjuvant treatment and had significant survival benefit ($p=0.002$) but because of selection bias the results are of doubtful significance. **Conclusion:** It is concluded that for tumours of lower 1/2 of oesophagus Ivor Lewis oesophagectomy with two-field lymphadenectomy is safe and effective procedure. It can be performed with low morbidity and mortality and good long-term survival. . Oesophageal cancer still remains a disease of old age and that on the basis of age alone no one should be denied the opportunity of surgical resection. Gastric outlet drainage had a strong influence on the incidence of postoperative leak. **Key Words:** oesophageal carcinoma, lymphadenectomy, gastro-oesophagectomy, survival

INTRODUCTION

Cancer of the oesophagus is one of the 10th most common cancers in the world [1]. The average incidence of this tumour in the Western world is between 5-10 cases per 100,000 populations per year. The highest incidence extends from the Caspian region of Northern Iran, across to the Southern Republics of former USSR and in to the Northern China. Although, Worldwide Squamous cell carcinoma is more common but it seems adenocarcinoma is increasing since the mid-1970`s by 5 to 10% per annum in the West. It accounts for 60-70% of all oesophageal cancers in the West. Chinese first described oesophageal cancer almost 2000 years ago. Twenty centuries later, it still remains a dreaded disease with a poor overall survival. Cancer

of the oesophagus has a tendency for early lymphatic spread and nearly 2/3rd of the patients already have lymph nodes metastasis at the time of presentation of this disease. While surgery still remains a gold standard treatment for this disease, controversy still exists as to the extent of lymph node dissection for better long-term survival. Most of studies including from Japan [1, 2] have touted the idea of radical oesophagectomy with three-field lymphadenectomy for better prognosis.

The purpose of this retrospective study was to review and analyse our long-term results of oesophageal resection, with two-field lymph node dissection.

PATIENTS AND METHODS

A retrospective review of 316 patients with carcinoma of the oesophagus was undertaken. These patients underwent oesophageal resection in our unit at Derriford hospital Plymouth between Jan 1992 to Mar. 1999, by a single Consultant Thoracic Surgeon and his team. This study included all tumour resections from cervical oesophagus and hypopharynx to gastro-oesophageal junction. All patients had standard preoperative investigations such as oesophagoscopy, computed tomography, bronchoscopy if tumour was in the upper half of the oesophagus and upper abdominal ultrasound in some cases, to rule out hepatic metastasis, whereby results of CT scan were inconclusive. In addition all patients had routine haematology and biochemistry profile. Staging of oesophageal cancer was performed according to the American Joint Committee on Cancer guidelines [3]. Ivor Lewis (no=277) was the operation of choice for tumours involving lower half of the oesophagus and Gastro-oesophageal junction, while McKeown`s three stage gastro-oesophagectomy (no=20) was performed for lesions involving upper 1/3rd of oesophagus. Total laryngo-pharyngo-oesopagectomy (no=14) was performed for lesions of cervical oesophagus and hypo pharynx. Reconstruction following resection was performed using Gastric tube interposition in all cases.

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Radical two field(abdominal and thoracic) lymph node dissection was performed by resecting left gastric, coeliac, splenic and common hepatic lymph nodes from abdomen and paraoesophageal, hilar, subcarinal, paratracheal lymph nodes from chest. Gastrointestinal tract continuity was re-established with a posterior mediastinal gastric tube interposition in every case. All intrathoracic anastomosis were performed using EEA stapler. In 109 patients 31 mm circular stapling device was used while 83 patients had 28 mm and 90 patients had 25mm size stapler used for anastomosis. In addition 234 patients also had ink welling of anastomosis using partial thickness horizontal mattress sutures between serosal surfaces of oesophagus and stomach about 1.5 cm from the anastomotic line. A Heinke-Mikulicz pyloroplasty was perfomed in 231patients while 27 patients had pyloromyotomy. All but 15 patients were extubated in theatre and sent back to the ward postoperatively. All but 22 patients received total parentral nutrition during postoperative period. All patients had gastromiro swallow before commencing oral feeding on day 4 in case of intrathoracic anastomosis and day 7 in case of hand-sewn anastomosis. In total 72 patients underwent adjuvant and/or neo-adjuvant treatment. Once the data collection at the base hospital was complete, it was sent to The Cancer Intelligence Unit Information Centre at Bristol for verification of data. All exchanges of data were encrypted and password protected using Norton Secret Stuff or PKZip. The actual matching was performed using the patient's name, the hospital number and diagnostic details. In total 128 patients were not known to have died at the date of last follow up, 31st of December 1999. These were coded as censored. The data analysis was then undertaken using SPSSv9.

The main technique utilized was the Kaplan-Meier survival estimate. Kaplan-Meier survival functions were produced and compared, using the log rank test, for a number of pre-specified variables and their associated levels. Multivariate analysis was performed using Cox's proportional hazards modelling

RESULTS

From a total numbers of 316 patients in this group, who underwent surgical resection at our unit at Derriford hospital between 1992 to march 1999, 66% (207) were male and 34% (109) were female patients

with a male to female ratio of 2:1. The average age at time of surgery was 63.5 years, with a range between 32 years and 87 years. 199 patients were below 70 while 117 patients were found to be above 70 years of age at resection. The total number of resections performed in each year is shown in table 1.

Table-1
Shows number of resections for cancer of the oesophagus per year at Derriford hospital Plymouth between 1992 – March 1999.

Year	No of resections
1992	40
1993	43
1994	56
1995	36
1996	50
1997	44
1998	38
1999	9
Total	316

The most common presenting symptoms include, dysphagia, weight loss, loss of appetite, anemia, haemetamesis either alone or in different combinations, while 10 patients were diagnosed on routine surveillance endoscopies for Barrett`s oesophagus. 86% of patients had some degree of dysphagia at the time of initial presentation. The average duration of symptoms at time of presentation was 13 week. As is clear from table 2, Ivor Lewis gastro-oesophagectomy was the resection procedure of choice, and hence 88% (277) had ILGO, while 6 % (20) had McKeon's and 1% (5) had their tumour resected with left thoracoabdominal approach. 5 %(14) of patients in this study, with the cancer of cervical oesophagus and or hypo pharynx underwent total pharyngo laryngo-oesophgectomy.

Table-2
Primary resection procedure

Type of resection	No of patients
Ivor Lewis gastro-oesophagectomy	277(88%)
McKeon's	20 (6%)
Left thoraco-abdominal	5 (2%)
Total laryngo-pharyngo-oesophagectomy	14 (4%)s

In total 197(62%) patients were found to have adenocarcinoma, 99(31%) patients had squamous cell carcinoma, 2 had anaplastic, 8 patients had mixed cell and only one was found to have oat cell carcinoma. In total nine patients had undifferentiated cellular pattern (table3).

Table-3
Histopathological diagnosis

	Men	Women	Total
Adenocarcinoma	158 197(62%)	39	
Squamous cell carcinoma	35 (31%)	64	99
Mixed	5	3	8 (3%)
Anaplastic	2	0	2 (1%)
Oat cell carcinoma	0	1	1(0%)

More than two third of patients (215) had metastatic spread to one or other regional lymph nodes at time of resection, while only one third (101) were found to be lymph node negative. The exact number of patients in each stage of disease is shown in table 4

Table-4
Postoperative morbidity

Morbidity	No of patients
Hemorrhage	4
Anastomotic leakage	25
Recurrent laryngeal nerve damage	3
Cardiovascular problems	12
Pulmonary embolism	3
Pulmonary infection/effusion	10
Deep venous thrombosis	5
Wound infection	8
Gastric tube stasis	6

In this particular study 73.5% of patients had pyloroplasty, while 7.5% of the patients had pyloromyotomy and 18 % did not have any gastric outlet drainage procedure.
The total number of anastomotic dehiscence in this series was 25, making it a rate of 8%. The 30 - day mortality in this particular group of patients was 40%, while 60% of these patients were successfully salvaged.

A total of 22 patients died within 30 days of resection, with a mortality rate of 7%. Ten of these patients initially developed anastomotic leak and subsequently various complications lead to their death.

The overall 5-year survival in this series was found to be 33%. No significant survival difference was found on the basis of gender (p=0.47) or histopathology differentiation (p=0.48). However, a highly significant difference in long-term survival (p=0.000) was found in patients with or without lymphatic involvement. 5-year survival in lymph nodes negative patients was 49% as compared to only 25%, once regional lymph were found to be involved. Chi square test for trend for depth of tumour invasion and lymph nodes involvement was highly significant (p>0.0001).

Age, preoperative weight loss and duration of symptoms before resection had no significant influence on the overall survival.

177 patients had both resection margins clear of tumour at resection, 82 had either one or other margin involved by the tumour, while 7 patients were found to have both margins involved at resection. The 5-year survival was found to be 40%, 26% and 14% respectively.

There was statistically significant difference in 5 year survival (48%vs29%) of those patients who received adjuvant or neo-adjuvant treatment (p=0.002) compared to those who did not have any treatment following resection.

The rate of anastomotic stricture, requiring dilatation, in this series was found to be 31%. On average, most patients resumed normal diet after three dilatations.

DISCUSSION

There is a real increase in the incidence of carcinoma of the oesophagus in the Western world including UK. This is true for both adenocarcinoma and squamous cell carcinoma. It is partly due to increasing age of the population but also because of an increased risk for successive generations.

The age distribution for all patients with the cancer of the oesophagus in the South West region, obtained from Cancer Intelligence Unit in Bristol, was found to be similar to that of those who had oesophageal resection in our unit (South West Devon).

The data available from CIU for 1989 – 98period has also shown that the overall incidence of cancer of the oesophagus in South West Devon is 9.18 per100, 000 population per year compared to 8.60 per 100,000 populations per year for the whole of the South West Region of England.

The mean age at time of resection was 63.5 years, which is broadly the same as published in other series from the West [1, 4.] There were even 37% of patients above the age of 70 years at time of resection in our series. The results from Dalrymple-Hay et al [5] from Southampton UK published in 1999, reported, 38% patients above the age of 70 years, which is in line with same age pattern as in our series.

The total number of anastomotic dehiscense in this series was 25 which make the leakage rate to be 8%. In our unit, it is standard practice to keep the patients nil by mouth, on total parentral nutrition (TPN) for feeding and perform a Gastromiro swallow on the 4th postoperative day, if a mechanical stapling gun was used or on 7th post-operative day in the case of hand - sewn anastomosis, before resuming oral intake.

Anastomotic dehiscence remains one of the most dreaded complications in post gastro-oesophagectomy patients and is a major source of morbidity and carries high rate of mortality. It results in mediastinitis and sepsis in cases of intra-thoracic anastomosis, with mortality as high as 80% in some cases.

In the current series the rate of mortality in this group of unfortunate patients was 40% within 30-days. We strongly believe that, while the patients with anastomotic leak in cervical anastomosis can be treated conservatively, those with a large dehiscense of intrathoracic anastomosis should be explored immediately and where possible, a new gastro-oesophageal anastomosis should be performed and that the pleural cavity should be thoroughly washed with antiseptic solutions and large size intercostal drains be left in situ, for continuous drainage of this potentially infected pleural space. These patients in our series, after exploration did receive strong intravenous antibiotics and in most cases were electively ventilated for 24 to 48 hours.

The leak rate in our first study [1] of 298 patients was 3%. The rate of dehiscense in the current series has been found to be 8% which is well within range of recently reported series in the literature [4, 6]. The use of anastomotic staplers (EEA) for oesophageal anastomosis had made this complication less common and in the recent published series [1, 6, 7, 8] leakage rate has been reduced to 0 – 10%.

We have found two independent predictors of anastomotic dehiscence in our series, as is clear from our findings shown above. Those predictors are as follows:

- If the patient had an anastomosis with a mechanical stapler or by hand-sutured technique. The stapling is being far superior to prevent dehiscence.
- Whether or not patients had gastric outlet drainage performed at the time of resection; risk of anastomotic breakdown increases significantly if no drainage is performed.

Hence, we conclude that for all intra-thoracic gastro-oesophageal anastomosis, the EEA stapler should be used routinely.

The rate of anastomotic stricture, following gastro-oesophagectomy, has been reported in literature, varying from 1% to more than 40%. In our current study it has been found to be 31%. It is comparable to that in other series, [1, 8], whereby EEA staplers are used for anastomosis. The rate of anastomotic stricture in our previous series [1] was 22%.

Ivor Lewis operative technique was first described in 1946, and since then it remains the most popular resection procedure for carcinoma of the lower half of the oesophagus and gastro-oesophageal junction. 88% of our patients in the current series had ILGO with pyloroplasty or pyloromyotomy.

Like others [6, 7, 9, 11], we have found this procedure to be safe, effective, and a practical middle ground between aggressive en block resections and the trans-hiatal resection, where the procedure is performed by blunt dissection. Hence, we believe that Ivor Lewis gastro-oesophagectomy, with two -field lymphadenectomy is a safe and effective approach for resection of lower half of the oesophageal cancer. On the other hand, for patients, with carcinoma of the upper 1/3rd of the oesophagus, McKeon's three-stage gastro-oesophagectomy and two-field lymph node dissection, with cervical lymph node sampling is a safe procedure with good long term survival.

The overall 5-year survival for all patients in this particular series is found to be 33%, which is much better than other reported series from the West [1, 6, 9, 10] but is comparable with the ones from Japan [2]. In our study 62% of the patients had adenocarcinoma and 31% had squamous cell carcinoma, but there was no statistically significant difference found in 5-year survival in these two groups of patients on the bases of histology. There was no difference in long term outcome detected on the bases of gender either. Baba *et al* [2], from Japan, published their results of oesophageal_resections in 1994. The study included oesophagectomy with three-field lymph node dissection in 106 patients. The 5-year survival was found to be 30.8% and ten year survival of 20.7%. The hospital mortality and morbidity was 10.4% and 65.1% respectively. Age above 71, lymph nodes metastasis and recurrent laryngeal lymph nodes metastasis were found to decrease overall survival. The 5-year survival results of this and other similar published studies, advocating extensive lymph node dissection, mainly from Japan, are comparable to our own results (30.8% vs. 33%). Our results are, in fact better. In addition, our series have a significantly less hospital mortality and morbidity as well. Our patients were submitted to far less extensive dissection, which have its own inherent risks. As compared to the above findings an important distinction in our study is, that, we found no difference in overall survival between the patients who were above (117) or below (217) the age of 70 years.

Despite the efforts to diagnose and treat this disease at an early stage, to achieve the best long-term survival, it still remains an elusive goal. Almost all studies [1, 2, 11], have found that, there is a highly significant difference in long-term survival in patients with or without regional lymph nodes involvement by primary tumour at resection. In the current series, there were only 101 (32%) patients, without lymph nodes metastases at resection as compared to 215 (68%) patients, who had lymphatic metastases at the time of resection of their tumour. A huge difference in 5-year survival was found in these two groups; 49% where no lymph nodes were involved, to only 25% once lymph nodes were involved by tumour. The overall 5-year survival for all patients in this study was found to be 33%.

The 30-day mortality in our series was found to be 7%, which is in line with the most of the recent published series [6, 7, 11, 12 13].

The results of our current study have proved, that, for carcinoma of the lower half of the oesophagus and gastro-oesophageal junction, Ivor-Lewis Oesophagectomy with two-field lymphadenectomy is safe and effective. It can be performed with low morbidity and mortality and good long-term survival. For carcinoma of the upper third of the oesophagus, a

three stage subtotal oesophagectomy remains procedure of choice, while Total laryngo-pharyngo-oesophagectomy should be reserved for cancer of the cervical oesophagus and hypo pharynx.

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