

Total thoracic oesophagectomy for oesophageal carcinoma: has it been worth it?

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Abstract

Objective: Anastomotic recurrence is a major cause of late mortality following oesophago-gastrectomy (OG) for carcinoma of the oesophagus and oesophago-gastric junction using either the Ivor Lewis or left thoraco-abdominal approach with intra-thoracic anastomosis. The aim of this study was to determine whether the more extensive total thoracic oesophagectomy (TTO) with cervical anastomosis would reduce the anastomotic recurrence rate while maintaining acceptable operative morbidity and mortality. **Methods:** From January 1988 to December 1996, 108 total thoracic oesophagectomies and 66 oesophago-gastrectomies were performed with curative intent in 174 patients (125 males, mean age 62.4 years) with carcinoma (squamous cell carcinoma in 34 and adenocarcinoma in 140) of the middle (31 patients) and lower (44 patients) oesophagus and oesophago-gastric junction (99 patients). **Results:** Minor complications occurred in 37 (34%) total thoracic oesophagectomy and 18 (27%) oesophago-gastrectomy patients, major complications in 15 (14%) and 5 (8%) and peri-operative death in 5 (4.6%) and 7 (11%) patients, respectively. Anastomotic leakage occurred in 10 (9%) total thoracic oesophagectomy and 5 (8%) oesophago-gastrectomy patients, and was fatal in 1 (1%) and 4 (6%). There was no incidence of tumour at or within 5 mm of the proximal limit in the total thoracic oesophagectomy group and this was reflected in the complete absence of anastomotic recurrence. In the oesophago-gastrectomy group there was a positive proximal resection margin in 13 (20%) and 13 anastomotic recurrences (22% of peri-operative survivors). The 5-year survival (including operative mortality) was 29% for total thoracic oesophagectomy compared with 21% for the other techniques ($P = 0.028$ log rank test). Median survival was 25.2 months after total thoracic oesophagectomy and 15.8 after oesophago-gastrectomy. **Conclusions:** Total thoracic oesophagectomy can be performed in oesophageal cancer patients with comparable morbidity to that of lesser resections. Incomplete proximal resection and anastomotic recurrence did not occur in this series of 108 total thoracic oesophagectomies and this is reflected in an increased medium term survival. The improved survival is most apparent for tumours of the oesophago-gastric junction. © 1999 Elsevier Science B.V. All rights reserved.

Keywords: Esophageal carcinoma; Resection; Cervical anastomosis; Anastomotic recurrence, Esophago-gastric junction

1. Introduction

A review of oesophageal resections performed between 1977 and 1985 in our unit showed an unacceptable level of positive proximal resection margins of 32%. This was reflected in a high anastomotic recurrence rate of 17% [1]. The resections at that time were performed either through a left thoraco-abdominal incision with anastomosis below the aortic arch, or using the Ivor Lewis approach with the anastomosis above the level of the azygos vein. In an attempt to reduce the anastomotic recurrence rate we began to use the total thoracic oesophagectomy (TTO) approach performed through left thoraco-abdominal and left cervical incisions as described by Matthews and Steel [2], developing previous work by Belsey.

The phased introduction of the new technique allowed us to compare it with the techniques of oesophago-gastrectomy (OG) commonly used in the United Kingdom, albeit not in a randomised trial.

2. Patients and methods

One hundred and seventy-four patients with carcinoma of the thoracic oesophagus and gastric cardia underwent TTO or OG with curative intent in the period from January 1988 to December 1996 (Table 1). Included in the study were all tumours of the middle and lower oesophagus or oesophago-gastric junction (OGJ) in which there was enough residual stomach to consider cervical anastomosis after resection of a gastric margin 5 cm distal to macroscopic tumour. The stage distribution is depicted in Table 2. Excluded from this analysis were upper third or post-cricoid tumours which

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Table 1
Patient characteristics

Characteristic	Total		TTO		OG	
	n	%	n	%	n	%
Number of patients	174	–	108		66	
Male:female	125:49	72:28	81:27	75:25	44:22	67:33
Site:						
middle third	31	18	24	22	7	11
lower third	44	25	32	30	12	18
cardia	99	57	52	48	47	71
Histopathology						
squamous cell carcinoma	34	20	24	22	10	15
adenocarcinoma	140	80	84	78	56	85
Mean age (years)	62.4		64.2		60.6	

were treated by cervical tumour and node dissection and trans-hiatal gastroplasty, incidental carcinomas found after a preoperative diagnosis of high grade dysplasia, and palliative resections. All patients had standard preoperative investigations required for major thoracotomy as well as barium meal, computed tomography scan, bronchoscopy and oesophagoscopy.

In the oesophago-gastrectomy group there were 18 Ivor Lewis resections and 48 left thoraco-abdominal resections with intra-thoracic anastomosis. TTO was performed in 108 patients. Frozen section was not performed routinely as previous experience has shown poor correlation with the permanent paraffin section findings. Frozen sections of the cuff also fail to detect ‘skip’ metastases in the more proximal oesophagus. A proximal or distal resection margin was defined as positive if tumour was present microscopically within 5 mm on the formalin-preserved specimen. Data on resection technique, histology and complications were collected prospectively. Follow-up was complete in all patients to death or review three years post-resection. Survival probability was calculated according to the Kaplan–Meier method using STATISTICA (StatSoft, Tulsa, OK, USA). Univariate comparisons were tested using the Log-rank test identifying parameters for multivariate analysis using a Cox proportional hazard model. This study was a non-randomised prospective audit during the gradual introduction of TTO to replace OG resection.

The TTO operative technique is similar to that described

Table 2
Tumour stage

Stage (TNM)	Total		TTO		OG	
	n	%	n	%	n	%
I (T1N0M0)	8	5	7	6.5	1	1.5
IIA (T2–3N0M0)	56	32	38	35	18	27
IIB (T1–2N1M0)	8	5	5	4.6	3	4.5
III (T3N1M0)	101	58	58	54	43	65
IV (T4N0M0)	1	1	–	–	1	1.5

previously [2,3]. The oesophagus is resected en-bloc with all the mediastinal fat and lymph nodes via a left thoraco-abdominal incision. A window in the supra-aortic mediastinal pleura allows the dissection to be taken to the neck. The stomach is mobilised on the right gastro-epiploic arcade and is placed in the posterior mediastinum after pyloro-myotomy. With the patient repositioned supine, the anastomosis is performed using a single-layer continuous 3/0 Vicryl suture (Ethicon, Edinburgh, UK) via an oblique left cervical incision.

All resections were carried out by a single surgical team. Thirty-three TTO resections (31%) and 15 OG (23%) were performed by surgeons-in-training.

3. Results

The average operative time for TTO was similar to that for the Ivor Lewis procedure. The OG via left thoraco-abdominal incision was shorter by approximately half-an-hour. Complication rates (Table 3) were comparable between the different operation groups despite the more extensive resection in the case of TTO. Though the anastomotic leak rate was similar only 10% of cervical anastomoses proved fatal following TTO whereas 80% of intra-thoracic anastomotic leaks were fatal. The mortality of TTO performed by surgeons in training was 3% compared to 27% for OG.

Death from chest infection occurred in two patients with pre-existing obstructive airways disease and another who previously had a thoracoplasty. Two patients who required local resection of the posterior wall of the left main bronchus to ensure tumour clearance also died of chest infection. A patient who had a splenectomy died of overwhelming pneumococcal pneumonia. Pulmonary emboli occurred in two cases with other major complications, one an anastomotic leak and the other a chest infection. One patient died of purulent pericarditis which occurred in the absence of a leak. Renal failure occurred in one patient with a previous nephrectomy. Recurrent laryngeal nerve injury occurred in 3 TTO patients.

By performing TTO we avoided any occurrence of positive proximal margin (tumour at or within 5 mm of the proximal limit in the fixed specimen). In comparison, despite taking a margin of oesophagus 7 cm above the gross tumour, 13 (20%) OG patients had a positive proximal margin on histological examination (Table 4). Symptomatic

Table 3
Complications

Complication category	TTO	Oesophago-gastrectomy
Fatal	5 (5%)	7 (11%)
Major	15 (14%)	5 (8%)
Minor	37 (34%)	18 (27%)
Anastomotic leak	10 (9%)	5 (8%)

Table 4
Incidence of resection limits and anastomotic recurrence

	TTO	Oesophago-gastrectomy
Proximal limit	Nil	13 (20%)
Distal limit	8 (7%)	8 (12%)
Anastomotic recurrence	Nil	13 (20%)

tumour recurrence at the site of anastomosis also occurred in 13 OG patients (22% of those who survived the peri-operative period), many without histological evidence of tumour at the proximal limit. Mediastinal recurrence, without involvement of the anastomotic site, occurred in 7 (6.5%) TTO patients. Of these two had positive gastric resection margins, four had tumour close to the deep resection margin and one had extracapsular lymphatic spread.

Univariate analysis (Table 5) has shown that patients undergoing TTO had significantly better ($P = 0.028$) 5-year survival (29%) than the OG group (21%). On multivariate analysis only wall invasion ($P = 0.005$), node metastasis ($P = 0.008$), positive proximal margin ($P = 0.01$) and squamous histology ($P = 0.05$) were all of independent prognostic significance. Surprisingly, the main improvement in 5-year survival following TTO was seen in tumours at the OGJ (TTO 30%, OG 17%) rather than the true oesophagus (TTO 29%, OG 29%), especially in node-negative tumours. However, between 18 and 36 months, the peak period for anastomotic recurrence, survival was better when middle and lower third tumours were treated by TTO. The survival curves for node metastasis and wall invasion confirm the importance of TNM staging. However, the survival according to overall staging suggests that Stage IIB and Stage III tumours behave identically, both categories being node-positive. Though the median survival of Stage IIB was 22.5 months, none of the 8 patients survived

Table 5
Univariate analysis

Parameter		Median (months)	5-year survival (%)	<i>P</i> value
N Stage	0	15.7	13	0.00008
	1	41.5	46	
T stage	1	Not reached	66	0.00005
	2	40.3	49	
	3	16.1	19	
Proximal limit	+ ve	9.6	Nil	0.0013
	– ve	22.6	28	
Histology	SCC	40.8	46	0.004
	Adeno	18.2	20	
Operation	TTO	25.2	29	0.028
	OG	15.8	21	
Distal limit	+ ve	10.5	12	0.052
	– ve	21.8	27	
Site	Middle third	35.0	38	0.32
	Lower third	22.1	22	
	OGJ	18.3	24	
Gender	Male	20.9	24	0.42
	Female	20.7	32	

more than 40 months. In Stage III, despite a median survival of only 14.6 months, there was a 5-year survival of 13%. While node metastasis is a poor prognostic sign, long-term survival does occur in this subgroup of patients. A positive proximal margin precludes long-term survival.

TTO was better tolerated by patients in the long term because of the reduced incidence of gastro-oesophageal reflux symptoms. This may be due to a very short remnant of oesophagus being preserved in an area of high tissue pressure. The main benign long-term complication was anastomotic stricture which was more common after TTO. Dilatation is straightforward and most strictures responded to either one or two dilatations.

4. Discussion

There are almost as many operations for oesophageal cancer as there are oesophageal surgeons. All operations must be tailored to a degree by the patient's physical attributes and the extent of the tumour. Our previous experience with oesophago-gastrectomy via the left chest was quite disappointing; early recurrence of malignant dysphagia being a rapidly fatal condition, often in patients with no other poor prognostic indicators such as T3 wall penetration or node metastases [1]. Intra-operative frozen section may have been able to slightly reduce the incidence of positive margins reported on the paraffin sections but this measure cannot confidently rule out subsequent anastomotic recurrence. Techniques which involved siting the stomach lateral to the aorta with an anastomosis high in the chest did not reduce the incidence of anastomotic recurrence. Ironically, the Ivor Lewis procedure had a higher incidence of recurrence than the left-sided oesophago-gastrectomy in this series. In line with the principles espoused by McKeown, we decided that only removal of almost the complete oesophagus could reduce anastomotic recurrence [4].

As the oesophagus passes through three surgical fields, the neck, the thorax and the abdomen, all approaches result in a compromise between the access and the surgical options. The 3-stage oesophagectomy, while being one of the best methods of obtaining tumour clearance, has the drawback that much of the dissection, particularly in the chest, needs to be performed before full assessment of the stomach, nodes and liver can be carried out. Trans-hiatal oesophagectomy may allow assessment of the abdomen but the tumour itself is not directly visualised. Described originally as a palliative procedure for high-risk patients, this procedure may have a place in the neoadjuvant setting but mediastinal recurrence is understandably high. We have found it most useful for reconstruction after oesophagectomy and cervical node dissection for upper third or pharyngeal tumours.

As most of the tumours presenting to our service are lower third and OGJ in position, we opted to use the technique described by Matthews [2], commencing with a left

thoraco-abdominal incision and later turning the patient to perform the cervical anastomosis. We were concerned that the more extensive resection would have a higher morbidity and mortality but the reverse was the case. As our experience grew we found that most OGJ tumours were amenable to TTO with resection of the lesser curve of the stomach, allowing a gastric tube to be fashioned after obtaining a clear macroscopic margin at the cardia.

A major advantage of the left thoraco-abdominal approach is the number of options available to the surgeon without performing unnecessary exploration or dissection and without repositioning the patient. TTO is now the preferred option for curable tumours in our unit. For tumours thought to be locally advanced with possible pancreatic or coeliac invasion, it is possible to commence with a small exploratory left upper quadrant oblique laparotomy. When tumours prove unresectable, a traction Celes-tin tube can be passed. When the tumour mainly involves the body of the stomach, a total gastrectomy and jejunal loop reconstruction is possible with good exposure via the thoraco-abdominal incision. If there is inadequate residual stomach to allow it to be brought to the neck, and there is a contra-indication to colon graft, oesophago-gastrectomy can be performed. Colon mobilisation is also possible via this approach, although usually if the tumour is too large to allow a gastric tube to be used it is unlikely to be cured by surgery alone. A further advantage of this approach is that the exposure of the short gastric vessels is particularly good.

Oesophago-gastrectomy with limited gastric and oesophageal resection is a compromise procedure. We now recognise that in the past we carried out inadequate resections due to adherence to this minimalist procedure, and now totally avoid this practice.

We reserve the right-sided approach for those tumours of the middle third of the oesophagus which may be invading the adventitia of the aortic arch. These are more easily accessed via the right chest. However, where the tumour abuts the aorta and there is no invasion, safe mobilisation is possible through the left chest with the added advantage that control of the aorta is infinitely easier.

The accepted endpoint in assessing an oesophageal cancer operation performed with curative intent is the 5-year survival, which for most patients equates to cure. In recognition that 70–80% of patients die from recurrent tumour after what was thought at the time to be a curative resection, other endpoints need to be considered. Such secondary endpoints include anastomotic recurrence, mediastinal or gastric remnant recurrence and the duration of effective disease palliation in those who may ultimately not be cured.

The TTO technique [2,3] has been shown to be safe, easily taught and reproducible. Subsequent experience has reduced the operative mortality for TTO, since its introduction in 1988, to 4%. The incidence of anastomotic leak, the most feared complication in oesophageal resection, did not

increase following cervical anastomosis, as has been reported in some series [5,6], confirming the data of Lam et al. [7].

Anastomotic recurrence has been eliminated by performing TTO. This has been reflected in the number of medium- and long-term survivors. Interestingly, this effect was most apparent for tumours of the OGJ rather than tumours of the true oesophagus. While some abdominal surgeons still claim they can obtain adequate clearance for OGJ tumours via a laparotomy alone, it is time to question this practice. The better outcome for OGJ tumours with TTO indicates that the mechanism of spread resembles that found in tumours of the true oesophagus. Because proximal submucosal tumour permeation is the normal mode of local spread, the only reliable way of avoiding recurrence in the proximal oesophagus is to remove virtually the whole organ.

In the TTO group, mediastinal recurrence and subsequent extrinsic compression of the stomach at various sites from the thoracic inlet to the hiatus is a more common feature and tends to occur later than anastomotic recurrence. It is hoped that the future addition of effective adjuvant therapies for patients with evidence of mediastinal node involvement or full-thickness penetration of the oesophageal wall will reduce such mediastinal recurrences.

Inadequate distal margin remains a problem for all oesophageal resections. In this series neither the Ivor Lewis nor the oesophago-gastrectomy resections were associated with improved distal margin clearance than TTO. This is because the oesophagus enters the stomach in a position well down the lesser curve and excising the fundus usually does not improve tumour clearance. Without performing a total gastrectomy and replacing the oesophagus and the stomach with colon, it is difficult to be certain of a clear distal margin. Statistically, tumour infiltration of the distal margin has not been as significant in terms of prognosis as the proximal margin as it is not involved in the anastomosis which is performed at the fundus of the stomach. This has achieved greater clinical importance with patients surviving longer. More recently, we have employed a more radical distal dissection, leaving only a tube remnant of the stomach. This has successfully reduced the incidence of positive distal margin.

A criticism of this study may be that it is not randomised and the decision to use a particular technique could have been biased. The pre-operative and post-operative management was similar for both groups and a single team managed all cases. For proximal tumours the surgical approach (Ivor Lewis or TTO) had to be decided prior to gaining informed consent. Tumours of the cardia were initially managed using OG. With experience gained over the 5-year period, the policy changed to performing a TTO in all patients with tumours of the cardia and oesophagus where there was adequate stomach to perform a cervical anastomosis. For lower tumours it could be argued that a bias could have occurred whereby tumours with a large gastric component were subject to a less radical proximal resection. Most such

resections were considered palliative and were therefore excluded from this study.

The study was primarily aimed at prospectively auditing a new technique which was gradually introduced to the unit and now has been universally adopted. We were unwilling to randomise patients between an established operation and a procedure which was new to the unit, and favoured initially limiting TTO procedures as the unit moved up the learning curve with the more radical operation. It has taken 10 years to produce a mature series with detailed analysis. The question now arises whether a randomised trial is necessary. There may be objections from those who believe that TTO is superior to OG, but to date there are no data to confirm this.

In conclusion, TTO is a safe oesophageal resection technique and, rather than increasing morbidity as feared, actually has a lower incidence of fatalities from anastomotic dehiscence. The latter is particularly evident for surgeons-in-training which suggests that TTO can successfully be taught to trainee surgeons. TTO provides improved proximal tumour clearance reflected in an absence of anastomotic tumour recurrence and an increase in survival, particularly in the medium term. This benefit being most pronounced for tumours of the oesophagogastric junction, we recommend that surgeons should strongly consider the TTO approach for these tumours. Multivariate analysis shows that in addition to node metastasis, wall invasion and squamous histology, proximal tumour clearance is of independent prognostic significance.

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