Selection for oesophagectomy and postoperative outcome in a defined population

Martin C Gulliford, Jeremy R Barton, Heather M Bourne

Abstract

Objective—To measure the extent of use of, and perioperative mortality from, oesophagectomy for carcinoma of the oesophagus, and to examine the association between oesophagectomy and long term survival.

Design—Retrospective cohort study of cases of oesophageal carcinoma notified to the Thames Cancer Registry.

Setting—South East Thames and South West Thames health regions.

Patients—3273 patients first registered with carcinoma of the oesophagus during 1985-9, 789 of whom were excluded because of incomplete data, leaving 2484 (75·9%) for further analysis.

Main measures—Treatment of oesophagectomy, mortality within 30 days of oesophagectomy, and duration of survival from date of diagnosis to death, according to patient and tumour characteristics.

Results—Oesophagectomy was performed in 571(23·0%) patients. Its use decreased with increasing age (odds ratio (95% confidence interval) 0·935(0·925 to 0·944) per year) and was less common for tumours of the middle or upper third of the oesophagus than the lower third (0·56(0·42 to 0·75)). The proportion of patients undergoing oesophagectomy varied threefold among the 28 districts of residence. The perioperative mortality rate was 15·1%(86/571) (12% to 18%); it increased with age (odds ratio 1·05(1·02 to 1·08) per year) and for tumours of the middle or upper third of the oesophagus compared with the lower third (2·52(1·31 to 4·84)). Long term survival was slightly higher for patients undergoing oesophagectomy (0·5% v 0·2%).

Conclusions—Despite a high perioperative mortality rate patients selected for oesophagectomy showed better long term survival than those who were not, suggesting that clinical judgements used in selection were independent markers of a better prognosis. The nature of this selection needs to be more completely characterised to permit a valid evaluation of outcome of oesophagectomy.

(*Quality in Health Care* 1993;2:17-20)

Introduction

Measuring the outcome of health care interventions routinely is recognised as an important yet infrequently performed activity in the NHS.[1] Reviewing the effectiveness of treatment for uncommon conditions poses particular problems because of the small numbers of cases seen at any one hospital and the lack of representativeness of reports from individual centres. The aim of evaluation should be to take into account all of the patients at risk in a defined population.

Oesophageal carcinoma causes about 5000 deaths a year in England and Wales,[2] and treatment is undertaken at both district hospitals and more specialised units. In the past oesophagectomy was difficult to justify, at least for squamous cell carcinoma, in view of the perioperative mortality rate of 30%.[3] More recently, perioperative mortality rates below 10% have been reported from selected centres,[4–8] and these results have been used to advocate increased use of oesophagectomy.[8] Others have emphasised that the aim of treatment should be to achieve palliation with minimum morbidity and mortality.[9] However, a randomised trial designed to evaluate the effectiveness of oesophagectomy for squamous cell carcinoma of the oesophagus was terminated prematurely because of low recruitment.[10] The justification for oesophagectomy is largely dependent on an accurate assessment of the perioperative mortality. A high perioperative mortality rate would make the operation difficult to justify whether it was used with curative or palliative intent.[3] Even if the operation could be justified for some patients the question of who should be selected for surgery remains to be answered. Surgeons who choose to report their experience are likely to form a biased sample of these who undertake such work.

We used cancer registrations to investigate the extent of use of oesophagectomy and the factors associated with selection for surgery in a defined population. We also evaluated the perioperative mortality rate and the eventual duration of survival in patients undergoing the operation.

Patients and methods

Data were obtained from the records of the Thames Cancer Registry in October 1991. Cases were selected if the patients were resident in the South East Thames or South West Thames regions and were registered with neoplasm of the oesophagus (International Classification of Diseases for Oncology (ICD-O) topographic codes 150·0-150·9) during 1985-9.[11] The site of the tumour was classified from the ICD-O topographic codes into the categories: lower third of oesophagus (150·5);

Department of Public Health Medicine, United Medical and Dental Schools of Guy's and St Thomas's Hospitals, St Thomas' Campus, London SE1 7EH
Martin C Gulliford, senior lecturer
Jeremy R Barton, assistant statistician

Thames Cancer Registry, Sutton, Surrey SM2 5NL
Heather M Bourne, special projects officer

Correspondence to:
Dr M C Gulliford, CAREC, PO Box 164, Port of Spain, Trinidad, West Indies
Accepted for publication 4 December 1992

middle and upper thirds of oesophagus (150·4 and 150·3); and not known (150·9). The tumour morphology was classified into the categories: squamous cell carcinoma (ICD-O morphology codes M80703 and M80713); adenocarcinoma (M81403 and M84813); carcinoma not specified (M80103 and M80003); all other codes. The simplified cancer registry staging system was used to classify the tumour stage into the categories "local" (meaning confined to the organ of origin), "local extension or nodal or distant metastases, or both," and "not known." Cases in which patients were treated by oesophagectomy were identified using the cancer registry operation codes. Perioperative mortality was defined as death within 30 days of operation. Place of residence was classified into 28 district health authorities. The 68 hospitals at which the patients were treated were classified according to the number of oesophagectomies performed over the five year period into: ≤5; 6–10; 11–15; 16–20; >20. One patient treated privately and two patients operated on at unidentified hospitals in another region were classified as having been treated at individual hospitals. The identity of all other hospitals was known. The patient's age was included as a continuous variable after showing that the effect of age was adequately explained by a linear relationship. Logistic regression was used to identify the characteristics associated with the use of oesophagectomy and the variables associated with perioperative mortality among those who underwent oesophagectomy.[12] Dates of diagnosis and death were obtained from the cancer registry, which obtains information both from clinical records and from the NHS Central Register. Survival rates from date of diagnosis to date of death were estimated by the product limit method, and the log rank test was used to test the significance of differences between groups.[13] The proportional hazards model was used to estimate the association of explanatory variables with survival. Hazard ratios were estimated relative to a baseline category; increasing values of the hazard ratio

indicated an increasing risk of death.[13] The likelihood ratio test was used to test the significance of the association of explanatory variables with survival.

Results

The Thames Cancer Registry identified 3273 cases meeting the entry criteria. In 768 (23·5%) cases, registration was from death certificate alone and additional data were not available for analysis; these cases were excluded. The district of residence was not known for 21 cases, which were also excluded. The mean age of patients was 73·8(SD 11·8) years for excluded cases compared with 71·2(11·0) years for analysed cases; the proportion of men was similar for the two groups (56% and 57% respectively). The proportion of cases excluded varied among the 28 health districts of residence (range 10–31%). Thus 2484 cases were available for further analysis; in 2288(92·1%) the patients were deceased.

Oesophagectomy was performed in 571(23·0%) patients. Older patients and patients with tumours in the upper two thirds of the oesophagus were less likely to receive surgery, as were patients with evidence of tumour spread (table 1). The tumour morphology was more likely to remain unclassified among patients who did not receive the operation. The proportion of patients who underwent oesophagectomy varied threefold among districts of residence. This variation was not explained by adjusting the age, tumour site, stage, and tumour morphology.

The overall perioperative mortality rate was 15·1(86/571(95% confidence interval 12%–18%)). The risk of perioperative death increased by 5% per year of age (table 2). Perioperative mortality was higher for patients with tumours of the middle and upper thirds of the oesophagus than of the lower third. Perioperative mortality was similar in men and women and was not associated with the tumour morphology nor district of residence. Oesophagectomy was undertaken at a total of 68 hospitals. There was no evidence that

Table 1 Variables associated with use of oesophagectomy in multiple regression analyses

Variable	(%) No treated by oesophagectomy	Odds ratio* (95% confidence interval)	χ^2†	Degrees of freedom	p Value
Age (per year):		0·935(0·925 to 0·944)	184·3	1	<0·001
Sex:					
Female	18·7(201/1076)	1·00	0·5	1	>0·05
Male	26·3(370/1408)	1·09(0·87 to 1·37)			
Tumour stage:					
Local	23·5(354/1508)	1·00	5·9	2	>0·05
Local spread or metastases	23·9(169/707)	0·74(0·58 to 0·95)			
Not known	18·2(48/269)	0·91(0·62 to 1·34)			
Tumour morphology:					
All other codes	34·2(42/123)	1·00	100·6	3	<0·001
Squamous cell	24·1(250/1036)	0·72(0·46 to 1·12)			
Adenocarcinoma	31·9(244/764)	0·92(0·59 to 1·44)			
Unclassified	6·2(35/561)	0·16(0·09 to 0·28)			
Tumour site:					
Lower third of oesophagus	30·6(290/947)	1·00	20·6	2	<0·001
Middle or upper third	17·3(109/629)	0·56(0·42 to 0·75)			
Not known	18·9(172/908)	0·63(0·49 to 0·81)			
District of residence:					
Highest proportion‡	39·4(39/99)		81·1	27	<0·001
Lowest proportion	13·2(12/91)				

* Adjusted for each of the other variables.
† Represents difference in goodness of fit with and without the variables.
‡ Highest and lowest proportion of patients receiving oesophagectomy among 28 district health authorities.

Table 2 Variables associated with perioperative mortality in multiple regression analyses

Variable	Perioperative mortality (%) (No)	Odds ratio* (95% confidence interval)	χ^2†	Degrees of freedom	p Value
Age (per year):		1·05(1·02 to 1·08)	15·0	1	<0·001
Sex:					
Female	17·4(35/201)	1·00	0·1	1	>0·05
Male	13·8(51/370)	0·90(0·53 to 1·55)			
Tumour stage:					
Local	13·6(48/354)	1·00	2·4	2	>0·05
Local spread or metastases	17·8(30/169)	1·50(0·88 to 2·56)			
Not known	16·7(8/48)	1·41(0·58 to 3·45)			
Tumour morphology:					
All other codes	19·1(8/42)	1·00	2·0	3	>0·05
Squamous cell	15·2(38/250)	0·51(0·20 to 1·26)			
Adenocarcinoma	14·3(35/244)	0·62(0·25 to 1·50)			
Unclassified	14·3(5/35)	0·58(0·16 to 2·11)			
Tumour site:					
Lower third of oesophagus	10·7(31/290)	1·00	9·6	2	<0·01
Middle or upper third	22·0(24/109)	2·52(1·31 to 4·84)			
Not known	18·0(31/172)	2·04(1·14 to 3·67)			
No of oesophagectomies at hospital, 1985-9 (No of hospitals):					
>20(6)	17·5(33/189)	1·00	7·8	4	>0·05
16-20(8)	11·6(16/138)	0·51(0·26 to 1·01)			
11-15(8)	17·9(19/106)	0·85(0·44 to 1·67)			
6-10(9)	18·3(13/71)	1·07(0·51 to 2·24)			
≤5(37)	7·5(5/67)	0·37(0·13 to 1·02)			

* Adjusted for each of the other variables.
† Represents difference in goodness of fit with and without the variable.

Table 3 One, two, and five year survival rates from diagnosis, according to use of oesophagectomy

Survival	Total (n=2484)	Non-operative treatment (n=1913)	Oesophagectomy (n=571)
One year	20·2	14·5	40·8
Two year	6·0	3·4	15·5
Five year	0·2	0·2	0·5

χ^2=182·4, df=1; p<0·001, difference in survival between non-operative and operative treatment.

hospitals where oesophagectomy was performed most frequently achieved lower perioperative mortality rates (table 2). Additional analyses showed that treatment at a teaching hospital was not significantly associated with perioperative mortality.

Survival rates from diagnosis were extremely low, both for patients treated by oesophagectomy and for those treated conservatively (table 3). Selection for oesophagectomy was associated with a slightly better prognosis.

Table 4 Variables associated with survival from date of diagnosis to death in proportional hazards regression analyses

Variable	Hazard rate (95% confidence interval)	χ^2	Degrees of freedom	p Value
	Univariate regression			
Oesophagectomy:				
No	1·00	196·9	1	<0·001
Yes	0·50(0·45/0·55)			
	Multiple regression			
Oesophagectomy:				
No	1·00	124·0	1	<0·001
Yes	0·54(0·48/0·60)			
Age (per year)	1·008(1·004/1·012)	13·8	1	<0·001
Sex:				
Female	1·00	2·2	1	0·136
Male	1·07(0·98/1·17)			
Tumour stage:				
Confined to oesophagus	1·00	26·5	2	<0·001
Local spread or metastases	1·24(1·13/1·37)			
Not known	1·31(1·14/1·51)			
Tumour morphology:				
All other codes	1·00	73·5	3	<0·001
Squamous cell	0·90(0·74/1·10)			
Adenocarcinoma	1·04(0·85/1·27)			
Unclassified	1·50(1·22/1·85)			
Tumour site:				
Lower third of oesophagus	1·00	9·0	2	0·011
Middle or upper third	1·06(0·94/1·18)			
Not known	1·17(1·05/1·29)			
District of residence		37·6	27	0·085

Additional analyses showed that this association was not accounted for by using the available information to adjust for age, sex, and tumour site, stage and morphology (table 4). However, the high proportion of "not known" or "unclassified" values for each of the explanatory variables, the unexpectedly high proportion of patients whose disease was classified as "confined to the organ of origin," and the very low survival for patients treated without oesophagectomy must be considered in interpreting this finding.

Discussion

These analyses provide an illustration of the potential value of cancer registrations in evaluating routine health care. In another study we found that those items of data which can be easily abstracted from medical records were reliably recorded at the Thames Cancer Registry (unpublished observations). Nevertheless, several potential biases in the present data must be acknowledged. The recording of tumour stage in clinical records is often inadequate,[14] and this was reflected in the low validity of this item in the cancer registry records. In the present data in an unusually high proportion of cases patients were reported to have disease confined to the organ of origin. This finding was probably explained by the limited documentation of tumour spread in the clinical setting. Similarly, the high proportion of "not known" or "unclassified" values for tumour stage, site, and morphology must be noted. The high proportion of misclassified values for these variables means that the results of multiple regression analyses must be viewed with caution, adjustment for confounding was probably incomplete or biased. The exceptionally short survival of patients treated without operation is also notable and this might be explained in terms of lead time bias. Thus patients presenting earlier in the course of the disease might be considered more suitable candidates for surgical treatment.

Recent discussion of the use of oesophagectomy has emphasised the uncertainty which surrounds the appropriate use of this procedure.[8-10] These data show that there was systematic variation in the use of the operation, which was partly explained by the prognostic characteristics of the patients. Thus older patients, those with tumours in the upper two thirds of the oesophagus, or those with evidence of spread were less likely to be selected for operation. In this sense oesophagectomy was used appropriately because these prognostic characteristics were also associated with an increased risk of perioperative death. Even after allowing for these variables there was systematic variation in use of the operation according to place of residence. These data did not allow a complete examination of the nature of judgements used in selecting patients for surgery. Clinicians may have used other information about prognostic characteristics of patients or the effectiveness of local surgical services before making decisions concerning the use of surgery. However, variation in the rate of use of the operation according to district of residence requires explanation.[15] A systematic examination of the clinical judgements used in selecting patients for surgery seems to be required, but such an examination is unlikely to be informative unless carried out at multidistrict or regional level.

In South East Thames and South West Thames regions perioperative mortality was lower than the figure of 33% reported from the North East Thames region in 1981[16] but substantially higher than the best reported rates.[4-8] We defined perioperative mortality as mortality occurring within 30 days of operation. This definition might have underestimated perioperative mortality through omission of deaths in hospital occurring after 30 days, but information concerning dates of admission and discharge was not available. Matthews *et al*, who also used cancer registrations, reported that patients treated by consultants who performed the operation infrequently experienced a particularly high perioperative mortality.[17] Our data did not support an association between volume and quality of care. One interpretation could be that hospitals at which oesophagectomy was performed most frequently were also more likely to accept higher risk patients for operation; for example, a higher proportion of palliative than curative operations might have been performed. Our data support the view that appropriate selection of patients as well as improved technical quality of surgical treatment are complementary approaches to reducing perioperative mortality.

Despite the high perioperative mortality patients who were selected for oesophagectomy experienced longer survival than those who were treated without the operation. This difference was not explained by using the available data to adjust for age, sex, and tumour site, stage, and morphology. However, the potential biases listed above must be emphasised. Although a therapeutic effect of

operation cannot be excluded, the most reasonable explanation in this non-randomised study was that clinical judgements used in selecting patients for oesophagectomy were independent markers of a good prognosis.[18] Thus until the nature of that selection is fully understood it is unlikely that the outcomes of the operation can be objectively evaluated.

The results of this analysis focus attention on the way treatment choices are made by patients, their doctors, and others responsible for purchasing care. Understanding the nature of selection for different forms of treatment is essential to understanding the subsequent outcomes. More objective and explicit methods for arriving at treatment choices are needed. The implementation of such protocols could then be evaluated as part of routine audit. For people with oesophageal carcinoma such methods should take into account the range of alternative treatments, the quality as well as duration of survival, and the considerable variation in attitudes to different costs and benefits among patients.[19] Such an approach would then preclude "paternalistic decisions based on 'my clinical experience with patients who have your disease.'"[19]

1 House of Commons Public Accounts Committee. *Quality of clinical care in National Health Service hospitals*. London: HMSO, 1989. (Tenth report: session 1988-9.)
2 Office of Population Censuses and Surveys. *Mortality statistics: cause, 1989*. London: HMSO, 1991. (Series DH 2, No 16.)
3 Earlam R, Cunha-Melo JR. Oesophageal squamous cell carcinoma. I. A critical review of surgery. *Br J Surg* 1980;67:381-90.
4 Dark JF, Mousalli H, Vaughan R. Surgical treatment of carcinoma of the oesophagus. *Thorax* 1981;36:891-5.
5 Pagliero KM. Treating carcinoma of the oesophagus [letter]. *BMJ* 1991;303:1202.
6 Kaul TK, Rowland CG, Pagliero KM. Carcinoma of the oesophagus: treatment of radical surgery or brachytherapy. In: RF Mould, ed. *Brachytherapy 2. Proceedings of the fifth international Selectron users' meeting, 1988*. Leersum: Nucletron, 1989:449-58.
7 Desa L, Raghunath AS, Chawla SL, Peel ALG, Dellipiani AW. Treatment policy for the management of carcinoma of the oesophagus. *Br J Surg* 1988;75:275-8.
8 Khoury GA. Squamous cell carcinoma of the oesophagus: 10 years on. *Ann R Coll Surg Engl* 1991;73:4-7.
9 Bown SG. Palliation of malignant dysphagia: surgery, radiotherapy, laser, intubation alone or in combination? *Gut* 1991;32:841-4.
10 Earlam R. An MRC prospective randomised trial of radiotherapy versus surgery for operable squamous cell carcinoma of the oesophagus. *Ann R Coll Surg Engl* 1991;73:8-12.
11 World Health Organisation. *International classification of diseases for oncology*. 1st ed. Geneva: WHO, 1976.
12 Harrell FE. The LOGIST procedure. In: *SAS Users' Group International. SUGI supplemental library users' guide*. Version 5, ed. Cary, North Carolina: SAS, 1986:269-93.
13 Dixon WJ. *BMDP statistical software manual. Vol 2*. Berkeley, California: University of California Press, 1990:759-806.
14 Fiegl P, Glaefcke G, Ford L, Diehr P, Chu J. Studying patterns of cancer care: how useful is the medical record? *Am J Public Health* 1988;78:526-33.
15 Bunker JP. Variations in hospital admissions and the appropriateness of care: American preoccupations? *BMJ* 1990;301:531-2.
16 Earlam R. Oesophageal cancer treatment in North East Thames region 1981: medical audit using hospital activity analysis data. *BMJ* 1984;288:1892-4.
17 Matthews HR, Powell DJ, McConkey CC. Effects of surgical experience on the results of resection for oesophageal carcinoma. *Br J Surg* 1986;73:621-3.
18 Pompei P, Charlson ME, Douglas RG. Clinical assessments as predictors of one year survival after hospitalisation: implications for prognostic stratification. *J Clin Epidemiol* 1988;41:275-84.
19 McNeil BJ, Weichselbaum R, Pauker SG. Speech and survival: tradeoffs between quality and quantity of life in laryngeal cancer. *N Engl J Med* 1981;305:982-7.