

Results of Surgical Resection of Oesophageal Carcinoma in Singapore

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Abstract

Introduction: The 5-year survival rate after resection of oesophageal cancer is still poor, reported to be between 5% to 34% in the literatures. We conducted this retrospective study to determine the prognostic factors and long-term survival rate for surgical resection of oesophageal carcinoma in Singapore. **Materials and Methods:** Sixty-seven consecutive patients who underwent surgical resection of oesophageal carcinoma from January 1989 to December 1996 were reviewed. **Results:** Majority of the patients were Chinese (94%), males (81%) with a history of dysphagia (96%), cigarette smoking (84%) and alcohol ingestion (58%). The median age at surgery was 63.6 (range 29 to 81) years. Sixty-four patients had squamous cell carcinoma of the oesophagus and 3 patients had adenocarcinoma. The lower one-third of the oesophagus was the most common site (48.6%) followed by the middle third (46%). Postoperative complications included pneumonia (43.3%), vocal cord paralysis/paresis (19.4%) and anastomotic leakage (17.9%). Thirty-day postoperative mortality was 7.5%. There was an almost equal number of patients undergoing transhiatal (34 patients) and transthoracic approach (33 patients). There was no significant difference in postoperative complications and survival outcome for both approaches. The median survival was 15.3 months after surgery. Tumour features such as depth of involvement and TNM stage were useful in predicting survival ($P < 0.05$, log-rank test). **Conclusions:** We conclude that the poor outcome of surgical resection (5-year survival rate was 18% by Kaplan-Meier survival plots) was mainly attributed to late presentation (80% patients had T3 or T4 tumour).

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Key words: Carcinoma of oesophagus, Chemo-irradiation, Transhiatal and transthoracic resection

Introduction

Although the incidence of oesophageal carcinoma is declining, it still remains a common cancer in Singapore. From 1988 to 1992, it was the ninth most common cancer in males (age-standardised rate, 8.9 per 100,000).¹ However, studies on oesophageal cancer locally were few and mainly on non-surgical modalities.²⁻⁴ A number of factors, such as age, sex, depth of tumour invasion, location, length, histological types, lymph nodes status and surgical methods of resection had been shown to be indicators for long-term results.^{5,6} The aim of this study was to review retrospectively the immediate postoperative outcome and influence of some of these factors on the long-term survival after surgical resection of oesophageal carcinoma in Singapore's predominantly Chinese population.

Materials and Methods

The records of 67 consecutive patients who had surgical resection for carcinoma of the oesophagus (excluding the cardio-oesophageal junction) at the Department of Surgery,

Singapore General Hospital over an eight-year period from 1 January 1989 to 31 December 1996 were reviewed.

Patient's presenting symptoms (grade and duration of dysphagia, regurgitation, weight loss and other complaints) were documented (Table I). Length of cancer involvement was determined preoperatively by endoscopy or radiological imaging. All patients had preoperative computed tomographic (CT) scan of the thorax and upper abdomen to stage the tumour. Staging of disease was according to the TNM (tumour, nodes and metastasis) classification.⁷ Histological type and grade were noted in all cases through biopsy or resected specimen (Table II). Operative morbidity and mortality were defined as postoperative complications and death within 30 days of surgery. Survival was measured from the date of operation. Statistical analysis was done using computer statistical software SPSS version 6.1. Univariate analysis was performed by Mann-Whitney U test for continuous variable and by chi-square test (or by Fisher Exact Test for small numbers) for categorical variable. Survival curves were calculated using the Kaplan-

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TABLE I: PRESENTING SYMPTOMS

Presenting symptoms	n (%)
1) Dysphagia	64(95.5)
a) to solid	36
b) to soft diet	11
c) to puree	10
d) complete	7
2) Loss of weight	35(52.2)
3) Regurgitation	26(38.8)
4) Melaena/haemetemesis	5 (7.5)
5) Dyspepsia only	1 (1.5)

TABLE II: TUMOUR CHARACTERISTICS

		n (%)
1) Histology	Squamous cell carcinoma	64 (95.5)
	Adenocarcinoma	3 (4.5)
2) Stage	Tis	2 (3.0)
	T1	1 (1.5)
	T2	10 (14.9)
	T3	42 (62.8)
	T4	12 (17.8)
	N0	38 (56.7)
	N1	29 (43.3)
	Stage 0	2 (3.0)
	Stage I	1 (1.5)
	Stage II	28 (41.8)
	Stage III	26 (38.8)
	Stage IV	10 (14.9)
3) Site	Upper 1/3	4 (6.0)
	Middle 1/3	31 (46.3)
	Lower 1/3	32 (47.7)

Meier method with log rank test for survival comparisons. Statistical significance was assumed at $P < 0.05$.

Results

Incidence and Patients Demography

Of the 67 patients in this study, 54 were males and 13 were females. Median age at surgery was 63.6 (range 29 to 81) years. Majority of the patients were Chinese (94%), with Malays (3%) and Indians (3%) contributing to the rest equally. Most of the patients had long history of cigarette smoking (83.6%) or alcohol drinking (58.2%). Only 2 patients had past history of caustic soda ingestion. As dysphagia is usually the first symptom of oesophageal cancer, 64 patients (95.5%) in our series presented with various degrees of dysphagia (Table I). The median time from the onset of dysphagia to the decision to operate was 1.5 months (range 2 weeks to 12 months). For the remaining 3 patients who did not have dysphagia, 2 patients had melaena and the other patient presented with dyspepsia only (Table I).

TABLE III: TRANSHIATAL VS TRANSTHORACIC APPROACH

	Transhiatal (n = 34)	Transthoracic (n = 33)	P value
Patients profile			
a) Median age (y)	66	63	0.48
b) Male/Female	29/5	25/8	0.32
c) Race (Chinese)	32	31	1.00
d) Chronic smoker	27	29	0.21
e) Pulmonary disease*	20	17	0.67
Site of tumour			0.02
Upper 1/3	1	3	
Mid 1/3	11	20	
Lower 1/3	22	10	
Stage of tumour			0.75
Stage 0 & I	2	1	
Stage II	14	14	
Stage III	14	12	
Stage IV	4	6	
30-days mortality	2	3	0.62
Postoperative morbidity			
a) Pneumonia	14	15	0.46
b) Pneumothorax	3	2	0.33
c) Hemothorax	3	2	0.33
d) Chylothorax	1	2	0.31
e) Vocal cord paresis	6	7	0.58
f) Anastomotic leak	5	7	0.25

* This includes chronic obstructive lung disease, bronchiectasis, pulmonary tuberculosis and others

Types of Surgical Resections

Approach to oesophageal resection was at the discretion of the surgeons. Almost equal number of patients underwent transhiatal or transthoracic resection (34 versus 33 patients). Of the 33 patients who had transthoracic resection, 26 patients had 3-stage resection and 7 patients had Ivor-Lewis 2-stage resection. In the transthoracic approach, lymph node dissection included the perioesophageal, carinal, peritracheal, cardiac, perigastric (excluding coeliac) and left gastric nodes. Transhiatal resection was the favoured operation for lower oesophageal carcinoma while 3-stage resection was the commonest approach for carcinoma of the upper and mid-oesophagus (Table III). The stomach was used in reconstruction for all cases. Sixty patients had cervical anastomoses and the remaining seven patients had intrathoracic anastomoses.

Postoperative Mortality and Morbidity

There were 5 postoperative deaths (7.5%) in this series. Two patients died from myocardial event, 2 patients died of pneumonia and the remaining patient died of septicaemia and acute renal failure. Major complications are shown in Table IV.

The patient profiles and tumour characteristics of patients who underwent transthoracic and transhiatal resection

TABLE IV: MAJOR POSTOPERATIVE COMPLICATIONS

Postoperative complications	n (%)	n (%)
Pneumonia		29 (43.3)
without respiratory failure	19 (28.4)	
with respiratory failure	10 (14.9)	
Vocal cord paresis/paralysis		13 (19.4)
Benign anastomotic stricture		12 (17.9)
Anastomotic leakage		12 (17.9)
clinical with fistula	8 (11.9)	
radiological only	4 (6.0)	
Re-operation		7 (10.4)
gastric outlet obstruction	2 (3.0)	
wound dehiscence	2 (3.0)	
haemostasis	1 (1.5)	
broncho-pleural fistula	1 (1.5)	
adhesiolysis	1 (1.5)	
Chylothorax		3 (4.5)

were almost similar. There were no significant differences in postoperative morbidity and mortality between these two groups of patients (Table III).

Survival Outcome and Prognosis

The median follow-up was 14.4 months (range 1.8 to 104 months). The median survival was 15.3 months after surgery. Thirty-nine patients (58.2%) were dead at a median of 12.9 months after surgery (range 1.8 to 55.0 months). Eighteen patients (26.9%) were still alive with 3 patients surviving more than 5 years. These 3 patients who survived for more than 5 years belonged to early stage of diseases (Stage 0 to IIa). Five patients (7.5%) were lost to follow up. The overall survival of all patients is shown in Figure 1. The 3- and 5-year survival rates were 33% and 18%, respectively. Only TNM stage, depth of tumour involvement and age of more than 70 years were of prognostic significance by univariate analysis (Table V, Figs. 2 & 3).

Seven patients received neoadjuvant chemo-irradiation prior to surgical resection. Three patients were in Stage III and the remaining 4 patients were in Stage IV radiologically. All patients had their diseases downstaged radiologically after neoadjuvant therapy, with complete histological resolution in 5 resected specimens. Postoperative morbidity was lower than the control group except for higher incidence of anastomotic leaks (28.6% versus 16.6%) and vocal cord paresis (28.6% versus 18.3%). However, there was no 30-day mortality. At the time of review, 5 patients were still alive with a median of 28 months (range 22 to 41 months). The remaining 2 patients developed systemic metastasis and died 5 and 10 months after surgery. Early results suggested improved survival for patients who had neoadjuvant chemo-irradiation. However, the number of patients was too small and the follow-up period was too

TABLE V: UNIVARIATE ANALYSIS OF SURVIVAL

	Log rank test
Patients factors	
a) Age (>70 years)	$P < 0.01$
b) Sex	ns
c) Race	ns
Presenting symptoms	
a) Degree of dysphagia	ns
b) Duration of dysphagia	ns
Tumours features	
a) TNM Stage	$P < 0.01$
b) Depth	$P = 0.01$
c) Lymph node status	ns
d) Length	ns
e) Site	ns
f) Histological grade	ns
Route of resection (Transhiatal vs transthoracic)	ns

ns: not significant

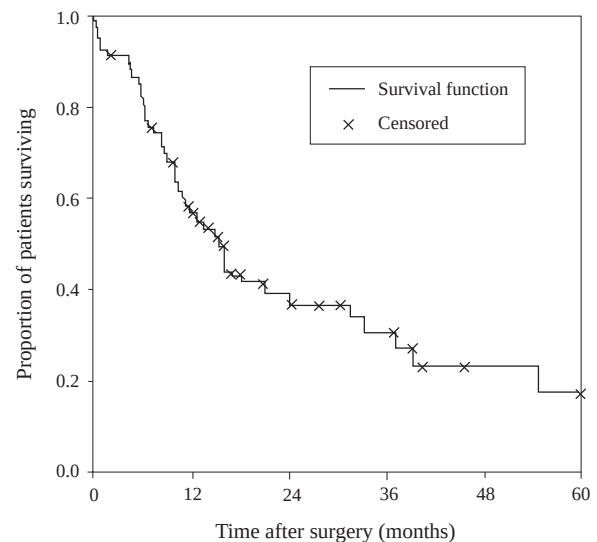


Fig. 1. Overall survival.

short to reach any statistical significance.

Discussion

The 5-year survival rate after surgical resection of carcinoma of the oesophagus is still poor, reported to be between 5% to 34%.⁸ Some authors argued that transthoracic approach achieved improved long-term survival as it allowed better oncological clearance with a more complete removal of involved lymph nodes than transhiatal route.^{5,9,10} However, this theoretical survival benefit was not evident in two recent prospective randomised trials comparing both resection routes.^{11,12} To the best of our knowledge, our series is the first published local data comparing both approaches in oesophagectomy for carcinoma of the oesophagus. Tumour staging was well-matched in both groups of patients (Table III). We found no survival benefit

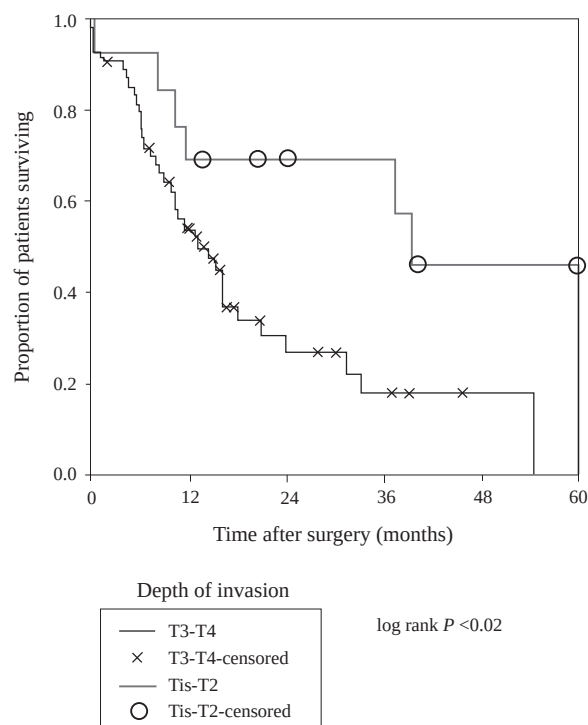


Fig. 2. Survival comparison by tumour depth.

in either approach. Thus, we conclude that the prognosis of oesophageal carcinoma depends mainly upon tumour stage at presentation, not on resection technique.

Transhiatal approach theoretically minimises pulmonary infection as it avoids painful thoracotomy incision and the need to collapse one lung.¹³ Results of retrospective studies were inconclusive in this aspect.¹⁴⁻¹⁶ Two recent prospective randomised trials showed no obvious respiratory benefit by the transhiatal route.^{14,15} However, there was no mention of distribution of patients with regard to preoperative respiratory-risk in one of the trials.¹¹ In our series, both groups of patients had similar chronic respiratory diseases and age distribution (Table III). There was no obvious decrease in incidence of pneumonia in transhiatal approach. As this is a retrospective study and the approach of resection was at the surgeon's discretion, we could not discount selection bias in our study. Transhiatal dissection of the oesophagus is blunt and sometimes blind, and could result in airway-injury, bleeding, chylothorax and recurrent nerve palsy. However, there was no significant increase of the above injuries in our series. Thus, we conclude that transhiatal resection is as safe as transthoracic approach.

Construction of oesophageal-gastric anastomosis in the neck was favoured in our department. It avoids the disastrous complications of intrathoracic leaks which are associated with a mortality rate as high as 50%.¹⁷ The zero mortality rate from anastomotic leak in our series could be accounted by the fact that only a small number of the patients in our

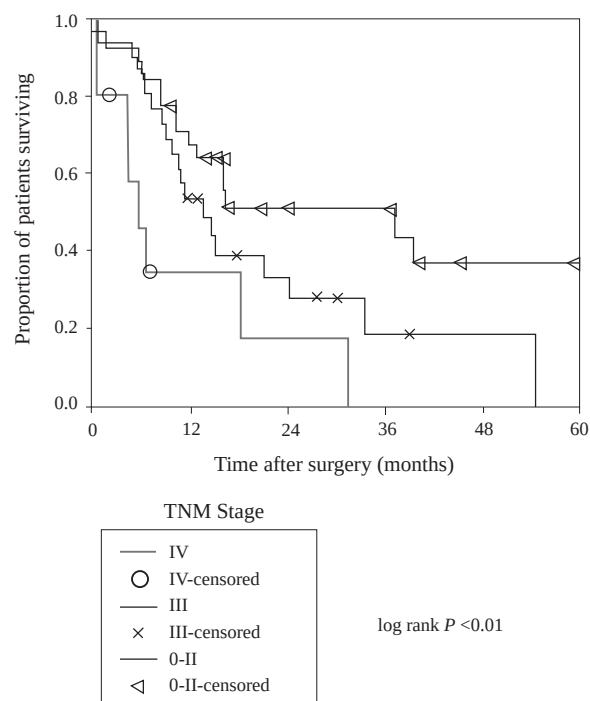


Fig. 3. Survival comparison by stage.

series ($n = 7$, 10.3%) had intrathoracic anastomoses. In addition, we did not find any significant increase of leak from cervical anastomoses compared to intrathoracic anastomoses (18.3% versus 14.3%) as suggested by some authors.¹⁴ They attributed the increase leaks to tension and ischaemia at the anastomotic site from maximal stretching of the organ for reconstruction to reach the neck. Our findings are similar to the series from Hong Kong on resection of 531 oesophageal cancer where the leakage rate was 18.8% versus 16.2% for cervical and thoracic anastomoses.¹⁷ All leaks in our series closed spontaneously between 3 weeks to 2 months after conservative therapy.

Our series 5-year survival rate of 18% is comparable with figures reported in Muller's review article (mean 20%, SD11%)⁸ on surgical resection for oesophageal cancer in over 75,000 patients. The poor prognosis of resection in our series could be related to late presentation of disease as almost 80% of the patients had cancer spread to adventitia and beyond at the time of surgery. This was further compounded by the fact that early detection of presenting surgical symptoms did not correlate well with early stage of disease and better long-term survival rate, in agreement with previous reports.^{6,18} This can be explained by the fact that rapid dissemination of the cancer is due to specific anatomical structure of the oesophagus (the thin muscular wall, absence of serosa and presence of aerolar fibro-fatty tissue rich in lymphatic surrounding the oesophagus).⁶

Thus, efforts to improve outcome of surgical resection of

the oesophageal carcinoma should focus on detection of early diseases. Abrasive cytology screening by the health authority in the People Republic of China had demonstrated increase in the detection of early cancer as well as improved survival.¹⁹ However, this is not feasible in Singapore as carcinoma of the oesophagus is not as prevalent as in China. Following the publication by Leichman et al in 1984,²⁰ intense interest has been focused on the use of neo-adjuvant chemo-irradiation in improving the survival outcome after surgical resection. About two-thirds of published trials have found that neoadjuvant therapy produces a survival advantage compared with controls.^{21,22} In our series of 7 patients with locally advanced cancer who received neoadjuvant chemo-irradiation, all had their diseases downgraded and early results suggested trends towards prolonged survival. Further prospective randomised trials are needed to evaluate the survival benefit of neo-adjuvant therapy. In the absence of any comprehensive screening programme for early detection in the local context, neoadjuvant chemo-irradiation may offer hope for this disease with such poor prognosis.

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