

Survival after resection of small cell carcinoma of the bronchus

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ABSTRACT Forty patients who underwent curative resection for oat cell carcinoma of the bronchus between 1959 and 1974 are reviewed. During the same period there were 24 patients who underwent thoracotomy but who were found to have inoperable lesions. Of the 40 patients who underwent curative resection, 11 patients remain alive and well with no evidence of recurrence. Ten of these patients have survived five years or more, an overall five-year survival rate of 25%. We consider that surgery should be considered as a possible first line of treatment in patients with small cell carcinoma of the bronchus.

The prognosis of patients with small cell carcinoma is reported to be poor.¹⁻⁶ The Medical Research Council Working Party, evaluating different methods of therapy for carcinoma of the bronchus, concluded in its report in November 1966 "that despite its very limited effect, radical radiotherapy is preferable to surgery in the treatment of small cell or oat cell carcinoma of the bronchus."⁷

This investigation and the conclusions reached have been questioned on the grounds that in all cases the diagnosis was made by rigid bronchoscopy and that too many surgeons were concerned in patient selection.^{8,9} However, surgery is often withheld since surgical results are still generally considered no better than those obtained with other modes of therapy. If this attitude persists as the incidence of preoperative histological typing increases with the introduction of the fiberoptic bronchoscope and greater familiarity with the technique of needle biopsy, more patients with small cell carcinoma will be denied surgery.

It has been our policy to exclude from surgery only those patients who have lesions judged inoperable on bronchoscopy, those who have evidence of distant metastasis, or those who are considered to be medically unfit to withstand lung resection. Otherwise we have used the same criteria for selection as with other histological types of carcinoma of the bronchus. Where it has

been possible to perform resection, we have attached great importance to as complete an extirpation of the lymphatic fields as possible.¹⁰

Patients selected for follow-up

Sixty-six patients with small cell carcinoma of the bronchus came under our care and were considered for surgery between 1959 and 1974 (table 1). Three patients were considered inoperable on radiological or bronchoscopic grounds. Sixty-three patients were subjected to thoracotomy, and of these 40 patients had curative resections, and the remainder were considered to have inoperable lesions. The number of patients undergoing resection represents 10% of all patients in whom a final diagnosis of small cell carcinoma was made at the Brompton Hospital.

This study concerns the follow-up of the 40 patients who had resections. There were nine women and 31 men with an average age of 60 years and an age range of 34 to 69 years. Twenty of these patients had pneumonectomies and 20 lobectomies. All surviving patients have been seen during the last 12 months.

Table 1 *Number of patients with oat cell carcinoma 1959-74*

Number rejected on radiological and/or bronchoscopic assessment	3
Number of thoracotomies	63
Number of curative resections	40
Number of pneumonectomies	20
Number of lobectomies	20
Total	66

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The percentage of patients submitted to thoracotomy and undergoing resection was, therefore, 63%. The resection rate is similar to that reported by Lennox *et al* (57%),⁸ Goldman (57%),⁵ and Kirklin *et al* (46%).² It is considerably higher than the 6% reported by Takita *et al*.

No case is included in this series in which there was any doubt about the histological diagnosis. This was made in each case by the same experienced pathologist.

Survival after curative resection

Among the 40 patients who had resections there were six hospital deaths (table 2). Five deaths followed pneumonectomy, a hospital mortality of 25%. There was only one death after lobectomy, a mortality rate of 5%. The operative mortality after pneumonectomy is high compared to the operative mortality rate for radical pneumonectomy of 15% reported by Brock.⁹ It is, however, similar to the operative mortality rate after resection for small cell carcinoma reported by Vincent *et al*¹¹ in 1976, although these authors do not say what percentage of these resections were radical pneumonectomies. Regardless of the histological type of carcinoma, they found the operative mortality increased with the magnitude of the operation to a level of 20% after radical pneumonectomy.

If the operative mortality after resection for small cell carcinoma is high, as appears to be the case, this may reflect both the radical approach

Table 2 *Survival of patients undergoing curative resection*

Hospital deaths	6
Late deaths	1
Unknown	1
Death caused by recurrence	21
Number of surviving patients	11 (10 longer than five years)

Table 3 *Surviving patients*

Patient number	Year	Age (yr)	Procedure	Length of survival (mo)	Outcome
1	1965	68	L	156	Died of squamous Ca of bronchus
2	1966	38	L	142	Alive and well
3	1969	56	L	104	Alive and well
4	1969	61	P	103	Alive and well
5	1969	34	P	99	Alive and well
6	1970	45	L	99	Alive and well
7	1971	59	L	79	Alive and well
8	1972	54	L	75	Alive and well
9	1972	61	L	75	Alive and well
10	1972	58	P	69	Alive and well
11	1974	48	L	40	Alive and well

Average age of survivors = 60 yr
Average age of all patients = 60 yr

to surgery, required for surgical "cure," and the nature of the underlying disease. There were 21 deaths from recurrent disease. One patient died one month after leaving hospital from unknown causes, and another patient died at eight months after the late development of a bronchopleural fistula.

Ten patients survived for five years or more and nine of these patients are alive and well (table 3). One patient died from a second carcinoma of the lung of the squamous cell type 156 months after surgery. The eleventh surviving patient is alive and well after four years. The survival rate after pneumonectomy was, therefore, 15% and 40% after lobectomy.

Preoperative diagnosis

A record of preoperative bronchoscopy is available in 36 of the 40 patients (table 4). Eight of these patients had a normal bronchoscopy. Twenty-eight patients had an abnormal bronchoscopy but in only 15 was a positive biopsy obtained by sputum cytology. Five of the 11 long-term survivors had an abnormal bronchoscopy and a positive biopsy was obtained in three. Expressing this another way, three out of 15, 20% of patients with a positive biopsy survived for five years or more.

Only 17 out of 40 patients had a preoperative diagnosis of small cell carcinoma. However, we would like to emphasise that the diagnosis was made by rigid bronchoscopy, and we feel with the introduction of the fiberoptic instrument a greater percentage of positive preoperative biopsies will, in future, be obtained. In other reported series the incidence of preoperative histological diagnosis varies from 27 to 77%.^{1 4 8 12}

Evidence of gland involvement

The incidence of microscopic evidence of gland involvement is shown in table 5. Ten patients had no evidence of gland involvement. Four of these patients survived more than five years and four patients died of recurrent disease. Of the 11 long-term survivors seven patients had hilar gland

Table 4 *Preoperative diagnosis*

	All patients (40)	Survivors (11)
Normal bronchoscopy	8	3
Abnormal bronchoscopy (negative biopsy)	13	5
Abnormal bronchoscopy (positive biopsy)	15	3
Sputum cytology only	2	
Unknown	2	

Table 5 Microscopic evidence of gland involvement

	None	Hilar	Mediastinal
All patients	10 (25%)	30 (75%)	6 (15%)
Survivors	4 (36%)	7 (63%)	2 (28%)
Dying of recurrence	4 (19%)	13 (66%)	4 (19%)

involvement.

Long-term survival is, therefore, possible in the presence of gland involvement and the advantages of a radical procedure are apparent.

Death from recurrent disease

Twenty-one of the 40 patients died from recurrent disease (table 6). Information from necropsy is available in 17 cases. The remaining four patients were reported to have died of carcinomatosis. Information from the 17 necropsies revealed that nine patients had metastatic disease only, seven patients had metastatic disease plus local recurrence, and one patient had evidence of local recurrence only.

The reason for failure of surgery in nine patients, therefore, is probably related to the inability to obtain adequate staging of systemic disease. With currently available techniques for staging, fewer patients with subclinical metastases should be subjected to surgical procedures and an increase in the survival rate of those undergoing resection might be expected.

In the figure the survival curves of 40 patients with small cell carcinoma are compared with those of 40 patients with squamous carcinoma matched for age, procedure, and year of operation, and operated upon by the same surgical team.

In the small cell group virtually all deaths from recurrent disease occur within 12 months of operation. In the squamous carcinoma group, deaths from recurrence accumulate steadily over three to four years. These curves illustrate the more aggressive nature of the small cell tumour.

As would be expected a greater percentage of surgical cures have been obtained in the squamous group. However, the five-year survival figure of 52% may not be representative as this number of cases is a small percentage of the total undergoing resection for squamous carcinoma between 1959-74.

Table 6 Death from recurrent disease

Carcinomatosis	4
Metastatic disease only, no local recurrence	9
Local recurrence ± metastases	8

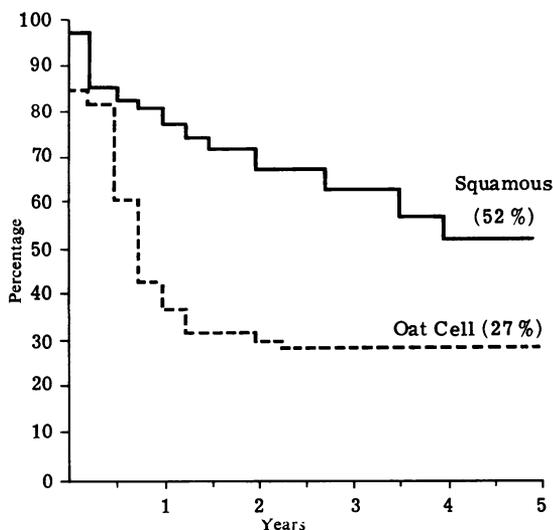


Figure Survival of patients with oat cell and squamous carcinoma undergoing surgical resection by the same surgical team and matched for year of operation, age, and procedure.

Discussion

The incidence of long-term survival in our series of patients justifies the incumbent mortality, morbidity, and discomfort of any operative procedure.

The five-year survival rate in other reported series varies between 0% and 36%. The highest survival rate of 36% reported by Higgins *et al*¹³ reflects the peripheral situation of the resected tumours. Friese *et al*¹⁴ reported a 37.5% survival rate in patients undergoing lobectomy for small cell carcinoma. They, like ourselves, do not regard mediastinal node involvement as a contra-indication to pulmonary resection. The number of surviving patients in our series who had histological evidence of hilar (64%) and mediastinal (18%) gland involvement clearly illustrates the benefit of radical surgery.

Postmortem findings in a series of patients with oat cell carcinoma reported by Takita *et al*⁶ suggested that the spread of the disease is not uniformly rapid and fatal. In addition, Goldman⁵ reported an association between improved survival and varying histological appearances with some features of differentiation such as rosette formation and pallasading of cells. There are histological and histochemical similarities between the small cell carcinoma and the carcinoid tumour,¹⁵ and attention has been drawn to the

“behavioural overlap” between the oat cell tumour and the atypical carcinoid. Long-term survival may occur when the tumour is at one end of a spectrum of malignancy.

Alternative methods of therapy with single or multiple agent chemotherapy have so far produced only isolated incidences of long-term survival although they do provide a high rate of remission and worthwhile palliation.¹⁶ Meyer¹⁷ recommended surgical resection in selected cases followed by a multiple agent chemotherapeutic regime, at the same time calling for controlled trials to establish the usefulness of adjuvant therapy.

At present, we conclude that surgery offers the best chance of long-term survival in small cell carcinoma of the bronchus. Avoidance of delay in diagnosis, early referral, and radical surgery, where possible, are strongly recommended.

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