

Survival in small cell lung carcinoma after surgery

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ABSTRACT In a retrospective study of long term survival in patients with small cell carcinoma of the lung who had been treated purely by surgery, 1820 patients with lung cancer seen during the 15 years 1962-77 were reviewed and reclassified histologically and according to the TNM system. Of these patients, 924 had had resections and 284 exploratory thoracotomies. Cancer chemotherapy was not used in this period and radiotherapy was given only occasionally as palliative treatment. Seventy seven of the patients having pulmonary resections had small cell carcinoma (8.4%), and there were six survivors among the 71 with T_{1-2} , N_{0-1} , M_0 tumours. The five and 10 year survival rates were both 12%. The histological specimens from these six patients with a small cell carcinoma who survived more than 10 years were re-evaluated and confirmed as small cell by an independent group of pathologists. It seems justified to conclude that a selected group of patients with small cell carcinoma should be treated by surgery alone without adjuvant chemotherapy, which might reduce the long term survival.

The results of surgery for lung cancer have not improved over the years, apart from the reduction of perioperative complications.¹ There has been a change in the approach to treatment, with a move from surgery alone to chemotherapy and irradiation, or combinations of these three modalities. This is especially so for small cell carcinoma.²⁻⁴ The histological classification may be difficult, but is of major importance in comparing results from different series.⁵ The TNM classification of small cell carcinoma is superior to staging purely on the basis of limited and extensive disease.⁶ We have found only one purely surgically treated series of patients with small cell carcinomas classified after the publication of the World Health Organisation criteria in 1981.⁷

The aim of this paper is to present the long term survival of an unselected series of patients with lung carcinomas treated purely surgically over 15 years, which we have reviewed and classified afresh on the basis of microscopy. During this period chemotherapy was not used, so small cell carcinomas had been evaluated for surgical treatment in the same way as other types of lung cancer.

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Patients and methods

The total number of patients with lung cancer seen at the department of thoracic and cardiovascular surgery in Odense from 1 September 1962 to 31 August 1977 was 1820 after reclassification. Of these, 924 underwent resection, the indication for operation being the possibility of cure. In 284 patients an exploratory thoracotomy was performed and the remaining 612 patients were not operated on. No patient received chemotherapy; a few had palliative radiotherapy after operation, but no combined treatment was planned.

The clinical records of all operated patients were re-evaluated by two surgeons and were reclassified according to the TNM system.⁸ Before operation all patients had chest radiographs performed in two planes and all underwent bronchoscopy. Mediastinoscopy was done in 45 of the 77 patients who had pulmonary resections and in 36 of the 58 patients who had explorations. During operation enlarged lymph nodes were removed and examined separately but proper mediastinal dissection was not performed routinely. The pathological description of the specimen included the tumour, the lymph nodes, and the resection line. In the classification of the primary tumour, T_3 tumours could easily be distinguished, whereas discrimination between T_1 and T_2 tumours

was not always possible. Classification according to nodal disease was fairly reliable, but a clearcut distinction between hilar disease and subtle disease of mediastinal nodes was not always possible, and in this way underestimation may have occurred. Classification according to distant metastases was based on the clinical description and the chest radiograph.

All histological specimens were reclassified blindly by one pathologist according to the WHO 1981 criteria.⁹ Among the patients who had explorations no histological material was available in 45 cases. Among the patients who had resections the material was missing in two cases. The microscopic material from the seven patients classified as having small cell carcinoma after the first review and who survived for more than five years was re-evaluated blindly by an independent group of pathologists. The diagnosis of small cell carcinoma of intermediate cell type was confirmed in six patients and changed to poorly differentiated squamous cell carcinoma in one patient.

Results

Of the 284 patients who had an exploratory thoracotomy, 58 (24%) had small cell carcinoma.

Among the 924 resected tumours, 77 (8.4%) were small cell carcinomas. In this group one patient classified as M_1 had a metastasis removed from the brain before the lung resection. Five other patients were classified as T_3 . None of these six patients survived for one year. Of the remaining 71 patients classified as T_{1-2} , N_{0-1} , M_0 , six have survived—for 10, 10, 10, 13, 16, and 17 years.

Analysis of survival after resection (table 1) for patients with small cell carcinoma compared with those with non-small cell carcinoma showed that 8% (6/77) of all patients with small cell carcinoma survived for five and 10 years, while the corresponding survival rates were 26% and 18% respectively for non-small cell carcinoma. The distribution of histological subtypes of small cell carcinoma in relation to lymph node classification is given in table 2. The metastatic rate is significantly higher in the oat cell group than in the intermediate cell type group ($\chi^2 = 6.33$; $p < 0.05$). All survivors were in the latter group and only at the N_0 and N_1 stages. Among the 19 patients at the N_2 stage only two lived longer than one year and none more than three.

The type of operation is correlated with the histological subtype of the tumour in table 3. The number of pneumonectomies is significantly higher in patients with oat cell carcinoma than in those with carcinoma of intermediate cell type ($\chi^2 = 8.77$; $p < 0.01$). Survival was found after segmental resection as well as

Table 1 *Survivors after surgical resection for non-small cell and small cell carcinoma*

Duration of survival	Number surviving	
	Non-small cell carcinoma	Small cell carcinoma
1 y	515/847	29/77
3 y	291/847	7/77
5 y	222/846	6/77
≥10 y	121/794*	6/77

*Not all survivors have been observed for 10 years.

Table 2 *Relationship between histological subtype and lymph node disease in T_{1-2} , M_0 small cell carcinoma (numbers in parentheses indicate five year survivors)*

	Number with cell type			Total
	Oat cell	Intermediate	Mixed	
N_2	13	5	1	19
N_1	9	6 (2)	0	15 (2)
N_0	9	24 (4)	4	37 (4)
Total	31	35 (6)	5	71 (6)

Table 3 *Relationship between histological subclassification and type of operation in T_{1-2} , N_{0-1} , M_0 small cell carcinoma (numbers in parentheses indicate five year survivors)*

	Number with cell type			Total
	Oat cell	Intermediate	Mixed	
Pneumonectomy	25	16 (3)	3	44 (3)
Sleeve resection	1	2	0	3
Lobectomy	5	14 (1)	2	21 (1)
Minor resection	0	3 (2)	0	3 (2)
Total	31	35	5	71 (6)

after pneumonectomy. One surviving patient had radiotherapy to the mediastinum after pneumonectomy and should be omitted.

Discussion

Small cell carcinomas constitute about 20% of all lung carcinomas.¹⁰ The question of long term survival of patients with small cell carcinoma is controversial: Fox and Scadding¹¹ and Mountain,¹² found no five year survivors after resection among 34 and 41 patients respectively. Other authors^{7 13-18} have had from 10% to 25% of patients surviving after treatment with surgery alone. The different series, however, have been collected over a considerable period and changes in classification have occurred, so direct comparison is difficult. Despite the relatively good interobserver agreement (about 95%) when small cell carcinoma is diagnosed as an entity by different pathologists,^{19 20} ensuring proper classification of the

few survivors is crucial in the evaluation of long term survival.

Moreover, in the typing of subgroups greater inter-observer variation is generally found.²¹ Consequently, to make sure that the number of long term survivors of small cell carcinoma was not inflated with questionable cases, we asked an independent group of pathologists to classify blindly our microscopical specimens from the surviving patients. In this way one of our original seven cases of small cell carcinoma was reclassified as possible squamous cell carcinoma and we moved it into that group. Exact classification should be easier with resection specimens than with preoperative biopsy material, which is often sparse and crushed,⁵ so the number of long term survivors with small cell carcinoma could be considered to include only definite cases.

We have only intermediate cell type carcinoma represented among our survivors, while others have equal numbers of oat cell and intermediate cell carcinoma,⁷ and differences in prognosis between oat cell and intermediate cell types are unsure. In the present series the oat cell carcinoma was generally in a higher N stage and extended more centrally. This caused a higher pneumonectomy rate as well as a poorer prognosis.

A good result after treatment of the intermediate cell type by surgery supplemented by chemotherapy was achieved by Hayata *et al*²: nine of 10 five year survivors had had carcinomas of the intermediate cell type and 10% of patients with this type survived for more than five years, although this cell type has been said to have a poorer response to chemotherapy than other types.²² Østerlind *et al*²³ on the other hand, found a poor long term survival after chemotherapy alone and also, for the group of "operable" small cell carcinoma, for surgery followed by chemotherapy. Toxic reactions in the bone marrow during chemotherapy are well known complications and may be lethal.²⁴ Volk *et al*²⁵ found that chemotherapy might even increase morbidity and mortality in those patients who were disease free more than 12 months after treatment. The value of chemotherapy, alone or in combination, although it has an indisputable positive effect on median survival, has been disappointing with regard to long term survival.²⁶

In our series the TN classification was based on operative findings and pathological material but the staging according to distant metastasis was based on the clinical findings in patients supported by chest radiography. A routine search for dissemination by bone marrow biopsy, peritoneoscopy, and radioactive scanning²⁷ or computed tomography²⁸ might reduce the number of M₀ cases and thereby the number of unnecessary operations.⁸ With this in mind, and the attitudes of others (summarised in ref 26), we

conclude that a small group of all histological subgroups of small cell carcinoma staged as T₁₋₂, N₀₋₁, M₀ should be treated by surgical resection alone without adjuvant chemotherapy, which might reduce the possibility of long term survival.

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