Chest wall invasion in carcinoma of the lung

Therapeutic and prognostic implications

From 1974 through 1983, 125 patients underwent operation at Memorial Sloan-Kettering Cancer Center for non–small cell carcinoma of the lung invading the chest wall. (Excluded are those with superior sulcus tumors or distant metastases at presentation.) Eighty patients were male and 45 were female. Ages ranged from 33 to 88 years (median 60 years). Histologically, the tumors were epidermoid carcinoma in 46%, adenocarcinoma in 46%, and large cell carcinoma in 8%. All patients underwent thoracotomy (pneumonectomy 19, bilobectomy seven, lobectomy 75, wedge resection 10, and no pulmonary resection 14), with an operative mortality of 4%. At thoracotomy, mediastinal lymph node dissection was routinely performed, and the postsurgical stage was T3 N0 M0 in 53%, T3 N1 M0 in 13%, and T3 N2 M0 in 34%. Extrapleural resection was performed in 66 patients. En bloc resection of chest wall and lung was performed in 45 patients with an operative mortality of 2%. Complete resection of tumor was possible in 77 patients (62%). Extension of tumor beyond the parietal pleura significantly decreased resectability. The median survival of 48 patients having incomplete resection was 9 months, despite perioperative interstitial and external radiation. The actuarial 5 year survival rate (Kaplan-Meier) of 77 patients having complete resection was 40%. This percentage was not significantly influenced by the patient's age or sex or by tumor size or histologic type. Lymphatic metastases significantly reduced survival, with a 5 year actuarial survival rate of 56% for patients with T3 N0 M0 disease and 21% for those with T3 N1 M0 or T3 N2 M0 disease (p = 0.005). The extent of tumor invasion of the chest wall appeared to influence survival, but in the absence of lymphatic metastases the difference at 5 years was not significant. Complete resection offers a significant chance for long-term survival in lung cancer directly extending into parietal pleura and chest wall. Extrapleural resection or en bloc chest wall resection can be performed with a low operative mortality and an expected 5 year survival in excess of 50% in the absence of lymphatic metastases.

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Although the majority of lung cancers are confined to the chest cavity, in about 5% of cases the tumor will invade the parietal pleura and chest wall. According to the American Joint Committee on Cancer, such tumors are T3 lesions and hence Stage III carcinomas. Chest wall invasion is considered by many to indicate incurability. Coleman in 1947 first reported long-term survival in patients with bronchogenic carcinoma invading the chest wall, who were treated by combined pulmonary and chest wall resection. In his select series of five patients, two were alive and well at 5 years. Several subsequent reports have supported the surgical treatment of these tumors.

We have reviewed the experience of the past 10 years at Memorial Sloan-Kettering Cancer Center to define the factors influencing the surgical treatment and prognosis when carcinoma of the lung invades the chest wall.

Patients and methods

Since 1973, all patients admitted to the Thoracic Surgical Service at Memorial Sloan-Kettering Cancer Center with primary carcinoma of the lung have had their disease staged according to the American Joint Committee on Cancer. Detailed staging (clinical, surgical, and pathological) was completed for all patients during their admission, and this information was entered.
into a computerized tumor registry. From January, 1974, through December, 1983, there were 2,521 patients with a primary carcinoma of the lung, 233 of whom had small cell lung cancer and 2,288 non–small cell lung cancer. This study has reviewed 125 patients with non–small cell lung cancer whose primary tumor was staged T3 after surgical exploration because of direct chest wall invasion. Patients with distant metastases at presentation were excluded as were patients with superior sulcus tumors. All patients were reviewed with respect to age, sex, clinical features, methods, and results of treatment, and pathological examination of resected specimens.

Follow-up was complete in all but two patients (98%). Calculation of actuarial survival employed the Kaplan-Meier method and included operative deaths and those resulting from lung cancer. Only two deaths during the period of follow-up were unrelated to lung cancer, and both patients had no evidence of lung cancer at autopsy. These patients were included in the analysis as cases lost to follow-up. The log-rank test was used to compare survival curves, and all differences in this study were tested for statistical significance by means of the chi square and two-sided t tests. A probability level of 0.05 was considered significant.

Results

Of the 125 patients included in this study, 80 were male and 45 were female. Ages ranged from 33 to 88 years with a median of 60 years. Forty-six patients (37%) presented with chest pain that had been present from 1 to 12 months prior to diagnosis. Serum alkaline phosphatase was measured in all patients and was elevated in 42 (34%). Preoperative bone scans demonstrated increased isotopic uptake in the chest wall overlying the tumor in 13 of 62 patients (21%) so examined. Evidence of chest wall invasion was evident preoperatively on computed tomograms in nine of 16 patients (56%) in whom this examination was performed.

The histologic tumor type was epidermoid carcinoma in 58 patients (46%), adenocarcinoma in 57 patients (45%), and large cell carcinoma in 10 patients (8%). The maximum diameter of the primary tumors ranged from 1.8 to 20 cm (mean 7.1 cm).

All patients without evidence of distant metastases or medical contraindication to operation underwent thoracotomy. The suspicion of mediastinal lymphadenopathy either on radiologic study or at bronchoscopy did not preclude thoracotomy, and preoperative assessment of the mediastinum by cervical mediastinoscopy or anterior mediastinotomy was not performed. At thoracotomy a systematic mediastinal lymph node dissection accompa-

Table I. Extent of pulmonary resection in 125 patients with T3 [chest wall] lung cancer

<table>
<thead>
<tr>
<th>Type of Resection</th>
<th>Number of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>No pulmonary resection</td>
<td>14</td>
</tr>
<tr>
<td>Pneumonectomy</td>
<td>19 (3)</td>
</tr>
<tr>
<td>Bilobectomy</td>
<td>7 (4)</td>
</tr>
<tr>
<td>Lobectomy</td>
<td>75 (33)</td>
</tr>
<tr>
<td>Wedge resection</td>
<td>10 (5)</td>
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</tbody>
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Legend: The number in parentheses indicates the number in whom en bloc chest wall resection was performed.

nied the pulmonary resection. Sixty-six patients had no nodal metastases, 17 had only peribronchial or hilar lymph node metastases (N1 disease), and 42 had mediastinal lymph node metastases (N2 disease). There was no significant difference between the different cell types and the incidence of lymphatic metastases (adenocarcinoma 51%, epidermoid carcinoma 45%, and large cell carcinoma 40%).

The extent of resection was determined by the nature of the chest wall invasion, the site and size of the primary tumor, the ability to resect all tumor, and the medical condition of the patient. One hundred eleven of the 125 patients underwent pulmonary resection, the extent of which is shown in Table I. There were five postoperative deaths (4%): The causes were bronchopneumonia with respiratory failure (three), hemorrhage (one), and aspiration pneumonia secondary to a bronchopleural fistula (one). In 66 patients extrapleural mobilization of the tumor in the region of its chest wall attachment facilitated the resection. However, 45 patients required en bloc resection of lung and segments of ribs and intercostal muscles because of tumor extension beyond the parietal pleura. Segments of from one to five ribs (most commonly three) were removed and the skeletal defect was reconstructed in 30 patients. Marlex mesh was used alone in 26 patients and Marlex combined with methyl methacrylate in four patients. Skeletal reconstruction was not performed in those patients with small chest wall defects or in those with posterolateral defects lying under cover of the scapula. There was only one postoperative death among these 45 patients (2%): A 57-year-old man developed bronchopneumonia following an en bloc right upper lobectomy with segments of ribs 3, 4, 5, and 6. Skeletal reconstruction with Marlex mesh had been performed in this patient, and there was no evidence of chest wall instability in the postoperative period.

Extension of tumor into the chest wall took three forms: infiltration of parietal pleura in 70 patients, invasion of intercostal muscles or ribs or both in 55 patients, and extension into the vertebral column in 12 of these 55 patients. A complete resection of all disease in the ipsilateral hemithorax was possible in 77 patients.
No Lymphatic Metastases
\(n = 45\)

Lymphatic Metastases
\(n = 32\)

Years after resection

Fig. 1. Probability of survival in patients with non–small cell lung cancer invading parietal pleura or chest wall. A marked survival advantage is afforded by complete resection.

Fig. 2. Probability of survival following complete resection in patients with non–small cell lung cancer invading parietal pleura or chest wall. The presence of regional lymph node metastases significantly reduces survival.

Gross disease was still evident after resection in 28 patients, and the residual tumor was implanted with radiation sources in 24 of them. Twelve patients received postoperative external radiation to the area of the residual tumor, and of 17 patients with mediastinal lymph node metastases, 14 received postoperative external radiation to the mediastinum. The median survival of these 28 patients was 10 months, and 13 had local recurrence of tumor.

Of the six patients with microscopic evidence of disease in the margin as the only sign of residual disease, three received external radiation postoperatively. None of the six patients had mediastinal lymph node metastases. Local recurrence developed in two (one had received postoperative external radiation), and all died of the disease within 12 months of operation.

Of the 77 patients whose tumor was completed resected, 19 underwent pneumonectomy, six bilobectomy, 48 lobectomy, and four wedge resection. The mean diameter of the resected tumors was 7.2 cm. Invasion of the parietal pleura alone was found in 54 patients, and 23 patients had intercostal muscle or rib involvement or both. Forty-eight of the 54 tumors with only parietal pleural invasion were resected by an extrapleural dissection in the region of attachment of the tumor to the chest wall. En bloc resection of lung and chest wall was performed in the other 29 patients. In all 77 patients a systematic mediastinal lymph node dissection was performed, and the pathological stage was T3 N0 M0 in 45 patients, T3 N1 M0 in 10 patients, and T3 N2 M0 in 22 patients. Seventeen of the patients with N2 disease received postoperative external radiation to the mediast-
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Parietal Pleura
(n = 31)

Chest Wall
(n = 14)

Fig. 4. Probability of survival following complete resection in patients with non-small cell lung cancer invading parietal pleura or chest wall. In the absence of lymphatic metastases, survival is not significantly influenced by the depth of invasion.

Fig. 3. Probability of survival following complete resection in patients with non-small cell lung cancer invading parietal pleura or chest wall. The depth of invasion appears to affect survival.

timum, as did four of those patients with N1 disease. Three patients had received external radiation to the primary tumor prior to presentation at Memorial Sloan-Kettering Cancer Center.

The actuarial survival rate of these 77 patients is shown in Fig. 1. At 5 years, the probability of survival was 40%. This was not significantly influenced by the patient's sex or age or by tumor size or histologic type. However, the presence of lymphatic metastases significantly reduced survival (Fig. 2). The 5 year actuarial survival rate was 56% in those without lymphatic metastases and 21% in those patients with nodal metastases (p = 0.005). Small numbers of patients precluded a statistical comparison of survival in those with N1 nodal metastases only, as opposed to those with N2 metastases. However, there was a trend favoring survival in the N1 group of patients (5 year actuarial survival rate 35% for N1, 16% for N2).

The depth of invasion appeared to affect survival (Fig. 3). At 5 years, the probability of survival for those patients with tumor confined to the parietal pleura was 48% compared with 16% in those patients with tumors invading muscle or ribs (p < 0.02). In the absence of lymphatic metastases (Fig. 4), the probability of surviving 5 years was 62% in those patients with only invasion of the parietal pleura and 35% in those with extension into muscle or rib (p = 0.1).

Discussion

Resection has been shown to offer a significant chance of cure for patients with carcinoma of the lung confined to the lung parenchyma, with reported 5 year survival rates of 70%. Evidence of direct extension of tumor into the chest wall and the presence of regional lymph node metastases often have been considered indicators of incurability, and a surgical approach has not been recommended. At our institution, neither of these findings in patients with non-small cell lung cancer precluded thoracotomy, provided there was no evidence of distant metastases. At thoracotomy, routine mediastinal lymph node dissection accompanied extirpative procedures with attempted resection of all gross disease and the use of intraoperative interstitial radiation for any residual tumor. Using this approach, we have demonstrated a 62% incidence of complete resection in patients with invasion of the parietal pleura or chest wall and a 5 year actuarial survival rate of 40% in those patients undergoing complete resection. In the absence of regional lymph node metastases, the probability of surviving 5 years rises to 56%. This survival rate is similar to that reported by Piehler and associates. Like Piehler's group, we could find no effect of the patient's sex, the size of the tumor, or the histologic type on survival. Piehler and associates noted an improved survival rate for those patients 60 years of age or younger compared with those older than 60 years. We found no such survival advantage for the younger patient.

Although the presence of regional lymph node metastases significantly reduced survival, 12 of 32 patients with lymphatic metastases remain alive and free of disease from 5 to 84 months after complete resection, with a 5 year actuarial survival rate of 21%.

In the absence of lymph node metastases, the depth of
chest wall invasion does not significantly affect survival provided a complete resection is performed with normal macroscopic and microscopic margins. However, the extent of surgical resection necessary for peripheral carcinomas of the lung found at thoracotomy to have a parietal attachment remains controversial. Some investigators have advocated that all patients with involvement of the parietal pleura should undergo en bloc resection of the lung and chest wall rather than an extrapleural dissection. Trastek and co-workers, in comparing small numbers of patients, reported an improved survival rate when a chest wall resection was performed. Eight of their patients with involvement of only the parietal pleura underwent en bloc chest wall resection and 14 underwent an extrapleural resection. The 5 year actuarial survival rates (excluding operative mortality) were 75% and 28%, respectively, for these patients. Our approach has been different, such that in the case of parietal attachment a trial of extrapleural dissection is attempted if there is no evidence of extension of disease beyond the parietal pleura. If a tumor-free plane is readily achieved, an extrapleural resection is performed. At pathological examination in many such cases, tumor will be found to be involving visceral pleura only, and the tumor will be staged T2 rather than T3. If any resistance to dissection is encountered during the extrapleural approach, dissection is ceased and en bloc resection of chest wall and lung is undertaken. By this technique, more than 88% of tumors invading only the parietal pleura could be resected. The 5 year actuarial survival rate of these patients (including operative mortality) was 62% in the absence of regional lymphatic metastases. In only six patients, in whom subsequent pathological examination revealed involvement of only the parietal pleura, was it necessary to perform en bloc resection of chest wall and lung. The pattern of survival in these patients was not different from that of patients undergoing an extrapleural resection.

Although we recommend an initial attempt at extrapleural dissection, we have no hesitation in proceeding to chest wall resection when we suspect or find tumor extending beyond the parietal pleura. En bloc resection of chest wall was performed in 45 patients with an operative mortality of only 2%. This is significantly less than figures from other reports, in which the operative mortality has been as high as 15%. Skeletal reconstruction after chest wall resection, with Marlex mesh alone or in combination with methyl methacrylate, was used in two thirds of our patient, and chest wall instability was not a problem in the postoperative management of these patients.

The importance of a complete resection is emphasized by the poor results in those patients in whom a complete resection was not possible. The median survival of these 48 patients was only 9 months, and only one patient was alive and free of disease more than 2 years after diagnosis. Even the presence of microscopic residual disease alone was associated with a poor prognosis. Postoperative external radiation did not appear to alter this prognosis. Preoperative external radiation did not form part of our treatment plan; therefore, we cannot comment on its efficacy. Postoperative radiation was used in most patients with known residual tumor. We plan the addition of systemic chemotherapy to the postoperative treatment regimen in these high-risk patients. When a complete resection was possible, postoperative adjunctive radiation was used only in those patients with lymphatic metastases in an attempt to sterilize the mediastinum of any possible residual microscopic tumor. There are no reported randomized studies to indicate any benefit from adjunctive radiation, although Patterson and associates noted an improved survival and lower local recurrence rate in a nonrandomized group of patients who received radiation.

All patients with non–small cell lung cancer directly invading parietal pleura and chest wall should undergo thoracotomy provided there are no distant metastases, the patient’s cardiopulmonary status does not preclude operation, and there is no evidence preoperatively of spinal invasion or extensive mediastinal lymph node metastases. The last two features identify patients in whom resection is unlikely to be complete, and innovative investigational approaches appear warranted in these groups of patients. Computed chest tomography is currently done routinely to correctly assess the extent of tumor involvement, particularly if invasion of the spine is suspected. The feasibility of a major resection to encompass all affected tissues is thus assessed preoperatively, including the extent of mediastinal involvement.

At thoracotomy, a complete resection will be possible in the majority of patients, with the prognosis determined primarily by the status of the regional lymph nodes. An extrapleural resection provides adequate tumor clearance for most tumors involving only the parietal pleura. Extension of tumor beyond the parietal pleura dictates the need for en bloc resection of lung and chest wall. Since involvement of the spine had precluded resectability in 12 patients, we are currently evaluating the merit of extending our resection to include the affected vertebrae by a combined thoracic-neurosurgical approach.

If macroscopic and microscopic tumor clearance cannot be achieved, local and/or distant recurrence
invariably follows. Radiation alone does not appear to alter survival in this high-risk group of patients, and the use of systemic chemotherapy warrants investigation.

REFERENCES