Surgical Treatment of Lung Cancer*

Manjit S. Bains, M.D., F.C.C.P.

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Carcinoma of the lung is the most common cause of death due to cancer in both men and women. The American Cancer Society has projected that 157,000 new cases of lung cancer will be detected in 1990 in the United States alone and that 142,000 persons will die of the disease.1 Ironically, carcinoma of the lung is caused predominantly by smoking and is a preventable disease.2,3 Hopefully, the increased awareness of the risks of smoking, the antismoking propaganda, and increased restrictions on smoking will significantly reduce tobacco use and eventually the incidence of lung cancer.

Resection remains the most effective form of treatment for lung cancer. Success of surgical treatment for lung cancer, however, is highly dependent on the proper selection of patients. The criteria for selection depend on the histology of the tumor, the anatomic extent of disease, and the physiologic status of the patient. Candidates for resection are patients with non-small cell lung cancer (NSCLC), patients with stage I and II disease, and a limited group of patients with stage III disease in whom a complete resection is feasible (Fig 1). A wide variety of histologic types are seen

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Table 1—Histologic Classification of Lung Cancer*

<table>
<thead>
<tr>
<th>Classification</th>
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<tbody>
<tr>
<td>Epidermoid carcinoma</td>
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<tr>
<td>Keratinizing squamous carcinoma</td>
</tr>
<tr>
<td>Small cell carcinoma</td>
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<tr>
<td>Oat cell carcinoma</td>
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<tr>
<td>Intermediate cell type</td>
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<tr>
<td>Adenocarcinoma</td>
</tr>
<tr>
<td>Acinar adenocarcinoma</td>
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<tr>
<td>Papillary adenocarcinoma</td>
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<tr>
<td>Solid carcinoma with mucin secretion</td>
</tr>
<tr>
<td>Bronchioloalveolar carcinoma</td>
</tr>
<tr>
<td>Large cell (undifferentiated)</td>
</tr>
<tr>
<td>Clear cell carcinoma</td>
</tr>
<tr>
<td>Giant cell carcinoma</td>
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<tr>
<td>Adenosquamous carcinoma</td>
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</table>

*Modified from reference 5.

in lung cancer. A number of classifications of lung carcinoma have been proposed, but the one proposed by the World Health Organization in 1981 is the most widely used (Table 1). Details have been discussed elsewhere. However, the frequency of various histologic types has been changing. Adenocarcinoma of the lung has become the most frequent histologic type, responsible for 50% of all lung cancers. Epidermoid or squamous cancer is the next most frequent cancer, accounting for 30%; oat cell or small cell lung cancer (SCLC) represents 15%; while large cell cancer makes up less than 5%.

From a clinical and therapeutic standpoint, one has to

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*Fig 1. Algorithm for mediastinal lymph node dissection. EOD = extent of disease.*

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Table 2—Role of Surgery in Lung Cancer, by Stage

<table>
<thead>
<tr>
<th>Cancer Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Consider Surgery?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Occult</td>
<td>TX</td>
<td>N0</td>
<td>M0</td>
<td>Yes</td>
</tr>
<tr>
<td>0</td>
<td>T1S</td>
<td>N0</td>
<td>M0</td>
<td>Yes</td>
</tr>
<tr>
<td>I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>Yes</td>
</tr>
<tr>
<td>II</td>
<td>T1</td>
<td>N1</td>
<td>M0</td>
<td>Yes</td>
</tr>
<tr>
<td>IIIA</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
<td>Yes</td>
</tr>
<tr>
<td>IIIB</td>
<td>Any T</td>
<td>N3</td>
<td>M0</td>
<td>No</td>
</tr>
<tr>
<td>IV</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
<td>No</td>
</tr>
</tbody>
</table>

divide all the histologic types into two major categories: SCLC and NSCLC. While SCLC is considered to be a systemic disease, best treated with chemotherapy, the most effective treatment for localized NSCLC is resection. Prognosis in carcinoma of the lung is a function of the stage of disease and the completeness of resection. Precise and accurate staging is vital in the selection of the most effective treatment to determine the prognosis and make meaningful comparison, as well as reporting of results. A new international staging system for lung cancer based on TNM classification was adopted in 1986 by the International Union Against Cancer and the American Joint Committee on Cancer (Table 2). It represents an improvement in accuracy and prediction of prognosis in stages I and II and a clearer breakdown of stage III, with stage IIIA disease falling within the realm of a surgical oncologist and stage IIIB disease being more appropriately treated with nonsurgical therapy.

Occult Cancer

Diagnosis of lung cancer can be made in a small group of patients before it becomes radiologically apparent. These individuals either participate in an early detection program or submit routine sputum cytologic specimens or are investigated for hemoptysis. A positive sputum cytologic result needs to be investigated for precise localization of the primary site by careful head and neck examination, bronchoscopy, and biopsy of a visible abnormality or, if the abnormality is not visible, repeated diagnostic bronchial brushings from the same bronchopulmonary segment at two separate bronchoscopic examinations. Occasionally, the use of a hematoporphyrin derivative for in vivo fluorescent staining may demonstrate the mucosal abnormalities and facilitate the precise localization.

There are only two techniques available for early detection of lung cancer: the chest roentgenogram and the sputum cytologic examination. While the chest x-ray film is the more reliable detector of a small, peripheral, early-stage adenocarcinoma, sputum cytologic study has been more useful in detection of early squamous cancer, generally involving a central position.

In a prospective screening program by the Cooperative Early Lung Cancer Group sponsored by the National Cancer Institute and involving Johns Hopkins, Mayo Clinic, and Memorial Sloan-Kettering Cancer Center, approximately 30,000 men aged over 45 years who smoked over 1 pack of cigarettes per day were randomized to two study arms. In one arm, the individuals had a yearly chest roentgenogram, while in the other arm they had a sputum cytology examination in addition to the chest radiograph.

The incidence of lung cancer was 4 cases per thousand, with the detection of adenocarcinoma being most efficient (64%), in contrast to 53% for squamous cancer and 27% for all oat cell cancers. Only 21% of symptomatic cancers in both groups were resectable, whereas 62% of all cancers discovered on chest radiographs taken during routine physical examination or in management of unrelated illness were resectable.

Occult cancers are almost always squamous cancers. Treatment of lung cancer at this stage is complete removal of all the tumor while conserving pulmonary parenchyma. Endoscopically visible tumors may extend proximally and necessitate a wider resection or a sleeve lobectomy. Complete resection is generally curative. Because most patients have coexisting chronic obstructive pulmonary disease, they are at increased risk for surgery. One viable alternative to a resection is phototherapy, providing an approximately 50% complete response rate in tracheobronchial superficial tumors that measure less than 3 cm in surface area. However, 20% to 45% of these individuals are at risk of developing a new primary cancer, with only half of these developing in the lung.

Stage I (T1N0M0 and T2N0M0) Tumors

Tumors confined to the pulmonary parenchyma without evidence of regional lymphatic metastases or extension into adjacent structures or distant metastases are referred to as stage I tumors. Most of these are asymptomatic and are picked up on a chest roentgenogram done as part of a routine physical examination or preoperative assessment of a patient for an unrelated procedure. An abnormal chest radiograph should be compared with a previous study if one is available. Assessment of the patient with a new abnormality should address cardiopulmonary status and the ability of the patient to undergo a resection, and usually should include a computed tomographic (CT) scan to evaluate the primary tumor and the mediastinum. Obtaining a few additional sections across the upper abdomen to include the liver and adrenal glands is desirable. Any bone and joint aches and pains or any neurologic symptoms should be selectively evaluated. When multigland radionuclide scanning is carried out in the absence of symptoms or signs of metastases, approximately 13% of the scans prove abnormal, and 94% of these are false-positive. The overall positive rate for scanning for metastatic cancer in the absence of symptoms is 0.78%.

A new pulmonary nodule without any calcification mandates establishment of a histologic diagnosis. This may be attempted with sputum cytologic study or fiberoptic bronchoscopy. The chance of obtaining a diagnosis with these studies is small. Transbronchial biopsy with fluoroscopic control or a fine needle aspiration biopsy may have a higher yield. However, a negative result does not necessarily mean absence of cancer. Invariably, a thoracotomy is needed to be certain of the histology. At the time of thoracotomy, a specimen obtained with a Tru-Cut needle (Travenol Laboratories, Deerfield, Ill) is almost always diagnostic. However, a wedge biopsy or sometimes even a lobectomy may be
necessary to obtain a diagnosis.

How much to resect is dependent on the location and the size of the tumor. Lobectomy is the procedure of choice when the tumor is confined to a lobe.\textsuperscript{10,11} When the tumor involves structures in the pulmonary hilum, crosses a fissure, or involves the main bronchus, a more extensive resection becomes necessary in order to encompass all the disease and obtain clear margins. We feel that the optimal treatment of NSCLC is complete resection of the primary tumor and excision of regional lymph nodes in a systematic and meticulous manner. The role of lymphadenectomy is not only to extirpate the tumor but also to stage it accurately. A complete mediastinal lymphadenectomy should be performed irrespective of extent of pulmonary resection. Lobectomy has provided a survival of 72% in stage I lung cancers, with 83% for T1 and 65% for T2 tumors (Fig 2, Table 3). Similar results were reported by other investigators.\textsuperscript{18,19}

When the lesion is small and peripheral, conservative resection is advocated by some on an elective basis.\textsuperscript{20,21} We have performed a wedge resection or a segmentectomy selectively in patients with limited cardiopulmonary reserve or poor general medical condition. McCormack and Martini\textsuperscript{22} reported on 61 patients undergoing a segmentectomy or a wedge resection from 1949 to 1978. Of the 53 postsurgical stage I patients, 43 were T1N0 and 10 were T2N0. The predominant histologic finding was adenocarcinoma. Recurrence was observed in 10 patients, giving a local recurrence rate of 19%. The 5-year actuarial survival was 33%. Jensik\textsuperscript{23} reported on their experience with segmental resections in 499 patients from 1957 to 1986. Of these, 296 patients had a stage I or II carcinoma. Almost three fourths of these patients had a T1 lesion, and 92% of the patients were free of nodal involvement. Half of these tumors were histologically adenocarcinomas, while 33% of the patients had a squamous cancer. Postoperative mortality was 1%. Persistent air leak was the most common complication. The 5-year survival was 52%. In 36 cases (12%) a local recurrence developed.

![Survival in resected stage I non-small cell lung cancer 1973-1977 (128 patients)](image)

**Figure 2.** Survival in resected stage I NSCLC.

<table>
<thead>
<tr>
<th>Stage</th>
<th>Five-Year Survival, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>72</td>
</tr>
<tr>
<td>T1N0</td>
<td>83</td>
</tr>
<tr>
<td>T2N0</td>
<td>65</td>
</tr>
<tr>
<td>II</td>
<td>49</td>
</tr>
<tr>
<td>T1N1</td>
<td>56</td>
</tr>
<tr>
<td>T2N1</td>
<td>46</td>
</tr>
<tr>
<td>IIIA</td>
<td></td>
</tr>
<tr>
<td>T3N0 (chest wall)</td>
<td>56</td>
</tr>
<tr>
<td>T3N2</td>
<td>30</td>
</tr>
<tr>
<td>T3N0 (proximity to carina)</td>
<td>36</td>
</tr>
</tbody>
</table>

Comparing these results to the survival obtained after a lobectomy, there is a better than 15% to 20% survival benefit in patients who have undergone resection of the tumor with a lobectomy rather than a segmental resection. Preliminary data from a randomized trial by the Lung Cancer Study Group (LCSG)\textsuperscript{24} randomizing resection to a lobectomy or a lesser resection seem to indicate that similar survival may be obtained in squamous cancers. However, adenocarcinomas do poorly with limited resections. More information is needed before drawing any conclusions.

**Stage II (T1N1 and T2N1) Tumors**

Fewer than 10% of the patients with NSCLC are found to have metastases confined to N1 nodes.\textsuperscript{25} One is concerned about more central spread. Nevertheless, it is potentially curable with a resection. The failure rate is high. The patterns of recurrence are different for various histologic types. The incidence of local and distant recurrence is equal in patients with epidermoid cancer. In contrast, distant metastasis is by far the most common type of recurrence in patients treated for adenocarcinoma of the lung. The most frequent site of metastasis is the brain.

In the experience at Memorial Sloan-Kettering Cancer Center reported by Martini et al.,\textsuperscript{26} the specific level of N1 nodes and the extent of nodal involvement did not appear to have any prognostic implications. The 5-year survival of patients with adenocarcinoma was 40% and that for patients with squamous cancer was 60%, with a somewhat poorer prognosis if visceral pleura was involved. There did not appear to be any survival advantage with the use of adjuvant chemotherapy or radiation therapy. However, the number of patients was small, and treatment was not uniform.

The LCSG analyzed over 1,000 cases of pulmonary resection for NSCLC and reported that 5-year survival in patients with T1N1 squamous carcinoma was 75% and that for patients with adenocarcinoma was 52%.\textsuperscript{27} For those with T2N1 disease, the survival rate was 53% with squamous cancer and 25% with adenocarcinoma. The Ludwig Lung Cancer Group\textsuperscript{28} reported median survivals for T1N1 and T2N1 disease of 4.8 years and 2.3 years, respectively. In patients with squamous carcinoma, the first site of recurrence was local in 41%, in contrast to 17% in patients with adenocarcinomas. In the latter group, the first recurrence was systemic in 66% and occurred in the brain in an additional 17%.

Randomization between no treatment and postoperative radiation therapy was carried out by the LCSG in 230
patients with resected stage II or III squamous carcinomas.\textsuperscript{30} Patients with N1 and N2 disease were not discriminated. Radiation therapy produced a significant reduction in local recurrence to 3\%, while the nonirradiated group had a local recurrence rate of 41\%. However, there did not appear to be any survival benefit.

The LCSG also found in the prospective randomized trial that combination chemotherapy (cyclophosphamide, doxorubicin, and cisplatin [CAP]) with radiation therapy was superior to radiation therapy alone in patients with advanced resectable adenocarcinomas and large cell cancers of the lung.\textsuperscript{31} The chemotherapy group had both a prolonged disease-free interval and a survival benefit.

\textbf{N2 Disease}

The presence of mediastinal lymph node metastases in NSCLC results in a significant worsening of the prognosis and may profoundly influence treatment selection. Even though pessimism prevails about the outcome of treatment and the controversy surrounding the role of surgery in the treatment, a select group of patients would benefit from a resection.\textsuperscript{32-34}

Metastasis to mediastinal lymph nodes is noted in nearly half of all patients with NSCLC. The factors affecting the outcome in these patients are the site of the involved lymph nodes, the number of the involved lymph nodes, whether the tumor is confined to the lymph nodes or has extranodal spread, and the histology and the size of the primary tumor in the lung.

Reporting on the experience from Memorial Sloan-Kettering Cancer Center, Martini and Flehinger\textsuperscript{35} noted that from 1971 to 1981, 1,598 patients with NSCLC were seen; 706 (44\%) had mediastinal node metastases. Of these, 404 were considered to have operable tumors, but only 151 tumors were completely resectable. Of the 404 patients who underwent surgical exploration, 224 were classified as having clinical N0 or N1 disease; of these, 119 (53\%) underwent complete resection. On the other hand, 179 patients had clinical N2 disease, and 32 of these (18\%) underwent complete resection. In the 151 patients with N2 disease who underwent resection, the histologic diagnosis was adenocarcinoma in 94 (62\%), epidermoid carcinoma in 46 (30\%), and large cell carcinoma in 11 (7\%). The overall survival of this group of patients was 29\%.

It has been our policy to carefully stage the mediastinum at the time of surgery. The mediastinal lymph nodes are carefully removed and classified by level and submitted for histologic review (Fig 3). In a right-sided thoracotomy and pulmonary resection, fairly complete dissection of ipsilateral mediastinal and subcarinal lymph nodes is possible. However, mediastinal node dissection is not complete in tumors involving the left lung. Three mediastinal lymph node compartments amenable to exploration and adequate dissection are (1) the superior mediastinum in a right thoracotomy, (2) the subaortic region in a left thoracotomy, and (3) the subcarinal region and inferior mediastinum in either a right- or left-sided approach.

Some Japanese surgeons have extended the resection to the opposite side of the mediastinum either through the same incision or through a median sternotomy.\textsuperscript{36,37}

In a recent report, Shields\textsuperscript{38} separated the patients with

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\textbf{FIGURE 3. Map of lymph nodes illustrating the sites by level and name.}

N2 disease into two broad categories: those with clinically evident disease and those with disease discovered only by means of an invasive procedure. He further subdivided each group into subsets, as follows: (1) clinically evident and symptomatic (superior vena caval syndrome, dysphagia,
etc, (2) clinically evident but asymptomatic, (3) N2 disease discovered at prethoracotomy mediastinal exploration, and (4) N2 disease discovered only at thoracotomy.

Resection has no role in the treatment of patients with superior vena caval syndrome or dysphagia. Most of these patients die of their disease in 6 months to a year.29

Patients with N2 disease evident on plain chest roentgenogram, manifested as mediastinal widening, or on bronchoscopy usually have unresectable disease. Martini and Flehinger30 reported a complete resection of the tumor in 32 (18%) of 179 patients who underwent exploration, with a survival of 9% at 3 and 5 years.

In most series,30-34 10 to 20% of patients with N2 disease discovered by routine mediastinal exploration may be considered for a resection. Pearson et al35 and Coughlin et al36 treated 20% and 10% of their patients with mediastinoscopic evidence of N2 spread with resection, with 5-year survival rates of 9% and 18%, respectively. Patients with unsuspected but completely resectable N2 disease discovered at thoracotomy have a better prognosis. Martini and Flehinger30 reported a complete resection of primary tumor and the involved mediastinal lymph nodes in 119 (53%) of 222 patients initially classified as having N0 or N1 disease. Actuarial survival rates at 3 and 5 years in patients with clinical N0 or N1 disease were 47% and 34%. Naruke et al37 reported a 19% survival rate in patients with N2 disease who underwent a complete resection. Patterson et al38 reported a 42% 5-year survival in patients who underwent a resection of lung cancer and were found to have unsuspected N2 disease in the aortopulmonary nodes. Martini reported a 35% 5-year survival in patients with similar nodal involvement during a discussion of the paper by Patterson et al.38

In the Memorial Sloan-Kettering Cancer Center experience,39 the overall 5-year survival was 30% (Fig 4). Thirty-seven patients lived 5 or more years. Of these, 25 were still alive and free of disease 5 to 11.5 years later at the time of last report in 1987.40 Five died of unrelated causes, and 7 died of the cancer. Five of the 7 who died of cancer were alive with disease at 5 years, while 2 had a recurrence after 5 years. The morbidity associated with the resection was acceptable, with only 2 postoperative deaths, both due to pulmonary embolism, 1 following a segmental resection and 1 after a pneumonectomy.

Better survival was noted in patients with smaller tumors (T1, 46%) as compared with larger tumors (T2, 27%; T3, 14%) (Fig 5).

The clinical nodal status of the disease on the basis of standard radiographic studies and bronchoscopic findings was a major determinant of survival. The 3- and 5-year survival rates in patients with clinical N0 or N1 disease were 47% and 34%, respectively, compared with 9% at 3 and 5 years in patients with clinically evident N2 disease before thoracotomy (Fig 6).

The extent of mediastinal lymph node involvement affected survival. Patients with a single involved N2 node did better (43% at 5 years) than those with multiple nodal involvement at one or more levels (30% at 5 years) (Fig 7). The size of the involved lymph node had no impact on survival as long as the node was encapsulated and completely removed.

The location of the involved lymph nodes appears to have an adverse effect if the subcarinal lymph nodes are involved (22% vs 33% at 5 years). Involvement of the upper paratracheal lymph nodes was associated with a 5-year survival rate of 20%, in contrast to 32% in patients who did not have positive nodes at levels I and II.

There was no survival advantage at 5 years for patients with epidermoid carcinoma (32%) compared with those with

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**Figure 5.** Survival in patients with NSCLC with N2 disease following resection as related to the T stage of tumor.

**Figure 6.** Survival in patients with NSCLC with N2 disease following resection as related to clinical status of regional lymph nodes.
blasting-cisplatin regimen reported by Kris et al. and the combination of cisplatin and 5-fluorouracil infusion have high response rates. Martini et al. reported an effective reduction of tumor burden in 73% of patients with NSCLC seen with bulky mediastinal lymph node metastases, improving the resectability rate to 75%. Previously, the resectability rate was reported by the same authors to be 18% in untreated patients with similar-stage disease. In 20% of all patients treated, no viable tumor could be found in the resected specimen. The survival in this group improved to 82% at 1 year and 54% at 3 years, with a median follow-up of 44 months and a median survival not yet attained. A number of recent reports of trials employing preoperative cisplatin-based combination chemotherapy have demonstrated a major objective response of at least 50% improvement in the resectability rate and survival.

Investigators at Rush-Presbyterian-St. Luke's Medical Center, Chicago, gave simultaneous cisplatin, fluorouracil infusion, and radiation followed by resection. Clinical response was noted to be complete in 8% of patients and partial in 48%, with 61% successfully undergoing the planned resection and sterilization noted in 23% of the resected specimens. The LCSG evaluated a similar regimen with an overall response rate of 65% in 78 patients. Chemotherapy with cyclophosphamide, doxorubicin, and cisplatin and radiation therapy also have been evaluated, with response rates in the range of 51% to 76% and a high resectability rate.

Preliminary results of these neoadjuvant trials are promising. However, a number of questions remain to be answered, among them: What is the best chemotherapy regimen? How many courses of chemotherapy should be given before and after the resection? What should the role and dosage of radiation therapy be before, during, and after the operation? Until these questions are answered in future trials, the use of neoadjuvant therapy should not be recommended as standard treatment for patients with locally advanced NSCLC.

**T3 CHEST WALL CANCER**

Invasion of the chest wall by lung cancer was viewed with great pessimism until Coleman in 1947 reported the cases of 2 patients who survived for 8 and 13 years following an en bloc resection of the lung and the involved chest wall. A number of investigators have published their experience since then, reporting an incidence of chest wall invasion by lung carcinoma of approximately 5% and a 5-year postresection survival rate of 30% to 40% when regional lymph nodes are negative.

McCaughan et al. reported on the experience at Memorial Sloan-Kettering Cancer Center from January 1974 to December 1983. Of the 125 patients in their study, 58 patients (46%) had epidermoid carcinoma, 57 (46%) had adenocarcinoma, and 10 (8%) had large cell carcinoma. Sixty-six patients had no nodal metastases, 17 had N1 disease, and 42 had N2 disease. Of the 125 patients, 111 underwent pulmonary resection, with 5 postoperative deaths (4%). Resection was performed by extrapleural mobilization in 66 patients, and en bloc resection of the lung and skeletal chest wall in 45, with reconstruction of the skeletal defect in two thirds of the patients.

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**Figure 7.** Survival in patients with NSCLC with N2 disease following resection as related to the number of involved lymph nodes and levels.
The tumor extended only into the parietal pleura in 70 patients but infiltrated the chest wall muscles and/or ribs in 55, with 12 having involvement of the vertebral column. Complete resection of the tumor was possible in 62% of all the patients, in 77% if only parietal pleura was involved, but in only 53% if intercostal muscle or rib invasion without vertebral invasion was present. There was no significant difference in resectability related to age, sex, presence of preoperative chest pain, histologic type of tumor, tumor size, or presence of lymph node metastases. Of the 77 patients who underwent a complete resection, 19 had a pneumonectomy, 6 a bilobectomy, 48 a lobectomy, and 4 a wedge resection. In all patients, a careful mediastinal lymph node dissection was performed. Pathologic staging in these patients was T3N0M0 in 45, T3N1M0 in 10, and T3N2M0 in 22. Four of the patients with N1 disease and 17 with N2 disease received external radiation therapy to the mediastinum. Only 3 patients had received external radiation therapy preoperatively elsewhere. Actuarial survival in patients with complete resection was 40% (Fig 8). There were no survivors beyond 30 months with residual disease. The presence of metastases to regional lymph nodes and the depth of penetration of tumor into chest wall greatly influenced the survival. The 5-year actuarial survival rate was 56% in patients without lymph node metastases and 21% in those with nodal metastases (Fig 9). Patients with tumor confined to parietal pleura had a 45% probability to survive 5 years, in contrast to 16% in those with tumors invading the chest wall. Chances of survival improved to 62% and 35%, respectively, in the absence of lymph node metastases.

Experience at the Mayo Clinic, reported by Pichlter et al., is quite similar. Five-year actuarial survival was 32.9% for all patients surviving the operation and 53.7% for patients with T3N0M0 tumors, with survival dropping to 7.4% when lymph node metastases were present. Major differences were in the operative mortality of 15.2% and a 5-year survival rate for patients aged 60 years or younger of 84.6%, compared with 27.7% for patients older than 60 years. No survival advantage was noted in younger persons by McCaughan et al.  

All thoracic surgeons agree that a full-thickness chest wall resection is indicated in patients with NSCLC invading the ribs or the chest wall muscles. However, there is some disagreement about the method and extent of resection if the tumor extension appears to be only up to the parietal pleura. We have felt that extrapleural dissection should be attempted initially and that if a tumor-free plane is readily achieved, an extrapleural resection should be performed. If any indication of tumor extension beyond the parietal pleura becomes obvious, a formal chest wall resection should be carried out. Objections to this approach are that a cancer plane is being violated and that even if the extrapleural dissection is satisfactory, some patients would have tumor extending to the resection margin. Trastek and co-workers reported a survival rate of 75% when en bloc chest wall resection was performed, compared with only 28% when extrapleural resection was performed, in patients in whom only parietal pleura was involved. McCaughan et al., however, reported that patients undergoing an extrapleural resection had a 5-year actuarial survival of 62% if regional lymph nodes demonstrated no metastases. Six patients had undergone en bloc resection of chest wall and lung with a survival pattern similar to that of patients undergoing extrapleural resection. Subsequent histologic examination had demonstrated involvement of the parietal pleura only.

The role of adjunctive radiation has not yet been defined. Its use was reported selectively at the Mayo Clinic and Memorial Sloan-Kettering Cancer Center. Patterson and associates reported 5-year survival rates of 56% in a nonrandomized group of patients receiving external radiation therapy and 30% in a nonirradiated group. Six of the 19 nonirradiated patients had a local recurrence, and 12 irradiated surviving patients had no recurrence.

As reported by McCormack et al., skeletal reconstruction was performed selectively with no reconstruction in small defects or defects lying under the scapula. Marlex mesh was found to be satisfactory in 26 of the 30 reconstructions. A rigid sandwich prosthesis constructed of 2 layers of Marlex mesh (C. R. Bard, Billerica, Mass) and methyl methacrylate was used in 4 patients with larger defects to maintain
function and cosmesis. Pairolo et al., however, feels that reconstruction of chest wall defects following an en bloc resection should always be done. He has preferred the use of Prolene mesh (Ethicon, Somerville, NJ) or more recently a 2-mm-thick polytetrafluoroethylene (Gore-tex W. L. Gore and Associates, Flagstaff, Ariz) soft-tissue patch.

**Superior Sulcus Tumor**

Pancoast first described the superior sulcus tumor in 1932. It is a carcinoma of the lung of any histologic type, but it is most commonly a low-grade epidermoid carcinoma that arises at the apex of the upper lobes in the region of the superior pulmonary sulcus and that invades the endothoracic fascia, the lower roots of the brachial plexus, the sympathetic chain, the adjacent ribs, and the vertebral bodies. Due to the precise location of the tumor, patients develop characteristic pain in the shoulder and in the distribution of the ulnar nerve, progressing to necessitate use of narcotics for relief of the pain and the Horner's syndrome.

There is often a delay in making a diagnosis since the patient has no pulmonary symptoms and often seeks relief of pain from an orthopedic surgeon or a chiropractor. A chest radiograph will show a lesion at the apex. However, a CT scan or a magnetic resonance imaging study is most useful for evaluation of the tumor and its extension into adjacent structures as well as the status of regional lymph nodes. Bronchoscopy is usually not diagnostic, but a fine needle aspiration biopsy is most valuable. A histologic evaluation of mediastinal adenopathy detected by radiologic studies is recommended.

Shaw et al. described combined preoperative irradiation and extended resection of superior sulcus tumors in 1961. Of the 131 patients with a proved superior sulcus tumor reported by the authors recently, 78 (60%) had a resection. Two patients (2.6%) did not survive the operation; 31% of the resected patients were alive at 5 years, 26% at 10 years, and 22% at 15 years. Survival was better in patients free of nodal metastasis, with 44% surviving at 5 years. At Memorial Sloan-Kettering Cancer Center, treatment of superior sulcus tumors has been a combined effort of thoracic surgeons, neurosurgeons, and radiation oncologists. The patient receives external radiation therapy to the primary tumor, the mediastinum, and the supraclavicular area to a total tumor dose of 4,000 cGy in 20 fractions over 4 weeks. A resection is performed on patients with localized tumor 4 weeks later. An en bloc resection of the lung and chest wall, in addition to a careful mediastinal lymph node dissection, is carried out. Resection includes laminecmy and excision of vertebral bodies, if involved. Any residual tumor is implanted with iodine-125 seeds.

Of the 129 patients who underwent exploratory surgery, 66 had epidermoid carcinoma, and 63 had adenocarcinoma or a large cell carcinoma. Eighty-seven patients had no metastases to the regional lymph nodes. Eighty-one patients had a complete or partial resection, and 103 received interstitial intraoperative brachytherapy. One patient died during the postoperative period due to a pulmonary embolus. The overall survival was 25% at 5, 10, and 15 years. The mediasinal nodal status and histology had an impact on survival. The 5-year survival was 29% in patients with N0 disease, in contrast to 10% in patients with N2 disease, 30% in patients with adenocarcinoma, and 19% in patients with squamous carcinoma. Patients who received preoperative irradiation had better 5-year survival.

Similar survival benefits have been noted in patients with negative regional lymph nodes in several other series. The benefits of routine use of preoperative radiation therapy have been questioned. Attar et al. have demonstrated significant long-term survival in a small selected series of patients treated by surgery alone where all disease was resected. However, if there is locally extensive disease, preoperative radiation therapy has been the treatment of choice universally.

**Small Cell Lung Cancer**

Small cell lung cancer accounts for 15% to 25% of all malignant lung tumors and is perceived as systemic nonsurgical disease due to its characteristic early and widespread dissemination. However, some groups have reported a 5-year survival rate of 30% following surgical management of SCLC. This difference can be explained on the basis of patient selection and stage of tumor since even an SCLC must be localized to the lung and hence curable by resection during its natural history.

Surgery, like radiation therapy, is a form of local treatment. Its role in treatment of SCLC will be limited to about 10% of all patients or about a third of the patients with limited disease at presentation when the tumor is completely resectable. Recently, a number of reports have appeared demonstrating improved local/regional control rate utilizing surgery and combination chemotherapy with or without radiotherapy.

Exclusively surgical management of SCLC has hardly any supporters since even in apparently localized tumors micrometastases are already present in most patients, resulting in a high incidence of treatment failure. However, surgical management may play a role in the treatment of SCLC in the following situations: (1) primary surgery with postoperative chemotherapy, (2) neoadjuvant chemotherapy followed by surgery with or without radiation therapy, and (3) as a salvage procedure.

**Primary Surgery with Postoperative Chemotherapy**

Included in this group are patients with a peripheral coin lesion or a central lesion of the lung with unknown or mistaken histology and those with a known diagnosis of SCLC where complete resection is likely in a study setting.

In the Veterans Administration Surgical Oncology Group trial reported by Shields et al., 146 patients underwent a potentially curative resection, with 10 postoperative deaths and a 5-year survival rate of 23%. Earlier-stage tumors (T1N0M0) had a survival benefit with a 5-year survival of 59.5%. Meyer reported on 10 patients with stage I and II disease who underwent resection and were treated for 1 year postoperatively; 7 patients survived at 5 years after resection, and only 1 patient died of recurrent tumor. Ginsberg reported on 63 patients who received postoperative chemotherapy and prophylactic cranial irradiation; the 5-year actuarial survival was 31% in the overall group and 45% in patients with N0 disease. Similar survival advantage has been reported by a number of other groups.

The possible advantage of this approach, as pointed out by

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Surgical resection in an adjuvant setting may be justified by the high incidence of local recurrence in limited disease despite attainment of clinically complete remission with chemotherapy alone or with the addition of radiation therapy. Meyer reported on 20 consecutive patients with stage III M0 disease. Of the 4 patients with T3N1 disease, 2 survived for more than 30 months after 2 courses of chemotherapy and resection; 1 died at 34 months of a myocardial infarction, and 1 survived at 5 years. Six of 16 patients with N2 disease did not undergo resection. All of these 16 patients died of recurrent disease, with a relapse occurring in 3 at 27, 30, and 37 months.

In a study by Eastern Cooperative Oncology Group, 37 patients with localized SCLC were treated with 2 cycles of chemotherapy, and those patients who achieved complete or partial remission were evaluated for resection. Postoperatively, patients received prophylactic cranial irradiation and chemotherapy for 11 months. Twelve patients underwent resection; residual cancer was found in the operative specimen in 10, and no residual disease was found in 2. Seven of these patients (58%) were alive with evidence of disease after a median follow-up period of 24 months. Five of the 7 patients who underwent resection proved to have mixed histology, and 5 (71%) were alive without evidence of disease after a median follow-up period of 36 months. Only 2 of the 16 patients who did not undergo resection were alive at 15 and 31 months. The remaining 14 died of their disease.

Ginsburg reported on 38 patients with limited SCLC who underwent 3 to 5 cycles of cyclophosphamide, doxorubicin, and vincristine, resection, postoperative thoracic irradiation, and prophylactic cranial irradiation with postoperative chemotherapy in many instances. The overall estimated 5-year survival was 38% (45% for N0 disease, 30% for N1 disease, and 40% for N2 disease). An additional 19 patients were fit for surgery but did not undergo an operation. The estimated 5-year survival in this group was 10%. A number of combined intragroup prospective randomized trials are currently going on. Results are awaited.

Persistence or recurrence of disease in a small number of patients with SCLC following treatment has been noted to be due to NSCLC histology. In a report by Baker et al, 7 of the 19 patients who underwent resection following 2 courses of chemotherapy had either residual foci of SCLC mixed with NSCLC (3 with adenocarcinoma and 1 with large cell carcinoma) or only focal areas of NSCLC. Five of these patients (71%) were alive at the time of the report (median follow-up, 36 months). Ginsberg reported on 14 patients who underwent salvage surgery; 3 were alive and well without evidence of disease at 3 to 6 years after resection.

In conclusion, combination chemotherapy remains the mainstay of treatment of SCLC. There is, however, increasing evidence that resection has a beneficial role in stage I disease and possibly in stage II disease when followed by polychemotherapy and prophylactic cranial irradiation. If there is evidence of nodal involvement, mediastinal irradiation is desirable. The role of neoadjuvant chemotherapy followed by surgery is unclear. Results from prospective randomized trials currently under way are awaited before definitive conclusions can be made.

Patients in whom there is a failure to respond or a recurrence at the primary site after initial response should be evaluated for salvage surgery since there may be coexisting NSCLC pathology.

**BRONCHOPLASTIC PROCEDURES**

Resection of the tumor may be possible with "sleeve lobectomy" as an alternative to pneumonectomy, conserving the lung and providing improved quality of survival. Sleeve lobectomy or the bronchoplastic procedures initially described by Paulson and Shaw in 1955 and by Price in 1956 were considered a compromise operation for the patient who was unable to undergo a pneumonectomy because of functional limitations. Extensive experience and encouraging results have gradually changed the restrictive attitudes toward broader indications. These procedures are no longer regarded as a compromise procedure but as a procedure of choice to be performed whenever the anatomic conditions of the tumor are favorable.

Bronchoplastic procedures were performed in 7% to 18% of the pulmonary resections reported by Grillo and Zanini, with survival rates of 32% to 45% at 5 years. The histologic characteristics were predominantly epidermoid, and the most frequently performed operation was right upper sleeve lobectomy. Bronchoplastic procedures are relatively safe, with a mortality of 1.7% to 9%. Bronchopleural fistula, bronchovascular fistula, and anastomotic stricture are the most common complications. Local recurrence varies from 4.5% to 17%.

Some authors have advocated the use of preoperative irradiation in patients with marginal pulmonary or cardiovascular status to improve resectability and maximize lung tissue salvage. However, others have reported increased risk of anastomotic complications, especially fistulae. A selective use of radiation therapy preoperatively in patients who would otherwise be unable to undergo a pneumonectomy may be prudent.

**BRAIN METASTASES**

The brain is one of the most common sites of extrathoracic metastases in NSCLC. The incidence is higher in patients with a histologic diagnosis of adenocarcinoma. Untreated patients with brain metastases have a median survival of about a month, which is doubled if the patient is treated with corticosteroids and is improved to 3 to 4 months with cranial irradiation. A few patients with primary tumor in the lung that is completely resected or resectable will present with a solitary lesion in the brain that is surgically accessible in most cases. Resection of metastases in these
patients is believed to be superior to other forms of
treatment. In a review at our institution of 43 patients with
NSCLC in whom solitary brain metastases were excised
followed by whole-brain irradiation, median survival was 26
months, compared with 14 months for 43 matched patients
treated by whole-brain irradiation alone. Similar experi-
ence was reported by Magilligan in recent reports. A
randomized trial comparing surgical removal of brain me-
 metastases followed by radiation therapy with radiation therapy
alone demonstrated a significantly longer survival in the
surgical group (median, 40 weeks vs 15 weeks in the radiation
therapy group). Also, recurrence at the site of the original
metastases was 20% in the surgical group, compared with
52% in the radiation therapy group.

It is our belief that in patients with NSCLC who have a
good prognosis based on the treatment of the primary tumor,
a solitary brain metastasis presenting synchronously or
metachronously should be surgically excised. The role and
extent of postoperative radiation therapy needs to be further
evaluated. Focal irradiation delivered by either external
focus beam or implantation of radioactive sources might
reduce the radiation-related cranial complications while
improving local control of tumor at the site of metastases.

Complications of Surgery

Safe execution of a surgical resection requires careful
patient selection. High-risk patients are those over the age
of 70 years, those with prior underlying cardiac disease, and
those with restricted pulmonary reserve. The severity of
morbidity and mortality is increased corresponding to the
extent of resection.

In a review of 961 patients undergoing a thoracotomy at
Memorial Sloan-Kettering Cancer Center from 1973 to
1980, Nagasaki et al reported that 780 (81%) patients had
an uneventful postoperative course, 78 (8%) had minor
complications, 83 (9%) had major nonlethal complications,
and 20 (2%) died of postoperative complications. The
mortality by procedure was essentially the same in all but
patients undergoing a pneumectomy. The incidence of
complications when related to age and cardiac history was
highest in elderly patients with cardiac disease (20%) and
lowest in younger patients without prior cardiac disease
(8%). The incidence of complications was also related to
pulmonary reserve.

In a report by Ginsberg et al, the overall 30-day
operative mortality for surgical resections in lung cancer
was 3.7% in 2,220 performed in the institutions within the
LCSG from 1979 through 1981. The extent of resection had
an impact on mortality: 44 of 569 patients who underwent a
pneumonectomy, 35 of 1,058 who underwent a lobectomy,
and 2 of 143 who underwent a segmentectomy or wedge
resection died within 30 days of their surgical procedure.
The age of the patient also had a significant impact: the
mortality was 1.3% for patients under 60 years of age, 4.1% for
patients who were from 60 to 69 years of age, and 7.1% in
patients older than 70 years.

Conclusions

Surgery remains the most effective mode of treatment for
NSCLC when tumor is localized to the pulmonary paren-
chyma. Tumor extension into the chest wall when completely
resectable is best treated surgically. In select circumstances
where tumor has metastasized to regional lymph nodes,
resection alone or in combination with preoperative chemo-
therapy may provide a chance of cure. In the presence of
extrathoracic metastatic disease, perhaps with the exception
of solitary brain metastases, surgery is not indicated.

Since the prognosis depends so much on resectability and
the stage of disease and since surgical treatment is not
without associated potential harm to the patient, it becomes
the responsibility of the treating physician to evaluate the
patient's ability to undergo an operative procedure safely
and to stage the tumor accurately to establish whether the
patient can benefit by resection of the tumor or whether
resection is likely to fail in long-term control of the disease.
Understanding the role of neoadjuvant therapy and using it
selectively would improve control and perhaps cure of the
disease.

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