Staging of the Mediastinum*
Role of Mediastinoscopy and Computed Tomography

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During the 1940s and 1950s, as many as 50% of thoracotomies identified nonresectable tumors. At present, better than 90% of patients undergoing thoracotomy for presumably resectable lung cancer are found to have operable tumors. This improvement is the result of major advances in the preoperative staging of this disease. Mediastinoscopy and computed tomography (CT) are the most valuable techniques for evaluating the mediastinum in patients with primary cancer of the lung. For each modality, the primary objective is to define the presence or absence of spread to mediastinal lymph nodes. In patients with non-small-cell lung cancer, surgical resection remains the treatment of choice so long as all recognizable tumor can be removed at operation. Both mediastinoscopy and CT provide critical information concerning the potential for a complete resection. Computed tomography remains the most effective noninvasive technique for the evaluation of mediastinal nodes.

Mediastinoscopy is a safe and highly accurate invasive procedure which, in experienced hands, will identify malignant lymph nodes in the superior mediastinum in 90% of patients. Contrary to some reports, we have observed that a select group of patients with N2 disease identified at mediastinoscopy will benefit from resection, as will patients with operable N2 disease discovered only at thoracotomy.

Mediastinoscopy and computed tomography (CT) are the most valuable techniques for the evaluation of mediastinal lymph node involvement in patients with primary lung cancer. For each modality, the primary objective is to define the presence or absence of spread to mediastinal lymph nodes. In patients with non-small-cell lung cancer, surgical resection remains the treatment of choice, so long as all recognizable tumor can be removed at operation. Both CT and mediastinoscopy provide critical information for determining the potential for a complete resection in patients with presumably operable tumors. In patients with N2 disease, only a select minority will benefit from surgical resection.

Advances in the surgical treatment of lung cancer during the past four decades have had little impact on the overall mortality rates associated with this disease. More accurate staging, particularly of lymphadenopathy in the mediastinum, however, has significantly reduced the incidence of fruitless exploratory thoracotomy during these years. A major advance has been the establishment of a consensus on the definition and nomenclature for the location of mediastinal and hilar lymph nodes. The nodal map developed by the American Joint Committee on Cancer (AJCC) has been widely adopted and has been employed as the standard in most of the publications referenced in this report. This map was developed from the original mapping outline described by Naruke et al. in 1978. At present, stage N1 is restricted to involvement of intrapulmonary and hilar nodes; stage N2 to ipsilateral mediastinal involvement, including the subcarinal area; and stage N3 to contralateral involvement in either the mediastinum, hilm, or supraclavicular regions.

Computed Tomography

At present, CT is the most effective noninvasive technique for the evaluation of mediastinal nodes. The accuracy of CT for this purpose is, however, highly variable. A review of publications during the past decade variably reports the sensitivity of CT between 52% and 88%. These differences are due to variations in the nodal size elected for the positive category, whether or not this measurement is made in the long or short axis of the node, the accuracy of nodal sampling for histologic confirmation at the time of mediastinoscopy or thoracotomy, and the accuracy of nodal mapping itself. Three publications report experience in a group of similar patients with presumably operable lung cancer, in whom complete nodal sampling was done at mediastinoscopy or thoracotomy.

Using a nodal size of 1 cm or greater, the sensitivity of CT varied in these three reports between 64% and 79%, and the specificity between 62% and 66% (Table 1). Both Libshitz et al. and McCloud et al. observed a higher incidence of false-positive lymph nodes (benign enlargement) in patients with an associated obstructive pneumonia. McCloud et al. evaluated sensitivity and specificity by nodal station. False-positives were more common in station 4R (right paratracheal), 10R (right tracheobronchial angle), and station 5 (subaortic). False-negative rates were highest in stations 10L (left tracheobronchial angle) and 7 (subcarinal). McCloud et al. also reported that five (15%) of 36 patients with T1 lesions were found to have N2 disease. Computed tomography is also capable of identifying nodes in locations which are inaccessible at mediastinoscopy (in lumen subcarinal) or at thoracotomy (contralateral nodes).

Current Recommendations

In patients with presumably operable non-small-cell lung cancer, CT is recommended prior to mediastinoscopy and/or thoracotomy in all cases. A diagnosis of N2 disease should be entertained if the nodal diameter is greater than 1 cm, and nodal location should be determined using the AJCC nodal map. All patients with CT-positive nodal involvement in superior mediastinal stations warrant mediastinoscopy and biopsy; approximately one third of such patients will have a benign

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adenopathy that does not modify operability.

**Mediastinoscopy**

Mediastinoscopy is a safe invasive technique that identifies malignant lymph nodes in the superior mediastinum. Because a biopsy and histologic diagnosis (including cell type) are obtained with mediastinoscopy, it is highly accurate in experienced hands. General anesthesia is usually required for this procedure, although a local anesthetic may be used safely in selected patients in a day surgery setting.

Not all mediastinal nodes are accessible by mediastinoscopy. All peritracheal nodes and the nodes at the tracheobronchial angle and proximally on the main bronchi are evaluable, as are the nodes in the anterior compartment of the subcarinal space. But nodes in the subaortic window and in the left anterior mediastinum (usually along the phrenic nerve) cannot be reached by conventional mediastinoscopy, nor can the inferior or posterior subcarinal lymph nodes. Obviously, nodes along the esophagus and in the inferior pulmonary ligament are not accessible either.

The procedure may be modified according to the location of the primary tumor. For example, tumor spread to the anterior mediastinal and left subaortic nodes almost always arises from tumors in the left hilum or left upper lobe. In such cases, our practice is to do a conventional cervical mediastinoscopy and to evaluate the biopsy specimens by frozen section. If the results are negative, we then proceed to a left anterior mediastinotomy through an interspace incision without removing cartilage, and explore and obtain biopsy specimens of the nodes in the subaortic region or the anterior mediastinum.

Ginsberg et al extended conventional cervical mediastinoscopy using the suprasternal approach as an alternative to left anterior mediastinoscopy. This entails developing a plane between the innominate and left common carotid arteries and introducing the scope through the front and lateral sides of the aorta to sample nodes in the subaortic arch. Left anterior mediastinoscopy or extended cervical mediastinoscopy may be used to identify nodes in stations 5 and 6 in patients with left hilar or left upper lobe tumors. Extended cervical mediastinoscopy may be employed to define the status of the primary lesion in cases of superior sulcus tumor by entering the pleural space on either the right or left side and then directly inspecting and sometimes performing a biopsy of the tissue. These procedures, however, should not be left to the inexperienced resident.

Mediastinal pleuroscopy may be used in patients with associated pleural effusions to aspirate effusions for cytologic examination. In appropriate cases, an open lung biopsy may be obtained during this procedure. More important, one may actually identify malignant pleural seeding, which indicates inoperability.

**Safety and Efficacy**

The safety and efficacy of mediastinoscopy as performed in 1,000 patients at Toronto General Hospital were reviewed retrospectively by Luke et al in 1986. The data showed left anterior mediastinoscopy was performed in a large number of patients with left upper lobar or left hilar lesions. A high incidence of metastases was observed in patients with small-cell lung cancer; the rate was lower in patients with adenocarcinoma, and lowest in those with bronchoalveolar cancers. No operative deaths occurred in this series; 2.3% of patients experienced complications: hemorrhage, pneumothorax, wound infection, and recurrent nerve palsy. The latter, which occurred more frequently early in the Toronto experience, can be avoided by maintaining gentle dissection at the left tracheobronchial angle, and by avoiding the use of cautery in the area of the left recurrent nerve.

Finger dissection is not usually possible at the subcarinal level. This dissection is usually done with the sucker tip with the scope positioned behind the right main pulmonary artery. Most bleeding complications associated with mediastinoscopy have occurred in this area. Fortunately, it is the bronchial vessels, and not the pulmonary artery, that bleed in almost all cases. Because the subcarinal space is a confined compartment, bleeding can usually be managed by applying local pressure with some form of packing for a period of approximately 5 min.

The accuracy of mediastinoscopy in the Toronto experience became apparent when data from 590 patients who underwent thoracotomy following a mediastinoscopy with negative results were analyzed; only 9% of these patients showed evidence of N2 disease at thoracotomy, usually in stations that were inaccessible at mediastinoscopy.

Mediastinoscopy thus has several advantages as follow: (1) A tissue diagnosis, including cell type, is obtained. (2) With experience, clinicians may use the findings to identify operability. Extranodal extension of the tumor with fixation to adjacent structures like the trachea or the aortic arch may preclude a complete resection. Contralateral spread precludes a complete resection using conventional approaches. (3) On occasion, the field can be extended to either pleural space. This is useful in the direct evaluation of the primary tumor in cases of superior sulcus cancer. A transpleural approach may also allow collection of pleural fluid and inspection of visceral and parietal pleura for the identification of pleural metastases. (4) Knowledge of N2 disease prior to thoracotomy may, in selected cases, prompt the use of neoadjuvant therapy, which in turn may modify the type of lymphadenectomy performed.

**Current Recommendations**

Mediastinoscopy is recommended in patients with T2 or T3 primary lesions, as well as in those with T1 lesions in whom the cell type is adenocarcinoma or large cell carcinoma, even when CT shows all superior mediastinal stations to be negative. If nodes can be identified, biopsy specimens should be obtained from all accessible superior mediastinal stations at cervical mediastinoscopy. Patients with T2 or T3

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**Table 1—Sensitivity and Specificity of CT Scanning for N2 Disease**

<table>
<thead>
<tr>
<th>Year</th>
<th>Author</th>
<th>No. Cases</th>
<th>Node Size, cm</th>
<th>Sensitivity, %</th>
<th>Specificity, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>1984</td>
<td>Libshitz et al</td>
<td>86</td>
<td>&gt;1</td>
<td>67</td>
<td>66</td>
</tr>
<tr>
<td>1988</td>
<td>Staples et al</td>
<td>151</td>
<td>&gt;1, Long axis</td>
<td>79</td>
<td>65</td>
</tr>
<tr>
<td>1992</td>
<td>McCloud et al</td>
<td>143</td>
<td>&gt;1, Short axis</td>
<td>64</td>
<td>62</td>
</tr>
</tbody>
</table>
lesions in the left upper lobe should undergo cervical mediastinoscopy with frozen section; if the nodal biopsy specimens are negative, a left anterior mediastinotomy through the second intercostal space should be performed. Mediastinoscopy may be omitted in patients with T1 lesions and negative findings on CT; cervical mediastinoscopy, however, is still indicated if the cell type is adenocarcinoma or large cell carcinoma. In patients with superior sulcus tumors, or significant pleural effusion, mediastinopleuroscopy may be performed on either side.

Operability of Patients With N2 Disease

Although patients with involved nodes in the superior mediastinum identified at mediastinoscopy have disease that has been deemed inoperable,10,11 our experience indicates that a select group of these patients may benefit from complete resection.12 In the early 1980s, a Toronto study compared 79 patients with positive ipsilateral and localized nodal involvement identified at mediastinoscopy and 62 patients with negative mediastinoscopy findings who were subjected to resection, in whom subsequent thoracotomy identified positive mediastinal nodes.13 Survival rates were 9% and 24%, respectively, for the two groups.

We conclude that a select group of patients with N2 disease identified at mediastinoscopy will benefit from complete resection, as will patients with operable N2 disease discovered at thoracotomy. Our analysis of the data for all patients with NSCLC and N2 disease undergoing a complete resection shows 24% have survived 5 years following surgery.14 Similarly, Martini et al15 observed a 29% 5-year survival rate in patients with NSCLC in N2 disease having complete resection.

The importance of selection cannot be overemphasized in these patients. Criteria for operability are summarized as follows: (1) non-small-cell histologic findings; (2) ipsilateral metastases where the involved nodes are discrete, usually surrounded by fat, and not adherent to the trachea, subcarinal airway, or great vessels (this includes patients with completely resectable subcarinal nodes). In such cases, it is determined that all gross disease can be resected, and that the most proximal stations in the superior mediastinum (usually level 2) are free of disease. In these patients, we recommend a resection and en bloc lymphadenectomy, followed by postoperative mediastinal irradiation. Currently, neoadjuvant therapy is restricted to patients in clinical trials and to a few carefully selected patients with bulky ipsilateral N2 disease.

REFERENCES

17. Pearson FG. Lung cancer: the past twenty five years. Chest 1986; 89:200-05