Flexible Transbronchial Needle Aspiration for Staging of Bronchogenic Carcinoma*

Ko Pen Wang, M.D., F.C.C.P.;† Roy Brower, M.D.;‡
Edward F. Haponik, M.D., F.C.C.P.;§ and Stanley Siegelman, M.D.||

Flexible transbronchial needle aspiration (TBNA) provides access to mediastinal lymph nodes, but its role in staging bronchogenic carcinoma is unknown. To determine the efficacy and safety of this procedure for staging the extent of mediastinal disease, the results of TBNA performed during fiberoptic bronchoscopy in 39 patients without known extrathoracic metastases were reviewed. Flexible TBNA was found to be a safe, effective method for determining the presence or absence of mediastinal metastases from bronchogenic carcinoma. Furthermore, TBNA results compare favorably with roentgenographic staging techniques, with the added advantage of providing cytopathologic information.

The ominous impact of mediastinal metastases on the prognosis of patients with bronchogenic carcinoma has been demonstrated convincingly.¹-⁴ Techniques for the diagnostic transbronchial needle aspiration (TBNA) of mediastinal tissue via the rigid bronchoscope have been described,⁵-²² and the recent introduction of a flexible needle has extended TBNA to the widely available fiberoptic instrument.²³ This technical innovation now permits the assessment of mediastinal lymph nodes at the time of diagnostic fiberoptic bronchoscopy. The yield, safety, and efficacy of flexible TBNA is reported in the staging of 39 patients with bronchogenic carcinoma, and compared with roentgenographic staging methods.

METHODS

Patient Population

Patients with known or suspected bronchogenic carcinoma who were referred to the bronchoscopy service of the Johns Hopkins Hospital between Nov 1, 1981, and Nov 17, 1982, were included in this study if a staging procedure was indicated at the time of bronchoscopy. In 28 patients with undiagnosed pulmonary lesions, bronchoscopy was performed primarily for diagnostic purposes. In the remaining 11 patients, bronchoscopy was performed solely for staging. Patients with known small cell carcinoma, extrathoracic metastases, malignant pleural effusions, chest wall involvement, and those with intratracheal tumors or neoplasms within 2 cm of the carina were excluded. Patients who had extrinsic compression of the trachea or carinal widening were included if the overlying mucosa appeared normal.

Flexible Transbronchial Needle Aspiration (TBNA)

Bronchoscopy with TBNA was performed by the same author (KFW) in all cases. The TBNA always preceded brushing, forceps biopsy, or washing of the primary tumor in order to avoid the spread of cellular material within the airway. Thus, the possibility of contamination of the aspirated specimen was minimized. Technical details of flexible TBNA have been reported previously.²⁴²⁵ The procedure is generally performed under topical anesthesia via the transnasal or transoral route and does not require placement of an endotracheal tube. The fiberoptic instrument is positioned in the airway with the lower trachea and carina in full view. The type 1 transbronchial needle is passed through the bronchoscopic channel with its smooth-tipped stylette protruding beyond the needle. When the needle and stylette tip appear in the viewing field, the stylette is partially withdrawn so that its tip remains within the lumen of the needle. This maneuver is essential in order to maintain enough rigidity for puncture of the airway. The carina or tracheal wall is then pierced with a quick needle thrust (Fig 1). The stylette is withdrawn completely from the plastic catheter, and a 30- or 50-ml syringe containing 3 to 5 ml of saline solution is attached to the proximal end of the translucent sheath. Suction is then applied, creating a fixed negative pressure in order to draw the specimen into the sheath. The needle and sheath are then removed from the bronchoscopic channel, and the specimen is collected by flushing the contents of the syringe back through the sheath and needle into a suitable container. Two or three punctures are made at each anatomic site, and a different needle is used at each location. Diagnostic material was processed for cytopathologic examination in a standard manner. The TBNA cytopathologic specimens were interpreted independent of bronchoscopic observations and roentgenographic findings and were considered positive when unequivocally malignant cells were present in the specimen. All other cytopathologic findings were regarded as negative TBNA.

Roentgenographic Procedures

Standard PA and lateral chest roentgenograms (CXR) were obtained in all 39 patients and computerized tomograms (CT) were obtained in 33 patients. In six patients, CT was not performed because CXR demonstrated obvious mediastinal abnormalities. The CXR and CT were reviewed prior to bronchoscopy and were used to guide optimal needle placement. All studies were read by one of the staff radiologists and one of us, and were classified as being positive or negative for the presence of mediastinal metastases. Mediastinal lymphadenopathy consistent with metastases was considered to be

*From the Division of Pulmonary Medicine, Departments of Medicine and Radiology, The Johns Hopkins Medical Institutions and Baltimore City Hospitals, Baltimore.
†Associate Professor of Medicine and Otolaryngology.
‡Fellow, Pulmonary Medicine.
§Assistant Professor of Medicine.
||Professor of Radiology.
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Reprint requests: Dr. Wang, Respiratory Division, Brady 4, The Johns Hopkins Hospital, Baltimore 21205

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present if nodes exceeded 8 mm in size. All radiologic classifications were made independent of the results of TBNA and other staging procedures.

**Correlative Histologic Studies**

All patients with negative TBNA were referred for additional invasive staging procedures which included mediastinoscopy and/or thoracotomy. Patients with positive TBNA did not undergo further staging procedures.

**Statistical Analyses**

The CXR and CT were considered "true-positive" (TP) if mediastinal abnormalities detected by these roentgenographic studies were confirmed as malignant by TBNA or surgery. They were considered "false-positive" (FP) if roentgenographic abnormalities which were believed to represent metastatic disease were not proven to be neoplastic by TBNA and surgery. Roentgenographic studies that did not demonstrate mediastinal disease were "true-negative" (TN) if no evidence of mediastinal tumor was found by both TBNA and surgery, and "false-negative" (FN) when evidence of neoplasm was detected by either TBNA or surgery. In this analysis, all positive TBNA were regarded as TP. The TBNA were TN when the absence of mediastinal metastases was confirmed by thoracotomy; FN aspirates occurred when subsequent surgical procedures detected metastatic disease. The efficacies of staging the mediastinum by TBNA, CXR, and CT were compared using calculations of the sensitivity (TP/TP + FN), specificity (TN/TN + FP), positive predictive value (TP/TP + FP), negative predictive value (TN/TN + FN), and diagnostic accuracy (TP + TN/TP + TN + FP + FN) of each technique. Statistical differences between groups were assessed with the Chi-square test.

**RESULTS**

Thirty-nine patients met criteria for inclusion in the study. Bronchoscopy and TBNA were repeated in one patient with an initial equivocal TBNA specimen for a total of 40 procedures. The histologic classifications and the primary anatomic locations of their neoplasms are summarized in Table 1. The diagnosis of carcinoid tumor was not made until thoracotomy in two patients, who are included in this series because they underwent preoperative staging with a presumptive diagnosis of bronchogenic carcinoma. Twenty-seven patients had primary tumors of the right lung, ten had primaries originating in the left lung, and two patients presented with mediastinal masses without apparent parenchymal primary lesions. Transcarinal (34) and ipsilateral paratracheal (35) specimens were obtained in most patients, and contralateral paratracheal aspirates were also obtained in two patients whose CT scans suggested abnormalities of these sites.

There was one complication (2.6 percent) of TBNA in this series, a pneumothorax which resolved with a chest tube. There were no bleeding complications.

The TBNA yielded malignant cytology (five adenocarcinoma, four epidermoid, six small cell, four large cell) in 19 patients (48.7 percent). These patients were considered to have unresectable disease, and they underwent no further staging procedures. Flexible TBNA were negative in the remaining patients (21 procedures in 20 patients). Subsequent thoracotomy confirmed the absence of mediastinal metastases in 15 of these, but revealed metastases in three (two adenocarcinoma, one epidermoid). Rigid transbronchial needle aspirates

<table>
<thead>
<tr>
<th>Type of Neoplasm</th>
<th>Right Lung</th>
<th>Left Lung</th>
<th>Mediastinum Only</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Epidermoid</td>
<td>5</td>
<td>4</td>
<td>0</td>
<td>9</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>9</td>
<td>3</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>Large cell</td>
<td>7</td>
<td>1</td>
<td>0</td>
<td>8</td>
</tr>
<tr>
<td>Small cell</td>
<td>4</td>
<td>2</td>
<td>2</td>
<td>8</td>
</tr>
<tr>
<td>Other (carcinoid)</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>27</strong></td>
<td><strong>10</strong></td>
<td><strong>2</strong></td>
<td><strong>39</strong></td>
</tr>
</tbody>
</table>
needle aspiration, percutaneous needle aspiration, and repeat flexible TBNA, respectively, provided cytopathologic diagnosis of small cell carcinoma in the other three patients.

The efficacy of TBNA with respect to the site and histologic findings of the primary neoplasm is summarized in Tables 2 and 3. No significant difference in the specificity and predictive value of a positive aspirate was correlated with these factors. However, the predictive value of a negative TBNA and the overall diagnostic accuracy of the procedure were significantly higher (p<0.05) for patients with right-sided primaries. The relationship between the anatomic sites of positive TBNA and location of the primary neoplasm is further detailed in Figure 2. Among patients with positive TBNA, 14 (73.7 percent) had positive aspirates obtained from N2 locations that are often inaccessible to mediastinoscopy (two left paratracheal, 12 subcarinal). Five patients had positive TBNA (one epidermoid, one adenocarcinoma, one large cell, two small cell) from two separate anatomic sites.

The relationship of TBNA results to the appearance of the airway at bronchoscopy is outlined in Table 4. The presence of extrinsic compression of the trachea or carina was associated with positive TBNA (p<0.01). However, a normal-appearing airway did not assure the absence of malignancy in surrounding tissue: 34.6 percent of patients had positive TBNA despite normal appearing airways. In addition, three patients with normal airways and negative TBNA had mediastinal metastases demonstrated at thoracotomy.

The usefulness of TBNA as a staging procedure in this selected population is summarized in Table 5 and compared with that of the roentgenographic studies. Both TBNA and CT scans were superior to CXR for staging purposes. The sensitivity of CT was slightly higher than that of TBNA, but the specificity, predictive value of a positive result, and diagnostic accuracy of TBNA appear to be superior to those of CT.

**DISCUSSION**

These data indicate that staging of bronchogenic carcinoma to define mediastinal nodal involvement (N status), as well as the extent of endobronchial disease (T status), can now be combined effectively with diagnostic fiberoptic bronchoscopy (Fig 1). Furthermore, this objective can be achieved both safely and accurately. The diagnostic efficacy of TBNA compared favorably with that of roentgenographic staging methods, with the added advantages provided by cytopathologic information. In many of these patients, flexible TBNA obviated the need for more invasive surgical staging procedures that are associated with increased morbidity, patient discomfort, the need for general anesthesia, and higher cost of hospitalization.

The documentation of positive TBNA in 48.7 percent of our patients, and of mediastinal metastases in 64 percent of our patients overall, is consistent with the high incidence of mediastinal nodal involvement that characterizes bronchogenic carcinoma. The histologic types of neoplasm in this series are also similar...
to those reported from other centers.\textsuperscript{1,8,10} There was no significant relationship between the histology of the primary neoplasm and TBNA results, but the number of patients in each category was too small for comparison. Three of the patients with false negative TBNA had small cell carcinoma. The overall efficacy of TBNA for staging is higher if patients with small cell carcinoma are excluded (Table 3). This is relevant, since at most institutions patients with this diagnosis would not be considered as surgical candidates and would not undergo staging procedures.

It is not surprising that patients with obvious extrinsic compression of the airway had an increased incidence of positive cytopathology. However, a normal appearance of the airway did not assure a negative TBNA; 34.6 percent of such patients had positive aspirates. Experience with paracarinal forceps biopsies has shown that a normal appearing carina may harbor submucosal tumor,\textsuperscript{8,13} and Versteegh's experience with rigid transcarinal needle biopsy is consistent with these findings.\textsuperscript{6} Our data reinforce the importance of obtaining specimens despite a benign appearance of the airway.

It is interesting that TBNA had a lower sensitivity, negative predictive value, and diagnostic accuracy in patients with left-sided primary neoplasms. This finding is similar to experience with more invasive staging procedures, and probably reflects both the complexity of lymphatic drainage patterns from the left lung\textsuperscript{14,17,83} and the more limited accessibility to these nodal sites.\textsuperscript{14} Nevertheless, five patients with left-sided tumors had positive TBNA. It is likely that some of these mediastinal metastases (two subaortic, three subcarinal) would have been inaccessible to mediastinoscopy.\textsuperscript{17} These patients would have required anterior mediastinotomy or thoracotomy to establish their unresectability.

The techniques of rigid\textsuperscript{14,17} and flexible\textsuperscript{9,14} TBNA have been described previously. Apart from factors related to needle placement and aspiration of the specimen, two important caveats must be rigorously observed in application of this procedure. First, the bronchoscopist must perform TBNA prior to any manipulation of a parenchymal or endobronchial abnormality in order to minimize the likelihood of contamination of the aspiration specimen. Second, and most importantly, the procedure cannot be performed unless appropriate, high-quality cytopathology services are available. The extremely high specificity, positive predictive value, and diagnostic accuracy observed for TBNA in this series assumed the absence of false positive cytopathology. Confidence in this assumption is based upon the low incidence (less than 1 percent) of false-positive cytopathology at our institution.\textsuperscript{42} In addition, TBNA were classified as positive only when unequivocally malignant cells were obtained. If suitable resources for cytopathology preparation and interpretation are unavailable, TBNA should not be attempted. Other potential limitations of the procedure should be recognized: initial experience suggests that TBNA may not be as useful in patients with lymphoma. Finally, TBNA does not permit the differentiation of intranodal from extranodal disease.

The TBNA safely provides specimens from N\textsubscript{2} sites which might otherwise be approached only by mediastinoscopy, mediastinotomy, or thoracotomy (Fig 2). The access TBNA provides to subcarinal nodes appears particularly important because of their central anatomic position and function as an intermediary station for the contralateral lymphatic extension of disease.\textsuperscript{83} Recognition of subcarinal involvement may prove to have unique prognostic value. None of Versteegh's 14 patients with positive rigid TBNA from subcarinal nodes who underwent thoracotomy had curative resec-

**Table 5—Efficacy of TBNA**

<table>
<thead>
<tr>
<th>Procedure</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Predictive Value if (+)</th>
<th>Predictive Value if (−)</th>
<th>Diagnostic Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>CXR</td>
<td>14/24 (58%)</td>
<td>11/15 (73%)</td>
<td>14/18 (78%)</td>
<td>11/21 (52%)</td>
<td>25/39 (64%)</td>
</tr>
<tr>
<td>CT</td>
<td>17/20 (85%)</td>
<td>8/13 (62%)</td>
<td>17/22 (77%)</td>
<td>8/11 (73%)</td>
<td>25/33 (76%)</td>
</tr>
<tr>
<td>TBNA</td>
<td>19/25 (76%)</td>
<td>15/15 (100%)</td>
<td>19/19 (100%)</td>
<td>15/21 (71%)</td>
<td>34/40 (85%)</td>
</tr>
</tbody>
</table>

*Assumes no false positive cytopathology; TBNA includes the patient who underwent two procedures as two cases, total n = 40.*

ANATOMIC LOCATIONS OF POSITIVE TBNA

(24 POSITIVE ASPIRATES IN 19 PATIENTS)

![Diagram of TBNA locations]

**Figure 2.** Positive TBNA were obtained from N\textsubscript{2} locations that otherwise might have required more invasive procedures to establish unresectability.
tions. Among 64 N₂ patients reported by Naruke and co-workers, those with subcarinal metastases had a significantly reduced five-year survival (9.1 percent) in comparison to N₁ patients without subcarinal disease (29 percent).

Findings on standard chest x-ray and computerized tomography in this series are similar to those reported from other institutions, and confirm the usefulness of the CT scan in the detection of mediastinal metastases. Information from this procedure proved valuable in identifying high-yield sites for TBNA, best exemplified in the two patients with otherwise unsuspected, contralateral nodal disease and in several patients with pretracheal lymphadenopathy. The diagnostic efficacy of TBNA exceeded that of roentgenographic procedures, but we do not believe that TBNA detracts from the usefulness of these imaging techniques. Nor does it diminish the value of other staging methods which obtain histologic information. Rather, these procedures are complementary, providing a number of options that might be modified according to the needs of each patient.

Patients with a radiologically abnormal mediastinum by either the standard chest roentgenogram or CT scan, and those who have clinical factors that have previously been correlated with mediastinal metastasis (unfavorable tumor histology, central location, parenchymal mass >3 cm) might benefit from TBNA. The interpretation of a positive TBNA in patients who lack roentgenographic evidence of mediastinal disease represents a still more difficult problem, and further experience is necessary to clarify the significance of this finding. In TBNA-negative patients, the more invasive but complementary procedures of mediastinoscopy or mediastinotomy might be required, depending on the location of the primary neoplasm and its associated lymphadenopathy. Most patients with roentgenographically-demonstrable mediastinal lymphadenopathy and positive TBNA from N₂ sites are not candidates for curative resection. This is based on the dismal prognosis for the subgroup of patients with perinodal extension of metastatic foci within the mediastinum. Whether positive TBNA identifies potentially curable patients who have intranodal micrometastases, however, is unknown. Recent data suggest that a subset of N₂ patients might benefit from surgical treatment. Thus, the decision regarding the risks and benefits of surgical approach for potential cure remains highly individualized and demands continued careful evaluation.

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REFERENCES
1 Bergh NP, Schersten T. Bronchogenic carcinoma. Acta Chir Scand 1965; 347(suppl):1
2 Rasmussen RA, Basinger CE, Harrison RW, Meade RH. Choice of operation in the treatment of bronchogenic carcinoma: a review of 813 cases of which 209 were treated by resection. Chest 1965; 46:190-97
7 Simecek C. Cytological investigation of intrathoracic lymph nodes in carcinoma of the lung. Thorax 1966; 21:369-71
18 Whitcomb ME, Barham E, Goldman AL, Green DC. Indica-

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Stratton, Inc, 1979; chap 6

26 Naruke T, Seumas K, Ishikawa S. Lymph node mapping and curability at various levels of metastasis in resectable lung cancer. J Thorac Cardiovasc Surg 1978; 76:832


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Needle Aspiration in Staging Bronchogenic Carcinoma (Wang et al)