Comparison of Video Thoracoscopic Lung Biopsy to Open Lung Biopsy in the Diagnosis of Interstitial Lung Disease*

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Background: Up to one third of patients with interstitial lung disease will require a lung biopsy for diagnosis. Open lung biopsy is generally accepted as the most reliable method of biopsy and tissue diagnosis. The purpose of this study was to compare the efficacy and safety of video thoracoscopic lung biopsy, a minimally invasive technique, with open lung biopsy in the diagnosis of interstitial lung disease.

Methods: From December 1990 to January 1992, 43 patients were referred for diagnostic lung biopsy. Twenty-two consecutive patients undergoing video thoracoscopic lung biopsy (VTLB) over a 6-month period were retrospectively studied and compared with 21 consecutive patients who had undergone open lung biopsy (OLB) in the preceding 6-month period.

Results: VTLB (46 ± 4 minutes) did not add to operative time when compared with OLB (38 ± 3 min, p = 0.09). The same number of biopsies per patient were performed (VTLB, 1.9 ± 0.1; OLB, 2.0 ± 0.1; p = 0.48), the same amount of tissue was obtained per biopsy (VTLB, 6.69 ± 0.82 cm³; OLB, 5.78 ± 0.54 cm³; p = 0.36), and the diagnostic accuracy of each method was comparable (VTLB, 95 percent; OLB, 100 percent). However, patients undergoing VTLB demonstrated a significant reduction in length of pleural drainage (1.36 ± 0.25 days) and hospital stay (2.57 ± 0.46 days) relative to patients undergoing OLB (3.20 ± 0.34 days, 5.71 ± 0.63 days; p < 0.05). Complications occurred in 2/22 VTLB patients (9 percent, 0 deaths) and 4/21 OLB patients (19 percent, 1 death).

Conclusions: When compared with OLB, VTLB does the following: (1) provides equivalent specimen volume; (2) achieves equal diagnostic accuracy; (3) does not add to operative time or complications; and (4) reduces the time necessary for pleural drainage and length of hospital stay. Our findings suggest that VTLB is an effective and safe alternative to OLB in the diagnosis of interstitial lung disease.

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Diffuse infiltrative diseases of the lung remain a diagnostic challenge despite exhaustive protocols and new diagnostic techniques. Commonly referred to as interstitial lung disease (ILD), diffuse infiltrative processes of the lung actually represent a heterogenous group of disorders that are classified together because of common clinical, roentgenographic, physiologic, and pathologic features. Over 100 different clinicopathologic entities remain in the differential diagnosis of ILD complicating the identification of a treatable etiology.

The diagnostic approach to these patients begins with careful history, physical examination, lung imaging studies, sputum analysis, blood serologic study, and pulmonary function studies. If the specific etiology remains in question, tissue sampling is necessary to (1) establish a diagnosis, (2) exclude an infectious or neoplastic disease, (3) identify potentially treatable causes of ILD, and (4) assess the activity of the disease, correlating anatomic changes and physiologic derangements. Progressively more invasive tests are employed to establish a histopathologic diagnosis, including bronchoscopy, bronchoalveolar lavage, transbronchial biopsy, transthoracic needle biopsy, and finally open lung biopsy (OLB).

Ultimately, nearly one third of patients with ILD will undergo OLB to establish a diagnosis. Despite the reluctance to subject these patients to the risk of general anesthesia and thoracotomy, OLB can be performed with acceptable morbidity and mortality. The development of new endoscopic techniques and improved endoscopic devices has revolutionized the surgical approach to procedures traditionally performed by open laparotomy, most notably cholecystectomy. Although, the use of thoracoscopy in the management of diseases of the chest is not new, recent advances in endoscopic techniques and equipment offer a minimally invasive alternative to procedures that have previously required thoracotomy. The purpose of this study was to (1) determine the efficacy and safety of video thoracoscopic lung biopsy (VTLB) in the diagnosis of ILD and (2) compare the results of VTLB with the results previously obtained in patients with OLB at the same institution.

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Methods

Patients and Study Design

Forty-three patients with ILD of unknown etiology were referred for lung biopsy between December 1990 and January 1992. Twenty-two consecutive patients undergoing VTLB (June 1991 to January 1992) were retrospectively studied and compared with 21 consecutive patients who had undergone OLB in the preceding 6 months (December 1990 to May 1991). In all cases, the patients were undergoing concurrent diagnostic evaluation for lung dysfunction of unknown etiology, referred for lung biopsy to obtain adequate tissue to facilitate pathologic diagnosis and to exclude an infectious or neoplastic etiology of the underlying lung condition.

All patients were admitted to the hospital the day of surgery. Data obtained included age, sex, use of immunosuppression, preoperative pulmonary function tests and arterial blood gas when available, operative time, length of pleural drainage (computed tomography [CT]), intensive care unit (ICU) stay, hospital stay, biopsy results (including number, size, histologic features, and culture), complications, and deaths.

Video Thoracoscopic Lung Biopsy

Patients received general anesthesia using a double-lumen endotracheal tube. Tube position was confirmed by fiberoptic bronchoscopy and the patient was placed in the lateral decubitus position. The ipsilateral lung was not ventilated. A pneumothorax was created with a Verres needle placed through the posterior chest wall and insufflating 0.5 L of carbon dioxide into the pleural space. A 12-mm trocar was then inserted through a 2-cm chest wall incision posterior to the scapula, and the videoscope was introduced into the pleural cavity. Two additional trocars (5 mm and 12 mm) were inserted under direct vision; the 5-mm port was placed anterior to the scapula and the 12-mm port was placed inferiorly as depicted in Figure 1. The videoscope was transferred to the inferiorly placed 12-mm trocar permitting inspection of the lung and associated intrathoracic structures. Following surgical exploration, a suitable biopsy site was chosen and the lung was grasped with atraumatic forceps. An endoscopic stapling device (Endo GIA-United States Surgical Corp, Norwalk, Conn) was inserted through the posterior port, placed across the lung, and fired transecting the lung with placement of a double staple line. The specimen was removed through the 12-mm port. The transected lung was inspected for bleeding, air leak, and proper application of the staples. Employing this technique, multiple biopsy specimens could be obtained from the grossly involved and uninvolved lung segments. A section of the specimen was sent to the microbiology department for bacterial, viral, and fungal cultures, while the remaining specimen was sent fresh to the pathology department for histopathologic analyses. The lung was reinspected and once hemostasis was ensured, the trocars were removed under direct vision. The videoscope was removed, a 32-French chest tube was inserted through the sheath, the sheath was removed, and the puncture sites were closed with simple sutures. The chest tube was attached to a closed drainage system and placed to suction.

Open Lung Biopsy

Patients were placed under general anesthesia using a single-lumen endotracheal tube. A 6-cm anterior thoracotomy incision in the fourth or fifth intercostal space was performed with the patient in the supine position. On entering the thoracic cavity, the lung and intrathoracic structures were inspected. Once a biopsy site was chosen, the lung was grasped with atraumatic lung clamps, the lung was divided with an automatic stapling device, and the specimen was removed. The specimen was sent for appropriate studies as outlined above. The transected lung was inspected for bleeding, air leak, and proper application of the staples. A 36-French chest tube was inserted through a separate incision and placed to a closed collection system, followed by closure of the incision.

Postoperative Management

All patients were allowed to emerge from anesthesia and if possible they were extubated in the operating room. Patients were transferred to the surgical ICU if postoperative mechanical ventilation was necessary or if following postoperative assessment by the attending surgeon and anesthesiologist, they were believed to require continuous monitoring (telemetry and/or pulse oximetry) and observation. If the patients appeared in stable condition or required only cardiac telemetry, they were transferred to the ward. Postoperative pain management consisted of administration of parenteral or oral narcotics. Alternate forms of pain management, including the infiltration of long-acting local anesthetics to the incision(s) or placement of epidural catheters were not employed. Once the presence of an air leak had been excluded, the chest tube was placed to waterseal, and a chest roentgenogram was obtained. If the lung remained expanded on waterseal, the chest tube was removed, and the patient was discharged home following a short period of observation.

Data Analyses

Results are presented as group mean ± SEM. The groups were analyzed for differences using a two-tailed, unpaired Student's t test. In all cases, a p value < 0.05 was considered significant.

Results

Patients

Forty-three patients with ILD of unknown etiology were referred for lung biopsy: 22 women and 21 men with a mean age of 51 ± 3 years. At the time of admission to the hospital, 19 of 43 (44 percent) patients were receiving daily immunosuppression therapy with an average prednisone dose of 32 ± 5 mg/d, and 6 of

Table 1—Characteristics of 43 Patients With Diffuse Interstitial Lung Disease Referred for Diagnostic Lung Biopsy

<table>
<thead>
<tr>
<th></th>
<th>Thoracotomy</th>
<th>Thoracoscopy</th>
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<tbody>
<tr>
<td>Patients</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>Sex, male/female</td>
<td>12 M/9 F</td>
<td>9 M/13 F</td>
</tr>
<tr>
<td>Age, yr</td>
<td>56 ± 3</td>
<td>46 ± 4</td>
</tr>
<tr>
<td>Steroids, No. (%)</td>
<td>7/21 (33)</td>
<td>12/22 (55)</td>
</tr>
<tr>
<td>Prednisone, mg/d</td>
<td>26 ± 8</td>
<td>36 ± 6</td>
</tr>
<tr>
<td>Abnormal chest radiograph, No. (%)</td>
<td>18/21 (86)</td>
<td>18/22 (82)</td>
</tr>
</tbody>
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Table 2—Preoperative Lung Function in 36 of 43 Patients Undergoing Diagnostic Lung Biopsy

<table>
<thead>
<tr>
<th></th>
<th>Thoracotomy</th>
<th>Thoracoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁, L</td>
<td>2.11 ± 0.20</td>
<td>1.98 ± 0.19</td>
</tr>
<tr>
<td>% Predicted</td>
<td>63 ± 4</td>
<td>58 ± 5</td>
</tr>
<tr>
<td>FVC, L</td>
<td>2.80 ± 0.26</td>
<td>2.61 ± 0.18</td>
</tr>
<tr>
<td>% Predicted</td>
<td>63 ± 5</td>
<td>62 ± 3</td>
</tr>
<tr>
<td>FEV₁/FVC, %</td>
<td>75 ± 3</td>
<td>75 ± 4</td>
</tr>
<tr>
<td>Dco, ml/min</td>
<td>22.7 ± 2.8</td>
<td>19.1 ± 1.3</td>
</tr>
<tr>
<td>% Predicted</td>
<td>65 ± 8</td>
<td>64 ± 5</td>
</tr>
<tr>
<td>PaO₂, mm Hg</td>
<td>64 ± 5</td>
<td>56 ± 4</td>
</tr>
</tbody>
</table>

43 (14 percent) patients required supplemental oxygen (Table 1). Hospital admission chest roentgenograms were abnormal in 36 of 43 (84 percent) patients. Preoperative pulmonary function tests and room air blood gases were available in 32 of 43 (74 percent) patients demonstrating a substantial reduction in lung volumes, mild resting hypoxemia, and impaired diffusion capacity. The patients in the two groups (VTLB, OLB) were comparable and no significant differences were found with respect to age, sex, degree and frequency of immunsuppression, or severity of lung disease (Tables 1 and 2).

Operative Procedure

Of 43 patients studied, 21 underwent OLB and 22 underwent VTLB. Biopsies were performed on the more affected side as suggested by preoperative chest roentgenogram: VTLB—upper lobe, 17; middle lobe/lingula, 3; lower lobe, 22; OLB—upper lobe, 16; middle lobe/lingula, 6; lower lobe, 21. If a pleural component was present on thoracic surgical exploration, then pleural biopsies were also performed (OLB 3, VTLB 3). The number of lung biopsies (pleural biopsies excluded) performed per patient was the same (p = 0.48) regardless of the method utilized (OLB, 2.0 ± 0.1; VTLB, 1.9 ± 0.2). The VTLB required 46 ± 4 min to perform and did not differ significantly from the operative time required for OLB (38 ± 2 min, p = 0.09). Although VTLB was associated with less blood loss (52 ± 6 ml) relative to OLB (136 ± 34 ml, p < 0.05), this difference was of little clinical importance due to the minimal blood loss with either method (Table 3).

Lung Biopsy

Specimen sizes, as determined by gross measurement, were equivalent regardless of the biopsy method utilized (VTLB, 6.69 ± 0.82 cm³ per specimen; OLB, 5.78 ± 0.54 cm³ per specimen; p = 0.36). All specimens obtained in the study were negative for bacterial, fungal, or viral growth. However, histopathologic diagnoses were obtained in all but one patient, resulting in a diagnostic accuracy of 100 percent for OLB (21/21) and 95 percent for VTLB (22/23). The tissue diagnoses obtained are shown in Table 4. In the one patient in whom the specimens were reported as normal lung, the biopsy was performed to exclude vasculitis; however, since the diagnosis could not be absolutely excluded, the biopsy specimen was considered nondiagnostic for study purposes.

Postoperative Course

Patients were admitted to the ICU (20 of 43, 47 percent) or ward (23 of 43, 53 percent) postoperatively. The ICU admissions were necessary in patients requiring postoperative mechanical ventilation (2 of 20) or continuous monitoring and observation (18 of 20). Twelve of 21 (53 percent) OLB and 8 of 22 (36 percent) VTLB patients required transfer to the ICU, with a mean length of stay 1.12 ± 0.47 days and 0.3 ± 0.09 days, respectively (range, 0 to 2.8 days; 0 to 1.0 days). While ICU stay appeared to be lower in the VTLB group, this difference did not achieve statistical significance (p = 0.06). However, VTLB (1.36 ± 0.25 days; range, 0.5 to 4.8 days) was associated with a significant

Table 3—Operative Results of Patients Undergoing Diagnostic VTLB or OLB*

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<th>Thoracotomy</th>
<th>Thoracoscopy</th>
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<tbody>
<tr>
<td>Biopsy (total)</td>
<td>43</td>
<td>42</td>
</tr>
<tr>
<td>Upper lobe</td>
<td>16</td>
<td>17</td>
</tr>
<tr>
<td>Middle lobe/lingula</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Lower lobe</td>
<td>21</td>
<td>22</td>
</tr>
<tr>
<td>Biopsy (per patient)</td>
<td>2.0 ± 0.1</td>
<td>1.9 ± 0.2</td>
</tr>
<tr>
<td>EBL, ml</td>
<td>136 ± 34</td>
<td>52 ± 6</td>
</tr>
<tr>
<td>OR, ml</td>
<td>38 ± 3</td>
<td>46 ± 4</td>
</tr>
<tr>
<td>Tissue, cm³</td>
<td>5.78 ± 0.54</td>
<td>6.69 ± 0.82</td>
</tr>
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*EBL = estimated blood loss; OR = operating room.
One death occurred in the study; a 68-year-old man undergoing OLB suffered multiple postoperative complications, including postoperative bleeding necessitating blood transfusion and prolonged pleural drainage, hospital-acquired pneumonia requiring antibiotic therapy, pulmonary embolus culminating in respiratory failure, and death on the 24th postoperative day (Table 4).

**Discussion**

We found that VTLB was an effective and safe alternative to OLB in the diagnosis of ILD. The number of biopsies performed as well as the amount of tissue obtained by VTLB were equivalent to that obtained by OLB; also, VTLB did not add to operative time or intraoperative complications (Table 3). Postoperatively, patients undergoing VTLB demonstrated a reduction in the time required for both pleural drainage and length of hospital stay (Fig 2). Despite the presence of underlying lung disease, impaired pulmonary function, and need for immunosuppression, VTLB was associated with minimal morbidity and zero mortality (Tables 1, 2, and 4). A histopathologic diagnosis was obtained in 22 of 23 patients (94 percent) that compared favorably with that obtained by OLB in both the present study and previously published series.\(^3\),\(^4\),\(^8\)

The accurate diagnosis of ILD is difficult, and numerous strategies have evolved to identify potentially treatable forms of the disease.\(^1\),\(^9\) A noninvasive approach appears preferable in these patients who characteristically demonstrate impaired lung function, limited pulmonary reserve, and the need for immunosuppressive therapy. However, Gaensler and Carrington\(^7\) have demonstrated repeatedly that up to one third of patients with chronic diffuse infiltrative lung disease will require OLB. In general, patients in the current study were referred for lung biopsy only after more conservative attempts at establishing a diagnosis were unsuccessful.

To date, OLB is the most reliable method of obtaining adequate lung tissue for histopathologic analysis.\(^5\) The reported diagnostic accuracy of OLB typically exceeds 90 percent,\(^8\) and Bell et al\(^10\) have demonstrated prospectively that neither needle biopsy nor transbronchial biopsy achieved the diagnostic accuracy of OLB. While the need for tissue diagnosis has been questioned by several authors,\(^9\) Walker et al\(^11\) have demonstrated that OLB is both reliable in establishing a specific diagnosis in diffuse infiltrative disease and will lead to a change in therapy in 54 percent of patients on the basis of the biopsy result alone. In the present study, a histopathologic diagnosis was obtained by OLB in 21 of 21 patients and VTLB in 22 of 23 patients, although we did not evaluate the role of biopsy results in the subsequent treatment of...
are unaware of any recent studies that have examined death and the endoscopic stapling device that allows resection earlier studies by accuracy achieved by open lung biopsy. While these demonstrated that thoracoscopic lung biopsy could be performed safely and approached the diagnostic accuracy achieved by open lung biopsy. While these studies demonstrate that traditional thoracoscopic lung biopsy can be used in the diagnosis of ILD, we are unaware of any recent studies that have examined the newer techniques of videoendoscopic surgery in diagnostic lung biopsy. Furthermore, the results of these previous studies should not be confused with the results of the present study. Both studies\textsuperscript{5,6} employed the traditional techniques of thoracoscopy at a time when the current techniques of videoendoscopy were unavailable.

Although diagnostic accuracy is similar, comparison of our results with those previously reported suggest several important differences and improvements. Boutin et al\textsuperscript{15} obtained lung tissue with electrocautery, while Dijkman et al\textsuperscript{16} used biopsy forceps yielding specimen sizes (1.25 cm\textsuperscript{3}, 0.3 cm\textsuperscript{3}, respectively) larger than those obtained with transbronchial or needle biopsy but considerably less than those obtained with VTLB (6.69 \pm 0.82 cm\textsuperscript{3}). These differences likely result from the improved visualization present with VTLB and the endoscopic stapling device that allows resection of specimens equivalent to those obtained by OLB (Table 3).

Secondly, a major determinant of ongoing hospitalization following lung biopsy is the need for pleural drainage. In both studies,\textsuperscript{5,6} the need for pleural drainage was considerably longer (3.4 \pm 0.3 days, 4.5 days, respectively) relative to VTLB (1.26 \pm 0.25 days) but comparable to that observed in OLB (3.20 \pm 0.34 days). While not available for comparison, hospital stay is likely reduced with VTLB relative to those methods previously reported.

The diagnostic accuracy, morbidity, and mortality of OLB reported in the present study (Tables 2 and 3) are similar to those reported by others\textsuperscript{3,4,11,12} and allow meaningful comparison of VTLB both within and outside our own institution. The patients undergoing either OLB or VTLB appeared well matched despite the use of retrospective analysis (Tables 1 and 2). No difference in biopsy number or specimen size was found on analysis of the two groups; and to our surprise, the minimally invasive technique of VTLB did not add significantly to operative time (Table 3). Again, these findings demonstrate that limited lung resection can be performed videoendoscopically and without the need for thoracotomy. Sufficient tissue could be provided for both microbiologic and histologic study such that the diagnostic accuracy of the two techniques was essentially equivalent.

Clearly, the length of hospital stay is dependent on a number of confounding variables. While it has been suggested that following thoracoscopy the incisions are no more painful than tube thoracostomy and substantially less than limited thoracotomy, we can only speculate on its importance in the present study. In both groups postoperative pain was managed similarly, utilizing parenteral or oral narcotics and therefore, it is unlikely to account for the observed differences. However, in our institution, a primary determinant of postoperative hospital stay following lung biopsy appears to be the need for continued pleural drainage ($r^2 = 0.81$). The time required for pleural drainage following lung biopsy was significantly shortened following VTLB, and as result, patients undergoing VTLB demonstrated a significant decrease in length of hospitalization (Fig 2). This apparent reduction in both the time needed for pleural drainage and hospital stay following VTLB appears valid in that patients undergoing OLB in our institution did not require prolonged pleural drainage or hospitalization relative to times previously reported.\textsuperscript{3,11,12}

With the refinements in endoscopic surgery and the introduction of specially designed endoscopic stapling instruments, VTLB has become an appealing alternative to OLB. Despite the limitations of retrospective analyses, our results demonstrate that VTLB is as safe and as equally effective as OLB in the diagnosis of ILD. Postoperative recovery, complications, and hospitalization appear substantially reduced by this minimally invasive technique. Therefore, we believe that VTLB is a superior method for obtaining a tissue diagnosis and is preferable to OLB in the evaluation of ILD.

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Video Thoracoscopic Lung Biopsy vs Open Lung Biopsy (Benaard et al)