Surgical Biopsy of Suspected Interstitial Lung Disease Is Superior to Radiographic Diagnosis

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Background. Different modalities are used to diagnose interstitial lung disease. We compared the effectiveness of minimally invasive surgical biopsy versus high-resolution computed tomography for the diagnosis of interstitial lung disease and report the mortality of the procedure.

Methods. We reviewed 194 patients undergoing video-assisted thoracoscopic lung biopsies for the suspicion of interstitial lung disease from January 2003 to February 2012 at Emory University. Demographics and patient characteristics were analyzed in addition to final diagnoses and clinical outcomes.

Results. Concordance of radiographic diagnosis with final diagnosis was poor, matching pathologic diagnosis in 15% of cases, and specific diagnoses were included in the radiographic differential in only 34% of cases. A specific diagnosis was made after surgical biopsy in 88% of cases. Overall mortality of surgical biopsy was 6.7% (13/194). Major risk factors for death were preoperative supplemental oxygen, ventilator dependence, and age (p < 0.0001, p < 0.0001, and p = 0.03, respectively). Among patients with ventilator dependence preoperatively, the mortality rate was 100% versus 4.8% in patients not ventilator dependent. All biopsy specimens were concordant 91% of the time, and the first two biopsy specimens were concordant 96% of the time.

Conclusions. Surgical biopsy should remain the gold standard for diagnosis of interstitial lung disease. The mortality is low with proper patient selection. More than two surgical biopsy specimens may not be needed because the concordance rates among pathologic specimens are very high.


Interstitial lung disease (ILD) encompasses a broad classification of parenchymal lung diseases, for which the diagnosis and treatment have evolved over time. One category of ILD is idiopathic interstitial pneumonias, of which there are seven recognized forms: idiopathic pulmonary fibrosis (IPF), nonspecific interstitial pneumonia, cryptogenic organizing pneumonia, acute interstitial pneumonia, respiratory bronchiolitis-associated ILD, desquamative interstitial pneumonia, and lymphoid interstitial pneumonia [1]. Other causes of ILD include granulomatous disease and hypersensitivity pneumonitis.

Differentiating the various ILDs from IPF is very important because many of these diseases will respond to therapies such as steroids or limiting exposure to environmental antigens. IPF, on the other hand, can be progressive, and mortality rates are high without lung transplantation. Historically, surgical lung biopsy has been the gold standard for the diagnosis of ILD. The current recommendation by the American Thoracic Society/European Respiratory Society [2] is for surgical lung biopsy in patients who are at acceptable risk to tolerate the procedure. However, with the advent of high-resolution computed tomography (CT) (HRCT), more patients are diagnosed without a tissue diagnosis, effectively reducing the number of patients undergoing surgical lung biopsy. HRCT offers the potential for diagnosis without the morbidity and mortality associated with a surgical biopsy. The popularity of HRCT is supported by data demonstrating surgical lung biopsy being performed in only a minority of patients with suspected IPF. Johnston and colleagues [3] found that 60% of patients with suspected IPF never underwent a surgical biopsy.

Presently, many surgical lung biopsies are performed by video-assisted thoracoscopic surgery (VATS). This approach is beneficial to patients by reducing length of stay in comparison with the traditional approach of open lung biopsy through a minithoracotomy [4]. However, few data exist on comparing results of CT scanning with the results of lung biopsy. The purpose of our study was to evaluate the hypothesis that for the diagnosis of ILD, VATS lung biopsy is superior in diagnostic accuracy to HRCT, and to determine whether this procedure can be done with low mortality.

Patients and Methods

Data were collected retrospectively on 194 consecutive patients who underwent VATS lung biopsy for suspected interstitial lung disease at Emory University between January 1, 2003, and February 29, 2012. The study was

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approved by the Institutional Review Board at Emory University (IRB #00019102). Both outpatients and inpatients were included. There were no additional exclusion criteria. Thoracic surgeons at this institution performed two or three biopsies on the basis of their respective clinical practices and review of the preoperative HRCT. All surgical specimens were reviewed by an institutional pathologist with a focus on interstitial lung disease. Data collected included patient demographics, oxygen supplementation, ventilator dependence, HRCT reports, pathology reports, length of stay, and 30-day mortality.

**Data Analysis**

A two-sample t test was used to compare continuous data. Categorical data were analyzed with the $\chi^2$ test. A $p$ value of $< 0.05$ was considered statistically significant.

**Results**

Of the 194 patients included in this study, 52% were male, and the mean age was 58. Sixty percent were not receiving supplemental oxygen, and 2% were ventilator dependent preoperatively. The final diagnoses are summarized in Table 1.

A 6.7% mortality was associated with VATS lung biopsy. The risk factors for mortality included age ($p < 0.03$), the need for preoperative supplemental oxygen ($p < 0.0001$), and preoperative ventilator dependence ($p < 0.0001$). Patients not ventilator dependent had a mortality of 4.7%. Patients with no oxygen requirement preoperatively had no associated mortality. Table 2 summarizes the risk factors for mortality.

A preoperative CT scan was available for review in 98.5% of patients. A pathologic specimen was obtained by surgical biopsy 100% of the time, and a specific pathologic diagnosis was determined in 88.6% of patients. Patients underwent two or three biopsies at the time of operation according to the surgeon’s preference. The biopsy specimens were 100% concordant in 91% of patients, and the first two biopsy specimens were concordant in 96% of patients. HRCT identified the specific pathologic diagnosis in 14.6% of patients. The specific diagnosis was included in the radiologist’s differential diagnosis 34.2% of the time. An accurate diagnosis of IPF on HRCT was much more likely than a diagnosis of another interstitial lung disease (21% vs 5%) ($p < 0.0001$).

**Comment**

The diagnosis of ILD has evolved to include clinical criteria, HRCT, and surgical lung biopsy [1]. Diagnosis based on clinical criteria alone remains moderately effective, with reported accuracy of up to 60% to 70%, and it remains unclear whether HRCT adds significant diagnostic accuracy [5, 6]. Additionally, there is significant interobserver variation in both clinical diagnosis and HRCT-based diagnosis [7, 8]. This study demonstrates that diagnosis without surgical lung biopsy led to an accurate diagnosis in only 15% of patients, with the specific diagnosis included in the differential from the CT scan interpretation in only a third of patients. HRCT was able to diagnose IPF more frequently than other ILDs; however, a specific diagnosis was still reached in only 21% of cases. In comparison, surgical biopsy revealed a pathologic process in all patients, and a specific diagnosis was made in 88% of cases. HRCT performed lower in this study than in other studies, in part perhaps because of surgical referral for difficult-to-diagnose cases. This study demonstrates that surgical lung biopsy has an extremely high diagnostic accuracy, and that is consistent with other published studies showing similar results [9, 10]. Surgical lung biopsy has not been previously favored because of the high morbidity and mortality. Currently, a significant number of lung biopsies are performed by use of VATS, with very low morbidity and mortality. For patients not risk stratified, the reported mortality ranges from 0% to 11% [9–12]. Among low-risk patients, the procedure is well tolerated, with a mortality rate of 0% to 2% [9, 10, 13] and low morbidity [9]. This study is consistent with the literature, demonstrating a low mortality with certain well-defined risk factors including age and preoperative oxygen requirement. Among ventilator-dependent patients, there is significant 30-day mortality [12], but this likely highlights advanced disease rather than the safety of the procedure.

Inasmuch as interstitial lung disease can be a heterogeneous process, performing multiple biopsies is
wherein it is difficult to assess the posterior portions of the lung and take biopsy specimens from them [16, 17]. This may contribute to the high concordance rate demonstrated in this study and suggests that with VATS lung biopsy and preoperative image guidance, fewer specimens may need to be obtained.

Conclusions

In summary, this study demonstrates the safety and efficacy of surgical lung biopsy in patients with ILD. VATS lung biopsy was found to be superior to the diagnostic accuracy offered by radiographic assessment. VATS biopsies are becoming even more important as clinical trials for new therapies emerge that mandate tissue biopsies and as the diagnostic criteria for specific ILDs become more complex. To this point, thoracoscopic lung biopsy should remain the gold standard for diagnosis of ILD.

References


INVITED COMMENTARY

Kayatta and colleagues [1] present their review of a single center’s experience with surgical lung biopsy for interstitial lung disease. This continues to be a controversial topic, particularly amongst the transplant community, where it is felt that a lung biopsy specimen may add little to the diagnostic pathway that ultimately leads to lung transplantation. Indeed, some surgeons believe that lung biopsy increases mortality unnecessarily and perhaps makes the explant more challenging.

The importance of this current review is in documenting favorable outcomes from the procedure when performed thoracoscopically. The authors demonstrate zero mortality in the cohort that is not oxygen-dependent. This should be contrasted with the 100% mortality in the ventilator-dependent patients.

Interstitial lung disease encompasses a wide variety of pathology. As imaging modalities have improved, idiopathic pulmonary fibrosis now has specific identifying features that, in the context of a multidisciplinary evaluation, can lead to a radiographic and clinical diagnosis in up to two-thirds of such patients, without the need for an invasive procedure.

However, in those patients in whom the diagnosis is less clear by established criteria, the potential benefits of an invasive procedure should be considered. Trunbronchial biopsy has a low risk but likewise a low yield in