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Original Article

Internal Medicine Section

Assessing the Safety and Clinical Impact of Thoracoscopic Lung Biopsy in Patients with Interstitial Lung Disease

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ABSTRACT

Introduction: The clinical relevance of surgical lung biopsy in Interstitial Lung Disease (ILD) is supported in the literature. Yet most reports reflect institutional or personal bias.

Aim: To evaluate the validity of radiologic diagnosis and clinical impact of lung biopsy to help clarify which patient benefit most from biopsy.

Materials and Methods: We performed a retrospective analysis of a prospectively managed database. All patients who had a surgical lung biopsy for ILD within a period of four year (2009 to 2013) were included. Data included patient demographics, peri-operative variables and outcomes. Preoperative Computed Tomography (CT) imaging was reviewed by a thoracic radiologist blinded to the original report and pathologic information.

Results: A total of 47 patients were included. Lung tissue was obtained via a thoracoscopic approach in all but two that had mini-thoracotomy. Mean operating time was 51.1 minutes (18-123), median hospital stay was two days (1-18). Most (87.2%) of the patients were discharged within 72 hours. Thirty day mortality for elective surgery was 4.5% (2/44). Post-operative complications occurred in about one third of the patients. Complications in elective procedures included pneumothorax (10.4%), re-intubation (5.4%) and prolonged intubation (2.7%). Full concordance of radiographic diagnosis with the final diagnosis was significantly higher when reviewed by a cardiothoracic radiologist (60.5% vs. 21.3%). The preoperative clinical diagnosis was fully concordant with the final diagnosis in only 28.2% of cases. In 13.0% of patients the preoperative diagnosis was incorrect. Malignancy was the final diagnosis in two (4.3%) patients. In 51.1% of the patients, results of the biopsy did alter therapy.

Conclusion: Diagnosis of specific ILD by a cardiothoracic radiologist is more specific and accurate and will probably lead to more appropriate therapy. Elective thoracoscopic surgical lung biopsy is a safe procedure, leads to a more accurate diagnosis of ILD and impacts therapy.

Keywords: Diffuse parenchymal lung diseases, High resolution computed tomography, Video-assisted thoracoscopic surgery

INTRODUCTION

Interstitial Lung Diseases (ILD) includes a wide variety of disorders with varied pathophysiology, clinical presentation, therapeutic options and overall prognosis. Accurate diagnosis requires a multidisciplinary team evaluating the clinical, radiologic and pathologic data. A Surgical Lung Biopsy (SLB) is considered to be the gold standard and is often suggested to clarify the diagnosis. Studies of SLB show considerable differences in the postoperative morbidity and mortality [1-5]. However, many of these series involved a thoracotomy approach with significant associated morbidity and mortality. Thoracoscopy offers a less invasive approach to obtain a specimen for biopsy which significantly reduces the procedural morbidity. Given that thoracoscopy reduces the risks of morbidity and mortality, we evaluated the impact of thoracoscopic lung biopsy on the diagnosis and therapy of patients with ILD.

MATERIALS AND METHODS

A prospectively managed database was retrospectively reviewed. All patients who had a SLB during a four year period (2009 to 2013) were included. All chest CT scans used as the basis for referral for lung biopsy were reviewed by a thoracic radiologist who was blinded to the original report and pathologic information. Thoracoscopic lung biopsy was performed by a standard two port technique a 15 mm and a 12 mm port allowing the introduction of a camera, grasper and stapler with single lung ventilation in lateral decubitus position. (Surgical biopsy was deemed elective if scheduled in advance and in the absence of related medical emergency. Those procedures performed in an inpatient setting where clinical variables necessitated immediate biopsy were designated non-elective). Two patients biopsied via mini-thoracotomy due to the intolerance of single lung ventilation were included to accurately represent the complete patient pool. Intraoperative variables including number of lobes biopsied and operative times were evaluated. Postoperative variables evaluated include length of stay in the hospital, postoperative morbidity and 30-day mortality. The original radiographic diagnosis (by "pool radiologists") was compared with that of the blinded thoracic radiologist. The concordance was deemed "Full" if there was complete agreement, "Partial" if there was partial agreement and "No" if there was no agreement. The pre-operative clinical and postoperative final diagnoses were similarly compared. An example of partial concordance is a preoperative diagnosis of ILD shown pathologically to be hypersensitivity pneumonitis with neuroendocrine cell hyperplasia. The final diagnosis was compared with the preoperative diagnosis to assess for changes, concordance with radiologic assessment and impact on therapy.

For comparison of the readings of the two groups of radiologists, nominal categorical parameters were analyzed by Fisher exact test/ Chi-square tests, in case of low observed frequencies.

RESULTS

Forty seven patients underwent a SLB for ILD during the study period. Mean age in years was 57.4±12.8, (21-77) and 55.3% were females. Forty five biopsies were performed via thoracoscopy and two biopsies were performed via a mini-thoracotomy. In nearly all cases two lobes were biopsied. The mean procedure time was 51.1 minutes (18-123 minutes), with a median hospital stay of two days

Postoperative events		No. of patients (n=47)	%
Complications	None	34	70.3
	Minor	10	21.3
	Major*	3	6.4
Pneumothorax (post chest tube removal)	Immediate	4	8.5
	Remote	1	2.1
	Total	5	10.6
Home oxygen requirement		2	4.3
Urinary retention		1	2.1
Nausea and vomiting		1	2.1
Post thoracotomy syndrome		1	2.1
Mortality at 30 days	Total	4	8.5
	Procedure related	1	2.1
	Non-procedure related†	3	6.4

[Table/Fig-1]: Morbidities and mortalities.
* Re-intubation or prolonged intubation of three of 45 patients not intubated prior to surgery, includes one mortality
† two urgent in patients, one elective considered non-procedure related due to severity of ILD prior to biopsy

Diagnosis	Number
Granulomatous Disease	1
Chronic Bronchiolitis	1
Epitheloid Hemangioendothelioma	1
Radiation Pneumonitis	1
Idiopathic Pulmonary Fibrosis (IPF)	11
Interstitial Fibrosis	1
Desquamative Interstitial Pneumonia (DIP)	4
Hypersensitivity Pneumonitis (HP)	6
Secondary to Inflammatory Bowel Disease	1
DIP with Neuroendocrine Cell Hyperplasia	1
Chronic Aspiration Pneumonitis	2
Pulmonary Langerhan's Cell Histiocytosis X	1
Pneumoconiosis (Welder's Lung)	1
Adenocarcinoma	1
Connective Tissue Disorder	3
Atypical Mycobacterium	1
Rituximab Toxicity	1
HP with Neuroendocrine Cell Hyperplasia	1
Microscopic Polyangitis	1
Organizing Pneumonia	1
Non-Specific Interstitial Pneumonia (NSIP)	1
NSIP v IPF	1
Granulomatosis with Polyangitis/Wegener's	1
Acute Interstitial Pneumonitis/Hamman Rich Syndrome	1
Viral Pneumonitis	1
Diffuse Alveolar Hemorrhage	1

[Table/Fig-2]: Final clinical diagnosis.

(1-18 days). Almost half (46.8%) of the patients were discharged the next day and most patients (87.2%) were discharged within 72 hours. Morbidities and mortalities are listed in [Table/Fig-1]. Four patients (8.5%) had a small pneumothorax after chest tube removal and required no further intervention. One patient had a significant (40%) asymptomatic pneumothorax identified at a routine clinic visit 20 days postoperatively. No chest tube was necessary. Two patients were re-intubated after post-operative extubation due to inadequate secretion clearance and laryngeal oedema, and there was one prolonged intubation. Two patients (both mortalities) were intubated prior to surgery.

Four patients died within 30 days of the procedure. Two were severely ill, ventilator dependent patients prior to the biopsy and underwent mini-thoracotomy. SLB was performed in these two patients for prognostication of their clinical status following extensive discussions with their families. The third was an elective patient with severe symptoms that progressed after the procedure. These three cases were classified as non-procedure related mortalities. The fourth mortality was classified as a procedure related mortality. The patient was found unresponsive at home the day after discharge after an otherwise uneventful procedure. No post-mortem examination was performed.

The final diagnoses combining clinical, radiologic and pathologic findings for all patients are listed in [Table/Fig-2].

Regarding the concordance of pre-operative radiologic assessment by a pool of radiologists and the blinded cardiothoracic radiologist: 65.1% of the preoperative CT scan readings were partially concordant and 25.6% were fully concordant. While the radiologic assessment by both groups was fully or partially concordant with one another over 90% of the time, the assessment of the cardiothoracic radiologist was almost three times more likely to be concordant with the pathologic diagnosis compared to the pooled radiologists (60.5% vs. 21.3%, p=0.0006).

The preoperative clinical diagnosis and the final diagnosis were only fully concordant in 28.2%. Of greater importance, in 13.0% the pre-operative diagnosis was wrong (no concordance). Furthermore, in two patients an unanticipated malignancy was diagnosed. Changes in therapy were defined as change in treatment strategy, cessation or previous therapy, or initiation of new treatment, as a result of the pathologic diagnosis. The management was altered in 51.1% of patients in response to biopsy results.

DISCUSSION

It is our opinion that biopsy late in the course of the disease process is less effective and more hazardous. The 45 elective procedures largely represent a group referred early in the disease process, at a time when there was often no extensive lung involvement and symptoms were mild to moderate. Currently many physicians rely on the CT scan for diagnosis and determination of initial therapy. These data show that the diagnostic accuracy of CT scans read by a pool of radiologists was low with full concordance with the final diagnosis in 21.3% and non-concordance in 6.4%. This contrasts with the improved accuracy of a thoracic radiologist but still was only 60.5% fully concordant and 2.3% non-concordant with the pathologic diagnosis. The principle difference between the pool radiologists and the cardiothoracic radiologist was the specificity of the report.

The final pathologic diagnosis was fully concordant with the preoperative clinical diagnosis in only 28.3% of patients. There was no concordance between preoperative and postoperative diagnosis in 13% of patients. Since many of these diagnoses were based on radiologic assessment this study confirms that all CT studies should be reviewed by a thoracic radiologist. Had these studies been reviewed by a thoracic radiologist the concordance of preoperative diagnosis with pathologic findings would have been significantly higher. The other alarming finding in this study was two malignancies in the pathologic sample. One patient had no symptom suggestive of malignancy, the other had intermittent hemoptysis.

The pathologic diagnosis led to alterations in therapy in 51.1% of patients. Fibla JJ et al., showed that treatment modifications resulting from SLB were noticed in 90% of patients including initiation of new treatment in 77%, changes in treatment strategy in 40.7% and cessation of previous treatment in 6.8% of patients [6].

While opinions vary regarding the value and safety of surgical lung biopsy, it has become more widely accepted as a useful diagnostic tool in those with interstitial lung disease. Conflicting data has been published regarding the morbidity and mortality of this procedure. Reported rates of morbidity range from 16% to 71% and mortality from 1.5% to 21.7% [1-5]. Vivienne Blackhall et al., reported a mortality rate of 4.9%, with no difference in the mortality rates between thoracoscopic and open biopsies [7]. Luo Q et al., showed a similar postoperative morbidity and mortality profile to our study [8]. Conflicting data on the postoperative morbidity and mortality may be due to variation in the preoperative status of the patient and timing of the biopsy relative to the stage of the disease process. One of our study's mortalities was in an elective patient whose disease process was quite advanced when he was referred for biopsy. Risk stratification as suggested by Fibla JJ et al., will allow better selection of patients who can benefit from biopsy and the best time in the disease process to perform the biopsy [6]. Including all deaths, the two ventilator dependent patients who required conversion to open thoracotomy, the one advanced lung disease oxygen dependent patient, and the one procedure related mortality, our mortality rate is 8.5%. While significantly higher, it is not unexpected as this mortality trend (up to 24%) is seen in multiple studies with a higher proportion of open lung biopsy [9-11]. Using the ILD risk score for SLB in ILD [6] the two patients who required open thoracotomy also required preoperative ICU care giving them a C classification (Class A patients would have a 90-day mortality risk of 2%; Class B, 12%; Class C, 40% and Class D, 86%). Clinicians, on an individual basis, will have to determine with the patient/family if biopsy is worthwhile in Class B and Class C patients given such high surgical risk. Furthermore, biopsy would not be recommended in Class D patients.

In the elective patient group referred for thoracoscopic biopsy the procedures were performed efficiently with minor morbidity. There were no conversions to open thoracotomy in this group. The two patients biopsied via mini-thoracotomy were end-stage, performed to determine prognosis and accounted for two of the four mortalities. Excluding these patients, in the elective group there were two mortalities. One was considered due to the progression of disease, leaving one that should be considered procedure related though the cause of death is unknown. These data show that thoracoscopic lung biopsy can be performed safely, provides significant therapeutic benefit and should remain the gold standard in diagnosing ILD.

LIMITATION

This study has a number of limitations. It is a retrospective study of a single cohort. There was no non-surgical cohort for comparison. The cohort of patients in this study was small but in agreement with similar studies of larger cohorts [12]. Though all patients who had a surgical lung biopsy were included, we do not know the total number of patients evaluated for ILD in this time period. Though the thoracic radiologist was blinded to the diagnosis he knew that the patient had been biopsied and his assessment may have been more thorough and specific than in the usual clinical setting. In addition, it should be noted that a change in clinical management based on surgical lung biopsy may not always resulted in clinical improvement. This was not investigated in this study.

CONCLUSION

Based on these findings we recommend that all diagnostic CT scans, used to determine the aetiology of interstitial lung processes be reviewed by a radiologist with expertise in pulmonary and thoracic diseases. Atypical radiologic appearance, uncertainty of radiologic diagnosis, unusual symptomatic presentation, or rapid progression should merit a thoracoscopic biopsy early in the course of the disease process as an effective and safe tool for diagnosis.

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