

Article

Time Is Lung: Inpatient Transbronchial Lung Cryobiopsy Decreases Wait Time to Treatment Initiation for Newly Diagnosed Interstitial Lung Disease

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ABSTRACT: Although performing lung biopsies on hospitalized patients with interstitial lung disease (ILD) has risk, initial studies have shown transbronchial lung cryobiopsy (TBLC) may be safely performed in this patient group. Data evaluating the value of this intervention in establishing a diagnosis and impacting management is lacking. We present a comparison of TBLC for inpatients and outpatients and provide data on the impact on medical therapy initiation and wait times from consultation to biopsy and treatment. Demographic data, pulmonary function values, chest imaging patterns, procedural information, diagnosis, and medical therapy changes, defined as medication initiation, adjustment, or cessation guided by TBLC results, were recorded from enrolled patients with newly identified ILD. Changes in medical therapy were the primary outcome. Time from consultation to biopsy and treatment was the secondary outcome. Fifty-four (54) patients (40 outpatient, 14 inpatient) were included. Inpatients underwent biopsy 2.5 ± 4.4 days after consultation compared to 15.5 ± 16.1 days for outpatients ($p < 0.001$). Medical therapy changes occurred 10.3 ± 7.9 days after biopsy for inpatients compared to 34.6 ± 37.0 days for outpatients ($p < 0.001$). There were no significant differences in medical therapy changes between the groups ($p = 0.45$). Our initial study suggests that performing TBLC on inpatients with newly identified ILD decreases wait times to treatment initiation and diagnosis. Efforts to understand the impact of a decreased wait time on ILD prognosis, including the development of progressive disease or fibrosis, symptom evolution, and quality of life, require further evaluation.

Keywords: Diffuse parenchymal lung disease; Interstitial lung disease; Transbronchial lung cryobiopsy; Lung biopsy; Treatment delay



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1. Introduction

Patients with interstitial lung disease often wait a prolonged time before a diagnosis is established. Surveys and retrospective studies of patients with idiopathic pulmonary fibrosis (IPF) show a median diagnostic delay of 2.1 years [1]. Similarly, 43% of patients with a self-reported diagnosis of interstitial lung disease (ILD) identified through the pulmonary fibrosis foundation reported a delay of at least one year, and 19% reported a delay of at least three years [2]. The patient's journey to diagnosis is also fraught with multiple misdiagnoses and invasive procedures during the evaluation [2]. Patients similarly report a clear lack of information and resources on pulmonary fibrosis at the time of diagnosis [3]. Efforts to improve the efficiency and accuracy of this diagnostic process are essential as delays have been associated with increased mortality for patients with IPF [4] and rheumatoid arthritis associated with ILD [5].

Once a concern for ILD exists, a presentation at a multidisciplinary discussion (MDD) to review all data is recommended [6]. When patient history, laboratory evaluation, and radiographic findings are unrevealing, guidelines recommend considering obtaining a tissue biopsy to guide diagnosis and management [7]. Although surgical lung biopsy (SLB) has been the standard method, a recent randomized clinical trial comparing TBLC and SLB has shown high concordance for both histopathological interpretation and MDD diagnoses [8]. A subsequent randomized clinical

trial comparing an upfront SLB diagnostic approach versus starting with TBLC followed by SLB if TBLC is inconclusive showed decreased chest tube duration, in-hospital length of stay, and similar diagnostic yields versus immediate SLB [9]. Recommendations now advocate for the use of transbronchial lung cryobiopsy (TBLC) at experienced centers [10] as when TBLC is used in conjunction with an MDD, it has comparable accuracy, decreased morbidity [11,12], and potential cost savings compared to SLB [13,14].

While outpatient lung biopsies have a low risk for complications [15–18], hospitalized patients have a higher historical risk. Studies of hospitalized patients with suspected ILD undergoing SLB may have significant morbidity post-procedure [16–18], with mortality rates as high as 16% [18]. In contrast, initial studies looking at inpatient TBLC appear to be relatively safe and effective in establishing a diagnosis [19,20]. While these studies are limited by a smaller sample size ($n = 17$ inpatients [19] and $n = 22$ inpatients [20]), inpatients had objectively higher levels of acuity based on comorbidities and American Society of Anesthesiology (ASA) scores, yet did not have a statistically significant increase in complications, including bleeding, pneumothorax, transfer to a higher level of care, or mortality [19,20].

While initial studies suggest that inpatient TBLC for newly identified ILD patients is safe, data evaluating the value of this intervention in impacting clinical management and establishing an ILD diagnosis is lacking. To help determine the potential benefit of inpatient TBLC on treatment initiation and wait times between identification of ILD on imaging and time to biopsy, we present a retrospective comparison of hospitalized and outpatients with newly identified ILD.

2. Methods

2.1. Study Cohort

All patients consecutively presenting to our interventional pulmonology (IP) clinic or inpatient consult service for evaluation of newly discovered ILD by high-resolution CT chest (HRCT) from November 2019 through May 2021 were consented for TBLC, underwent the procedure by one interventional pulmonologist in a dedicated bronchoscopy suite as previously described [20], and were enrolled. During the study period, 77 total patients underwent TBLC, with 55 outpatients and 22 inpatients (Figure 1). Ten (10) patients received an alternative diagnosis to ILD diagnosis (six outpatients, four inpatients), and 13 patients (nine outpatients, four inpatients) did not have treatment guided by TBLC results (medication initiation, adjustment, or cessation was not directly impacted by results of the TBLC procedure) and were thus excluded from the final analysis. The study was approved by the institutional review board of the Medical College of Wisconsin PRO00036023.

Demographic data, pulmonary function test (PFT) values, chest imaging pattern, final MDD diagnosis, time from consultation to biopsy and medical therapy change, and specific medical therapy changes, defined as medication initiation, adjustment, or cessation guided by TBLC results, were extracted from the medical record. Procedural information, including biopsy location, number of lobes biopsied, total biopsies performed, and procedure complications, including pneumothorax, bleeding severity, worsening respiratory status, change in level of care, and 30-day and 60-day mortality, were previously reported [20]. Changes in medical therapy were the primary outcome. Time from consultation to biopsy and treatment initiation was the secondary outcome.

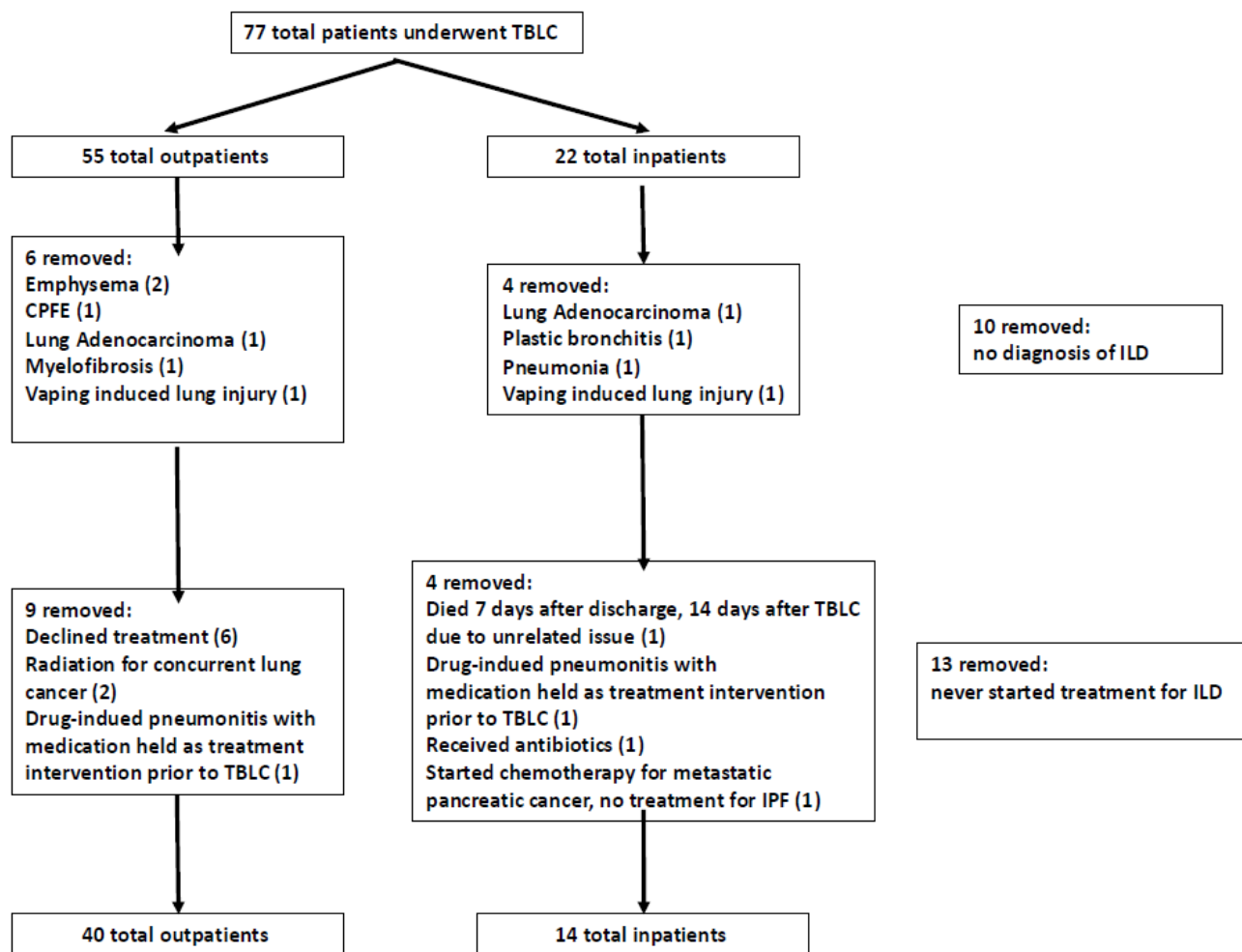


Figure 1. Evaluation of patients undergoing transbronchial lung cryobiopsy and those included in the study. CPFE = combined pulmonary fibrosis and emphysema, ILD = interstitial lung disease, IPF = idiopathic pulmonary fibrosis, TBLC = transbronchial lung cryobiopsy.

2.2. Statistical Analysis

Categorical variables were expressed as a number and percentages, and comparisons were performed with the Chi-square test or Fisher's exact test. Continuous variables were expressed as mean with standard deviation or as an interquartile range with overall range, and comparisons were done with the Student's *t*-test or Mann-Whitney *u*-test. All *p*-values were two-sided, and $p < 0.05$ was considered statistically significant. Statistical analysis was performed with SAS version 9.4 (SAS Institute, Cary, NC, USA).

3. Results

During the study period, 54 patients (40 outpatient, 14 inpatient) underwent TBLC, were diagnosed with ILD, and had treatment guided by the TBLC results. There were no significant differences in sex, race, PFTs, or chest imaging patterns between the groups (Table 1). There was a significant difference in age between the groups, with inpatients being younger (59.4 ± 9.5 years) compared to outpatients (65.9 ± 11.3 years) ($p = 0.02$). As described previously [20], inpatients had a statistically significant increased ASA score (3.3 ± 0.48) compared to outpatients (3.0 ± 0.51) ($p = 0.0062$) in addition to more total comorbidities (inpatient: 2.9 ± 1.6 vs. outpatient: 1.9 ± 1.2) ($p = 0.0070$), including history of malignancy (inpatient: 68% $n = 15$ vs. outpatient: 24% $n = 13$) ($p = 0.0002$) or history of transplant (inpatient: 31% $n = 7$ vs. outpatient: 4% $n = 2$) ($p = 0.0017$). Inpatients were more likely to be treated with steroids for non-pulmonary disease (45% $n = 10$ vs. 18% $n = 10$) ($p = 0.0137$), immunosuppressive therapy (36% $n = 8$ vs. 13% $n = 7$) ($p = 0.0266$), and to require supplemental oxygen (55% $n = 12$ vs. 18% $n = 10$). Reasons for hospitalizations varied for inpatients, including hypoxic respiratory failure ($n = 11$), COVID-19 pneumonia ($n = 2$), dyspnea ($n = 2$), interstitial

lung disease ($n = 2$), altered mental status ($n = 1$), cholecystitis ($n = 1$), pneumonia ($n = 1$), pulmonary nodules ($n = 1$), and severe sepsis ($n = 1$).

Table 1. Patient Characteristics.

	Outpatient	Inpatient	Total	<i>p</i> Value
Age (mean \pm SD)	65.9 \pm 11.3	59.4 \pm 9.5	64.2 \pm 11.1	0.02
Sex (<i>n</i> , %)				0.43
Male	18 (45.0%)	8 (57.1%)	26 (48.1%)	
Female	22 (55.0%)	6 (42.9%)	28 (51.9%)	
Race (<i>n</i> , %)				0.13
Caucasian	30 (75.0%)	9 (64.3%)	39 (72.2%)	
Black	6 (15.0%)	2 (14.3%)	8 (14.8%)	
Hispanic	1 (2.5%)	3 (22.4%)	4 (7.4%)	
Asian	3 (7.5%)	0 (0.0%)	3 (5.6%)	
PFTs (mean \pm SD)				
FEV1 % predicted	68.6 \pm 16.4	67.7 \pm 14.3	68.5 \pm 16.0	0.89
FVC % predicted	65.3 \pm 13.9	62.3 \pm 14.8	64.8 \pm 13.9	0.60
TLC % predicted	73.0 \pm 18.3	79.0 \pm 18.6	74.0 \pm 18.2	0.47
DLCO % predicted	58.0 \pm 17.4	49.4 \pm 21.7	56.5 \pm 18.2	0.27
HRCT Pattern (<i>n</i> , %)				0.81
Alternative	34 (85.0%)	13 (92.9%)	47 (87.0%)	
Probable UIP	3 (7.5%)	0 (0.0%)	3 (5.6%)	
Indeterminant for UIP	3 (7.5%)	1 (7.1%)	4 (7.4%)	

DLCO = diffusing capacity for carbon monoxide, FEV1 = forced expiratory volume in 1 s, FVC = forced vital capacity, HP = hypersensitivity pneumonitis, HRCT = high-resolution CT chest, NSIP = non-specific interstitial pneumonitis, PFT = pulmonary function test, SD = standard deviation, TLC = total lung capacity, UIP = usual interstitial pneumonia, Bold denotes $p < 0.05$.

As previously reported [20], there were no statistically significant differences in adverse events between hospitalized and outpatients, including the incidence of pneumothorax (9%, $n = 2$ vs. 5%, $n = 3$), tube thoracostomy placement (5%, $n = 1$ vs. 2%, $n = 1$), grade 2 bleeding (defined as suctioning for more than 1 min or instillation of vasoconstricting agents) (9%, $n = 2$ vs. 0%, $n = 0$), escalation in level of care (5%, $n = 1$ vs. 0%, $n = 0$), 30-day mortality (9%, $n = 2$ vs. 2%, $n = 1$), and 60-day mortality (9%, $n = 2$ vs. 4%, $n = 2$) ($p > 0.05$ for all). No deaths were attributed directly to the procedure.

A final MDD diagnosis was obtained in 96% ($n = 52$) of patients (inpatient 100%, $n = 14$ vs. outpatients 95%, $n = 38$) ($p = 1$) (Table 2). The most common overall diagnosis was chronic hypersensitivity pneumonitis (31.5%, $n = 17$), which was primarily driven by the outpatient group (40.0%, $n = 16$), followed by connective tissue disease-related interstitial lung disease (11.1%, $n = 6$), NSIP (11.1%, $n = 6$), and organizing pneumonia (9.3%, $n = 5$). Two (3.7%) patients (both outpatients) were determined to have unclassifiable ILD and did not receive a definitive diagnosis.

Table 2. Multidisciplinary Conference Diagnoses.

	Outpatient N = 40	Inpatient N = 14	Total N = 54	<i>p</i> Value
MDD Diagnosis Received (N, %)	38 (95.0%)	14 (100%)	52 (96.3%)	1
Specific MDD Diagnoses (N, %)				
Chronic HP	16 (40.0%)	1 (7.1%)	17 (31.5%)	
CTD-ILD	5 (12.5%)	1 (7.1%)	6 (11.1%)	
NSIP	4 (10.0%)	2 (14.3%)	6 (11.1%)	
Organizing Pneumonia	1 (2.5%)	4 (28.6%)	5 (9.3%)	
Drug Induced Pneumonitis	2 (5.0%)	2 (14.3%)	4 (7.4%)	
Granulomatous Pneumonitis	4 (10.0%)	0 (0.0%)	4 (7.4%)	
Unclassifiable ILD	2 (5.0%)	0 (0.0%)	2 (3.7%)	
CFILD	1 (2.5%)	1 (7.1%)	2 (3.7%)	
IPF	2 (5.0%)	0 (0.0%)	2 (3.7%)	
¹ Other	3 (7.5%)	3 (21.4%)	6 (11.1%)	

CFILD = chronic fibrosing interstitial lung disease, CTD-ILD = connective tissue disease-related interstitial lung disease, HP = hypersensitivity pneumonitis, ILD = interstitial lung disease, IPF = idiopathic pulmonary fibrosis, MDD = multidisciplinary conference, NSIP = non-specific interstitial pneumonitis, ¹ Other = bronchiolitis (1), CMV pneumonitis (1), graft versus host disease

(1), granulomatous and lymphocytic interstitial lung disease (1), interstitial pneumonia with autoimmune features (1), respiratory bronchiolitis interstitial lung disease (1).

The inpatient group had significantly shorter time intervals from initial IP consult to biopsy (2.5 ± 4.4 days vs. 15.5 ± 16.1 days, $p < 0.001$), from biopsy to medical therapy change (10.3 ± 7.9 days vs. 34.6 ± 37.0 days, $p < 0.001$), and from initial IP consult to medical therapy change (12.8 ± 10.8 days vs. 50.1 ± 38.5 days, $p < 0.001$) (Table 3). Inpatients also had less variability in time intervals compared to outpatients, as reflected by their corresponding smaller standard deviations, narrower interquartile ranges, and smaller overall ranges.

Table 3. Time Intervals Between Events.

	Outpatient	Inpatient	Total	<i>p</i> Value
Consult to Biopsy Days (mean \pm SD)	15.5 \pm 16.1	2.5 \pm 4.4	12.1 \pm 15.1	<i>p</i> < 0.001
Consult to Biopsy Days (IQR, Range)	20.5, 0–71	3.0, 0–17	18.5, 0–71	
Biopsy to Treatment Days (mean \pm SD)	34.6 \pm 37.0	10.3 \pm 7.9	28.3 \pm 33.7	<i>p</i> < 0.001
Biopsy to Treatment Days (IQR, Range)	28.0, 6–189	13.3, 1–24	23.3, 1–189	
Consult to Treatment Days (mean \pm SD)	50.1 \pm 38.5	12.8 \pm 10.8	40.4 \pm 37.3	<i>p</i> < 0.001
Consult to Treatment Days (IQR, Range)	37.5, 6–196	10.8, 1–41	41.0, 1–196	

IQR = interquartile range, SD = standard deviation, Bold denotes $p < 0.05$.

Patients in whom treatment was directly impacted by TBLC results were evaluated for differences in the types of medical therapy changes, defined as medication initiation of immunosuppression, anti-fibrotic, or other medications or medication changes, including adjustment or cessation (Table 4). There were no significant differences in medical therapy changes between the groups ($p = 0.45$). Initiation of immunosuppression was most common (70%, $n = 38$) and was similarly enacted between inpatients (64%, $n = 9$) and outpatients (72.5%, $n = 29$).

Table 4. Medication Changes.

	Outpatient N = 40	Inpatient N = 14	Total N = 54	<i>p</i> Value
Treatment Medications (N, %)				0.45
Immunosuppression	29 (72.5%)	9 (64.3%)	38 (70.4%)	
Prednisone	14 (35.0%)	8 (57.1%)	22 (40.7%)	
Mycophenolate	7 (17.5%)	1 (7.1%)	8 (14.8%)	
Mycophenolate + Prednisone	3 (7.5%)	0 (0.0%)	3 (5.6%)	
Methotrexate	1 (2.5%)	0 (0.0%)	1 (1.9%)	
Azathioprine	1 (2.5%)	0 (0.0%)	1 (1.9%)	
Azithromycin	3 (7.5%)	0 (0.0%)	3 (5.6%)	
Anti-fibrotic	4 (10%)	1 (7.1%)	5 (9.3%)	
Nintedanib	3 (7.5%)	1 (7%)	4 (7.4%)	
Pirfenidone	1 (2.5%)	0 (0.0%)	1 (1.9%)	
Other	6 (15.0%)	2 (14.3%)	8 (14.8%)	
Antibiotic	4 ¹ (10.0%)	1 ² (7.1%)	5 (9.3%)	
Rituximab	1 (2.5%)	0 (0.0%)	1 (1.9%)	
Ruxolitinib	0 (0.0%)	1 (7.1%)	1 (1.9%)	
Inhaled therapy	1 ³ (2.5%)	0 (0.0%)	1 (1.9%)	
Medication Change	1 ⁴ (2.5%)	2 ⁵ (14.3%)	3 (5.6%)	

¹ Antibiotics = cefepime (1), fluconazole (1), three-drug therapy for mycobacterium avium complex (1), voriconazole (1), ² Antibiotics = valacyclovir for CMV pneumonitis (1), ³ Inhaled therapy = budesonide-formoterol fumarate for bronchiolitis (1), ⁴ Medication Change = everolimus stopped for drug-induced pneumonitis (1), ⁵ Medication Change = everolimus held (1), osimertinib held (1).

4. Discussion

Patients with ILD often wait a prolonged time between the initial presentation, the establishment of a diagnosis, and the initiation of medical therapy [1,2]. Therefore, it is important to identify opportunities to improve efficiency in the diagnostic process. With the development of more data supporting the efficacy of TBLC for diagnosing ILD, acutely ill, hospitalized inpatients with ILD may benefit from an expedited diagnosis to guide treatment. Our initial results evaluating wait times for newly identified ILD inpatients and outpatients show that inpatients have a significantly decreased wait time from initial consultation to lung biopsy and to changes in medical therapy.

A potential concern when performing TBLC on inpatients is the severity of the illness that warranted their hospitalization. SLB has been shown to be potentially prohibitive for hospitalized patients due to higher mortality compared to elective, ambulatory patients [16–18]. In contrast, initial studies on inpatients undergoing TBLC have shown that while they are more acutely ill as measured by ASA score, supplemental oxygen need, and comorbidities, complication rates are not higher compared to outpatients for pneumothorax, bleeding, need for a higher level of care, or mortality [19,20]. While the size of these studies is limited ($n = 17$ inpatients [19] and $n = 22$ inpatients [20]), these findings are supported by other studies comparing inpatients and outpatients for other bronchoscopic procedures, such as endobronchial ultrasound-guided transbronchial needle aspiration [21] and flexible bronchoscopy with bronchoalveolar lavage on intubated patients [22]. Although the indications for these various procedures and patient populations are certainly different, the safety profiles further support performing bronchoscopic procedures on inpatients. Thus, consideration of inpatient TBLC to facilitate a diagnosis of ILD and treatment initiation appears reasonable.

HRCT is a crucial component in the diagnostic algorithm for ILD [23]. The positive predictive value of an HRCT diagnosis of UIP is at least 90% in studies looking at patients with biopsy-proven diagnoses [6]. While overt radiographic abnormalities are regularly recognized, subtle imaging changes are more challenging to identify, demonstrating the complexity of HRCT interpretation [24]. This potential for conflicting data between imaging and biopsy results presents another concern regarding inpatient TBLC. While there are limited data looking at ILD resolution on serial imaging, it is possible that hospitalized patients with newly identified ILD could have short interval follow up imaging that refutes the possibility of ILD similar to incidentally found pulmonary parenchymal nodules [25] and airway nodules of the tracheobronchial tree [26]. In our study population, ten patients (six outpatients, four inpatients, Figure 1) received an alternative diagnosis despite the presence of what appeared to be ILD on imaging, further reflecting this potential discordance between radiographic and histopathologic diagnoses. However, we were able to establish an alternative diagnosis for these patients that guided their treatment, supporting the benefit of the biopsy procedure in their overall management. To mitigate the risk of an unnecessary procedure, it will be imperative to ensure that all alternative explanations for an ILD pattern on imaging, such as infection, interstitial edema, or malignancy, amongst others, are thoroughly examined before proceeding. Optimizing this process will be an area of future discussion.

ILD is uncommon in younger patients, with the mean age at diagnosis for IPF being 68 [27]. Unfortunately, older age at diagnosis is associated with worse outcomes for patients with IPF [4–28], other progressive fibrosing interstitial lung diseases [29], and rheumatoid arthritis associated with ILD [5]. Because establishing a diagnosis of ILD is often delayed and exposes patients to unneeded procedures [1,2], years may pass before starting a treatment plan [1,2], potentially missing the opportunity to intervene earlier in the disease course before inflammation evolves into fibrosis. Interestingly, in our study, inpatients (59.4 ± 9.5 years) presented at a significantly earlier age than outpatients (65.9 ± 11.3 years; $p = 0.02$, Table 1) for TBLC. Although we are limited by our small sample size, this finding potentially suggests that these patients may be able to take advantage of a diagnosis at a significantly earlier age than outpatients, further supporting the finding of significant delays that outpatients with ILD experience. It is possible that the worse outcomes associated with advancing age may reflect the negative impact of a prolonged delay from symptoms to diagnosis and treatment. Thus, improving the efficiency of the diagnostic process may have the potential to impact morbidity and mortality.

A portion of ILD patients will develop chronic, fibrosing, and progressive disease. While IPF is the exemplar of this process, non-IPF ILDs may also evolve into a progressive pulmonary fibrosis (PPF) phenotype, which is characterized by worsening symptoms, radiographic progression, and physiological progression over the past year [10]. PPF leads to a decline in lung function, decreased quality of life, and early mortality [30]. Unfortunately, prognosticating which patients will develop this phenotype is challenging [31]. Because fibrosis is irreversible, treatment should be initiated as soon as a diagnosis is confirmed for IPF [32,33] and once evidence of PPF is confirmed based on established criteria [10]. In our study, inpatients undergoing TBLC waited significantly less time from IP consultation to biopsy

(2.5 ± 4.4 days vs. 15.5 ± 16.1 days, $p < 0.001$), from biopsy to treatment (10.3 ± 7.9 days vs. 34.6 ± 37.0 days, $p < 0.001$), and most importantly from initial IP consult to treatment initiation (12.8 ± 10.8 days vs. 50.1 ± 38.5 days, $p < 0.001$) (Table 3) compared to outpatients. It is reasonable to hypothesize that these findings suggest a potential positive impact on patient outcomes if lung function and lung structure are preserved through a more expeditious and efficient diagnostic and management process. Longitudinal studies assessing this possibility will be an area of future research.

While TBLC may present an efficient means to obtain an ILD diagnosis and establish a treatment plan, the need to obtain prior insurance authorization for certain medications may prevent patients from receiving their prescribed therapy. Studies from multiple medical specialties have shown that when prior insurance authorization is required, the time between medical therapy prescription and initiation of therapy is delayed, often due to denials for prior insurance authorization [34–36]. Delays in initiating medications may lead to worse outcomes, as seen in post-cardiac stent patients who are unable to obtain anti-platelet therapy in a timely manner [34]. Efforts to combat this barrier include the utilization of a centralized pharmacy [37] and identifying individuals or teams to champion the process [38]. Further efforts to accelerate the prior insurance authorization process will be needed to ensure that once a diagnosis is established and medical therapy is prescribed, patients will be able to begin their treatment quickly.

Although not examined in this study, there may also be a role for TBLC in evaluating inpatients with known ILD admitted for an acute exacerbation or concern for disease progression. While guidelines recommend ruling out cardiac failure or volume overload as part of the diagnostic criteria for an acute exacerbation of IPF [39] or other ILDs [40], the role of bronchoscopy with bronchoalveolar lavage to evaluate for infection as the inciting event or TBLC to obtain histopathology in this evaluation requires additional investigation [39]. In lung transplant patients undergoing both surveillance bronchoscopy and those suspected of experiencing acute cellular rejection, TBLC, compared to the gold standard conventional transbronchial forceps biopsy [41], improved the diagnostic accuracy of acute cellular rejection and led to treatment changes with an acceptable safety profile [42,43]. Extrapolating from this population, it may be beneficial to understand if histopathology for ILD patients with a suspected acute exacerbation or progression shows a change from an inflammatory state that requires additional or alternative immunosuppression to a fibrotic state that would be better suited by treatment with anti-fibrotic therapy. The potential impact of the information gained by TBLC on altering treatment regimens will require formal studies in the future.

Our study has limitations. These include its design as a single center and retrospective analysis with a small sample size, thus potentially impacting the rate of complications seen in our groups. Additionally, patients were not able to be randomized between the two groups, given the nature of their presentation for evaluation. However, it is strengthened by its inclusive nature of all patients with new ILD from both the inpatient and outpatient environments and the ability to obtain complete data points on all patients. We were able to show that inpatients with a new diagnosis of ILD present at a younger age (Table 1) and wait less time to initiate medical therapy and to obtain a treatment determining TBLC procedure (Table 3) compared to outpatients.

Because patients with ILD experience significant delays in establishing a diagnosis and initiating treatment, efforts to improve this process are essential. TBLC is a guideline recommended option to obtain a tissue diagnosis for patients with ILD. Our study shows that inpatients undergoing TBLC have a significantly decreased wait time from initial consultation to biopsy and to medical therapy changes, including medication initiation, adjustment, or cessation. Accelerating this process has the potential to positively impact patients by preventing progressive lung loss due to prolonged wait times. Evaluating the clinical impact of using TBLC to expedite and ILD diagnosis will require future prospective, longitudinal studies.

Author Contributions

All authors were responsible for data collection and accuracy of data, analysis of results, finalization of the manuscript, and approval of the submitted article. C.C. and B.S.B. conceived and wrote the manuscript and take responsibility for the integrity of the work as a whole.

Ethics Statement

Approval was obtained from the institutional review board of the Medical College of Wisconsin PRO00036023, Date of Approval: 5 March 2020.

Informed Consent Statement

Patient consent was waived by the institutional review board due to the retrospective nature and minimal risk of this research study.

Data Availability Statement

The data that support the findings of this study are available on request from the corresponding author.

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Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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