Diagnostic Yield of Computed Tomography-Guided Transthoracic Lung Biopsy in Diffuse Lung Diseases

Eva Padrão^a Márcio Rodrigues^b Susana Guimarães^c Patrícia Caetano Mota^{a, d}
Natália Melo^a Conceição Souto Moura^{c, d} António Morais^{a, d}
José Miguel Pereira^{b, d}

^aDepartment of Pulmonology, Centro Hospitalar de São João, Porto, Portugal; ^bDepartment of Radiology, Centro Hospitalar de São João, Porto, Portugal; ^cDepartment of Pathology, Centro Hospitalar de São João, Porto, Portugal; ^dFaculty of Medicine, University of Porto, Porto, Portugal

Keywords

Computed tomography-guided transthoracic lung biopsy · Complications · Diagnostic yield · Diffuse lung diseases · Organizing pneumonia · Surgical lung biopsy

Abstract

Background: Accurate diagnosis is essential for successful management of diffuse lung disease (DLD). Histopathology may sometimes be necessary. Surgical lung biopsy, the gold standard, carries a risk of morbidity and mortality. Computed tomography (CT) guided transthoracic lung biopsy (CT-TLB) is a minimally invasive method for obtaining lung tissue. However, its diagnostic yield is unknown in DLD. **Objective:** To assess the diagnostic yield of CT-TLB in DLD according to the predominant high-resolution CT (HRCT) patterns. **Methods:** Between January 2009 and December 2016, we enrolled all consecutive adult patients with suspicion of DLD who underwent CT-guided transthoracic lung biopsy during the diagnostic work-up. All biopsies were performed by a senior interventional radiologist using CT fluoroscopy. **Results:** The study included 169 patients (50.3% men) with a mean ($\pm$ SD) age of 58.3 ± 14 years. Consolidation was the

predominant HRCT pattern. A definitive or probable diagnosis was made in 66.3%. The most frequent diagnosis was organizing pneumonia (36.2%). Diagnostic yield was higher when the predominant HRCT pattern was consolidation or nodular. The most common complication was pneumothorax (17.8%); other complications included mild hemoptysis (7.7%), hemothorax (1.2%), and death (0.59%). No acute exacerbation of the underlying condition was observed. **Conclusions:** CT-TLB proved to be accurate and safe for the diagnosis of DLD. The overall diagnostic yield of the procedure was 66.3%. Given its low complication rates, CT-TLB can be an option in patients whose respiratory function is seriously impaired and in those with substantial comorbidities, where more invasive procedures cannot be performed for reasons of safety.

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Introduction

Diffuse lung disease (DLD) comprises a large and heterogeneous group of acute and chronic diseases that predominantly affect the pulmonary interstitium [1–3].

Establishing an accurate and confident diagnosis, while frequently challenging, is essential for the successful management of patients with DLD [1–3]. Therefore, a multidisciplinary approach should be taken and based on clinical data, laboratory tests, and functional, imaging, and histopathological findings [4–6]. While the diagnosis can be established on the basis of compatible clinical and radiologic findings combined with specific bronchoalveolar lavage (BAL) findings, it may be necessary to use histopathology, which is more invasive [1, 4, 5]. Transbronchial lung biopsy can be an appropriate initial procedure, although its diagnostic accuracy is highly variable and depends on a range of factors, such as disease distribution, crush artifacts, and sample size, which might not be representative of the predominant process; therefore, it is not considered useful in a significant number of DLDs [4, 5, 7, 8]. Several recent publications have reported on the high diagnostic accuracy of transbronchial lung cryobiopsy (TBLC), a bronchoscopic procedure that yields sufficiently large and high-quality lung samples [9–12]. Most recommendations and published data refer to surgical lung biopsy (SLB) and its diagnostic yield in DLD [4, 5, 7]. However, this approach may increase morbidity and mortality and requires appropriate patient selection, taking into account age, comorbidities, functional status, and disease severity; consequently, in many cases it is unlikely to be performed [13–16]. Computed tomography (CT)-guided transthoracic lung biopsy, a minimally invasive method, is an option for obtaining lung tissue that significantly reduces the morbidity of more invasive approaches such as SLB. Few data have been reported on the value of CT-guided transthoracic lung biopsy in the diagnosis of DLD, and its actual diagnostic yield in this context is unknown.

Aims

The aim of this study was to evaluate the diagnostic yield of CT-guided transthoracic lung biopsy in patients with DLD based on the predominant patterns in high-resolution CT (HRCT). We also analyzed its role in the multidisciplinary approach of this group of diseases and associated complications.

Materials and Methods

Subjects and Diagnostic Procedures

We included all consecutive adult patients (≥ 18 years) whose HRCT scan showed features of diffuse lung involvement and who underwent a CT-guided transthoracic lung biopsy during their diagnostic work-up at a tertiary referral center, Centro Hospitalar de São João, from January 2009 through December 2016. Before pro-

posing the procedure, each case was discussed at a multidisciplinary meeting. All participants provided their written informed consent after an explanation of the purpose and methodology of the biopsy procedure, its associated risks, and possible adverse outcomes. The study was approved by the Institutional Review Board of Centro Hospitalar de São João.

Patients underwent a complete blood count, with platelet count, basic blood biochemistry, and a coagulation study. Anticoagulant and antiplatelet therapy had been discontinued.

All lung biopsies were performed by a senior interventional radiologist using CT fluoroscopy. The biopsies were taken with an 18-gauge automated cutting needle after administration of local anesthesia with a subcutaneous injection of 5 mL of 2% lidocaine. In most of the biopsies, only one specimen was obtained, with a maximum of 2 specimens per procedure.

After the procedure, each patient was transferred to the ward and positioned in such a way that the biopsy puncture site was in the dependent position. A chest radiograph was performed within 2 h to identify possible complications. If there was no evidence of complication (pneumothorax, hemoptysis, hemorrhage) the patient was discharged on the day of the procedure. Asymptomatic patients with mild pneumothorax were followed with no intervention. A chest tube was inserted in symptomatic patients and in those with evidence of large or increasing pneumothorax.

Clinical, Radiological, and Functional Assessment, BAL, and Histopathology

Clinical data and demographic information were obtained from electronic medical records. A retrospective analysis of the information recorded was performed, taking into account clinical data, smoking habits, predominant HRCT pattern, respiratory function tests, BAL features, histopathology findings, procedure complications, and need for further study, namely, SLB.

The HRCT pattern was classified as micronodular, nodular, ground-glass opacity, reticulation, consolidation, mass, cystic, and mosaic according to the glossary of the Fleischner Society [17]. Patterns were also classified as combined if equally dominant.

Pulmonary function tests were performed in accordance with the standard recommendations of the American Thoracic Society (ATS) and European Respiratory Society (ERS) and findings categorized as normal, obstructive, restrictive, or mixed abnormalities [18].

BAL was performed following the recommendations of the ERS [19]. BAL cellular patterns were classified as lymphocytic ($>15\%$), neutrophilic ($>3\%$), and eosinophilic ($>1\%$).

Biopsy specimens were processed and stained for histopathology. Samples were considered nonrepresentative if there was inadequate or insufficient tissue. A histopathological analysis was performed only in biopsy specimens that met the minimal criteria of acceptability (at least 10–20 mm in length and at least 1 mm in width). If the biopsy specimens met sufficient histopathologic criteria to define a specific DLD pattern, a histologic diagnosis was established. When only some specific pathologic features of a specific DLD were present but criteria were incomplete, the diagnosis was classed as probable. Samples that lacked major histopathologic criteria for establishing a pattern of DLD were considered nonspecific/nondiagnostic.

DLDs were classified case by case after discussion at a multidisciplinary meeting, taking into account the current international consensus criteria of the ATS and the ERS [4, 5].

Statistical Analysis

All data analyses were performed using SPSS version 21.0 (IBM SPSS Statistics for Windows, version 21.0, IBM Corp., Armonk, NY, USA). Exploratory and descriptive analyses were applied to the variables. For each comparison, *p* values were calculated and considered statistically significant if less than 0.05.

Results

The study population included 169 patients with a mean ($\pm$ SD) age of 58.3 ± 14 years (range 18–85 years). Of these, 85 (50.3%) were men and 91 (53.9%) had a history of smoking. Pulmonary function testing revealed ventilatory abnormalities in 51.7% of subjects. Diffuse lung capacity for carbon monoxide (D_LCO) was impaired in 67.2%, in whom the mean ($\pm$ SD) percentage of predicted D_LCO was $53.1 \pm 14.8\%$ (Table 1). A differential cell count was performed in BAL in 115 patients (68%) and revealed lymphocytosis to be the most frequent feature. General demographic information and clinical characteristics are summarized in Table 1.

The most frequent predominant HRCT pattern was consolidation, which was seen in 29% of patients. The other notable CT patterns included nodular (13%), micronodular (10%), ground-glass opacity (7.7%), cystic (6.5%), reticulation (6.5%), and combination of patterns (24.9%). The main CT features are shown in Table 2.

The diagnostic accuracy of CT-guided transthoracic lung biopsy is shown in Table 3. Sufficient histopathologic tissue was obtained in 92.9% of patients. A definitive or probable diagnosis was confirmed in 66.3% of patients.

In the case of patients with a histopathology-based definitive/probable diagnosis ($n = 112$), the most frequent diagnosis was organizing pneumonia (OP), which was detected in 36.2%, followed by sarcoidosis, silicosis, acute fibrinous and OP, eosinophilic pneumonia, hypersensitivity pneumonitis (HP), pleuroparenchymal fibroelastosis (PPFE), and usual interstitial pneumonia (UIP). The remaining detailed information on the histopathologic diagnosis is listed in Table 4. Figures 1–3 illustrate 3 cases in which the diagnosis was based on a CT-guided transthoracic lung biopsy.

CT-guided transthoracic lung biopsy had a significantly higher diagnostic yield when the predominant HRCT pattern was consolidation ($p < 0.01$). In these cases, the yield was 87.7%. A nodular pattern also indicated a high diagnostic yield (77.3%). A ground-glass opacity or cystic pattern was significantly associated with a nondiagnostic CT-guided transthoracic lung biopsy ($p = 0.018$

Table 1. Demographic and clinical characteristics

Variable	Total
Age, years, mean $\pm$ SD	58.3 $\pm$ 14
Gender, <i>n</i> (%)	
Male	85 (50.3)
Female	84 (49.7)
Smoking habits, %	
Nonsmoker	46
Ex-smoker	30.2
Smoker	23.7
Pack-years, mean $\pm$ SD	36.6 $\pm$ 30.5
Pulmonary function pattern, %	
Normal	48.3
Obstructive	25.9
Restrictive	22.4
Mixed	3.4
Diffuse lung capacity for carbon monoxide	
Decreased, %	67.2
Percentage of predicted, mean $\pm$ SD	53.1 $\pm$ 14.8
Normal	32.8
Percentage of predicted, mean $\pm$ SD	87 $\pm$ 10.8
Bronchoalveolar lavage cellular pattern, %	
Normal	21.9
Lymphocytic	27.6
Eosinophilic	13.3
Neutrophilic	12.4
Lymphocytic and neutrophilic	9.5
Neutrophilic and eosinophilic	8.6
Lymphocytic and eosinophilic	6.7

Table 2. Radiologic evaluation

Predominant high-resolution CT pattern	Total, <i>n</i> (%)
Consolidation	49 (28.99)
Nodular	22 (13.02)
Micronodular	17 (10.06)
Ground-glass + consolidation	16 (9.47)
Ground-glass + reticulation	16 (9.47)
Ground-glass	13 (7.69)
Cystic	11 (6.51)
Reticulation	11 (6.51)
Reticulation + honeycombing	5 (2.96)
Reticulation + honeycombing + ground-glass	5 (2.96)
Mass	2 (1.18)
Mosaic	2 (1.18)

and $p = 0.009$, respectively). The overall diagnostic yield of the technique according to the predominant HRCT pattern is shown in Table 5.

Among subjects with nondiagnostic biopsies ($n = 45$), 11 subsequently underwent a second CT-guided transthoracic lung biopsy, 7 (58.4%) of which confirmed the

Table 3. Diagnostic accuracy of CT-guided transthoracic lung biopsy

Variable	Total, n (%)
Definite diagnosis	102 (60.4)
Probable diagnosis	10 (5.9)
Nondiagnostic	45 (26.6)
Nonrepresentative	12 (7.1)

Table 4. Histopathologic diagnosis obtained ($n = 112$)

Variable	Total, n (%)
OP	42 (37.5)
Sarcoidosis	11 (9.82)
Silicosis/silicoanthracosis	11 (9.82)
AFOP	10 (8.93)
Eosinophilic pneumonia	6 (5.36)
HP	6 (5.36)
PPFE	6 (5.36)
UIP	6 (5.36)
Vasculitis ^a	4 (3.57)
Langerhans cell histiocytosis	2 (1.79)
Rheumatoid nodule	2 (1.79)
NSIP	1 (0.89)
RB-ILD	1 (0.89)
Other	
Amyloid tumor	1 (0.89)
Emphysema	1 (0.89)
CMV infection	1 (0.89)
Granulomatous process in the context of MAC infection	1 (0.89)

^a Two cases were positive for antineutrophil cytoplasmic antibody (ANCA) to myeloperoxidase (MPO), one was positive for ANCA proteinase 3 (PR3) and one was negative for ANCA.

AFOP, acute fibrinous and organizing pneumonia; CMV, cytomegalovirus; HP, hypersensitivity pneumonitis; MAC, *Mycobacterium avium* complex; NSIP, nonspecific interstitial pneumonia; OP, organizing pneumonia; PPFE, pleuroparenchymal fibroelastosis; RB-ILD, respiratory bronchiolitis interstitial lung disease; UIP, usual interstitial pneumonia.

following diagnoses: antineutrophil cytoplasmic antibody (ANCA) to myeloperoxidase (MPO) vasculitis ($n = 2$), OP, eosinophilic pneumonia, lipoid pneumonia, hyalinizing granuloma, and connective tissue disease-related interstitial lung disease (rheumatoid arthritis). Another 13 patients were referred for SLB, which confirmed the diagnosis in 11 cases (84.6%), as follows: HP ($n = 5$), OP ($n = 2$), respiratory bronchiolitis interstitial lung disease ($n = 2$), pulmonary hemosiderosis ($n = 1$), and epithelioid hemangioendothelioma ($n = 1$). Of note, in the last 2 cas-

es, the diagnosis had already been suggested by the CT-guided transthoracic lung biopsy, although SLB was performed to confirm the diagnosis.

Most of CT-guided transthoracic lung biopsy procedures (72.8%, $n = 123$) were performed without complications. The most common complication was pneumothorax, which developed in 30 biopsy procedures (17.8%). In 9 cases (30%) it was necessary to insert a chest drain; the remaining cases improved spontaneously, without intervention. Mean prolonged hospital stay due to this complication was about 4 ± 3 days. Mild hemoptysis occurred in 7.7% of patients and hemothorax in 1.2%. None of the events reported was life-threatening. No acute exacerbation of the underlying condition was observed. Only one procedure-related death (gas embolism) was reported. Significantly more complications were observed in patients with decreased D_LCO ($p = 0.031$), although no differences in the HRCT pattern were observed ($p > 0.05$).

Discussion

We found that CT-guided transthoracic lung biopsy proved to be an accurate and safe procedure for the diagnosis of DLD. The overall diagnostic yield of CT-guided transthoracic lung biopsy in this cohort of patients with suspected DLD was 66.3%; the procedure proved more sensitive when the radiologic pattern was consolidation or nodular.

Most published data on CT-guided transthoracic lung biopsy to date are on lung nodules or masses, which are mainly assessed to determine whether they are benign or malignant. In this context, this technique has widespread acceptance as a preferred method of diagnosis, since it has already been demonstrated to be significantly accurate and safe [20–24]. The diagnostic yield of CT-guided transthoracic lung biopsy in nodules or masses has been reported to be as high as 95% [23–26].

The multidisciplinary meeting is currently the gold standard when establishing a diagnosis of DLD [4–7, 27]. This approach has significantly improved diagnostic accuracy, overall agreement, and diagnostic confidence [6, 28]. When DLD is suspected, the information recorded (history, physical examination, thoracic imaging, lung function, and other tests [e.g., BAL data]) must be thoughtfully reviewed and analyzed. When these investigations are considered to be insufficient to provide a confident diagnosis, additional and more invasive procedures, such as lung biopsy, are useful [4, 5, 7]. Until recently, SLB was considered the recommended diagnostic procedure in

Fig. 1. Organizing pneumonia secondary to amiodarone-induced toxicity in a 75-year-old man. **a, b** Axial HRCT images demonstrate the presence of bilateral multifocal consolidations, with a predominant peripheral and peribronchial distribution; some of

the consolidation foci present a surrounding ground-glass halo. **c** Transthoracic lung biopsy sample showing airspaces filled with plugs of loose fibroblasts, inflammatory cells, and myxoid stroma (H&E, ×100).

Fig. 2. Hypersensitivity pneumonitis (HP) in a 61-year-old man who had been exposed to pigeons and had a previous medical history of non-Hodgkin lymphoma treated with chemotherapy. **a, b** Multiple centrilobular nodules with ground glass attenuation scat-

tered throughout the lungs. A small cyst is noted in the right middle lobe. **c** Transthoracic lung biopsy sample showing lymphocytic infiltrate in the alveolar walls, a small poorly formed granuloma and organizing pneumonia (H&E, ×200).

Fig. 3. Idiopathic pulmonary fibrosis in a 73-year-old man. **a, b** Axial HRCT images show extensive reticulation and multilayered subpleural honeycombing with traction bronchiectasis. Asymmetry is noted, with more pronounced findings in the right lung. No

inconsistent features are seen. **c** Transthoracic lung biopsy sample showing collagenous fibrosis with transition to preserved parenchyma (not shown), fibroblastic foci, and mild chronic interstitial inflammation; no honeycombing (H&E, ×200).

Table 5. Diagnostic yield of CT-guided transthoracic lung biopsy according to the predominant HRCT pattern

HRCT pattern	Diagnostic yield, %*
Consolidation	87.7
Nodular	77.3
Ground-glass + consolidation	75
Micronodular	64.7
Reticulation	54.6
Ground-glass	38.5
Ground-glass + reticulation	31.2
Cystic	27.3

* Definite and probable diagnosis.

DLD. In fact, the role of SLB is well established in DLD [13]. Published data show that, in most cases, a confident diagnosis was reached in more than 90% of patients who underwent SLB [13, 29–31]. However, despite the high diagnostic yield of this procedure, associated morbidity and mortality are high, mainly because of acute exacerbation of the underlying disease [13, 14, 31–36]. Therefore, the procedure may not be feasible in patients with serious comorbidities or severe disease. Moreover, TBLC is increasingly used in the diagnosis of DLD and has a diagnostic yield of between 75 and 85%, or even higher in some series [11, 12, 37–39]. Even in cases of fibrosing DLD, with a UIP or UIP-like HRCT pattern, in which the differential diagnosis is more problematic, TBLC has also provided a good diagnostic yield [12].

Few data are available on the role of CT-guided transthoracic lung biopsy for the diagnosis of DLD, and reports almost only refer to its role in OP, in which the technique has been used for diagnosis in isolated cases [40–42]. The procedure was also reported in a small cohort of patients for the diagnosis of PPFE and was considered a valuable tool in this context [43]. Our literature search revealed only 2 small series on CT-guided transthoracic lung biopsy for diagnosing DLD, in which the authors made an etiological diagnosis in about 80% and 73% of cases [44, 45]. However, their relatively small sample sizes ($n = 15$ and $n = 22$, respectively) inevitably limit the interpretation of these results owing to potential sampling biases. Although the overall diagnostic yield of our study is slightly lower than those cited, we emphasize that, to the best of our knowledge, ours is the largest cohort in which the role of CT-guided transthoracic lung biopsy has been established in patients with suspected DLD and the only one to show a clear correlation between HRCT pattern and diagnostic yield.

The diagnosis of patients who underwent CT-guided transthoracic lung biopsy was established after evaluation at the multidisciplinary meeting, where the histological pattern was contextualized with both clinical and radiological features. Diagnosis based on histopathology (Table 4) was reliable in some cases, such as OP, sarcoidosis, and acute fibrinous and OP, whereas other cases (e.g., UIP or nonspecific interstitial pneumonia pattern [NSIP]) were more complex, usually required larger samples, and could not be diagnosed with a high degree of confidence. The initial diagnosis was HP in 6 patients, although in 3, histology findings were considered low-confidence, and the final diagnosis was only established at the multidisciplinary meeting. The other 3 were considered high confidence, since an interstitial infiltrate was present in all 3 (associated with granulomas in 2 and with OP in 2). As for the UIP pattern, it is noteworthy that none of these patients could undergo SLB because of their comorbidities. Six patients were considered to have a UIP pattern; of these, 2 had patchy fibrosis associated with fibroblastic foci and honeycombing, 2 had patchy fibrosis with fibroblastic foci, and one patchy fibrosis with honeycombing, which can be considered a high-confidence diagnosis. One of the patients, however, had patchy fibrosis, which enables a low-confidence diagnosis, and a definitive diagnosis was obtained only after the multidisciplinary evaluation. After the multidisciplinary meeting, 2 of these cases of UIP were assumed to be in the context of HP, whereas the remaining in the context of idiopathic pulmonary fibrosis. In the only patient diagnosed with NSIP, the histology sample revealed diffuse interstitial fibrosis with a significant inflammatory infiltrate and aggregates of lymphocytes and plasmocytes that were consistent with his rheumatoid arthritis. In this case, transthoracic lung biopsy had been performed as part of a differential diagnosis with imaging features analyzed previously in the multidisciplinary meeting. Of the 4 cases with vasculitis, 2 proved to be ANCA MPO+ and one ANCA PR3+. All 3 underwent transthoracic lung biopsy, which revealed granulomatous vasculitis and capillaritis with hemosiderosis in the first 2. In the ANCA PR3+ case, the biopsy showed hemosiderosis and capillaritis. Two of these cases corresponded to patients who initially (at onset of disease) were ANCA- negative; ANCA titers were shown to be positive during the course of the disease and after the CT-guided transthoracic lung biopsy. In both cases, ANCA values remained only feebly positive. The other patient was admitted to hospital with persistent fever of unknown origin. In addition to the identification of ANCA positivity, a superinfection gave cause for concern

and led to the CT-guided transthoracic lung biopsy. One patient with a final diagnosis of granulomatosis with polyangiitis was ANCA-negative, and the diagnosis was based on pulmonary hemorrhage in the biopsy and extrapulmonary features compatible with vasculitis.

One could question whether the result of this study would have been more robust if subsequent surgical biopsy specimens had been used to validate the diagnostic accuracy of CT-guided biopsy. However, as previously mentioned, given the high degree of confidence when establishing the diagnosis in the cases presented in this series, it would not be ethical to pursue to SLB merely to validate the diagnosis, since it would eventually (and needlessly) contribute to an increased risk of complications. Moreover, it should be noted that cases in which it was not possible to establish a diagnosis with a high degree of confidence after CT-guided transthoracic lung biopsy were subsequently referred for SLB, unless this was not feasible owing to safety concerns.

Complications of CT-guided transthoracic lung biopsy were detected in 27.2% of cases, which is consistent with the literature. The most common complication was pneumothorax (17.8%), followed by mild hemoptysis (7.7%) and hemothorax (1.2%); these data are in line with other reports on this technique, even though reported complication rates are highly variable [21, 25, 26, 46]. Apart from the patient who died from procedure-related complication, none of the other events that occurred in our study were considered life-threatening for patients undergoing CT-guided transthoracic lung biopsy. Conversely, SLB, a widely accepted and costly procedure, may unnecessarily increase the risk of serious complications in some cases. In fact, it carries considerable risks, namely, an overall mortality of 2–6% and an associated morbidity of approximately 10–20%, both of which are largely associated with the occurrence of acute exacerbation [13, 14, 31, 32, 34, 35, 47, 48]. In the present cohort, it should be noted that there were no exacerbations after CT-guided transthoracic lung biopsy. In fact, concerns about morbidity and mortality and risk of exacerbation are a major constraint when selecting patients for histological assessment to resolve an inconclusive diagnosis. The decision to perform a lung biopsy should always be taken on an individual basis, weighing the potential risks inherent to the procedure against the benefit of establishing a confident diagnosis. In fact, it is not uncommon for patients with suspected DLD in whom SLB is deemed necessary to be excluded from this procedure owing to serious comorbidities or severe lung disease, since the risk of complications may outweigh the potential benefits of

biopsy. Additionally, as SLB is invasive and is associated with significant morbidity and mortality, many patients frequently do not consent to undergo the procedure. In this context, CT-guided transthoracic lung biopsy might be considered an appropriate method for histological assessment. One of the main advantages of the procedure is that it can be performed under local anesthesia, without the need for deep sedation or intubation. Thus, CT-guided transthoracic lung biopsy can be envisaged for patients with severely impaired respiratory function and substantial comorbidities. As the technique is minimally invasive, it reduces the risk of complications and life-threatening events.

Our study is limited by its retrospective design. It is also subject to a certain degree of selection bias, because of the intrinsic notion that CT-guided transthoracic lung biopsy could be particularly sensitive for the diagnosis of patients whose HRCT patterns are characterized by consolidations and nodules, which are the main radiologic findings registered in this cohort. This selection bias became even more evident after the introduction of TBLC in our center. In addition, OP was the most frequent diagnosis in the cohort, although this does not fully represent the patients followed at our DLD outpatient clinic. Furthermore, and while inherent to the technique, the dimensions of the lung tissue samples obtained through CT-guided transthoracic lung biopsy tend to be significantly smaller than those sampled through SLB, thus affecting the diagnostic accuracy of the former. In fact, in the present study, CT-guided transthoracic lung biopsy did not provide an accurate diagnosis in 26.6% of patients. However, it must be noted that when a patient undergoes CT-guided transthoracic lung biopsy, tissue sampling is guided directly on-site. With SLB and TBLC, sampling errors might occur if the biopsy does not cover an affected area in cases of patchy impairment by a DLD.

On the other hand, while biopsies are usually taken at multiple sites in SLB, with CT-guided transthoracic lung biopsy, the biopsy is usually performed only at one site. This can be considered another limitation of the study. In fact, as a minimally invasive technique, CT-guided transthoracic lung biopsy is usually performed at a single site in order to minimize the risk of complications. However, all the cases included in the present study were discussed at the DLD multidisciplinary meeting prior to the procedure, and the biopsy site was chosen according to the presumptive higher diagnostic yield and taking into account the distribution of the radiologic abnormalities. After performing the biopsy, the interventional radiologist

evaluated the specimen obtained macroscopically, and, if this was considered unsuitable, a second biopsy was performed near the area. Nevertheless, we recognize the relevance of obtaining biopsies from multiple sites, especially when UIP or NSIP is suspected, since both these patterns can coexist in the same patient and may also be associated with other entities, such as HP. However, the cases with UIP or NSIP in our series corresponded to patients who presented no conditions for further invasive procedures.

Diagnostic decisions with respect to patients with DLD must be taken on an individual basis. In specific patients, lung biopsy might provide valuable diagnostic information and could therefore confirm diagnosis of a specific DLD. The decision as to which histological sampling procedure is the most appropriate depends on the availability of the different methods in the various centers, the experience of health care professionals, the diagnostic

yield of the technique in the specific context, the general status of the patient, and the patient's preferences.

In conclusion, this study describes our experience and provides important insights into the role of CT-guided transthoracic lung biopsy in the diagnosis of DLD, specifically, in radiologic patterns in which the diagnostic yield was higher, such as consolidation and nodular pattern. Given the low complication rates, CT-guided transthoracic lung biopsy can be considered an alternative in patients whose respiratory function is seriously impaired and in those with substantial comorbidities, where more invasive procedures cannot be performed for reasons of safety.

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