Video-assisted thoracoscopy for the diagnosis of diffuse parenchymal lung disease*

A videotoracoscopia no diagnóstico das doenças difusas do parênquima pulmonar

Renato Tadao Ishie, João José de Deus Cardoso, Rafael José Silveira, Lucas Stocco

Abstract

Objective: To evaluate the role of video-assisted thoracoscopy in the diagnosis of diffuse parenchymal lung diseases. **Methods:** The medical charts of patients suspected of having diffuse parenchymal lung disease were retrospectively reviewed, as were the results of the anatomopathological examination of lung biopsy specimens collected through video-assisted thoracoscopy. **Results:** Of the 48 patients included in the study, 25 (52.08%) were female and 23 (47.92%) were male. The mean age was 58.77 years (range, 20-76 years). A total of 54 biopsy fragments were submitted to anatomopathological examination: 24 (44.44%) from the lingula; 10 (18.52%) from the left lower lobe; 7 (12.96%) from the right middle lobe; 6 (11.11%) from the right lower lobe; 5 (9.26%) from the left upper lobe; and 2 (3.71%) from the right upper lobe. The mean duration of thoracic drainage was 2.2 days. Adverse events included conversion to thoracotomy, in 2 patients (4.17%), and residual pneumothorax, in 1 (2.08%). The definitive diagnosis was made in 46 patients (95.83%), and idiopathic interstitial pneumonia was the predominant diagnosis (in 54.18%). The most common diagnoses were usual interstitial pneumonia (in 29.27%), nonspecific interstitial pneumonia (in 16.67%) and hypersensitivity pneumonia (in 12.50%). **Conclusions:** Lung biopsy through video-assisted thoracoscopy is a safe, effective and viable procedure for the diagnosis of diffuse parenchymal lung diseases.

Keywords: Lung diseases, interstitial; Thoracoscopy; Diagnosis.

Resumo

Objetivo: Analisar o papel da videotoracoscopia no diagnóstico das doenças difusas do parênquima pulmonar. **Métodos:** Os prontuários de pacientes com suspeita de doenças difusas do parênquima pulmonar e os resultados do exame anatomopatológico das amostras de biópsia pulmonar por videotoracoscopia foram analisados retrospectivamente. **Resultados:** Dos 48 pacientes incluídos no estudo, 25 (52,08%) eram do sexo feminino, e 23 (47,92%) eram do sexo masculino. A idade média foi de 58,77 anos, variando entre 20 e 76 anos. Foi realizado o exame anatomopatológico de 54 fragmentos de biópsia pulmonar: 24 (44,44%) da língula; 10 (18,52%) do lobo inferior esquerdo; 7 (12,96%) do lobo médio; 6 (11,11%) do lobo inferior direito; 5 (9,26%) do lobo superior esquerdo; e 2 (3,71%) do lobo superior direito. O tempo médio de drenagem torácica foi de 2,2 dias. Como eventos adversos, houve conversão para toracotomia em 2 pacientes (4,17%) e pneumotórax residual em 1 (2,08%). O diagnóstico definitivo foi obtido em 46 (95,83%) casos, com predomínio das pneumonias intersticiais idiopáticas (54,18%). Os diagnósticos mais frequentes foram pneumonia intersticial usual (29,27%), pneumonia intersticial não-específica (16,67%) e pneumonia por hipersensibilidade (12,50%). **Conclusões:** A videotoracoscopia com biópsia pulmonar é um procedimento eficaz, seguro e viável para o diagnóstico das doenças difusas do parênquima pulmonar.

Descritores: Doenças pulmonares intersticiais; Toracoscopia; Diagnóstico.

Introduction

Diffuse parenchymal lung diseases (DPLDs) constitute a heterogeneous group of lung diseases, including more than two hundred different interstitial diseases, characterized by varying degrees of inflammation and fibrosis. These non-neoplastic disorders primarily affect the lung interstitium, although the alveolar space, bronchioles and pulmonary vessels can also be affected.[1,2] In addition to the histological aspects, these disorders present similar

* Study carried out at the Federal University of Santa Catarina, Florianópolis, Brazil.
Correspondence to: Renato Tadao Ishie. Rua Professora Maria Flora Pausewang, 277, apto. 202, Trindade, CEP 88036-800, Florianópolis, SC, Brasil.
Tel 55 48 9912-8697. E-mail: renatoishie@yahoo.com.br
Financial support: None.
Submitted: 1 June 2008. Accepted, after review: 26 August 2008.

clinical, functional and radiological manifestations, justifying the fact that they are classified into the same group.[2]

Epidemiological data regarding DPLDs are scarce, since this is a group of diseases that are underdiagnosed and under-reported. In the United States, it is estimated that the prevalence of DPLDs is 80.9 cases/100,000 population among males and 62.2 cases/100,000 population among females, with an incidence of 31.5 and 26.1 new cases/100,000 population per year among males and females, respectively.[3]

The importance of the study of DPLDs is underscored by the increase in incidence observed in western countries in recent years. In addition, DPLDs account for approximately 15% of the noninfectious diseases diagnosed by pulmonologists. These diseases can also cause significant morbidity, resulting in secondary pulmonary hypertension and right heart failure accompanied by cor pulmonale, as well as disabling dyspnea. In addition, even with appropriate treatment, some DPLDs, such as usual interstitial pneumonia, have an unfavorable prognosis comparable to that of neoplastic diseases.

According to the American Thoracic Society/European Respiratory Society,[1] DPLDs can be divided into four categories: DPLDs of known etiology; granulomatous DPLDs; idiopathic interstitial pneumonia; and other forms of DPLD (Figure 1).

The process of diagnosing a DPLD is dynamic. The diagnostic reasoning is based on the joint analysis of clinical, radiological and anatomopathological aspects.[1]

The radiological presentation of a DPLD typically varies. Routine chest X-rays present low sensitivity and specificity,[4] typically identifying the presence of pulmonary disease and indicating the need for additional tests that are more complex. A common presentation is the development of honeycomb cystic areas.

Among imaging tests, an HRCT scan of the chest is the best suited to the evaluation of a DPLD. Such scans can be used not only to identify the presence of disease but also to evaluate its extent and characterize its pattern. In addition, an HRCT scan of the chest helps reduce the number of differential diagnoses and define the site from which the biopsy specimen is to be taken, as well as allowing the clinical course of the disease and the response to therapy to be evaluated.[5] However, HRCT lacks diagnostic specificity and therefore, in most DPLD patients, does not preclude the need for histological confirmation,[6] as shown in Figure 2.

Pulmonary function tests are often recommended. These tests can estimate severity and prognosis, as well as monitoring response to therapy and disease progression.[7] The recommended tests include spirometry, DLCO determination and evaluation of the degree of reduction in oxygenation during exercise

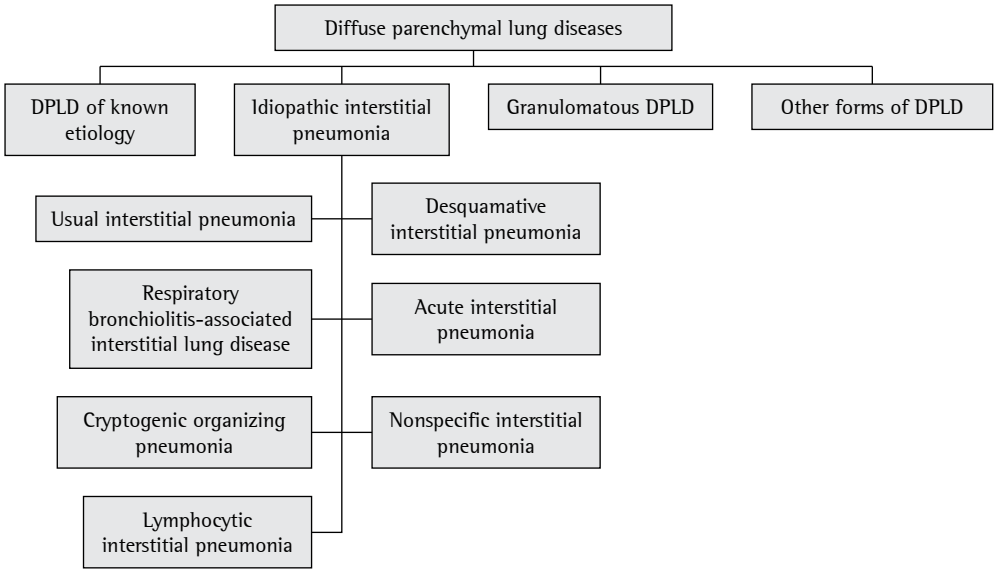

Figure 1 - Classification of diffuse parenchymal lung diseases.[1] DPLD: diffuse parenchymal lung disease.

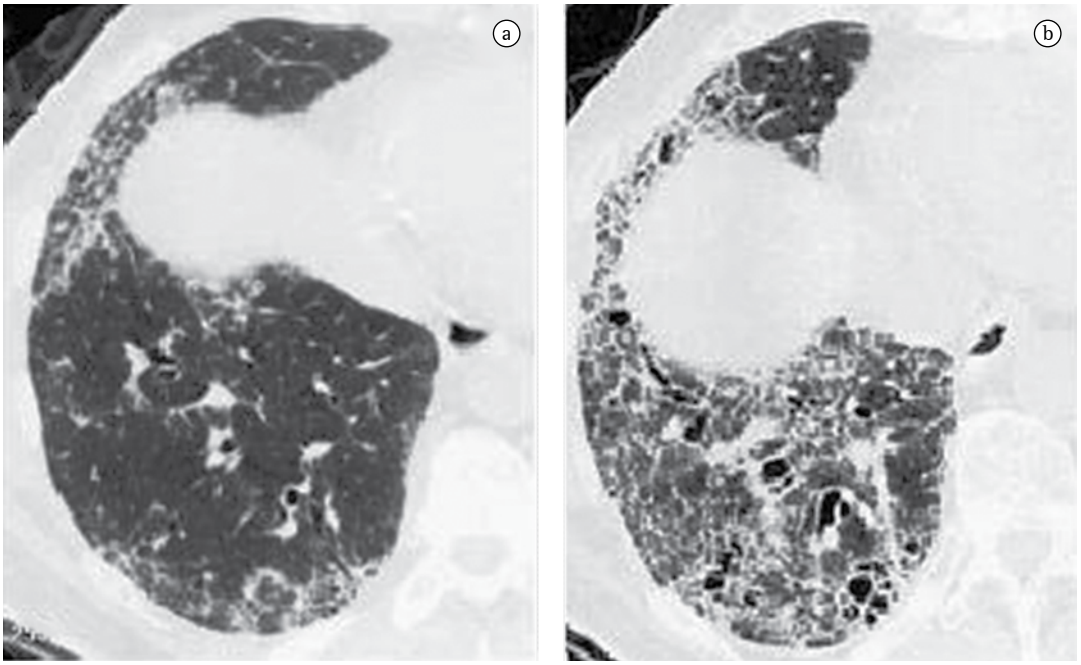

Figure 2 - HRCT scans revealing fibrosis progression and lung honeycombing in a patient with idiopathic pulmonary fibrosis.[1]

through the use of blood gas analysis or pulse oximetry. Usually, DPLDs present a characteristic functional pattern, with restrictive ventilatory failure and reduced diffusing capacity.

Bronchoalveolar lavage is a test that allows the analysis of cells in the airway and alveolar space, as well as of soluble substances from the extracellular mucus layer.[5] Bronchoalveolar lavage is a useful technique for the investigation of pneumoconiosis, opportunistic infections, suspected malignancy, some hematologic diseases and alveolar proteinosis, as well as diseases related to lung transplantation or drug-induced diseases.[2]

Frequently, the definitive diagnosis of DPLD can be established only through anatomopathological examination of the material obtained by lung biopsy. In addition to diagnostic confirmation, this procedure provides information regarding disease activity, disease progression and response to therapy.[2] The options for lung biopsy include bronchoscopy with transbronchial biopsy, open lung biopsy and lung biopsy through video-assisted thoracoscopy.

Bronchoscopy with transbronchial biopsy is useful in cases in which the disease presents peribronchial, peribronchiolar or diffuse distribution. One limitation of this procedure is the small quantity of lung tissue obtained in the biopsy, which is why it is not recommended for the investigation of idiopathic interstitial pneumonia.[1,4] In addition, its accuracy in the diagnosis of DPLD in immunocompetent patients is only 7-37%.[8,9]

The gold standard for the diagnosis of DPLD is surgical lung biopsy, which should be used whenever it is not possible to establish a definitive diagnosis based on the available clinical and radiological data.[10] It can be performed as an open procedure or through video-assisted thoracoscopy.

Open lung biopsy has a high diagnostic yield (92%), as well as low rates of morbidity and mortality (2.5% and 0.3%, respectively).[5] The most common technique is minimal inframammary thoracotomy, through which lung biopsy is performed, using either manual or mechanical sutures.

Video-assisted thoracoscopy is considered a minimally invasive technique. It provides excellent visualization of the intrathoracic structures and allows the collection of a greater number of lung samples, when necessary. Since it is a less invasive procedure, video-assisted thoracoscopy has come to be used as the principal means of diagnosing DPLD, and the number of surgical

lung biopsies has increased.[5] However, its use must be evaluated in terms of safety and diagnostic resolution. Therefore, the objective of the present study was to analyze the role of this method, which is currently widely used, in the diagnosis of DPLD.

Methods

The medical charts of patients being monitored in order to diagnose DPLD were evaluated, as were the results of the anatomopathological examination of lung biopsy specimens collected through video-assisted thoracoscopy. All of the eligible patients had been monitored in the Department of Thoracic Surgery of the Nereu Ramos Hospital in the city of Florianópolis, located in the state of Santa Catarina, between July of 1999 and July of 2007. The inclusion criteria were as follows: being under outpatient follow-up treatment in order to diagnose DPLD; not having received a diagnosis by noninvasive evaluation; and not having received a histopathological diagnosis in the transbronchial biopsy, when performed.

The exclusion criteria were as follows: requiring mechanical ventilation in an intensive care unit and being oxygen-dependent.

There were 48 patients who met the criteria adopted, and the charts of those patients were therefore selected for study.

Data regarding gender and age of the patients were analyzed. Age (in years) was defined as that at the time of lung biopsy. The distribution of biopsy sites and the anatomopathological diagnoses obtained were also analyzed. Regarding the surgical procedure, the variables studied were surgical complications, duration of thoracic drainage in the postoperative period and postoperative complications.

Results

A total of 48 patients met the study criteria and were included. Of those, 25 (52.08%) were female and 23 (47.92%) were male. Patient ages ranged from 20 to 76 years (mean, 58.77 years).

A total of 54 lung biopsy samples were sent for anatomopathological analysis: 39 (72.22%) from the left lung and 15 (27.28%) from the right lung. Table 1 shows the biopsy site distribution.

Table 1 - Lung biopsy site distribution.

Biopsy site	n	%
Lingula	24	44.44
Left lower lobe	10	18.52
Middle lobe	7	12.96
Right lower lobe	6	11.11
Left upper lobe	5	9.26
Right upper lobe	2	3.71
Total	54	100.00

The mean duration of thoracic drainage in the postoperative period was 2.2 days (range, 1-4 days).

Regarding intraoperative complications, 2 patients (4.17%) required 4-5 cm auxiliary incisions. Only 1 patient (2.08%) presented a postoperative complication (residual pneumothorax after chest tube removal).

The anatomopathological results of the video-assisted thoracoscopic lung biopsies are listed in Table 2.

Table 2 - Distribution of the diagnoses and findings made by video-assisted thoracoscopic biopsy.

Diagnosis/finding	n	%
DPLDs of known etiology		
Hypersensitivity pneumonia	6	12.50
Pulmonary tuberculosis	1	2.08
Paracoccidioidomycosis	1	2.08
Amioradone-induced interstitial lung injury	1	2.08
Idiopathic interstitial pneumonia		
Usual interstitial pneumonia	14	29.17
Nonspecific interstitial pneumonia	8	16.67
Lymphocytic interstitial pneumonia	2	4.17
Cryptogenic organizing pneumonia	2	4.17
Granulomatous DPLDs		
Wegener's granulomatosis	2	4.17
Sarcoidosis	1	2.08
Other forms of DPLD		
Eosinophilic pneumonia	4	8.34
Eosinophilic granuloma	1	2.08
Papillary adenocarcinoma	1	2.08
Alveolar proteinosis	1	2.08
Airway-centered interstitial fibrosis	1	2.08
Other findings		
Lung honeycombing	1	2.08
Normal lung tissue	1	2.08
Total	48	100.00

DPLD: diffuse parenchymal lung diseases.

Discussion

The DPLDs constitute a heterogeneous group of lung diseases characterized by varying degrees of inflammation and fibrosis. In some DPLDs, significant morbidity and unfavorable evolution, comparable to those of neoplastic diseases, are seen. Therefore, an efficient and safe method for the diagnostic confirmation of DPLD is needed. Currently, lung biopsy through video-assisted thoracoscopy is widely used for this purpose.

The objective of the present study was to analyze the role of this technique in the diagnosis of DPLD. To that end, the medical charts of 48 patients who underwent lung biopsy through video-assisted thoracoscopy were analyzed.

In our study sample, there was a slight predominance of females (52.08%) over males (47.92%). The same was found in another study,[11] in which 55.13% of the patients were female and 44.87% were male. However, other authors have found a slight predominance of males.[3,12] Most of our patients (89.59%) were over 41 years of age (mean, 58.77 years). This finding is similar to those reported in the studies cited above.

A total of 54 lung biopsy samples were obtained from 48 patients. The samples were representative and sufficient to establish the diagnosis in 46 patients (95.83%). In 1 patient (2.08%), histopathological confirmation was not possible due to extensive honeycombing with distortion of the lung architecture. In another case, the histopathological analysis revealed normal lung parenchyma.

In 42 patients (87.50%), a single biopsy was performed. In 6 (12.50%), multiple biopsies, of 2 samples each, were performed.

In the multiple biopsies analyzed, the biopsy sites were the right upper lobe/lingula in 2 cases, the right middle lobe/right upper lobe in 1 case and the right middle lobe/right lower lobe in 1 case. In the remaining 2 cases, it was not possible to define the site of the second biopsy due to lack of information in the medical charts. In the multiple biopsies, the definitive diagnosis was made in 5 cases. The remaining case is the one in which the definitive diagnosis was not possible due to honeycombing. When the anatomopathological results of the two samples from the same patient were compared, the diagnoses were concordant.

In the present study, a definitive diagnosis was established in all 42 cases in which a single biopsy was performed. When multiple biopsies were performed, the results of the two samples were the same. This is in agreement with the findings of another study,[13] in which it was concluded that a single sample obtained from a region pre-selected using radiology is sufficient for the diagnosis. Yet another study,[14] although not demonstrating greater diagnostic efficacy with the use of multiple biopsies, recommended that such biopsies be performed whenever possible. Various authors have stated that multiple biopsies increase the probability of establishing the definitive diagnosis.[15]

The justification for performing multiple biopsies is probably the difficulty in choosing the segment to be biopsied, since extensive areas of fibrosis make it difficult to identify the specific characteristics of the underlying disease.

The data obtained in the present study, although limited, show that a single sample is sufficient for the diagnosis. Nevertheless, preplanning, with the aid of HRCT, is necessary for choosing the appropriate site to be biopsied. In addition, multiple biopsies would probably increase the diagnostic accuracy of the test, although the high cost of endoscopy can be a limiting factor for this option in Brazil.

The most common biopsy site was the lingula, accounting for nearly half (44.44%) of the samples obtained. In the left lung, the most common site was the middle lobe. The choice of these sites for biopsy is controversial. Some authors[16] recommend that these sites be avoided since they are common sites of nonspecific infectious processes, inflammation, cicatrization and vascular congestion. This would affect the quality of the sample, which would present more fibrosis and vascular alterations than would those collected from other pulmonary areas. However, various studies have demonstrated that biopsy samples obtained from the lingula or from the middle lobe have the same diagnostic yield as do those obtained from other lung segments.[14,17,18]

The samples obtained from the middle lobe were sufficient for the diagnosis, except for that obtained in 1 case, in which there was pronounced honeycombing. It is likely that, in that case, the lung presented an advanced degree of diffuse fibrosis, since multiple biopsies

were performed, and the result of the anatomopathological analysis of the right lower lobe was the same. All of the samples obtained from the lingula were appropriate for the diagnosis. Therefore, these two sites can be considered representative of other lung segments, provided that the underlying disease diffusely affects the lung. In addition, the site to be biopsied should include areas of active disease, whereas regions of honeycombing should be avoided. The fact that, in the present study, the lingula was the most frequently biopsied site can be explained by the greater technical ease of resection at that site. The lingula is attached by a narrow pedicle, easily resected, and offers a large quantity of lung tissue for analysis.

In the patients studied, there was a higher prevalence of diseases that belong to the idiopathic interstitial pneumonia group (54.18%), especially usual interstitial pneumonia (29.17%) and nonspecific interstitial pneumonia (16.67%). Hypersensitivity pneumonia was the third most common (12.50%).

One group of authors also described a higher prevalence of idiopathic interstitial pneumonia, accounting for 38.58% of the 744 cases studied.[12] Among those, usual interstitial pneumonia was also the most common. However, hypersensitivity pneumonia accounted for only 5.11% of the total, and the number of cases of nonspecific interstitial pneumonia was not communicated by the authors. Other studies have described a lower prevalence of nonspecific interstitial pneumonia than that found in the present study; in one study, the prevalence was reported to be 4%.[11]

In the literature, the prevalence of hypersensitivity pneumonia ranges from 1.5% to 14%.[19,20]Similarly, the prevalence of pneumoconiosis ranges from 4% to 10.4%.[19,20]

In the present study, the absence of pneumoconiosis and the frequency of hypersensitivity pneumonia can be explained by the environmental conditions to which the patients were exposed, that is, the characteristics of a region that has a relatively low concentration of industries and is more agricultural, with greater exposure to organic dust. In addition, the diagnosis of pneumoconiosis might have been established by means of other diagnostic methods, there being no need for confirmation by lung biopsy.

Sarcoidosis was found in only 1 case (2.08%). In contrast, in the literature, sarcoidosis is described as a common DPLD. In a study involving 3,152 patients,[21] sarcoidosis was the most common disease (in 33.72% of the cases), followed by idiopathic pulmonary fibrosis (in 27.41% of the cases). This is due to the fact that sarcoidosis, due to its characteristic peribronchial or peribronchiolar distribution, is preferably diagnosed by transbronchial biopsy.[22] Therefore, in suspected cases of sarcoidosis, surgical lung biopsy is used only when the diagnosis cannot be made by transbronchial biopsy.

In 12.08% of our cases, the histological finding was normal lung parenchyma. In the subsequent diagnostic investigation of this patient, gastroesophageal reflux disease was diagnosed. This might have been due to an atypical clinical presentation, the differential diagnosis being made only after the surgical lung biopsy.

Many studies have compared video-assisted thoracoscopy and open lung biopsy in the diagnosis of DPLD. These techniques have been compared in terms of diagnostic efficacy and safety in surgical lung biopsy.

As discussed above, video-assisted thoracoscopy provided adequate lung tissue samples with high diagnostic efficacy. The definitive diagnosis was made in 95.83% of the cases. This finding is in agreement with those of another study,[15] in which the diagnosis was established in 98.39% of the cases. Open lung biopsy produces findings similar to those of video-assisted thoracoscopy.[18]

In the present study, the mean duration of thoracic drainage in the postoperative period was 2.2 days (range, 1-4 days). In a study comparing video-assisted thoracoscopy with open lung biopsy, it was reported that the duration of thoracic drainage was equivalent (video-assisted thoracotomy, 38 ± 28 h; and thoracotomy, 31 ± 26 h).[23] Some authors have questioned the need for thoracic drainage after biopsy through video-assisted thoracoscopy in certain patients.[24,25] They state that, in the absence of air leak after the procedure, thoracic drainage is optional, and that foregoing thoracic drainage can shorten hospital stays and avoid procedure-related morbidity.

Regarding surgical complications, 2 patients (4.17%) required 4-5 cm auxiliary incisions. In

1 patient, there was difficulty in maintaining single-lung ventilation, whereas, in the other, it was not possible to introduce the camera and visualize the lung parenchyma due to extensive pleural adherences. This was also described by another group of authors,[26] who recommended that video-assisted thoracoscopy be avoided in these situations.

Only 1 patient (2.08%) presented a postoperative complication (residual pneumothorax after chest tube removal, with no need of additional pleural drainage). In the patient sample studied, there were no deaths in the immediate postoperative period.

In the literature, the rate of postoperative complications varies. A study presented similar results, with only 1 case (2.94%) of pneumothorax as an adverse event.[27] In other studies, complications were reported in 3.6% of the cases,[28] and morbidities were described in 19.1% of the patients.[29] In that study, the most common complications were pneumothorax, need for postoperative mechanical ventilation and hematoma in the incision site. In the literature, the mortality rate over a 60-day postoperative period was found to be 4.4%.[29]

The comparison of the two techniques of surgical lung biopsy in terms of safety revealed no significant differences between open lung biopsy and video-assisted thoracoscopy.[23]

In the present study, variables such as intraoperative blood loss, need for analgesics in the postoperative period and length of hospital stay were not evaluated. Various authors state that video-assisted thoracoscopy is superior to open lung biopsy in terms of those variables.[30] However, there are studies stating that there are no differences.[23] Therefore, further studies are needed in order to elucidate this point.

Currently, video-assisted thoracoscopy is the most widely used tool for performing lung biopsy in the diagnosis of DPLD. Since it is considered a minimally invasive technique, its use has increased. Therefore, the present study was needed in order to evaluate its role. Our results demonstrate that video-assisted thoracoscopy is highly efficient in diagnostic resolution. In addition, video-assisted thoracoscopy has proven to be safe for this purpose, since postoperative complications occurred in only 2.08% of the cases. The analysis of the results of our study revealed that, as long as there is an investigation and appropriate pre-planning, as well as careful selection of candidates, video-assisted thoracoscopy is an option with a good success rate when surgical lung biopsy is indicated.

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About the authors

Renato Tadao Ishie
Medical Student. Federal University of Santa Catarina, Florianópolis, Brazil.

João José de Deus Cardoso
Adjunct Professor IV. Department of Clinical Surgery, Federal University of Santa Catarina, Florianópolis, Brazil.

Rafael José Silveira
Thoracic Surgeon. University Hospital, Federal University of Santa Catarina, Florianópolis, Brazil.

Lucas Stocco
Medical Student. Federal University of Santa Catarina, Florianópolis, Brazil.