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EXPERT REVIEW

Idiopathic fibrotic interstitial pneumonias: state of the art

Neumonías intersticiales idiopáticas fibróticas: estado del arte

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Abstract

In the diagnosis of diffuse interstitial lung diseases, the gold standard is multidisciplinary evaluation. This means a clinical, radiological and histopathological consensus. The ideal is to have an experienced team of specialists, mainly in cases that present difficulty in definitive diagnosis, without categorical characteristics of a specific pathology. High-resolution computed tomography is the imaging test of choice that contributes to the definitive diagnosis. The purpose of this article is to analyze the imaging patterns of idiopathic fibrotic diseases: usual interstitial pneumonia, idiopathic pulmonary fibrosis, combined pulmonary fibrosis and emphysema, non-specific interstitial pneumonia and pleuroparenchymal fibroelastosis. Initially we will also analyze the interstitial lung abnormality. Finally, we will refer to the growing use of artificial intelligence in the evaluation and progression of diffuse lung diseases, and to the application of a recently developed technique, photon counting computed tomography.

Keywords: *Interstitial lung abnormality. Usual interstitial pneumonia. Idiopathic pulmonary fibrosis. Non-specific interstitial pneumonia. Pleuroparenchymal fibroelastosis. Hypersensitivity pneumonitis.*

Resumen

En el diagnóstico de las enfermedades pulmonares intersticiales difusas, el método de referencia es la evaluación multidisciplinaria. Esto significa un consenso clínico, radiológico e histopatológico. Lo ideal es contar con un equipo experimentado de especialistas, principalmente en casos que presentan dificultad en el diagnóstico definitivo, sin características categóricas de una patología específica. La tomografía computada de alta resolución es la prueba de imagen de elección que contribuye en el diagnóstico definitivo. El propósito de este artículo es analizar los patrones imagenológicos de las enfermedades idiopáticas fibróticas: fibrosis pulmonar usual o idiopática, fibrosis pulmonar y enfisema combinados, fibrosis pulmonar no específica y fibroelastosis pleuroparenquimatosa. Analizaremos además al inicio la anormalidad pulmonar intersticial. Finalmente, haremos referencia al creciente uso de la inteligencia artificial en la evaluación y la progresión de las enfermedades pulmonares difusas, y a la aplicación de una técnica de desarrollo reciente, la tomografía computada con conteo de fotones.

Palabras clave: *Anormalidad pulmonar intersticial. Fibrosis pulmonar usual. Fibrosis pulmonar idiopática. Fibrosis pulmonar no específica. Fibrosis pulmonar y enfisema combinados. Fibroelastosis pleuroparenquimatosa. Neumonitis por hipersensibilidad*

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Introduction

Numerous conditions have been described that make up the group of diffuse interstitial lung diseases, including idiopathic interstitial pneumonia. In this article we will focus on those idiopathic diseases that present fibrosis as a predominant component. Within the multidisciplinary evaluation, high-resolution computed tomography (HRCT) plays an essential role both in the diagnosis and in the evolutionary analysis of them. The use of antifibrotic agents has demonstrated satisfactory effectiveness in slowing the progression of fibrotic involvement.

Technique

Simple chest x-ray is usually the initial imaging examination in the study of diffuse interstitial diseases. However, it is low-yielding, nonspecific, and frequently normal in early stages.

HRCT with volumetric acquisition is the examination of choice, using the lowest possible radiation dose (ALARA, *as low as reasonably achievable*). It requires fine slices (< 1.5 mm) with high spatial frequency reconstruction algorithm and ideally iterative reconstruction. It allows multiplanar reconstructions to be performed, especially useful in differentiating between bronchiectasis and traction bronchiolectasis and honeycombing. Prone evaluation is a priority to distinguish subpleural interstitial involvement from decubitus atelectasis[1,2] (Fig. 1).

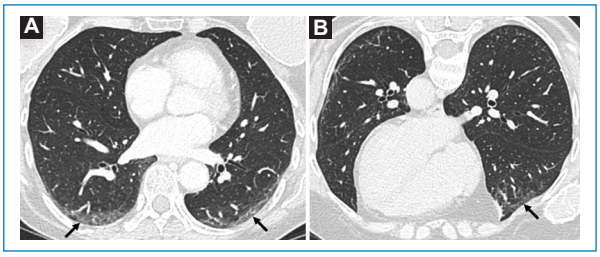

Figure 1. Importance of prone evaluation. **A**: subpleural opacities are seen in the inferior lobes (arrows). **B**: the prone view shows almost complete regression of them, which correspond to decubitus atelectasis. Note that in the prone position the opacities have moved towards the dependent areas, especially evident in the lingula (arrow).

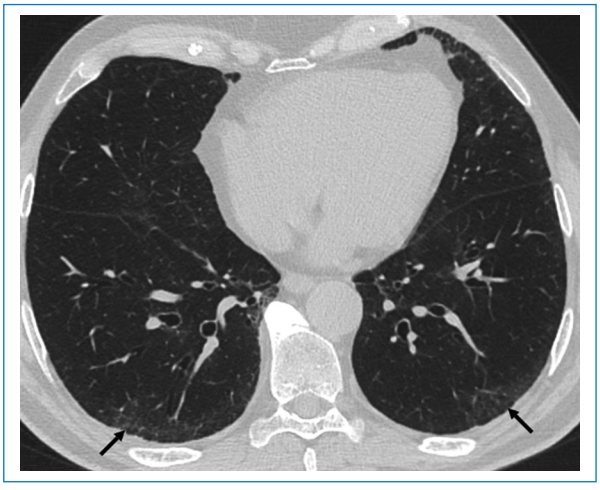

Figure 2. Non-fibrotic interstitial lung abnormality. Faint subpleural reticulation in both inferior lobes, without other findings suggesting fibrosis (arrows).

Interstitial lung abnormality

Incidentally, mild interstitial involvement is observed on HRCT in older adults, usually over 60 years of age. Its incidence is up to 10%, being more common in smokers. For a long time, this finding was attributed to a manifestation inherent to aging. However, it has been shown that the interstitial alterations detected in these patients frequently progress in more than 50% of cases. Its progression is insidious and is usually evident over a period of 5 years or more[3].

An involvement of > 5% of any lung area is considered interstitial lung abnormality (ILA). Three lung zones are delimited[4]:

– Superior: above the superior margin of the aortic arch.
– Middle: under the inferior margin of the aortic arch and the right inferior pulmonary vein.
– Inferior: distal to the right inferior pulmonary vein.

Six lung zones are thus differentiated: three on the right and three on the left. Involvement of more than three sites may be classified as advanced ILA or rather considered a diffuse interstitial disease (eg, *usual interstitial pneumonia* [UIP]).

The tomographic findings of ILA can be ground glass or reticulated glass, distortion of lung architecture, bronchiectasis or traction bronchiolectasis, honeycombing or non-emphysematous air cysts[3].

The distribution of ILA can be central or subpleural. Subpleural ILA has a higher risk of progression and is classified as non-fibrotic and fibrotic (Figs. 2 and 3). The latter implies a probability of evolving towards a specific fibrotic disease[4].

Not considered ILA[3,4] are:

– Centrilobular nodules in ground glass.
– Decubitus opacities (evaluate in prone).
– Abnormality < 5% or unilateral.

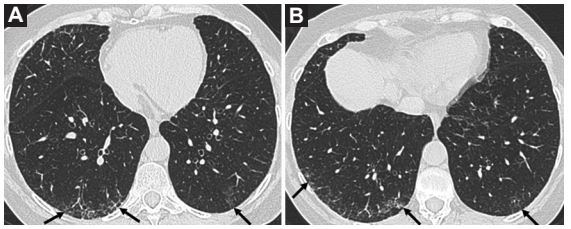

Figure 3. Fibrotic interstitial lung abnormality. Thick reticular images associated with some traction bronchiolectasis and minimal ground glass in the subpleural region of the inferior lobes, more extensive on the right (arrows in **A** and **B**).

– Focal fibrosis due to compression of vertebral osteophytes.
– Patchy ground glass or tree-in-bud with a clear clinical history of aspiration.
– History of autoimmune disease, such as collagen disease and familial interstitial disease, and exposure to inhalation of certain dusts in suspension (such as asbestos).

Risk factors for ILA are advanced age, smoking, and exposure to certain toxic fumes. On the other hand, a patient with ILA is at increased risk of lung lesion if exposed to thoracic surgery, radiotherapy, chemotherapy, or immunotherapy (Figs. 4 and 5).

Clinical manifestations, especially in more advanced cases, are usually dry cough, dyspnea, and altered respiratory function tests. In particular, progression of fibrotic ILA is associated with increased mortality. As

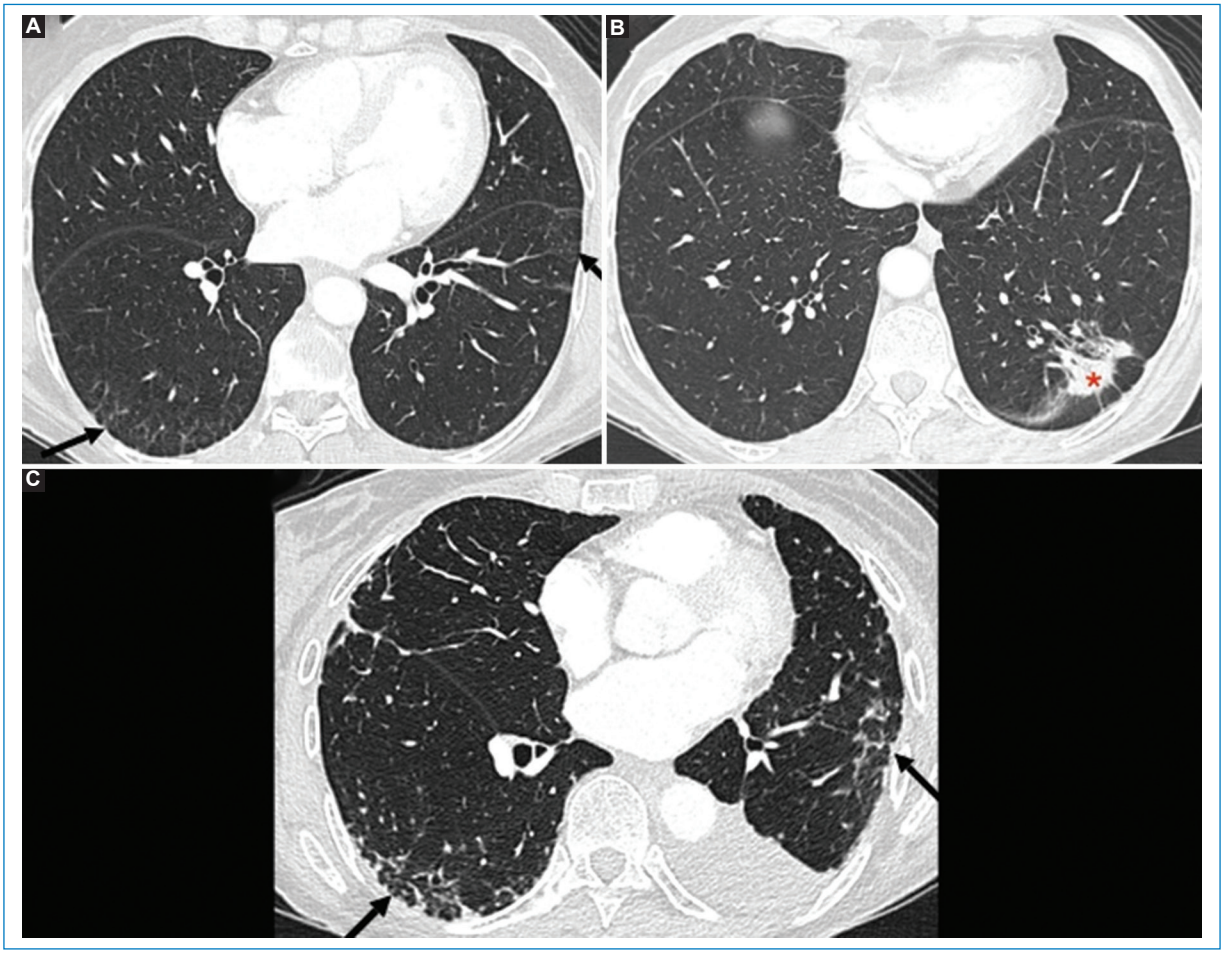

Figure 4. Interstitial lung abnormality. Subpleural reticulate in the inferior lobes, greater on the right (arrows in **A**), and adenocarcinoma in the left inferior lobe (asterisk in **B**). After a lobectomy, accentuation of interstitial involvement is observed with distortion and septal thickening, and traction bronchioloectasias, findings of a fibrotic nature (arrows in **C**). Post-surgical left pleural effusion.

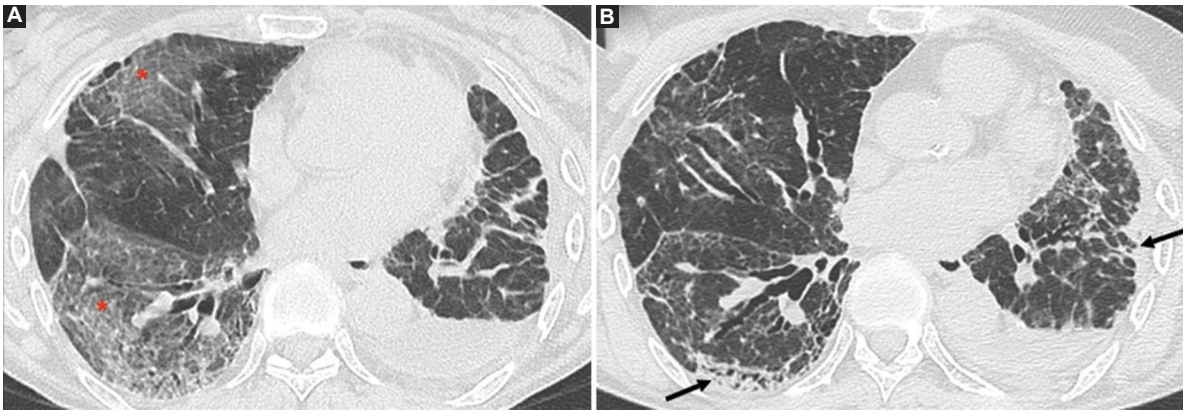

Figure 5. Same patient as in Fig. 4. Two years after the left inferior lobectomy, two metastatic nodules appear and are resected in the right superior lobe. Immunotherapeutic treatment (pembrolizumab) is initiated. Areas of ground-glass opacity are evident in the right middle and inferior lobes (asterisks in **A**). Once treatment is stopped, a significant regression of the ground-glass areas and progression of fibrotic changes is noted (arrows in **B**). Note the persistence of the left pleural effusion.

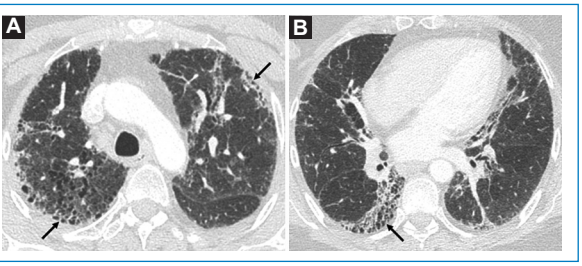

Figure 6. Pattern of probable UIP. Both images (**A** and **B**) show predominantly subpleural interstitial involvement, somewhat asymmetric, with a cephalocaudal gradient and more pronounced in the right inferior lobe. It is characterized by fibrotic reticulation associated with bronchiectasis and traction bronchiolectasis (arrows in **A** and **B**).

already mentioned, patients undergoing thoracic surgery, radiotherapy or chemotherapy are at higher risk[5].

Given the slow progression of interstitial involvement in ILA, controls are suggested every 1 to 2 years. In cases with progression of clinical symptoms or worsening of lung function, these times are usually shortened[4].

Idiopathic pulmonary fibrosis and usual interstitial pneumonia

Idiopathic pulmonary fibrosis (IPF) is a chronic, progressive and irreversible pathological process. As its name indicates, it is of unknown origin. Approximately 60% of cases have a history of smoking. Genetic factors are known, with family history in a percentage that varies between 5% and 20%[1].

It is the most common fibrotic interstitial pneumonia and has a higher incidence in men, usually over 60 years of age. It is characterized by the histological and tomographic pattern of UIP[2].

UIP can also be a manifestation of connective tissue diseases (eg, rheumatoid arthritis), hypersensitivity pneumonitis, asbestosis, and drug toxicity[1].

Currently, the average survival of patients with IPF can reach up to 10-11 years after diagnosis, probably due to earlier detection and the use of antifibrotic drugs, such as pirfenidone and nintedanib[1]. In previous evaluations, the average survival fluctuated between 2.5 and 3.5 years after diagnosis.

Clinically, patients present symptoms such as chronic dry cough and dyspnea, which in many cases appear up to 2 years before the diagnosis is made. On physical examination, crackling sounds on lung auscultation and digital clubbing are usually evident. Respiratory function is restrictive and alterations in gas exchange are observed.

Histologically, UIP is mainly characterized by dense peripheral fibrosis associated with characteristic proliferating fibroblastic foci at the inner margin of the fibrosis[1].

UIP on HRCT usually shows[1,2,6]:

- Distortion of the parenchymal architecture with accentuation of septal thickening and intralobular reticulation, predominantly peripheral, subpleural and basal.
- Bronchiectasis and traction bronchioloectasis. They are characterized by a serpiginous course with a corkscrew morphology due to adjacent fibrosis (Figs. 6 and 7).

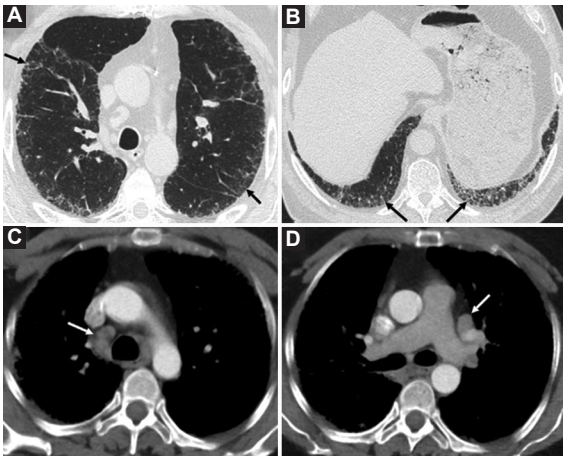

Figure 7. Pattern of probable UIP. Subpleural reticulation with septal distortion and thickening, associated with bronchiectasis and traction bronchiolectasis (arrows in **A** and **B**). The mediastinal window shows lymphadenopathy in the right paratracheal location and in the aortopulmonary window (arrows in **C** and **D**).

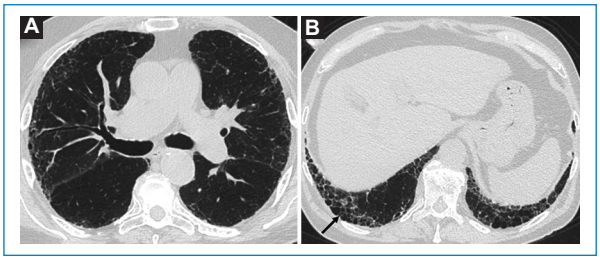

Figure 8. Typical pattern of UIP (**A** and **B**). The most pronounced subpleural fibrosis stands out at the bases, where bronchiectasis and traction bronchiolectasis, and honeycomb outline are evident, especially in the right inferior lobe (arrow in **B**).

– Honeycombing: subpleural cysts that share thick walls in one or several rows with diameters most frequently between 3 and 5 mm (Fig. 8). Occasionally they can reach up to 20 mm or more. Differentiation from traction bronchioloectasis is usually difficult. In these cases, multiplanar reconstructions and MiniP can be useful.
– Non-homogeneous patchy distribution of fibrotic involvement. Areas with different degrees of fibrosis and areas of normal parenchyma are combined (temporal heterogeneity). As already noted, it is usually more pronounced in the periphery and at the lung bases (cephalocaudal gradient). In cases of familial IPF this distribution may be diffuse or more accentuated in the superior lobes.

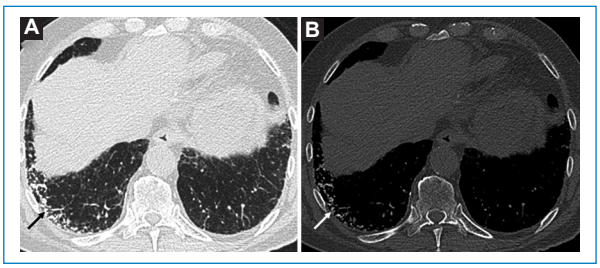

Figure 9. Usual pulmonary fibrosis. Major subpleural fibrotic involvement at the bases, with radiopaque micronodules compatible with ossification, some with branches of similar density, called dendriform branches (arrows in **A** and **B**).

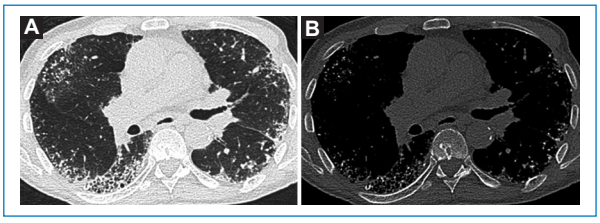

Figure 10. (**A** and **B**) UIP with extensive ossification in relation to the fibrotic areas.

– Sometimes radiopaque micronodules associated or not with branches of similar density can be seen in the fibrotic areas that correspond to ossification, which can also manifest, less frequently, in other fibrotic lung diseases[7] (Figs. 9 and 10).
– Progressive reduction in lung volume due to fibrotic progression.
– Mediastinal lymphadenopathy in approximately 70% of cases with diameters generally < 15 mm in the short axis. The most frequent location is low right paratracheal and subcarinal (Fig. 7C and D).

Three tomographic signs have been described that tend to be more frequent in UIP secondary to connective tissue diseases than to IPF[1,8] (Table 1).

The tomographic diagnostic criteria for UIP established by the Fleischner Society in 2018 are largely consistent with the clinical practice guidelines of the American Thoracic Society (ATS), the European Respiratory Society (ERS), the Japanese Respiratory Society (JRS) and the Latin American Thoracic Society (ALAT) of the same year, distinguishing four categories[2,9] (Table 2) (Figs. 11-13).

Both the Fleischner Society and the ATS/ERS/JRS/ALAT guidelines consider, in the appropriate clinical context, performing a surgical biopsy in indeterminate UIP and in fibrosing pneumonia with a pattern

Table 1. Most frequent tomographic signs in UIP due to connective tissue diseases[1,8]

Predominant fibrotic involvement in the subpleural region in the anterior segments of the superior lobes, regardless of its usual distribution in the rest of the lung parenchyma
Exuberant honeycombing that compromises > 70% of the pulmonary fibrotic volume
Straight edge sign: fibrosis of the lung bases that is separated from the normal lung by a horizontal limit, without significant cranial extension along the lung margins. It has also been described in non-specific pulmonary fibrosis

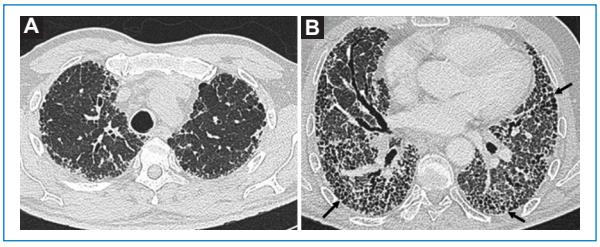

Figure 11. Advanced UIP (**A** and **B**). Extensive fibrotic involvement predominantly peripheral and basal, with distortion of the parenchymal architecture, bronchiectasis and traction bronchiolectasis, and honeycomb. The latter significantly more extensive in the inferior lobes (arrows in **B**).

suggestive of an alternative non-UIP disease. The ATS/ERS/JRS/ALAT guidelines recommend performing a surgical biopsy in probable UIP, but the Fleischner Society does not. Surgical biopsy is not free of risks, mainly in morbidity. The most common complication is pneumothorax, which is usually difficult to resolve. It can also cause acute exacerbation[2].

An alternative to surgical biopsy is transbronchial cryobiopsy, which is lower risk, although significantly less effective than surgical biopsy[2,10].

The histological correlation of typical UIP and probable UIP is 90% and 80%, respectively, while that of indeterminate UIP or non-compatible fibrosis is 50%[1].

Acute exacerbation is a complication that affects up to 15% of patients with IPF annually. Surgery, especially pulmonary surgery, increases the risk. To consider an exacerbation, it is necessary to rule out infection (sometimes due to opportunistic pathogens), pulmonary thromboembolism, and heart failure. The prognosis is poor, with a mortality rate close to 50%[11]. Exacerbation is not exclusive to IPF; it can also be seen in other fibrotic diseases, such as non-specific interstitial pneumonia (NSIP), connective tissue diseases, and hypersensitivity pneumonitis. Histology shows diffuse alveolar damage, in some cases associated with organizing pneumonia.

HRCT shows areas of ground-glass opacity or condensation of variable extent, superimposed on fibrotic involvement. Patients who survive frequently show worsening fibrosis[11] (Fig. 14).

Lung cancer is a not uncommon association in IPF[6]. Approximately 10% of these patients die from this cause. Although less frequently, it can be seen in any other fibrotic lung pathology. In general, it develops in areas of severe fibrosis and can present as dense condensation, leading to a differential diagnosis with

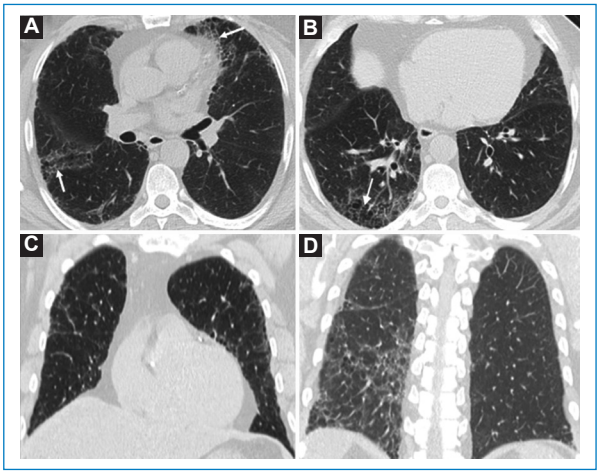

Figure 12. Asymmetric pulmonary fibrosis with predominantly peripheral distribution with reticulation, bronchiectasis and traction bronchiolectasis, and areas of honeycombing (arrows in **A** and **B**). Note the distribution of fibrotic involvement mainly in the right inferior and left superior lobes, and the absence of this in the left inferior lobe (**C** and **D**). This pattern is compatible with indeterminate usual pulmonary fibrosis.

compact fibrosis. When neoplastic suspicion is present, positron emission tomography is useful for confirmation and staging (Fig. 15).

Infections, particularly opportunistic pathogens, can complicate both IPF and other fibrotic lung diseases. Infections due to *Pneumocystis jirovecii,* tuberculosis and other non-tuberculous mycobacteria are the most common[1].

The follow-up of patients with IPF or UIP is carried out considering the clinical evolution, including respiratory function tests and eventually control with HRCT. The latter, in cases without conclusive clinical progression, may not present significant changes in periods of less than 1 year[2].

Table 2. HRCT diagnostic criteria for UIP pattern

Definitive or typical UIP (Figs. 8 and 11)	Probable UIP (Figs. 6 and 7)	Indeterminate UIP* (Fig. 12)	Pattern suggestive of alternative diagnosis (non-UIP)* (Fig. 13)
Distortion of parenchymal architecture	Distortion of parenchymal architecture	Fibrosis with a variable or diffusely distributed cephalocaudal gradient	Predominance of ground glass or condensation
Reticulated	Reticulated	Other findings that may suggest an alternative diagnosis	Small airway involvement: Areas of mosaic attenuation, particularly in non-fibrotic areas. Air trapping in expiration
Bronchiectasis or traction bronchiolectasis	Bronchiectasis or traction bronchiolectasis		
Honeycombing	Predominantly basal and subpleural distribution		
Predominantly basal and subpleural distribution			

UIP: usual interstitial fibrosis.
*In cases of indeterminate UIP or fibrosis with an alternative non-UIP pattern, it is advisable for the radiologist to suggest a differential diagnosis in his report. In some cases, it is pertinent to include more than one diagnostic alternative[6].

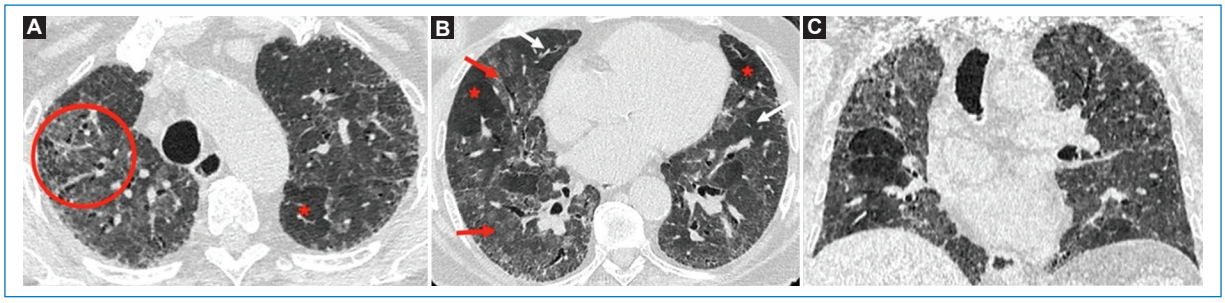

Figure 13. Diffuse fibrotic disease with a pattern that suggests an alternative diagnosis to UIP. Peripheral reticulation with peribronchovascular component and traction bronchiectasis (circle in **A**). There are also areas of ground glass opacity (red arrows in **B**), normal parenchyma (white arrows in **B**) and increased transparency (asterisks in **A** and **B**); the latter suggests small airway disease. Findings compatible with pneumonitis due to fibrotic hypersensitivity (coronal reconstruction in **C**). The diagnosis is confirmed with bronchoalveolar lavage and transbronchial biopsy.

Combined pulmonary fibrosis and emphysema

This condition is characterized by the predominant presence of pulmonary emphysema in the superior lobes and UIP in the inferior lobes (Fig. 16). Its prognosis is similar to that of IPF alone. Pulmonary hypertension is more frequently present, probably due to the association of fibrosis and emphysema. Patients with combined pulmonary fibrosis and emphysema (CPFE) also have an increased risk of lung cancer compared to those with fibrosis alone. Furthermore, acute exacerbations are more frequent[12,13].

It has been suggested not to consider CPFE as a disease in itself, but rather as two coexisting conditions. Fibrotic involvement, as noted, is UIP in approximately 80% of cases; the remaining percentage corresponds more frequently to desquamative interstitial pneumonia, predominantly associated with tobacco. Some cases of fibrotic NSIP have also been described[1,14].

Non-specific interstitial pneumonia

Idiopathic NSIP is less common than UIP and its prognosis is significantly better, with a 5-year survival rate of around 80%. In the vast majority of cases it is not idiopathic, but secondary to connective tissue diseases (eg, scleroderma), hypersensitivity pneumonitis, or drug toxicity. It generally occurs in younger patients, between 40 and 50 years old, with symptoms such as dry cough, dyspnea on exercise and altered, predominantly restrictive, lung function. It is more common in women and non-smokers[15].

Histology shows interstitial inflammatory infiltration with lymphocytes and plasma cells in purely cellular NSIP (rare), and varying degrees of interstitial fibrotic

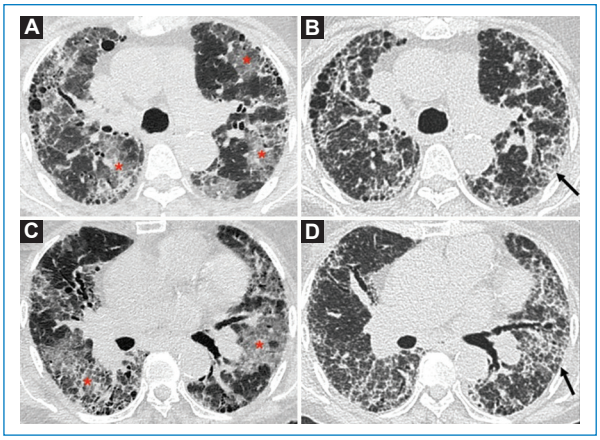

Figure 14. Known UIP that presents a sudden decompensation. After ruling out infection, heart failure and thromboembolism, it is treated as acute exacerbation. In images **A** and **C**, extensive ground glass is observed superimposed on the areas of fibrosis during the acute process (asterisks). Images **B** and **D** show an adequate response to treatment, with a significant decrease of ground glass. An increase in fibrosis as a consequence of the exacerbation is impressive (arrows in **B** and **D**).

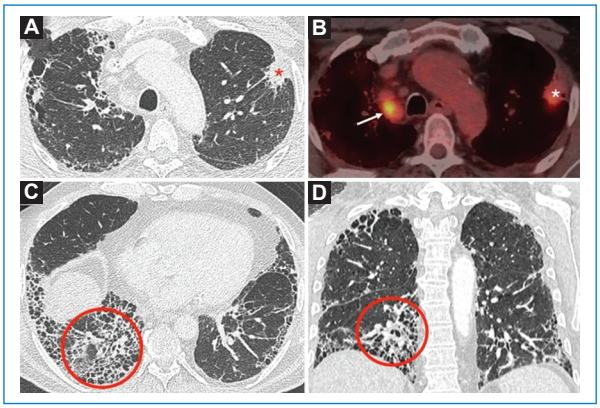

Figure 15. Images **C** and **D** show fibrosis with a cephalocaudal gradient of asymmetric distribution, more accentuated in the right inferior lobe, where the presence of honeycomb (circles) is evident, consistent with UIP. Peripheral mass-like consolidation with extensive pleural contact in the left superior lobe, with significant metabolic activity on positron emission tomography, where a contralateral paratracheal metastatic adenopathy is also identified (arrow in **B**). It corresponds to an adenocarcinoma (asterisk in **A** and **B**).

involvement in cases of mixed NSIP and fibrotic NSIP (predominant). Temporal homogeneity of lung involvement stands out, unlike UIP[1].

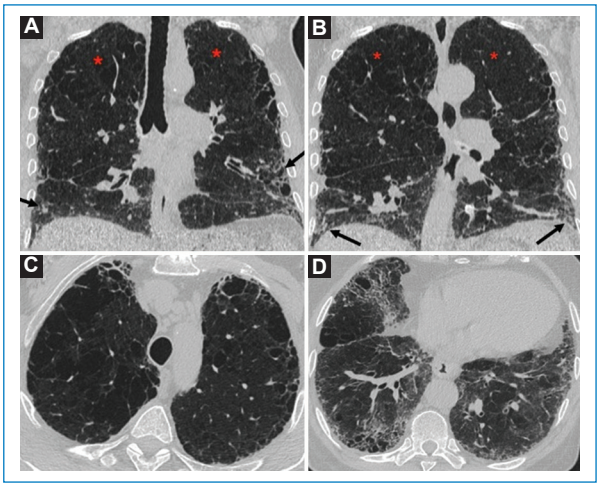

Figure 16. Combined pulmonary fibrosis and emphysema. Coronal reconstructions (**A** and **B**) show extensive predominantly centrilobular emphysema in the superior lobes (asterisks in **A** and **B**), and fibrosis at the lung bases (arrows in **A** and **B**). Axial slices confirm extensive emphysema in the superior lobes (**C**) and bibasal fibrosis with reticulation, distortion of interlobular septa, and bronchiectasis and traction bronchioloectasis (**D**).

HRCT is characterized by[15]:

- Ground glass, which can have a diffuse, patchy distribution, although it predominates towards the lung bases. The presence of ground glass without other findings may correspond to cellular NSIP, which is rare. In this case, treatment, usually steroids, can achieve complete regression.
- Frosted and reticulated glass, which suggests a fibrotic component (Fig. 17).
- Bronchiectasis or traction bronchioloectasis. In typical fibrotic NSIP, they are observed with a predominantly peribronchovascular distribution and in the inferior lobes, associated with reticulation and ground glass; the latter usually corresponds to microscopic fibrosis (Figs. 18 and 19). There is frequently a decrease in volume of the inferior lobes.
- Partial sparing of the immediate subpleural space, when there is peripheral involvement, visible in up to 60% of cases (Fig. 17).
- Honeycombing, rare (0-40% of cases in follow-up).
- Mediastinal lymphadenopathy, similar to UIP.

Acute exacerbation can be seen in NSIP, although less frequently than in IPF.

Clinical and imaging follow-up of NSIP, as in other fibrotic interstitial diseases, is essential to evaluate its evolution and response to treatment. Some cases of fibrotic NSIP progress to UIP[16].

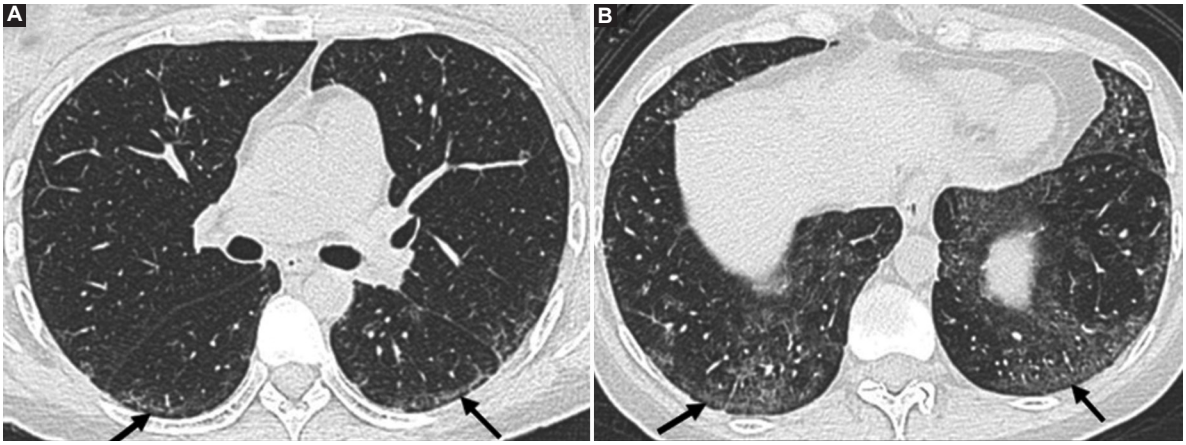

Figure 17. Ground glass, and peribronchovascular and subpleural minimal reticulation in the inferior lobes, middle lobe, and lingula. Note the partial sparing of the immediate subpleural space in the inferior lobes (arrows in **A** and **B**). This is probably a mixed, predominantly cellular, non-specific pulmonary fibrosis.

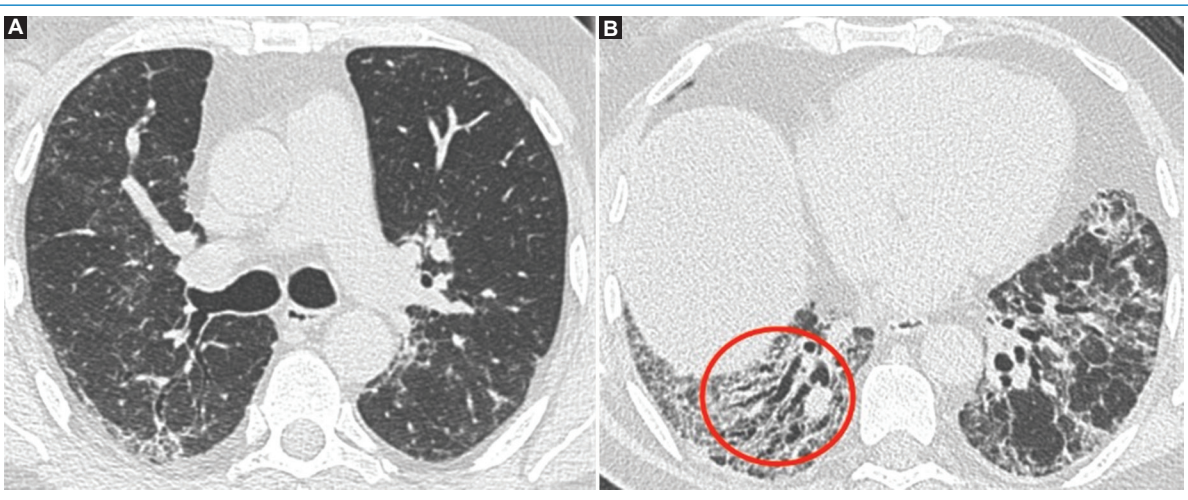

Figure 18. Reticulation, septal distortion and traction bronchiectasis with a peribronchovascular and peripheral distribution (**A** and **B**) more pronounced in the right inferior lobe (circle in **B**). Findings compatible with non-specific fibrotic pulmonary fibrosis. The accompanying ground glass usually reflects microscopic fibrosis.

Pleuroparenchymal fibroelastosis

Pleuroparenchymal fibroelastosis (PPFE) is a rare disease characterized by biapical pleural fibrotic thickening associated with pulmonary fibrosis with predominant involvement of the superior lobes, which decrease in volume as the process progresses, causing cranial traction of the pulmonary hilum. It is mostly idiopathic. It has no gender predilection and usually occurs between 40 and 70 years of age. No effective treatment has been proven; low doses of corticosteroids and immunosuppressants have been used in some cases, without conclusive results. The use of prophylactic antibiotics can benefit patients with PPFE, since they have a higher incidence of respiratory infections[17,18].

PPFE is not always idiopathic, and can be observed in association with other pathologies such as connective tissue diseases (e.g., rheumatoid arthritis), chemotherapy treatments (alkylating agents), exposure to asbestos, and chronic infections (non-tuberculous mycobacteria and aspergillosis). It may also have a family component. An identical pattern usually occurs in lung and bone marrow transplantation[1].

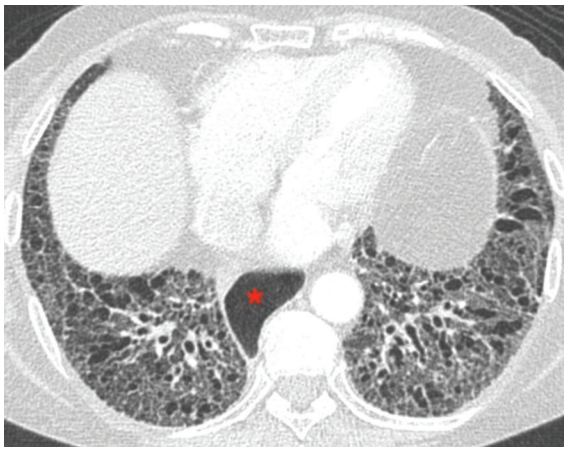

Figure 19. Fibrotic non-specific pulmonary fibrosis in a patient with scleroderma. Extensive peribronchovascular and peripheral fibrosis in the inferior lobes, and accompanying ground glass. Note the dilation of the esophagus (asterisk).

The symptoms are usually chronic, with dry cough and dyspnea, which is present months or years before diagnosis. Pulmonary function tests show generally restrictive alterations. The chest x-ray basically shows bilateral apical pleural thickening, decreased volume of the superior lobes, and cranial traction of the hilum.

The presence of pleuritic pain may be a manifestation of pneumothorax, a common complication in this condition. Although of lower incidence, pneumomediastinum may also occur. For these reasons, surgical biopsy is avoided if possible.

The average survival rate of patients with PPFE is approximately 10 years. There is, however, a subgroup of patients who present a more accelerated phenotype of the disease, with an average survival rate of no more than 5 years, both in idiopathic and secondary cases.

Histology shows marked fibroelastic thickening of the visceral pleura and adjacent parenchyma, usually in the superior lobes, with septal thickening and fibrosis of the alveolar interstitium.

HRCT is characterized by irregular pleural and subpleural thickening, associated with consolidation and interstitial reticulation in addition to traction bronchiectasis (Fig. 20).

Progressively the superior lobes decrease in volume, producing cranial traction of the hilum. Sometimes, the involvement can extend to the fissures (Fig. 21).

A significant number of patients with PPFE develop platythorax, a decrease in the anteroposterior diameter of the thorax, probably due to loss of muscle mass and reduced volume of the superior lobes. In these cases, deviation and posterior displacement of the trachea can be observed, to end up presenting a paravertebral location[18].

25% to 30% of PPFE cases are associated with other fibrotic interstitial pneumonia, located preferentially in the inferior lobes, generally UIP and less frequently NSIP (Fig. 20). It is not specifically defined whether these associations affect the prognosis of this disease[1].

Unclassifiable interstitial pneumonias

Despite careful evaluation and multidisciplinary discussion, there is an approximate percentage of 12-15% of diffuse interstitial diseases that present characteristics that do not allow a definitive classification. The multidisciplinary discussion is usually complex in these cases. The clinical reasons that contraindicate surgical biopsy are an important factor that prevents correct classification in many of these patients[1,19].

Application of artificial intelligence in diffuse lung diseases

The important development of artificial intelligence (*machine learning, deep learning*) in different fields of medicine, including imaging, is a reality in recent years, using algorithms with a large database.

Its application in diffuse lung diseases, especially those with a fibrotic component, has an accuracy of up to 80%, similar to that achieved by experienced thoracic radiologists in this field. It has great performance in the early diagnosis, the evaluation of the progress and prognosis of the disease, as well as the response to antifibrotic treatment. It has been possible to clearly differentiate areas of normal lung from areas of reticulation and honeycombing. It constitutes not a threat, but rather an aid, for the radiologist, speeding up his diagnostic work[20]. More information on the topic of artificial intelligence is not contemplated in this article.

Photon counting computed tomography

This new technology allows significant progress in the quality of tomographic images. In particular, in the study of diffuse lung diseases, computed tomography with electron counting allows the peripheral vascular and bronchial structures to be defined with greater resolution, as well as the interstitial involvement that characterizes them.

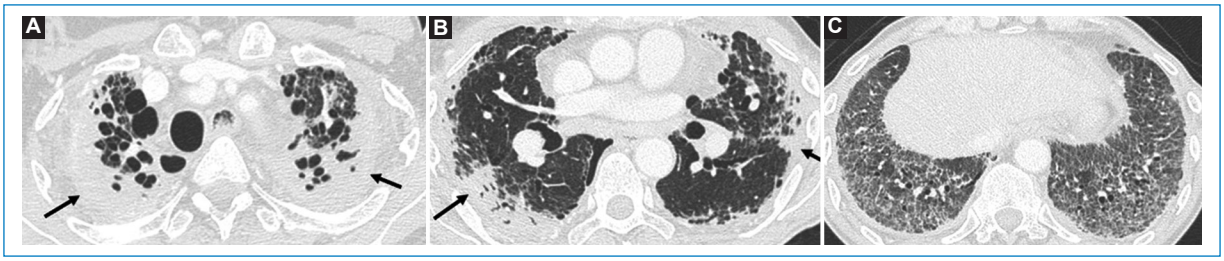

Figure 20. Pleuroparenchymal fibroelastosis. Images **A** and **B** show significant pleural thickening in the superior lobes, more pronounced at the vertices (arrows). It is associated with elements of pulmonary fibrosis with thickening and distortion of interlobular septa and some peripheral condensations. In **C**, fibrotic involvement suggestive of non-specific pulmonary fibrosis is observed.

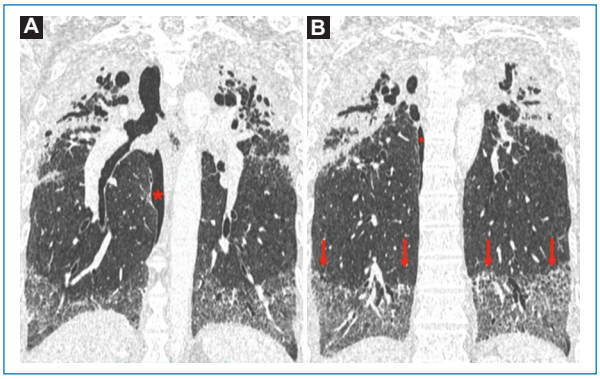

Figure 21. Pleuroparenchymal fibroelastosis. In the coronal reconstructions (**A** and **B**) the pleuroparenchymal involvement of the superior lobes is clearly evident, which are markedly reduced in volume, causing cranial traction of the hilum. The straight edge sign is also observed, which separates the fibrosis from the uninvolved lung (arrows). Small pneumothorax (asterisk).

The notable improvement in images is due to the use of detectors substantially different from the energy-integrating detectors (solid-state scintillation detectors) used by conventional CT scanners. Photon counting detectors have the ability to directly measure photon energy and are composed of smaller pixels.

The advantages of photon counting detectors lie in the direct conversion of X-ray photons into electrical signals. It improves spatial resolution, as well as the contrast/noise ratio, with a lower radiation dose and without loss of image quality. In addition, it reduces artifacts and beam hardening[21,22].

Conclusions

The diagnosis of diffuse lung diseases, including fibrotic diseases, is essentially based on multidisciplinary discussion. Sometimes, the definitive diagnosis is not achieved. There is a minority group, although no less important, of unclassifiable interstitial diseases. With regular multidisciplinary meetings and considering the evolution of the case, a consensus classification can sometimes be achieved.

ILA acquires diagnostic importance due to its frequently evolving nature, especially when it presents a fibrotic component.

HRCT is essential in the evaluation of fibrotic interstitial diseases. The application of artificial intelligence and CT with photon counting to imaging makes it possible to optimize diagnostic accuracy in these pathologies.

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Conflicts of interest

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Ethical disclosures

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Data confidentiality. The authors declare that no patient data appear in this article.

Right to privacy and informed consent. The authors declare that no patient data appear in this article.

Use of artificial intelligence to generate texts. The authors declare that they have not used any type of generative artificial intelligence in the writing of this

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References

1. Desai S, Devaraj A, Lynch D, Sverzellati N, editores. Webb, Müller and Naidich's High-Resolution CT of the Lung. 6th ed. Philadelphia: Wolters Kluwer Health; 2020.
2. Lynch DA, Sverzellati N, Travis WD, Brown KK, Colby TV, Galvin JR, et al. Diagnostic criteria for idiopathic pulmonary fibrosis: a Fleischner Society White Paper. Lancet Respir Med. 2018;6:138-53.
3. Hatabu H, Hunninghake GM, Richeldi L, Brown KK, Wells AU, Remy-Jardin M, et al. Interstitial lung abnormalities detected incidentally on CT: a position paper from the Fleischner Society. Lancet Respir Med. 2020;8:726-37.
4. Hata A, Schiebler ML, Lynch DA, Hatabu H. Interstitial lung abnormalities: state of the art. Radiology. 2021;301:19-34.
5. Chae KJ, Jin GY, Goo JM, Chung MJ. Interstitial lung abnormalities: what radiologists should know. Korean J Radiol. 2021;22:454.
6. Hobbs S, Chung JH, Leb J, Kaproth-Joslin K, Lynch DA. Practical imaging interpretation in patients suspected of having idiopathic pulmonary fibrosis: official recommendations from the Radiology Working Group of the Pulmonary Fibrosis Foundation. Radiol Cardiothorac Imaging. 2021;3: e200279.
7. Egashira R, Jacob J, Kokosi M, Brun AL, Rice A, Nicholson AG, et al. Diffuse pulmonary ossification in fibrosing interstitial lung diseases: prevalence and associations. Radiology. 2017;284:255-63.
8. Chung JH, Cox CW, Montner SM, Adegunsoye A, Oldham JM, Husain AN, et al. CT features of the usual interstitial pneumonia pattern: differentia- ting connective tissue disease–associated interstitial lung disease from idiopathic pulmonary fibrosis. Am J Roentgenol. 2018;210:307-13.
9. Raghu G, Remy-Jardin M, Myers JL, Richeldi L, Ryerson CJ, Lederer DJ, et al. Diagnosis of idiopathic pulmonary fibrosis. An official ATS/ERS/ JRS/ALAT clinical practice guideline. Am J Respir Crit Care Med. 2018;198:e44-68.
10. Lodhi T, Hughes G, Stanel S, Chaudhuri N, Hayton C. Transbronchial lung cryobiopsy in idiopathic pulmonary fibrosis: a state of the art review. Adv Ther. 2019;36:2193-204.
11. Leuschner G, Behr J. Acute exacerbation in interstitial lung disease. Front Med. (Lausanne). 2017:4:176.
12. Ufuk F. Combined pulmonary fibrosis and emphysema. Radiology. 2020;296:275.
13. Jankowich MD, Rounds SIS. Combined pulmonary fibrosis and emphysema syndrome. Chest. 2012;141:222-31.
14. Cottin V, Selman M, Inoue Y, Wong AW, Corte TJ, Flaherty KR, et al. Syndrome of combined pulmonary fibrosis and emphysema: an official ATS/ERS/JRS/ALAT research statement. Am J Respir Crit Care Med. 2022;206:e7-41.
15. Kligerman SJ, Groshong S, Brown KK, Lynch DA. Nonspecific interstitial pneumonia: radiologic, clinical, and pathologic considerations. RadioGraphics. 2009;29:73-87.
16. MacDonald SLS, Rubens MB, Hansell DM, Copley SJ, Desai SR, du Bois RM, et al. Nonspecific interstitial pneumonia and usual interstitial pneumonia: comparative appearances at and diagnostic accuracy of thin-section CT. Radiology. 2001;221:600-5.
17. Chua F, Desai SR, Nicholson AG, Devaraj A, Renzoni E, Rice A, et al. Pleuroparenchymal fibroelastosis. A review of clinical, radiological, and pathological characteristics. Ann Am Thorac Soc. 2019;16:1351-9.
18. Bonifazi M, Montero MA, Renzoni EA. Idiopathic pleuroparenchymal fibroelastosis. Curr Pulmonol Rep. 2017;6:9-15.
19. Skolnik K, Ryerson CJ. Unclassifiable interstitial lung disease: a review. Respirology. 2015;21:51-6.
20. Zhang G, Luo L, Zhang L, Liu Z. Research progress of respiratory disease and idiopathic pulmonary fibrosis based on artificial intelligence. Diagnostics. 2023;13:357.
21. Dack E, Christe A, Fontanellaz M, Brigato L, Heverhagen JT, Peters AA, et al. Artificial intelligence and interstitial lung disease. Invest Radiol. 2023;58:602-9.
22. Farhadi F, Rajagopal JR, Nikpanah M, Sahbaee P, Malayeri AA, Pritchard WF, et al. Review of technical advancements and clinical applications of photon-counting computed tomography in imaging of the thorax. J Thorac Imaging. 2021;36:84.