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Post-COVID-19 lung Fibrosis: Imaging Characteristics and Differentiation from Fibrosing ILDs

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ABSTRACT

Background: Background: Lung fibrosis is a progressive and irreversible disease that impairs lungs' function. The global impact of COVID-19 lung infection has brought attention to fibrotic lung disease. Post-COVID-19 lung fibrosis is an important long-term complication that tend to occur in patients with prolonged ICU stays, mechanical ventilation, or comorbidities. Differentiation of post-COVID-19 lung fibrosis from other fibrosing interstitial lung diseases (FILDs) such as idiopathic pulmonary fibrosis (IPF), and hypersensitivity pneumonitis (HP) is essential for determine patients' prognosis and guide their treatment. High-resolution computed tomography (HRCT) plays a significant role in this differentiation by identifying the different imaging patterns.This review article highlights the role of HRCT imaging in identifying and differentiating post-COVID-19 lung fibrosis from FILDs.

Keywords*:* Post-COVID-19 lung fibrosis; FILD; HRCT; subpleural sparing

INTRODUCTION

Lung fibrosis refers to chronic progressive lung disease characterized by fibrotic tissue deposited in the lungs' interstitium, resulting in irreversible architectural distortion and respiratory failure eventually [1]. Given that lung fibrosis is frequently progressive and linked to high rates of morbidity and mortality, prompt diagnosis is essential [1,2].

The recent pandemic of COVID-19 infection resulted in a significant number of patients at the risk of developing post-COVID-19 lung fibrosis, particularly among those who experienced moderate to severe COVID-19 pneumonia with prolonged intensive care stays and mechanical ventilation [2,3]. Distinguishing post-COVID-19 lung fibrosis from other fibrosing interstitial lung diseases (FILDs), including idiopathic pulmonary (IPF) fibrosis, ILDs associated with connective tissue diseases, and fibrotic hypersensitivity pneumonitis, is crucial [4,5]. While these conditions exhibit similar imaging characteristics, precise diagnosis greatly influences treatment approaches and prognosis [4].

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High-resolution computed tomography (HRCT) remains the cornerstone of imaging in fibrotic lung disease. It can accurately detect structural abnormalities related to lung fibrosis, such as reticular opacities, ground-glass opacities (GGO), traction bronchiectasis, honeycombing, interlobular septal thickening, and architectural distortion [5–7]. Importantly, the specific patterns and distribution of these findings can offer diagnostic clues to differentiate various FILDs, including post-COVID lung fibrosis [8].

Adequate HRCT scanning methods and image clarity are essential to achieve accurate diagnosis [9]. Radiologists need to have a solid understanding of the HRCT characteristics that identify and differentiate FILDs and post-COVID-19 lung fibrosis. Importantly, recent findings indicate that the subpleural sparing sign observed on HRCT could assist in distinguishing post-COVID lung fibrosis from fibrosing nonspecific interstitial pneumonia (NSIP) [8].

Pathogenesis of Post-COVID-19 Lung Fibrosis

The pathogenesis of post-COVID-19 lung fibrosis involves virus-induced (SARS-CoV-2) lung damage combined with immune response and repair process through fibroproliferation. This repair process might either restore the damaged lung parenchyma or cause permanent lung fibrosis [10]. Lung fibrosis arise during the acute phase of infection as the body attempts to heal inflamed regions after lung damage [11].

Several risk factors increase the likelihood of fibrotic sequelae in COVID-19 survivors, including advanced age, male sex, and comorbidities such as diabetes and hypertension [12]. The severity of the COVID-19 infection is often related to an increased occurrence of lung fibrosis. The development of lung fibrosis is associated with the duration of ICU admission and mechanical ventilation support, which can lead to additional lung damage [13,14].

To aid in clinical evaluation, patients with post-COVID lung fibrosis are frequently categorized according to the degree of respiratory support required during their acute illness: scale 3 (no oxygen therapy), scale 4 (requiring supplemental oxygen), and scale 5–6 (requiring high-flow nasal cannula, noninvasive ventilation, or mechanical ventilation). Survivors in the latter group frequently exhibit reduced total lung capacity and impaired diffusion capacity of carbon monoxide, both of which correlate with persistent radiological changes and functional disability [15].

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HRCT Features of lung fibrosis

Key HRCT findings of lung fibrosis include lung reticulations, traction bronchiectasis, honeycombing, architectural distortion, ground-glass opacities (GGO), mosaic attenuation, emphysema, and lung nodules. Each finding contributes to differentiating ILDs and assessing disease severity [16].

Lung reticulations are the most reliable characteristics of lung fibrosis, and appear as a network of overlapping linear opacities due to thickening of both the intralobular and interlobular septa. Lung reticulations frequently are more evident in subpleural and basal lung regions and associate with lung volume reduction. When combined with GGO and traction bronchiectasis, reticulations are highly suggestive of advanced fibrotic lung disease [17–20]

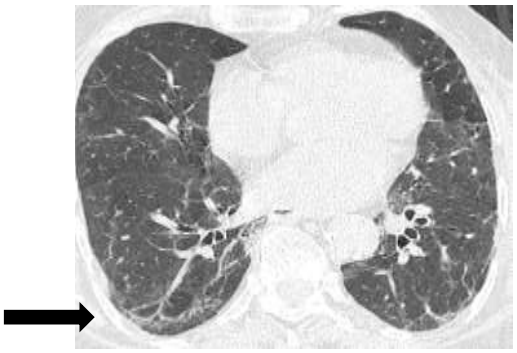

Fig. 1 Lung reticulations. Axial HRCT image of the chest demonstrating thickening of the intralobular lines and ground-glass opacities (arrow) secondary to lung fibrosis.

Traction bronchiectasis is another key feature of lung fibrosis. It refers to permanent widening of airways from fibrotic retraction of surrounding lung tissue. It commonly occurs alongside reticulations and GGO, particularly in the periphery of lower lobes in FILDs like usual interstitial pneumonia (UIP) and NSIP [16,21]. Central and upper lobe predominance may suggest sarcoidosis or fibrotic hypersensitivity pneumonitis [22].

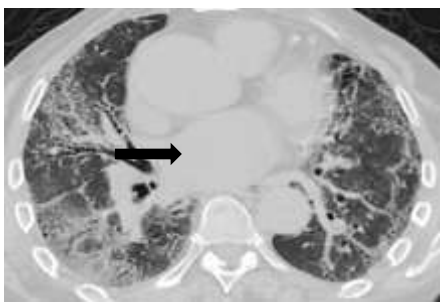

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Fig. 2 Traction bronchiectasis. Axial HRCT image of the both lower lung lobes showing basal predominant reticulation adjacent to traction bronchiectasis (arrow).

Honeycombing signifies advanced fibrosis and is marked by grouped cystic airspaces with thick walls, usually found at the basal subpleural lung regions. Honeycomb cysts frequently present as multilayered and are closely related to traction bronchiectasis [16,23]

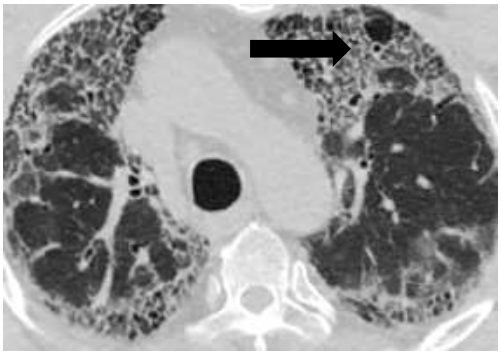

Fig. 3 Honeycombing. Axial HRCT image of the chest showing honeycombing (arrow).

Architectural distortion is an additional characteristic of advanced fibrosis, detected as the displacement or overcrowding of bronchi, vessels, and fissures. It indicates significant parenchymal restructuring and is frequently associated with loss of lung volume [24,25]

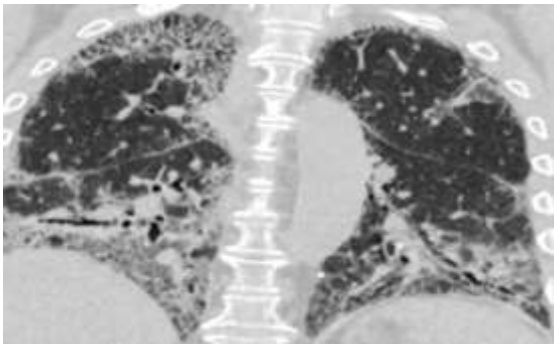

Fig. 4 Architectural distortion. Coronal HRCT image of the chest demonstrates reticulations, traction bronchiectasis, and architectural distortion.

Mosaic attenuation refers to a quilt-like look of the lung on HRCT, frequently observed in lung fibrosis. It might indicate the presence of small airways disease, vascular abnormalities, or varied parenchymal involvement.Correlation with expiratory images and vascular patterns helps distinguish the underlying cause [26].

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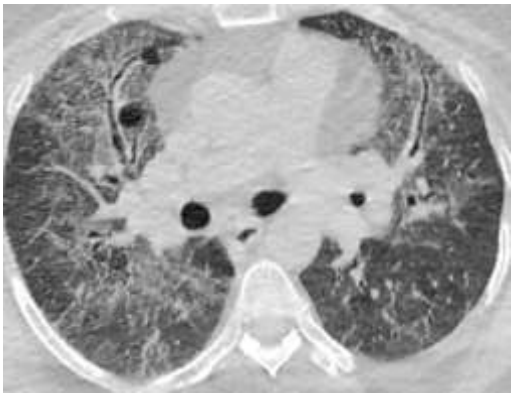
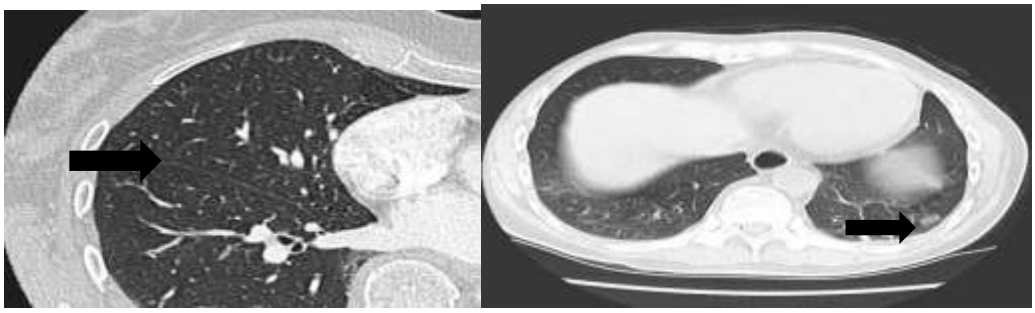


Fig. 5 Mosaic attenuation. Axial HRCT image showing heterogeneously distributed GGO that produces mosaic appearance in lung bases on a background of traction bronchiectasis, and subpleural reticulations.

GGOs are misty regions of high attenuation not hiding the bronchovascular structures beneath them.Although GGO may arise from active inflammation, their continued presence in patients with lung fibrosis frequently indicates microscopic fibrosis or subtle interstitial thickening [27,28].

Ultimately, lung nodules—solid, part-solid, or ground-glass—can manifest in lung fibrosis [29].



A B

Fig 6 A) Axial contrast enhanced HRCT of the chest showing right lung perifissural nodule (arrow). B) Axial HRCT of the chest showing left lower lobar pleural based nodule (arrow).

HRCT Features of Post-COVID-19 lung fibrosis

HRCT plays a vital role in assessing post-COVID-19 lung fibrosis, highlighting both remaining inflammatory changes and permanent fibrotic changes.HRCT features of post-COVID-19 lung fibrosis include parenchymal bands, coarse reticulations, traction bronchiectasis, and honeycombing, although the latter is less common than in idiopathic pulmonary fibrosis (IPF) [30].

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GGOs are commonly noted in post-COVID-19 lung fibrosis, indicating resolving inflammation or minor fibrosis, particularly if these opacities last for more than three months following acute infection. These opacities commonly appear alongside reticulations and traction bronchiectasis, especially in the posterior and basal lung regions [31,32].

Lung consolidation can also be seen in the acute and subacute phases of COVID-19 infection but usually resolves. If consolidation persists it may indicate organizing pneumonia or progression to fibrosis [16].

In instances of confirmed post-COVID-19 lung fibrosis, architectural distortion and abnormal bronchovascular interfaces become more apparent. Nodules, bronchial wall thickening, and crazy-paving patterns may be seen, especially in patients with prior severe disease or those with secondary infections during hospitalization [16].

The assessment of fibrotic burden in patients with post-COVID-19 lung fibrosis on HRCT is typically performed through visual means. Every lung lobe can receive a score ranging from 0 to 5 based on the level of involvement (0 = no involvement; 5=>75% involvement). The overall CT score (from 0 to 25) aids in classifying the severity of the disease: mild (0–8), moderate (9–14), and severe (>14) [33].

Follow-up HRCT at six months post-infection frequently reveals persistent fibrotic changes (e.g., reticulations, traction bronchiectasis, and subpleural linear opacities) in over half of patients with initial severe disease. These changes might reveal gradual improvements over one year but can continue or advance in a certain subset of patients, especially among older patients or those with comorbidities [16].

Differentiation Between Post-COVID-19 lung Fibrosis and FILDs on HRCT

Differentiating post-COVID-19 lung fibrosis from FILDs is essential for precise diagnosis, patient guidance, and management planning. While imaging findings on HRCT may be similar, slight variations in distribution, patterns, and radiologic context can guide differentiation [34].

FILDs including IPF, NSIP, fibrotic hypersensitivity pneumonitis typically show distinct HRCT patterns. For instance, IPF is characterized by a usual interstitial pneumonia (UIP) pattern, with basal and subpleural reticulation, traction bronchiectasis, and honeycombing, often without significant GGO. In contrast, NSIP typically shows GGOs, fine reticulations, and traction bronchiectasis with relative subpleural sparing. Fibrotic hypersensitivity pneumonitis often affect upper lobes with a centrilobular distribution and mid-zone preference [35].

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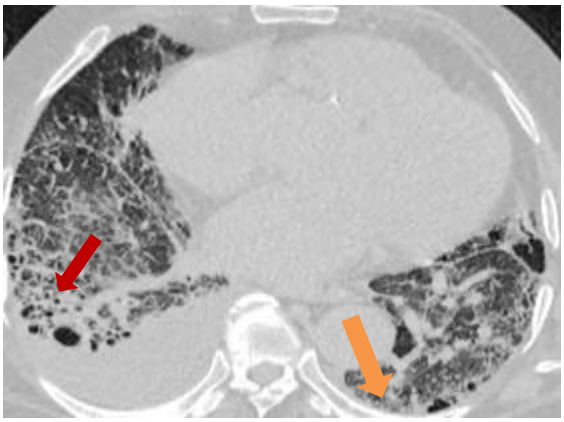

Fig 7 Axial HRCT image of the chest showing HRCT findings in IPF patient including…bilateral diffuse cenrtilobular and subpleural pulmonary reticulations (red arrows) and honeycombing (orange arrow).

In post-COVID-19 lung fibrosis, the imaging characteristics might resemble UIP or NSIP, yet there are crucial distinctions. The fibrosis frequently appears as coarse reticulation, traction bronchiectasis, and parenchymal bands predominantly in posterior and basal lung zones [36]. Significantly, honeycombing occurs less frequently, and the presence of GGOs or crazy-paving patterns may persist for months after the acute phase [36]. A highly promising differentiator is the observation of the"subpleural sparing" sign, a HRCT finding where a rim of normal lung is preserved between the pleural surface and fibrotic changes. This feature appears more frequently in post-COVID-19 lung fibrosis than in NSIP, and when the subpleural distance exceeds 3 mm, it may serve as a valuable imaging feature [8].

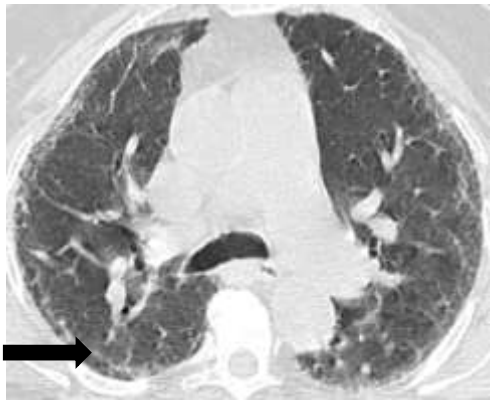

Fig 8 Axial HRCT image of the chest showing subpleural sparing sign (arrow).

Alongside pattern analysis, the distribution of fibrosis (subpleural, centrilobular, or mixed) and zonal dominance (upper, lower, diffuse) further aid in differentiation. Post-COVID-19 lung fibrosis generally displays a predominance in the posterior and basal areas, characterized by peripheral band-like

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opacities and irregularities in the pleura. Conversely, IPF exhibits a more uniform pattern, whereas fibrotic HP often display nodular infiltrates primarily in the upper lobes [16,37-39].

Conclusion

In conclusion, while post-COVID-19 lung fibrosis shares many features with FILDs, the combination of its clinical context (recent COVID-19 infection), imaging patterns, and distinctive signs like subpleural sparing can help radiologists and clinicians distinguish it from other fibrotic lung diseases. comprehensive knowledge of HRCT findings, and distinguishing imaging features is vital for radiologists and clinicians to manage the growing number of patients presenting with post-COVID-19 pulmonary fibrosis.

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