



The challenge of diagnosing interstitial lung disease by HRCT: state of the art and future perspectives

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Chest HRCT is the gold standard for the recognition of lung alteration patterns underlying interstitial lung diseases (ILDs) and those entities with potential for fibrotic evolution. In the era of antifibrotic therapies, the central role of imaging to achieve early diagnosis and prognosis is unquestionable. The diagnostic accuracy of chest HRCT is indeed sufficiently high to detect even subclinical alterations that occur in ILDs at an early stage. Any alteration is a component of a puzzle that should be carefully analyzed and revised over time by combining additional elements. The capacity of the skillful mind of the observer to interpret their meaning and insert them into a specific pattern will reduce, within the appropriate clinical context, the range of possible disease entities.

The review article by Torres et al.⁽¹⁾ published in the present issue of the *Jornal Brasileiro de Pneumologia*, emphasizes the role of chest HRCT in the diagnostic workup of ILDs. The first aspect that deserves attention is the methodology, which requires adequate procedural and technical parameters. They include the placing of the patient in the prone position, acquisition at maximal inspiration, volumetric image acquisition, thin-slice reconstruction (1.00-1.25 mm), use of a high resolution reconstruction filter, and adoption of the shortest rotation time and the highest pitch to reduce acquisition time and movement-related artifacts. Among these, volumetric image acquisition is fundamental to differentiate traction bronchiectasis from honeycombing, which is crucial to diagnose or rule out idiopathic pulmonary fibrosis (IPF).^(2,3) In addition, multiplanar image reconstruction of the entire lung, which enables the evaluation of distribution and extent of interstitial abnormalities, can be exclusively obtained with volumetric CT. Integrated image acquisition in the prone position helps differentiate very early reticulation in the lower subpleural regions from gravity-induced nonpathological increase in lung density (lung dependent). Finally, thin-slice, volumetric image CT acquired at end-expiration further improves the diagnostic reliability of small airway diseases.

The authors⁽¹⁾ correctly describe the tomographic features commonly found in fibrosing ILDs and analyze in detail those signs that differentiate the imaging pattern of IPF from that associated with other fibrosing ILDs. On the basis of the most recent international guidelines on the diagnosis of IPF,⁽²⁾ the authors⁽¹⁾ discuss the new CT classification for IPF in four patterns: UIP, probable UIP, indeterminate for UIP, and alternative diagnosis. There is a certain tendency to consider the first two patterns as only one, because traction bronchiectasis and honeycombing have the same prognostic value regarding

the profusion of fibroblastic foci on histology.⁽⁴⁾ Indeed, in the appropriate clinical context and in the absence of elements suggestive of other ILDs, the sole CT imaging pattern of probable UIP is highly consistent with the diagnosis of IPF, according to the Fleischner Society.⁽³⁾ Conversely, the indeterminate for UIP and alternative diagnosis patterns, although not indicative of IPF, do not exclude a histological UIP pattern. CT imaging in these scenarios represents a crucial component of the diagnostic workup, because it facilitates the identification of the best site where to perform biopsy, increasing sampling performance. This means that the combination of radiology with histology is essential, along with clinical information, in the diagnostic workflow of ILDs. Finally, for those patients whose diagnosis remains indeterminate despite all efforts, clinical behavior and disease progression will guide the decision-making process. This is in line with a study⁽⁵⁾ recommending that a multidisciplinary team (MDT) discusses about atypical cases in order to achieve a "working diagnosis"; a procedure that can achieve high confidence levels (> 70%). The MDT is perceived as the gold standard for diagnosis of ILDs other than IPF, including a broad panel of entities ranging from ILDs with autoimmunity features to chronic hypersensitivity pneumonia and nonspecific interstitial pneumonia.⁽⁶⁾ The lack of classification and standardized diagnostic criteria for some of these entities is still a diagnostic challenge, mainly because a non-negligible proportion of cases of inflammation-mediated ILDs may evolve to fibrosis.

The timing of chest HRCT in the follow-up of patients is still an issue of debate because there is no consensus. It does enable the differentiation between nonfibrotic and fibrotic ILDs; among the latter, it allows differentiation between forms with a slow progression and those with a rapid progression. In particular, Torres et al.⁽¹⁾ underscore the importance of chest HRCT in the follow-up of progressive forms of fibrosing ILDs, characterized by episodes of acute exacerbation and disease acceleration, in which superimposed ground-glass opacities on the fibrotic background may assume a different value.⁽⁷⁾ Currently, the attention paid to the identification of interstitial lung abnormalities (ILAs) is also a topic of interest. ILAs present with early, subclinical, and limited interstitial radiological findings. Initially ascribed to senescence or aging, ILAs are incidentally found in most cases and are relatively common in elderly smokers/former smokers in the absence of a clinically relevant condition.⁽⁸⁾ In this setting, chest HRCT is the only available diagnostic tool that distinguishes nonfibrotic from fibrotic ILAs. This differentiation has prognostic implications as fibrotic ILAs

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can evolve to pulmonary fibrosis over a few years of monitoring in up to 40% of the cases.

CT imaging is an evolving field of application and study. There is an increasing need to improve diagnostic performance by integrating visual interpretation with quantification of tissue damage. The advancement of technology has made this objective easier to achieve. Both open-source and commercially available tools have been generated to improve patient profiling and prognosis stratification, providing mathematical and statistical data.^(9,10) Artificial intelligence for human support is an emerging possibility that is expected with hope. Fibrotic ILDs represent a highly complex

sector of medicine that requires integration of specific and in-depth knowledge, as well as close interaction among different (and complementary) professionals. Nintedanib and pirfenidone have been currently used for IPF treatment, but emerging evidence suggests that they can also be used as a reliable strategy to counteract non-IPF progressive fibrotic ILDs.^(11,12)

The radiologist is an irreplaceable component of the MDT. Chest HRCT is of fundamental importance in the natural history of ILDs, including early diagnosis, severity assessment, prognosis stratification, disease progression, and prompt identification of any short- and long-term complications.

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