Co-Relation of Chest X-Ray and HRCT in Patients with Interstitial Lung Diseases

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Abstract: **Background:** Interstitial lung diseases (ILD)⁴⁻⁷ refer to a large group of diseases which inflame or scar the lung interstitium. HRCT provides a global anatomic assessment of the lung, thus imaging technique improves significantly the sensitivity and specificity of clinical and histopathological diagnosis. The radiographic signs are nonspecific so conclusions on the etiology of the findings are normally based on associated and indirect and indirect signs. Although some diseases can have common findings, making differentiation difficult, others have specific characteristics that frequently indicate diagnosis.⁵⁻⁶⁻¹² **Materials and Methods:** This is a prospective study comprising of 100 patients with a provisional clinical diagnosis of interstitial lung disease, as referred to the Department of Radio-diagnosis at GCS Medical College and Hospital, Ahmedabad, Gujarat from Jan 2020 till date. PA views and lateral views X-rays were taken in full inspiration. In HRCT, 1 to 1.5 mm collimation sections were obtained. Five to eight slices with thin collimation were obtained at different anatomic levels of the lung 2 cm, or 3 cm intersection gap was used. Scanning was performed using a field of view large enough to encompass both lungs (35-40cm). **Results:** Out of the 100 cases with suspected ILD, majority of them belonged to the age group of forty to seventy years of age. Out of the 25 cases of idiopathic pulmonary fibrosis, 5 were males and 25 were females. The remaining (non-IPF) 75 cases were of 30 males and 45 females. **Conclusion:** HRCT is the most sensitive modality in diagnosing ILD. It offers the ability to distinguish responders and non responders to treatment in ILD. Overall, HRCT is the most sensitive parameter to detect the early interstitial changes in non-IPF patients. HRCT can show evidence of interstitial lung changes even when clinical and pulmonary function tests parameters are normal. HRCT is superior to plain chest radiograph in the evaluation of early interstitial lung changes.

**Keywords:** HRCT, ILD, IPF, Radiograph

1. Introduction

HRCT is particularly helpful in the evaluation of diffuse interstitial lung disease (DILD), as clinical presentation and histo-pathologic patterns can show significant overlap and there can be significant heterogeneity of disease throughout the lung. These modalities together provide a clinicoradiological- histopathological approach to the patient with DILD that allows for accurate diagnosis and optimal management. Using thin slices and high-resolution reconstruction techniques, HRCT has the ability to detect discrete abnormalities as small as 0.3 mm. While this resolution is significantly less than that of pathologic examination. Approximately 200 entities manifest as diffuse lung disease. Fortunately, only about 10 of these account for about 90% of all diffuse lung diseases, that are assessed by open lung biopsy. The radiographic signs are nonspecific so conclusions on the etiology of the findings are normally based on associated and indirect and indirect signs. Although some diseases can have common findings, making differentiation difficult, others have specific characteristics that frequently indicate diagnosis.

2. Aims and Objectives

- To find the correlation between chest x-ray and HRCT findings in various interstitial lung diseases.
- To study age and gender wise distribution of interstitial lung diseases.
- To determine the sensitivity of HRCT and chest x-ray in diagnosing interstitial lung diseases.
- To determine the relative frequencies of different interstitial lung diseases in region.
- To study the correlation of HRCT and chest x-ray in idiopathic pulmonary fibrosis (IPF).
- To study the correlation of HRCT and chest x-ray in patients of non-idiopathic pulmonary fibrosis (non-IPF) type of interstitial lung diseases.

3. Materials and Methods

This is a prospective study comprising of 100 patients with a provisional clinical diagnosis of interstitial lung disease, as referred to the Department of Radio-diagnosis at GCS Medical College and Hospital, Ahmedabad, Gujarat from January 2020 till date. All patients were subjected to chest x-ray followed by HRCT, at the same time using:

1) X-ray Machine – Meditronix 300mA,or
2) X-ray Machine – Meditronix 800mA,or
3) X-ray Machine – Siemens 500mA, and
4) 16 Slice CT Scan Machine – Siemens Somatom

High-resolution images were obtained at 1 mm collimation at 1- mm intervals from the apices to the lung bases. Images were reconstructed into a bow algorithm using standard window setting (window level: 700HU; window width: 1500 HU). The CT scan was interpreted for the presence of bronchiectasis severity, pattern, distribution, and associated disease process such as emphysema and small airway

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disease by 2 radiologists who were blinded to other clinical and laboratory results; decisions were reached by consensus.

**Inclusion Criteria**
- Patients with a clinical suspicion of interstitial lung disease.
- Known cases of interstitial lung disease who are being treated medically.
- Biopsy proven cases of interstitial lung disease.

**Exclusion Criteria**
- Known cases of tuberculosis (except silico-tuberculosis).
- Known cases of lung masses (except mesothelioma).
- Pregnant females.

The 100 patients included in our study are sub-divided into two categories depending on the underlying disease condition which includes:
- Idiopathic pulmonary fibrosis (males and females)
- Non-IPF patients (males and females).

4. Results

(a) Tables

<table>
<thead>
<tr>
<th>Total Cases = 100</th>
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<tbody>
<tr>
<td>IPP CASES = 25</td>
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<tr>
<td>NON-IPP CASES = 75</td>
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<tr>
<td>MALES = 5</td>
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<tr>
<td>FEMALES = 20</td>
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<tr>
<td>MALES = 30</td>
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<tr>
<td>FEMALES = 45</td>
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</tbody>
</table>

**Observations in Patients of Idiopathic Pulmonary Fibrosis (IPF):**
- Total patients of IPF studied (N) =25.
- There were 5 males (20%) and 20 females (80%).
- The male: female ratio was 1:3.
- Average age of male patients was 48.4 years and for females it was 45.8 years.
- Majority of the patients had the duration of illness between one and three years.
- The mean duration of illness was 2.9 years.
- 18 of the 25 patients had respiratory complaints (72%).
- The symptoms included cough, breathlessness, wheeze, sputum production and chest pain.
- Of the 18 patients, 14 patients (77.78%) had clinical evidence of respiratory involvement presenting with rhonchi and crackles.
- In our study population, 21 patients (84%) with positive clinical features had HRCT findings consistent with IPF.
- 11 patients had abnormalities detectable on chest x-rays (44%).

<table>
<thead>
<tr>
<th>Table 1: Age and gender predilection in patients of idiopathic pulmonary fibrosis</th>
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<tbody>
<tr>
<td>Category</td>
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<tr>
<td>----------------</td>
</tr>
<tr>
<td>Total</td>
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<td>Males</td>
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<td>Females</td>
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<th>Table 2: Comparative analysis of clinical features and radiological investigations in detecting lung involvement</th>
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<td>Procedure</td>
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<tr>
<td>Clinical features</td>
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<td>Chest x-ray</td>
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<td>HRCT</td>
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<th>Table 3: Incidence of IPF in various age groups</th>
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<td>Age group in years</td>
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<td>51-60</td>
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<td>61-70</td>
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<td>71-80</td>
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<th>Table 4: Incidence of IPF in various age groups</th>
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<tr>
<td>Age group in years</td>
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<td>61-70</td>
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<tr>
<td>71-80</td>
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</tbody>
</table>

**Observations In Non-IPF Patients**
- Total no. of patients (N) =75
- There were 30 males and 45 females.
- Their mean age was 48.2 years.
- Median age at diagnosis in men and women was 52 and 49 years respectively.
- 9 men (25.7%) and 11 women (26.8%) were aged more than 60 years.

**Chest radiographic findings included:**
- Reticular shadows: n=23, 30.67%
- Reticulonodular shadows: n=40, 53.33%
- Hilar enlargement: n=04, 5.33%

**Abnormalities noted on HRCT thorax included:**
- Reticular pattern: n= 23, 30.67%
- Reticulonodular pattern: n= 40, 53.33%
- Honeycombing: n= 60, 80 %
- Ground glass opacity: n= 16, 21.33%
- Parenchymal nodules: n= 07, 9.33%
- Mediastinal lymphadenopathy: n= 04, 5.33%

Mild air trapping was observed in three patients. All three were smokers, and air trapping was considered to be related to smoking-associated small airway obstruction.
Table 5: Relative frequencies of interstitial lung diseases in our study

<table>
<thead>
<tr>
<th>S. No.</th>
<th>Interstitial lung disease</th>
<th>No. of patients</th>
<th>Relative frequency (%)</th>
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<tbody>
<tr>
<td>1.</td>
<td>Occupational and environmental</td>
<td>28</td>
<td>28</td>
</tr>
<tr>
<td>2.</td>
<td>Idiopathic pulmonary fibrosis</td>
<td>25</td>
<td>25</td>
</tr>
<tr>
<td>3.</td>
<td>UIP and NSIP</td>
<td>11</td>
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</tr>
<tr>
<td>4.</td>
<td>Lymphangioleiomyomatosis (LAM)</td>
<td>10</td>
<td>10</td>
</tr>
<tr>
<td>5.</td>
<td>Hypersensitivity pneumonitis</td>
<td>08</td>
<td>08</td>
</tr>
<tr>
<td>6.</td>
<td>Connective tissue disorders</td>
<td>07</td>
<td>07</td>
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<tr>
<td>7.</td>
<td>Langerhans’ cell histiocytosis (LCH)</td>
<td>05</td>
<td>05</td>
</tr>
<tr>
<td>8.</td>
<td>Drugs and radiation</td>
<td>03</td>
<td>03</td>
</tr>
<tr>
<td>9.</td>
<td>Sarcoidosis</td>
<td>02</td>
<td>02</td>
</tr>
<tr>
<td>10.</td>
<td>Others</td>
<td>01</td>
<td>01</td>
</tr>
<tr>
<td></td>
<td>Total</td>
<td>100</td>
<td>100</td>
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Table 6: X-ray features in non-IPF patients (%)

<table>
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<tr>
<th>X-ray features</th>
<th>No. of Patients</th>
<th>Percentage</th>
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<td>Reticular</td>
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<td>30.67</td>
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<tr>
<td>Reticulonodular</td>
<td>40</td>
<td>53.33</td>
</tr>
<tr>
<td>Hilar enlargement</td>
<td>4</td>
<td>5.33</td>
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Table 7: HRCT findings in non-IPF patients (%)

<table>
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<tr>
<th>HRCT findings</th>
<th>No. of patients</th>
<th>Percentage</th>
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<td>30.67</td>
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<td>40</td>
<td>53.33</td>
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<tr>
<td>Honeycombing</td>
<td>60</td>
<td>80</td>
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<tr>
<td>Ground glass opacity</td>
<td>16</td>
<td>21.33</td>
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<tr>
<td>Parenchymal nodules</td>
<td>7</td>
<td>9.33</td>
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<tr>
<td>Mediastinal lymphadenopathy</td>
<td>4</td>
<td>5.33</td>
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Table 8: Age and gender distribution in non-IPF patients

<table>
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<tr>
<th>Category</th>
<th>No. of patients</th>
<th>Mean age (years)</th>
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<td>Patients</td>
<td>75</td>
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<tr>
<td>Males</td>
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<td>52</td>
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<tr>
<td>Females</td>
<td>45</td>
<td>49</td>
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Table 9: Incidence of non-IPF patients in different age groups

<table>
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<th>Age groups in years</th>
<th>Number of patients</th>
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<td>61-70</td>
<td>13</td>
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<tr>
<td>71-80</td>
<td>4</td>
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<tr>
<td>81-90</td>
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Table 10: Incidence of non-IPF patients in different age groups

<table>
<thead>
<tr>
<th>Age groups in years</th>
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<tbody>
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<td>21-30</td>
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<td>71-80</td>
<td>4</td>
</tr>
<tr>
<td>81-90</td>
<td>1</td>
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</tbody>
</table>

Figure 1: Chest x-ray and HRCT thorax in idiopathic pulmonary fibrosis (IPF) showing traction bronchiectasis, fibrosis and honeycombing
Figure 2: Progressive massive fibrosis in a case of coal worker’s pneumoconiosis (CWP) delineating upper lobe conglomerates with radiating fibrotic strands.

Figure 3: Progressive massive fibrosis appearing as sausage shaped conglomerate nodules in a case of silicosis.

Figure 4: Chest x-ray and HRCT thorax of hypersensitivity pneumonitis showing perihilar alveolar infiltrates with ground glass opacities and mosaic attenuation.
Figure 5: Chest x-ray and HRCT thorax in **usual interstitial pneumonia (UIP)** demonstrating classic honeycombing.

Figure 6: Chest x-ray and HRCT thorax in **non-specific interstitial pneumonia (NSIP)** delineating patchy ground glass opacities with fibrosis and honeycombing.

Figure 7: Chest X ray and HRCT thorax in a known case of tuberous sclerosis with classic thin-walled cysts in **lymphangioleiomyomatosis**
Figure 8: Chest X ray and HRCT thorax in a young adult smoker delineating submillimeter cysts with centrilobular nodules and interstitial septal thickening, in a case of Langerhans’ cell histiocytosis.

Figure 9 – Evidence of interseptal thickening with subpleural nodules in a 50 year old male who is a known case of gastric carcinoma. Findings suggest lymphangitis carcinomatosis.
5. Discussion

Interstitial lung disease (ILD) is a group of lung disorders in which the deep lung tissues become inflamed or scarred. It includes a variety of illnesses with diverse causes, treatments, and prognoses. These disorders are grouped together because of similarities in their clinical presentations, plain chest radiographic appearance, and physiologic features.

Often, the identification of interstitial opacities on chest x-ray focuses the diagnostic approach towards one of the ILDs. ILDs represent a large number of conditions that involve the parenchyma of the lung- the alveoli, the alveolar epithelium, the capillary endothelium, and the spaces between these structures, as well as the perivascular and lymphatic tissues. This heterogeneous group of disorders is classified together because of similar clinical, roentgenographic, physiologic, or pathologic, or pathologic manifestations. These disorders are often associated with considerable morbidity and mortality, and there is little consensus regarding the best management of most of them.

One useful approach to classification is to separate the ILDs into two groups based on the major underlying histopathology:

- a) Those associated with predominant inflammation and fibrosis,
- b) Those with a predominantly granulomatous reaction in interstitial or vascular areas.

This process of granulomatous lung disease is characterized by an accumulation of T lymphocytes, macrophages, and epithelioid cells organized into discrete structures (granulomas) in the lung parenchyma. The granulomatous

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**Figure 10:** Chest x-ray, CT thorax (mediastinal window) and HRCT thorax showing hilar lymphadenopathy with perilymphatic nodules in a biopsy proven case of sarcoidosis.
lesions can progress to fibrosis. Many patients with granulomatous lung disease remain free of severe impairment of lung function, or, when symptomatic, they improve after treatment. The main differential diagnosis is between sarcoidosis and hypersensitivity pneumonitis [23,26].

The proposed mechanism of pulmonary fibrosis suggests that the lung is naturally exposed to repetitive injury from a variety of exogenous and endogenous stimuli. Several local and systemic factors (e.g., fibroblasts, circulating fibrocytes, chemokines, growth factors, and clotting factors) contribute to tissue healing and functional recovery. Dysregulation of this intricate network through genetic predisposition, autoimmune conditions, or superimposed diseases can lead to aberrant wound healing with the result of pulmonary fibrosis. Alternatively, excessive injury to the lung may overwhelm even intact reparative mechanisms and lead to pulmonary fibrosis. On cellular level, multiple micro injuries damage and activate alveolar epithelial cells, which in turn induce an antifibroinolytic environment in the alveolar spaces, enhancing wound clot formation. Alveolar epithelial cells secrete growth factors and induce migration and proliferation of fibroblasts and differentiation into myofibroblasts. Subepithelial myofibroblasts and alveolar epithelial cells produce gelatinases which may increase basement membrane disruption and allow fibroblast – myofibroblast migration. Both intraalveolar and interstitial myofibroblasts secrete extracellular matrix proteins, mainly collagens. An imbalance between interstitial collagenses and tissue inhibitors of metalloproteinases provokes the progressive deposit of extracellular matrix. Signals responsible for myofibroblast apoptosis seem to be absent or delayed in usual interstitial pneumonia, increasing cell survival. Myofibroblasts produce angiotsinogen, which as angiotensin II provokes alveolar epithelial cell death, further impairing reepithelialization. Abbreviations: FGF-2, fibroblast growth factor 2; MMPs, metalloproteinases; PAI-1, PAI-2, plasminogen activator inhibitor 1, 2; PDGF, platelet-derived growth factor; TGF-transforming growth factor; TIMPs, tissue inhibitors of metalloproteinases; VEGF [27,28].

The HRCT study by Johkoh T et al. [29] of patients with interstitial pneumonias revealed a high prevalence of ILD (44%). If all forms of HRCT diagnosed ILD that is, changes or IPF, GGO and interlobular thickening are combined, there is a closer level of prevalence (37%) of ILD to that study. Lynch DA et al. [30] found that interstitial pneumonias with evidence of ILD on HRCT have abnormalities which cannot be confidently given on any other non-invasive test, considering HRCT as gold standard.

6. Conclusion

HRCT has been in use since introduction in 1970s and has now become an indispensable tool for radiologists around the world. The use of HRCT in thoracic imaging has been progressively increasing. The plain radiograph and HRCT in IPF reveal bilateral, peripheral and basilar predominant disease with reticulo-nodular infiltrates, often with honeycombing and cystic changes. Ground glass abnormalities, increased attenuation of the lung tissue without distortion of the underlying blood vessels or bronchi, are absent or minimal in classic IPF. As the burden of disease increases, the chest x-ray examination can reveal multiple tiny cysts in the most markedly involved regions. This cystic pattern, called honeycombing, reflects end-stage fibrosis and is a feature of many end-stage ILDs. [31]

There is a good correlation among chest x ray and HRCT findings in IPF. Although we earlier relied heavily on histopathological confirmation of disease, many more patients (especially those unable to undergo lung biopsy) are now being diagnosed based on HRCT scans. In our present study, typical radiographic findings were observed on HRCT in 88% patients. In non-IPF patients, usual interstitial pneumonia, non-specific interstitial pneumonia, occupational lung diseases, hypersensitivity pneumonitis and rheumatoid arthritis are the commonest abnormalities. The HRCT findings include pleural thickening and effusion, honeycombing, septal thickening, bronchiolitis obliterans organizing pneumonia (BOOP), bronchiectasis and bronchiolitis obliterans. With progression of disease, the reticular pattern becomes more coarse and diffuse, and honeycombing may be seen. We observed that 16% patients had no abnormality in any of the parameters related to the pulmonary involvement. 12% patients had relevant clinical symptoms consistent with ILD in the absence of clinical or chest radiographic changes. 28% patients had relevant clinical symptoms consistent with HRCT findings in the absence of chest x ray features. 44% patients had consistent clinical features with chest X-ray and HRCT findings. No patient had absence of relevant clinical features with positive HRCT and chest x-ray. Sensitivity of HRCT thus surpasses that of chest x-rays and clinical features. HRCT is thus, the radiological imaging technique best suited to revealing changes in lung structure. Various HRCT findings, taken together, can represent typical patterns. [32,33] These patterns, in conjunction with the anatomical distribution of findings and with clinical data, can narrow the differential diagnosis of diffuse interstitial lung disease and, in many cases, indicate the correct diagnosis with a high degree of accuracy. The most common HRCT patterns seen in cases of diffuse interstitial lung diseases are the nodular pattern, linear/reticular opacities, cystic lesions, ground- glass opacities and consolidations. This study reviews the correlations between HRCT patterns and pathologic findings, summarizing the most common causes, as well as detailing the methods of investigation employed in order to diagnose the most common types of chronic diffuse lungdisease. As per the results of our study, the interstitial lung changes affect a significant proportion of the patients. Overall, HRCT is the most sensitive parameter to detect the early interstitial changes in non-IPF patients. HRCT can show evidence of interstitial lung changes even when clinical and pulmonary function tests parameters are normal. HRCT is superior to plain chest radiograph in the evaluation of early interstitial lungchanges.

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