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Differentiating Connective Tissue Disease-Associated Interstitial Lung Disease from Idiopathic Pulmonary Fibrosis Using CT Characteristics of the usual Interstitial Pneumonia Pattern

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ABSTRACT— Many studies show that it might be challenging to identify in order to diagnose the usual Interstitial Pneumonia, this study would assess the effectiveness of chest computed tomography to differentiate Connective Tissue Disease-Associated Interstitial Lung Disease from Idiopathic Pulmonary Fibrosis. a retrospective evaluation of 48 patients admitted to our hospital was conducted 2019-2022, who had a UIP pattern on a diagnostic-quality CT study and a multidisciplinary diagnosis of CTD-ILD or IPF. 31 (64.6 %) were male, and 17 (35.4 %) were female with a mean age of 56.96±11.31 years. 34 (70.8%) had IPF, 14 (29.2%) had CTD-ILD. 40 (41.7%) of them smokers. Rheumatoid arthritis was the most common type of CTD-ILD. There were significant differences between IPF and CTD-ILD in terms of the distribution of lung involvement. Also significancy founded in the prevalence of ground-glass opacities, consolidation, honeycomb lung, and lymphadenopathy. the sensitivity and specificity values show that different imaging features can help distinguish between IPF and CTD-ILD with varying accuracy. CT can help in diagnosing the causative features of usual Interstitial Pneumonia in most of patients diagnosed with UIP had IPF.

KEYWORDS: Usual Interstitial Pneumonia Connective Tissue Disease-Associated Interstitial Lung Disease Idiopathic Pulmonary Fibrosis Chest CT Nasiriyah

1. INTRODUCTION

Usual Interstitial Pneumonia (UIP) is characterized by a distinctive pattern of lung tissue damage and inflammation [1]. The exact incidence and prevalence of UIP are not well-established, but it is estimated to affect 10-15 per 100,000 people per year [2]. The cause of UIP is not well understood, but several risk factors have been identified. These include age, smoking, environmental exposures and genetics [3]. UIP due to Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD) and Idiopathic Pulmonary Fibrosis (IPF) are both forms of interstitial lung disease that share similar clinical features, including progressive dyspnea and cough. However, they have different underlying causes and treatment approaches. Differentiating between UIP-CTD-ILD and IPF is important for appropriate management and prognosis [4].

Chest computed tomography (CT) imaging plays a critical role in distinguishing between these two conditions. Here are some of the CT features that can help differentiate UIP-CTD-ILD from IPF: Distribution of fibrosis; IPF typically has a predominantly peripheral and basal distribution of fibrosis, while UIP-CTD-ILD may have a more diffuse and upper lobe distribution [5], [6]. Ground-glass opacities (GGOs); GGOs are typically more prominent in UIP-CTD-ILD than in IPF. In UIP-CTD-ILD, GGOs tend to be patchy and involve multiple lobes, whereas, in IPF, they tend to be limited and peripheral [7]. Consolidation: Consolidation is more common in UIP-CTD-ILD than in IPF and may be patchy or diffuse

[8]. Honeycombing: Honeycombing is a hallmark of IPF but is less common in UIP-CTD-ILD [9]. Also, associated features: Certain imaging features may suggest an underlying connective tissue disease, such as ground-glass opacities with a reticular pattern, lymphadenopathy, pleural effusions, or pericardial effusions [10].

It is important to note that while these CT characteristics can be helpful in distinguishing between UIP-CTD-ILD and IPF, a definitive diagnosis often requires a combination of clinical, imaging, and histopathologic findings [11]. A multidisciplinary approach involving pulmonologists, radiologists, and pathologists can help ensure accurate diagnosis and optimal management of these conditions [12]. The purpose of this study was to use the CT features to assess each finding's diagnostic value in distinguishing between CTD UIP and IPF UIP.

2. Materials and methods

In the study, patients with suspected interstitial pulmonary diseases (ILD) who were admitted to Al-Hussein Teaching Hospital in Nasiriyah, Iraq between January 1, 2019, and May 31, 2022, and who had a UIP pattern on a diagnostic-quality CT study and a multidisciplinary diagnosis of CTD-ILD or IPF, were reviewed retrospectively. Patients' incomplete data were excluded. 48 out of the 71 patients with lung diseases in the ILD registry had a UIP CT pattern based on a diagnostic-quality investigation and were given the diagnosis of CTD-ILD or IPF.

The following questions were included in a designed questionnaire that was filled out in combination with reviewing the records of patients suspected of having ILD: Age and gender are sociodemographic factors. Smoking history, CTD-ILD subtype, and CT scan results. The Al-Hussein Teaching Hospital's Ethics Committee gave the study procedure its approval. The privacy of patient information was respected.

A CT scan was deemed to be of diagnostic quality if it had thin acquisition or reconstruction intervals (2.0 mm) and was devoid of motion artifacts that precluded the detection of fine detail inside the lung parenchyma. Many scanners were used to obtain chest CT scans (16- to 64-MDCT, Multislice siemens somatom). With 120 kVp, 220 mAs, and a 512 512-pixel image reconstruction matrix, a supine helical CT capture was carried out during complete inspiration. Using a lung methodology, continuous axial image reconstruction was performed at 1- and 3-mm slice thickness. Images in the coronal and sagittal planes were produced.

Certain signs within the UIP pattern are more suggestive of being due to CTD-ILD rather than IPF, these include: The accumulation of fibrosis in the anterior region of the upper lobes with relative sparing of other parts of upper lobes and concurrent lower lobe involvement, were the characteristics of the *anterior upper lobe sign* (figure:1). The profuse growth of cysts resembling honeycombs greater than 70% of fibrotic changes, was the *exuberant honeycombing sign* (figure:2), and in coronal images, the *straight-edge sign* (figure :3) was isolated fibrosis to the lung bases lacking notable extension all along lateral borders of the lungs.

The Statistic Package for the Social Science Software was used to do statistical analysis (SPSS, 25). The data were presented in the form of mean±standard deviation. For categorical measurements, frequencies and percentages were utilized and appropriate statistical tests were performed, Chi-square was used for categorical variables and Fisher’s exact test was used when expected variables were less than 20%. Tables and/or graphs were used to convey the findings and $P<0.05$ was regarded as statistically significant.

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3. Results

This study included 48 (67.6%) patients who were diagnosed with UIP and were admitted to our hospital. 34 (70.8%) had IPF, and 14 (29.2%) had CTD-ILD. The age group of the participants was varied; 8 (16.7%) patients were younger than 40, 15 (31.3%) patients were from 40–60 years old, and the majority, 25 (52.1%) patients, were older than 60 years old, with a mean and standard deviation of 56.96±11.31 years (37- 75 years). There was a significant association between age Group and UIP ($p<0.05$). Participants with IPF were older than those with CTD-ILD (Table 1).

In the current study, the majority were males, as there were 31 (64.6 %) while the rest were females, with only 17 (35.4 %). There was a significant association between age group and UIP ($p<0.05$). Most of the patients with IPF were males, and most of those with CTD-ILD were females (Table 1).

Finally, for smoking cigarettes, 40 (41.7%) of the patients were smokers. There was a significant association between smoking and UIP ($p<0.05$). Patients with IPF had smoked more than the patients with CTD-ILD (Table 1).

Table 1 Demographics according interstitial lung diseases (N=48)

		Usual Interstitial Pneumonia				P value
		IPF		CTD-ILD		
		N=34	%	N=14	%	
Age Group	< 40 years old	1	2.9%	7	50.0%	**.000**
	45-60 years old	9	26.5%	6	42.9%	
	>60 years old	24	70.6%	1	7.1%	
Age (Mean±SD)		62.27 ± 7.824		47.40 ± 10.266		**0.0001**
Gender	Male	26	76.5%	5	35.7%	**.007**
	Female	8	23.5%	9	64.3%	
Smoking	Yes	15	44.1%	3	21.4%	**.000**
	Ex	16	47.1%	2	14.3%	
	No	3	8.8%	9	64.3%	
*Significant difference between different percentages using Pearson Chi-square test (χ^2-test) at 0.05 level						

Table 2 presents the distribution of different types of Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD) among patients in the study.

The results show that rheumatoid arthritis was the most common type of CTD-ILD, accounting for 35.7% (5) of cases. Systemic sclerosis and Sjogren's syndrome were the next most common types, each accounting for 21.4% of cases. Systemic lupus erythematosus accounted for 14.3% of cases, while mixed connective

tissue disease accounted for only 7.2% of cases (Table 2).

Table 2 Frequency of Relevant Types of Connective Tissue Disease-Associated Interstitial Lung Disease (N=14)

Type of CTD-ILD	Frequency	Percentage
Rheumatoid arthritis	5	35.7%
Systemic sclerosis	3	21.4%
Systemic lupus erythematosus	2	14.3%
Sjogren's syndrome	3	21.4%
Mixed connective tissue disease	1	7.2%

Table 3 presents the results of a study comparing the CT scan findings between patients with Usual Interstitial Pneumonia (UIP) and Connective Tissue Disease-Associated Interstitial Lung Disease (CTD-ILD).

The results show that there were significant differences between IPF and CTD-ILD in terms of the distribution of lung involvement, with 79.4% of IPF patients showing peripheral-basal distribution compared to only 21.4% of CTD-ILD patients. In contrast, diffuse-upper lobe distribution is more common in CTD-ILD patients, with 78.6% compared to only 20.6% in UIP patients (Table 3).

Other significant differences were found in the prevalence of ground-glass opacities, consolidation, honeycomb lung, and lymphadenopathy. Ground-glass opacities were more common in CTD-ILD patients (64.3%) compared to IPF patients (17.6%), whereas consolidation was more common in CTD-ILD patients (78.6%) than IPF patients (11.8%). Honeycomb lung was more prevalent in IPF patients (35.3%) compared to CTD-ILD patients (7.1%), while lymphadenopathy was more common in CTD-ILD patients (50%) compared to IPF patients (2.9%) (Table 3).

Finally, there were no significant differences between IPF and CTD-ILD patients in terms of the prevalence of pericardial effusions and pleural effusions (Table 3).

For instance, in the case of honeycomb lung, the sensitivity is 7.1%, which means that 7.1% of patients with CTD-ILD had honeycomb lung on imaging. The specificity for the same feature is 64.7%, which implies that 64.7% of patients with IPF did not have honeycomb lung on imaging (Table 3).

Similarly, for consolidation, the sensitivity is 78.6%, indicating that only a proportion of CTD-ILD patients had consolidation on imaging, while the specificity is 88.2%, implying that most patients with CTD-ILD did have consolidation on imaging (Table 3).

Finally, the sensitivity and specificity values reported in the table suggest that different imaging features can help distinguish between IPF and CTD-ILD with varying degrees of accuracy. For example, ground-glass opacities had a relatively high sensitivity of 64.3%, suggesting that this feature is more commonly observed in patients with CTD-ILD. On the other hand, lymphadenopathy had a very high specificity of 97.1%, indicating that this feature is more commonly absent in IPF patients (Table 3).

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Table 3 CT scan findings according to interstitial lung diseases (N=48)

		Usual Interstitial Pneumonia				**Sensitivity**	**Specificity**	P value
		IPF		CTD-ILD				
		No=34	%	No=14	%			
Distribution	Peripheral-basal	27	79.4%	3	21.4%	78.6%	79.4%	**.000**
	Diffuse-upper lobe	34	20.6%	11	78.6%			
Ground-glass opacities	Yes	6	17.6%	9	64.3%	64.3%	82.4%	**.002**
	No	28	82.4%	5	35.7%			
Consolidation	Yes	4	11.8%	11	78.6%	78.6%	88.2%	**.000**
	No	30	88.2%	3	21.4%			
Honeycomb lung	Yes	12	35.3%	1	7.1%	7.1%	64.7%	**.046**
	No	22	64.7%	13	92.9%			
lymphadenopathy	Yes	1	2.9%	7	50.0%	50.0%	97.1%	**.000**
	No	33	97.1%	7	50.0%			
pericardial effusions	Yes	6	17.6%	6	42.9%	42.9%	82.4%	.067
	No	28	82.4%	8	57.1%			
pleural effusions	Yes	9	26.5%	3	21.4%	21.4%	73.5%	.714
	No	25	73.5%	11	78.6%			
*Significant difference between different percentages using Pearson Chi-square test (χ^2-test) at 0.05 level								

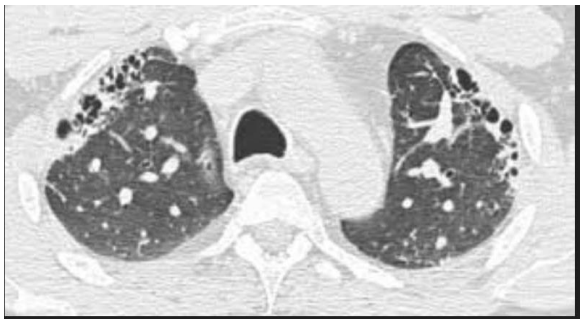

Figure:1-axial CT section, anterior upper lobe sign.

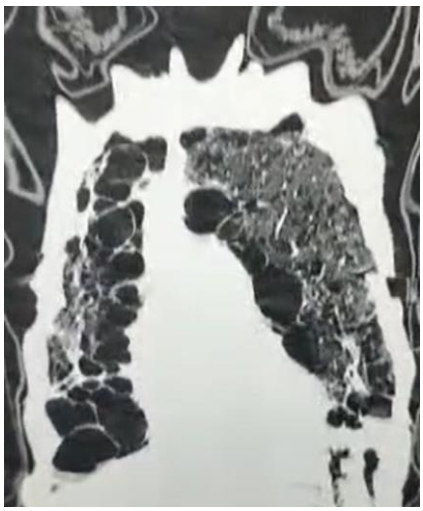

Figure: 2 – coronal CT image shows an exuberant honeycombing sign, macrocystic type.

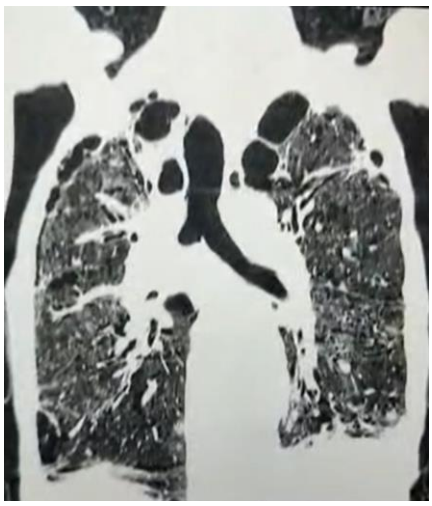

Figure :3 – coronal CT image shows straight-edge sign

4. Discussion

The study aimed to evaluate the diagnostic utility of thoracic CT in determining the underlying cause of UIP in patients with suspected ILD. The study included a total of 48 patients who underwent thoracic CT, and among these patients, 34 (70.8%) were diagnosed with IPF and 14 (29.2%) were diagnosed with CTD-ILD. This information suggests that the majority of patients diagnosed with UIP in this study had IPF. Our findings are consistent with a study done by [13] in US, which revealed there were 62 (36.2%) CTD-ILD and 109 (63.6%) IPF patients.

The age distribution of the participants in the study shows that the majority of the patients were older than 60 years old, with a mean age of 56.96±11.31 years. This finding is consistent with the fact that IPF is a disease that primarily affects older adults. Our findings are consistent with a study done by [14], which revealed IPF is a form of interstitial lung disease that primarily affects older people. IPF is typically diagnosed in individuals over the age of 60, whereas CTD-ILD can occur at any age. The age difference between the two groups may also reflect differences in the underlying mechanisms of disease. IPF is thought to be primarily driven by age-related changes in lung tissue, while CTD-ILD is associated with autoimmune and inflammatory disorders that may affect individuals of any age. A study done by [15] in India revealed a total of 2,005 patients, mean age was 48.5±11.9 years and 65.8 ±7.9 years for IPF.

The study results indicate that smoking is associated with a higher risk of developing UIP. The study found that 41.7% of the patients were smokers, and there was a significant association between smoking and UIP. This finding is consistent with previous research that has shown smoking to be a risk factor for ILDs, including IPF. It is believed that smoking causes damage to the lung tissue, which can lead to inflammation and scarring, ultimately leading to the development of UIP and other ILDs. Additionally, the study found that patients with IPF had smoked more than patients with CTD-ILD. This may suggest that smoking is a more significant risk factor for IPF than for CTD-ILD. A study done by [16] in South Korea revealed Dose-dependent increase was reported for smoking as a risk factor for IPF.

The statement describes the prevalence of various types of CTD-ILD among patients. Rheumatoid arthritis was found to be the most common type, accounting for 35.7% of cases. Systemic sclerosis and Sjogren's syndrome were the next most common types, each accounting for 21.4% of cases. Systemic lupus erythematosus accounted for 14.3% of cases, while mixed connective tissue disease accounted for only 7.2% of cases. Our findings are consistent with a study done by [17] in South Korea.

These results are important for clinicians and researchers to better understand the prevalence and distribution of CTD-ILD, which can help guide diagnosis and treatment strategies. For instance, rheumatoid arthritis is a common underlying condition in CTD-ILD, so clinicians should consider it as a potential diagnosis when patients present with respiratory symptoms [18], [19].

There are significant differences in the distribution of lung involvement between the two diseases. Specifically, peripheral-basal distribution is more common in IPF patients, with 79.4% of cases showing this pattern, compared to only 21.4% of CTD-ILD patients. On the other hand, diffuse-upper lobe distribution is more common in CTD-ILD patients, with 78.6% of cases showing this pattern, compared to only 20.6% of IPF patients. These differences in lung involvement patterns may have implications for the diagnosis and treatment of these diseases. Our findings are consistent with a study done by [20] in the UK, which revealed the importance of separating disease distribution into that typical of IPF (peripheral, basal, or subpleural predominant) and disease distributions not typical of IPF (middle or upper zone predominant).

In the current study, there is a significant difference found between IPF and CTD-ILD in terms of radiological findings, specifically ground-glass opacities, consolidation, honeycomb lung, and lymphadenopathy. Ground-glass opacities were found to be more common in CTD-ILD patients (64.3%) compared to IPF patients (17.6%). This difference may be due to the fact that connective tissue diseases often involve inflammation and immune system activation, which can lead to the development of ground-glass opacities. A study done by [21] in Spain revealed that ground-glass is a common pathologic diagnostic in both UIP and non-UIP, however it usually occurs in fibrotic regions in UIP.

Consolidation was found to be more common in CTD-ILD patients (78.6%) compared to IPF patients (11.8%). Consolidation is often seen in acute lung injury and infection, which are more common in CTD-ILD in IPF. Our findings are consistent with a study done by [22] in India in which revealed that consolidation was 20% in CTD-ILD while 0% in IPF.

Honeycomb lung was found to be more prevalent in IPF patients (35.3%) compared to CTD-ILD patients (7.1%). Honeycomb lung is a hallmark feature of IPF, and its presence on imaging is often used to aid in diagnosis. This finding suggests that honeycomb lung may be a useful distinguishing feature between IPF and CTD-ILD. Our findings are consistent with a study done by [23] in US which revealed that honeycomb was present in 240 (48.8%) patients with IPF and in 111 (22.6%) patients with connective tissue disease–

associated.

Lymphadenopathy was found to be more common in CTD-ILD patients (50%) compared to IPF patients (2.9%). Lymphadenopathy can be seen in a variety of connective tissue diseases, which are more commonly associated with CTD-ILD than IPF [24], [25].

Ground-glass opacities were found to have a relatively high sensitivity of 64.3% in differentiating between IPF and CTD-ILD. This suggests that ground-glass opacities are more commonly observed in patients with CTD-ILD than in patients with IPF. In contrast, lymphadenopathy had a very high specificity of 97.1%, indicating that this feature is more commonly absent in IPF patients. This suggests that the absence of lymphadenopathy on imaging may help distinguish IPF from CTD-ILD. However, it is important to note that lymphadenopathy is not a common finding in CTD-ILD, and its presence may suggest an alternative diagnosis such as lymphoma or sarcoidosis. Our findings are consistent with a study done by [26] in India.

5. Conclusion

The majority of patients diagnosed with UIP had IPF, which is a disease that primarily affects older adults. Smoking was found to be a significant risk factor for UIP, with patients with IPF having smoked more than patients with CTD-ILD. Rheumatoid arthritis was found to be the most common type of CTD-ILD, followed by systemic sclerosis and Sjogren's syndrome. The differences in lung involvement patterns and radiological findings between IPF and CTD-ILD may have implications for diagnosis and treatment strategies. Ground-glass opacities were more common in CTD-ILD patients, while consolidation was more common in CTD-ILD than in IPF.

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