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Significance of Using the Interstitial Lung Disease Reporting and Data System (ILD-RADS) in Diagnosis of ILDs

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ABSTRACT

Background: A standardized template for reporting interstitial lung diseases (ILDs) at high-resolution computed tomography (HRCT) called the Interstitial Lung Disease Imaging Reporting and Data System (ILD-RADS) was recently introduced.

Objective: The aim of the current work was to assess the significance of using the ILD-RADS in the diagnosis as well as categorization of ILDs at HRCT.

Patients and methods: This retrospective cross-sectional study comprised 42 ILDs patients. All patients underwent multi-detector HRCT scans, which were reviewed and categorized according to the ILD-RADS by an experienced radiologist. The final diagnoses of ILDs were determined by multidisciplinary diagnosis with transbronchial lung biopsy (n=4) or without lung biopsy (n=38).

Results: The study included 18 males and 24 females, (with median age 57 years, and interquartile range=52-64 years). Based on the final diagnoses, cases were classified into two groups: cases with idiopathic pulmonary fibrosis (IPF) (n=8) and with non-IPF ILDs (n=38). The most commonly found HRCT pulmonary finding in all patients was pulmonary reticulations (n=42, 100%). The presence of honeycombing was significantly different between patients with IPF and those without IPF. (*P=0.02*). The detected extra-pulmonary findings did not differ significantly between IPF and non-IPF patients. 87.5% of IPF patients were assigned ILD-RADS-1 versus 23.5% of non-IPF patients (*P=0.0008*). 47.1% of the non-IPF patients were assigned ILD-RADS-4 versus none of the IPF patients (*P=0.014*).

Conclusion: It could be concluded that using the ILD-RADS can help differentiate between IPF and non-IPF ILDs at HRCT.

Keywords: Interstitial Lung Disease Reporting and Data System (ILD-RADS); Idiopathic pulmonary fibrosis; High-Resolution Computed Tomography.

INTRODUCTION

Interstitial lung diseases (ILDs) include more than two hundred lung diseases characterized by inflammation of the lung interstitium that eventually results in pulmonary fibrosis, reduced pulmonary capacity, pulmonary failure, and death [(1–2)]. Among these conditions, idiopathic pulmonary fibrosis (IPF) is an irreversible, and progressively fatal ILD of unknown etiology that usually affects old male patients (>65 years) [(3–4)].

Management and prognosis of IPF vary from other ILDs, thus, accurate diagnosis is essential. Diagnosis of ILDs is challenging and requires careful assessment of medical history, serological tests, imaging, and pathological results [(5–7)]. High-resolution computed tomography (HRCT) of the chest has a leading role in the diagnosis of ILDs [(8)].

Four HRCT patterns are identified in ILDs: typical UIP, probable UIP, indeterminate for UIP, and incompatible with UIP [(2)]. In the proper clinical context, various ILDs show characteristic HRCT patterns that suggest specific diagnoses (e.g., hypersensitivity pneumonitis, sarcoidosis) [(8)].

To standardize HRCT reporting of ILDs, the Interstitial Lung Disease Imaging Reporting and Data System (ILD-RADS) was introduced. The ILD-RADS presents a reporting template and four categories based on well-established previously described HRCT findings [(9)].

This study was performed to assess the significance of introducing ILD-RADS in the diagnosis and categorization of ILDs at HRCT.

SUBJECTS AND METHODS

This single-institutional retrospective cross-sectional study included a total of 42 consecutive ILDs patients who underwent chest HRCT, attending at Department of Radio-diagnosis, Faculty of Medicine, Zagazig University. This study was conducted between April 2022 and September 2022.

Inclusion criteria: Patients had (1) chest HRCT of optimal quality and (2) available medical records.

Exclusion criteria: Nine patients were excluded due to (1) inadequate quality of the CT images (n=3); (2) unavailable medical records (n=6).

Demographic data (age, sex), detailed medical history including, smoking history, history of occupational or environmental exposures, history of autoimmune diseases, history of medications, and histopathological data of patients were retrieved by reviewing their medical records.

Chest HRCT

All patients underwent non-contrast HRCT scans using a 128-multidetector CT scanner (Philips

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Healthcare Ingenuity). No specific patient preparation was required. All patients were scanned in a supine position and were instructed to remain stable and hold their breath at full inspiration during the scan. Axial images were acquired with coronal and sagittal reformations.

Technical parameters of the employed chest HRCT protocol were as follows: scan range, from the thoracic inlet to the diaphragm; slice thickness, 0.625-1mm; scan time, 0.5-1 second; Kvp,100-120; MAs, 100-200; collimation, 1.5-3 mm; reconstruction algorithm, high spatial frequency algorithm; and window, lung (level, 800 HU and width,1000 HU) and mediastinal (level, 0 HU and width, 250 HU) windows.

HRCT image analysis

HRCT image analysis was performed on the picture and archiving system (PACS) "PaxeraUltima". In each HRCT scan, the pulmonary and extra-pulmonary findings were assessed and recorded by an experienced radiologist (with 13 years of experience in radiology).

The pulmonary findings involved pulmonary volume (normal/hyper-inflated/hypo-inflated), honeycombing, reticulations, GGO, nodules, cysts, traction bronchiectasis, mosaic attenuation, emphysema, as well as consolidations and were classified as present or absent. Their axial (central, peripheral, or diffuse) and zonal (upper, middle, lower, or diffuse) distributions were recorded.

Extrapulmonary findings included enlarged hilar or mediastinal LNs, pleural thickening, pulmonary artery dilatation, pleural effusion, pneumothorax, cardiomegaly, calcification of the trachea and main bronchi, calcified pleural plaques, pericardial effusion, hepatomegaly, gallbladder stones, as well as liver cirrhosis, and splenomegaly, soft tissue and bone findings (e.g., subcutaneous emphysema, or osteolytic or sclerotic bony lesion). Extra-pulmonary findings were classified as either present or absent.

ILD-RADS categorization

Based on the identified HRCT pattern, each HRCT scan was classified according to ILD-RADS categories into ILD-RADS 1 (typical UIP), ILD-RADS 2 (probable UIP), ILD-RADS 3 (indeterminate UIP), and ILD-RADS 4 (non-UIP) **[9].**

Reference standard

The final diagnoses of ILDs were made by multidisciplinary consensus integrating clinical and HRCT findings with the histopathological data of lung biopsy, if available. Based on the final diagnoses of ILDs, the 42 patients were divided into two groups: patients with IPF and patients with non-IPF ILDs.

***Ethical Consideration*:**

This study was ethically approved by Zagazig University's Research Ethics Committee (ZU- IRB #9714). Written informed consent of all the participants was obtained. The study protocol conformed to the Helsinki Declaration, the ethical norm of the World Medical Association for human testing.

Statistical analysis

The "SPSS version 20" was used to evaluate the gathered data. The Shapiro-Wilk test was used to ensure that the data were normally distributed, and then the median and interquartile range (IQR) were used to summarize the quantitative data. The median ages of IPF and non-IPF patients were compared using the Mann-Whitney U test. The pulmonary findings, extrapulmonary findings, and ILD-RADS categories were compared between the study groups using the Chi-square test (X2) or Fischer's exact tests. A P value of less than 0.05 was considered statistically significant.

RESULTS

Study patients' characteristics

42 patients (median age, 57 years; IQR, 52-64 years) were included in the study. 18/42 patients (42.9%) were males, and 24/42 patients (57.1%) were females. The most affected age group was (≥ 50- <60) which included (35.7% of the patients). The most prevalent presenting symptom of the patients was dyspnea, present in 36 (85.7%) patients, followed by cough in 32 (76.2%) patients. Twelve patients (28.6 percent) were found to be smokers, making this the most common risk factor observed. Study patients' characteristics are presented in **Table 1**.

Only four patients underwent transbronchial lung biopsy with a histopathological examination, and the remaining 38 patients were diagnosed by multidisciplinary consensus based on clinical and HRCT data without lung biopsy. The final diagnoses of ILDs are listed in **Table 2**.

The IPF patients' group included 8 (19.1%) patients while the non-IPF patients' group included 34 (80.9%) patients. A non-significant difference was found between IPF and non-IPF patients regarding recorded demographic or clinical data (**Table 1**). The most common diagnosis identified among patients with non-IPF ILDs was post-infection pulmonary fibrosis (n=8, 19.1%), followed by CTD-ILD (n=6, 14.2%) (**Table 2**).

Table (1): Study patients' characteristics.

	Total n=42	IPF patients n=8	Non-IPF patients n=34	*P-value*
Age (years)				0.808
Median (IQR)	57 (52-64)	57 (56-78)	57.5 (49-64)	
Sex				0.653
Male	18 (42.9%)	4 (50%)	14 (41.2%)	
Female	24 (57.1%)	4 (50%)	20 (58.8%)	
Clinical symptoms				0.373
Cough	34 (80.9%)	7 (87.5%)	27 (79.4%)	
Dyspnea	36 (85.7%)	8 (100%)	28 (82.3%)	
Chest pain	2 (4.8%)	-	2 (5.8%)	
Risk factors				0.476
Smoking history	10 (23.8%)	3 (37.5%)	7 (20.5%)	
History of pneumonia	7 (16.7%)	-	7 (20.5%)	
Environmental exposure	4 (9.5%)	-	4 (11.7%)	
Occupational exposure	2 (4.8%)	-	2 (5.8%)	
Exposure to drugs	3 (7.1%)	-	3 (8.8%)	
Exposure to radiation	3 (7.1%)	-	3 (8.8%)	

IPF.Idiopathic pulmonary fibrosis = IQR=interquartile range.

Table (2): Final diagnoses of ILD patients.

Final diagnoses	Patients (n=42)	
	Number	Percentage
Idiopathic pulmonary fibrosis (IPF)	8	19.1%
Non-IPF ILDs	34	80.9%
1-Connective tissue disease (CTD)-ILD	6	14.2%
Rheumatoid arthritis	4	9.5%
Scleroderma	2	4.8%
2-Granulomatous disease	3	7.1%
Sarcoidosis	2	4.7%
Chronic granulomatous disease	1	2.3%
3- Chronic hypersensitivity pneumonitis (CHP)	4	9.5%
4-Occupational	2	4.8%
5-Post-infection pulmonary fibrosis	8	19.1%
Tuberculosis	2	4.8%
COVID-19	4	9.5%
Other	2	4.8%
6-Radiation-induced pulmonary fibrosis	3	7.1%
7-Chemotherapy-induced pulmonary fibrosis	2	4.8%
8-HIV-associated ILD	2	4.8%
9-Smoking related ILD	2	4.8%
10-Intravenous drug abuse-related ILD	1	2.4%
11-Neoplastic: *lymphangitis carcinomatosis*	1	2.4%

ILD=Interstitial lung disease.

Chest HRCT pulmonary and extrapulmonary findings

As presented in **Table 3**, the most commonly found ILDs pulmonary findings were pulmonary reticulations (n=42; 100%) followed by traction bronchiectasis (n=31; 73.8%), minor GGO (n=26; 61.9%), and honeycombing (n=19; 45.2%). On comparing IPF and non-IPF patients regarding the identified pulmonary findings, honeycombing was significantly more prevalent in IPF patients than in non-IPF patients (*P=0.02*). Most of the study patients had bilateral lung involvement (n=39, 92.9%) with diffuse zonal (n=25, 59.5%) and peripheral axial (n=23, 54.8%) distributions of the ILD pulmonary findings, with no significant differences betweenIPF and non-IPF patients (**Table 4**). A low proportion (n=8, 19.1%) of the patients had no extrapulmonary findings on HRCT scans. The most frequent extrapulmonary findings were hilar/mediastinal lymphadenopathy (n=20, 47.6%) followed by pulmonary artery dilatation (n=12, 28.6%). There were no statistically significant differences between IPF and non-IPF patients regarding the HRCT extra-pulmonary findings (**Table 5**).

Table (3): HRCT pulmonary features of ILD patients.

Pulmonary findings	Total (n=42)	IPF patients (n=8)	Non IPF patients (n=34)	P-value
Lung volume				0.51
Normal	32 (76.2%)	7 (87.5)	25 (73.5)	
Hypoinflated	5 (11.9%)	1 (12.5)	4 (11.8)	
Hyperinflated	5 (11.9%)	-	5 (14.7)	
Reticulations				
Present	42 (100%)	8 (100%)	34 (100%)	NA
Absent	-	-	-	
Honeycombing				***0.02***
Present	19 (45.2%)	7 (87.5%)	12 (35.3%)	
Absent	23 (54.8%)	1 (12.5%)	22 (64.7%)	
Traction bronchiectasis				0.06
Present	31 (73.8%)	8 (100%)	23 (67.6%)	
Absent	12 (26.2%)	-	11 (32.4%)	
GGO				
Extensive	2 (4.7)	-	2 (5.9%)	0.48
Minor	26 (61.9)	8 (100)	18 (52.9%)	
Absent	14 (33.3)	-	14 (41.2%)	
Mosaic attenuation				0.65
Present	2 (4.8%)	-	2 (5.9%)	
Absent	40 (95.2%)	8 (100%)	32 (94.1%)	
Consolidation				0.402
Present	12 (28.6%)	1 (12.5%)	11 (32.4%)	
Absent	30 (71.4%)	7 (87.5%)	33 (67.6%)	
Nodules				0.32
Present	8 (19%)	-	8 (23.5%)	
Absent	34 (81)	8 (100%)	26 (76.5%)	
Cysts				0.61
Present	8 (19.1%)	1 (12.5%)	7 (20.6%)	
Absent	34 (80.9%)	7 (87.5%)	27 (79.4%)	
Emphysema				0.78
Present	9 (21.4%)	2 (25%)	7 (20.6%)	
Absent	33 (78.6%)	6 (75%)	27 (79.4%)	

NA= not applicable. IPF.Idiopathic pulmonary fibrosis =

Table (4): Distribution of HRCT pulmonary features in ILD patients.

Distribution	Total (n=42)	IPF patients (n=8)	Non-IPF patients (n=34)	P-value
Laterality				0.48
Unilateral	3 (7.1%)	1 (12.5%)	2 (5.9%)	
Bilateral	39 (92.9%)	7 (87.5%)	32 (94.1%)	
Zonal distribution				
Upper	11(26.2%)	-	11 (32.4%)	0.542
Middle	11(26.2%)	-	11 (32.4%)	
Lower	8 (19%)	1 (12.5%)	7 (20.6%)	
Diffuse	23 (54.8%)	7 (87.5%)	16 (47.1%)	
Axial distribution				
Central	2 (4.7%)	-	2 (5.9%)	0.683
Peripheral	27 (64.3%)	6 (75%)	21 (61.8%)	
Diffuse	13 (31%)	2 (25%)	11 (32.4%)	

IPF.Idiopathic pulmonary fibrosis =

Table (5): HRCT extra-pulmonary findings of ILD patients

Extra-pulmonary findings	Total (n=42)	IPF patients (n=8)	Non-IPF patients (n=34)	P-value
No findings	8 (19.1)	1 (12.5)	7	0.61
Pleura				
Effusion	-	-	-	
Thickening	6 (14.3)	-	6 (17.6)	0.58
Pneumothorax	1 (2.4)	-	1 (2.9)	0.11
Tracheobronchial tree calcifications	4 (4.8)	-	4 (11.8)	0.57
Mediastinal/hilar lymphadenopathy	20 (47.6)	6 (75)	14 (41.2)	0.08
Heart				0.87
Cardiomegaly	6 (14.3)	1 (12.5)	5 (14.7)	
Pulmonary artery dilatation	12 (28.6)	4 (50)	8 (23.5)	0.14
Soft tissue/bone abnormalities				
Bone deposits	1 (2.4)	-	1 (2.9)	0.11
Upper abdomen abnormalities				
Hepatomegaly	6 (14.3%)	0	6 (17.6%)	0.58
Splenomegaly	1 (2.4)	0	1 (2.9%)	0.11
GB stones	1 (2.4)	0	1 (2.9%)	0.11

IPF.Idiopathic pulmonary fibrosis =

ILD-RADS categorization

As shown in **Table 6,** most of the study patients (n=16, 36.1%) were categorized as ILD-RADS-4, followed by ILD-RADS-1 (n=15, 35.7%). The majority of IPF patients (n=7, 87.5%) were categorized as ILD-RADS-1 versus eight (23.5%) non-IPF patients and this difference is highly statistically significant (*P=0.0008*). Most of the non-IPF patients were assigned ILD-RADS-4 (n=16, 47.1%), while no IPF patients were assigned ILD-RADS category 4, and this difference is highly statistically significant (*P=0.014*) (**Figure 1**).
Illustrative cases are presented in **Figures 2** and **3**.

Table (6): ILD-RADS categories of ILD patients.

ILD-RADS categories	Total (n=42)	IPF patients (n=8)	Non-IPF patients (n=34)	P-value
ILD-RADS 1	15 (35.7%)	7 (87.5%)	8 (23.5%)	**0.0008**
ILD-RADS 2	4 (9.5%)	1 (12.5%)	3 (8.8%)	0.75
ILD-RADS 3	7 (16.7%)	0	7 (20.6%)	0.16
ILD-RADS 4	16 (36.1%)	0	16 (47.1%)	**0.014**

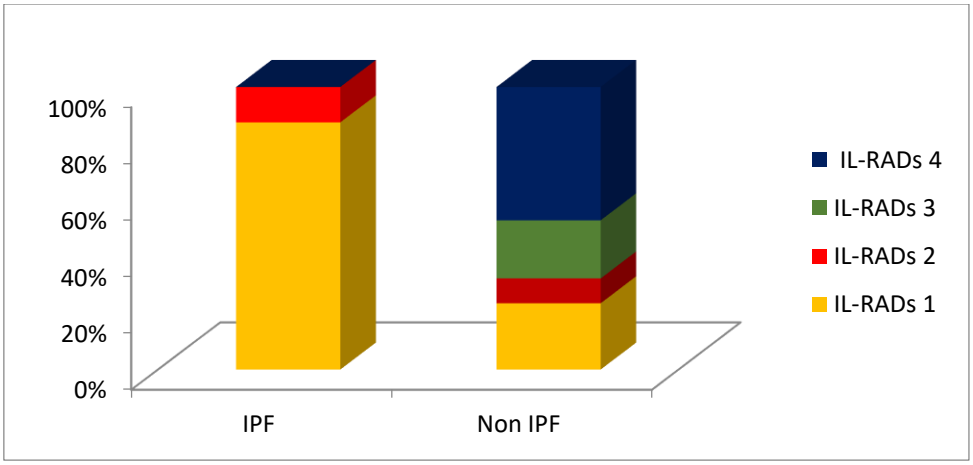
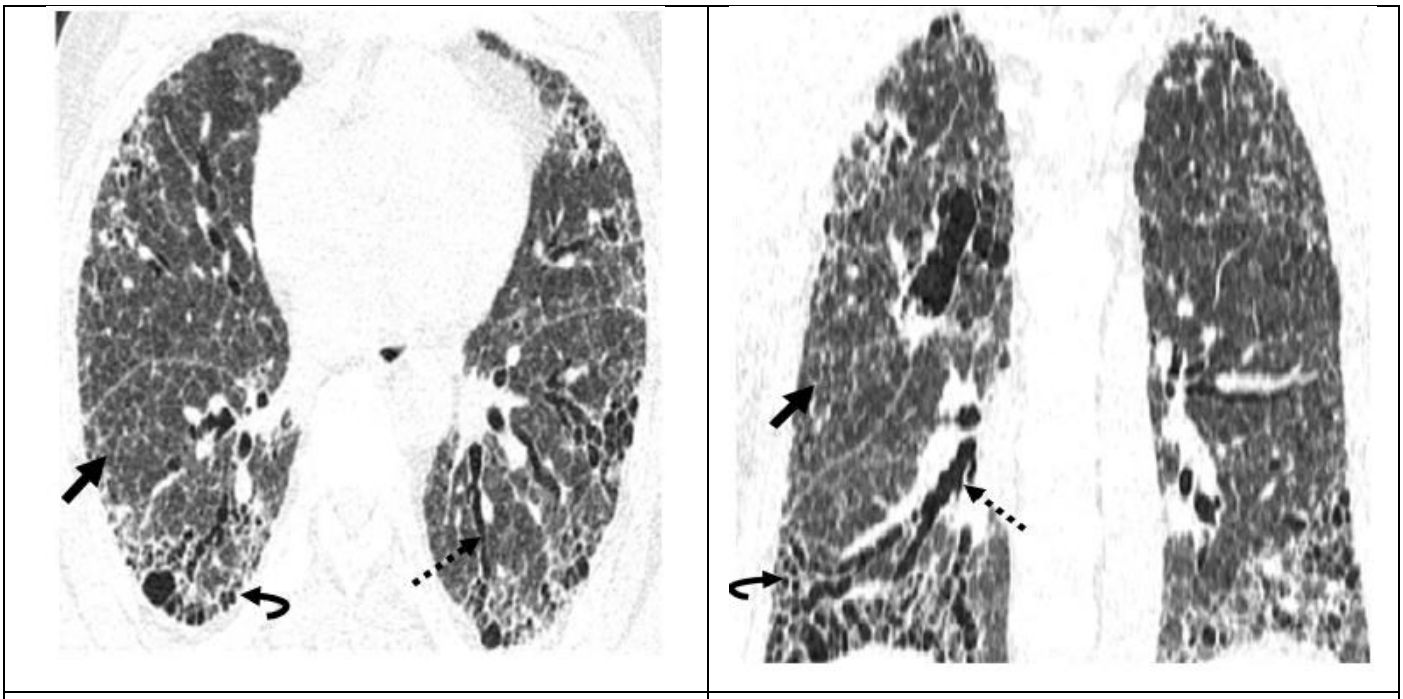
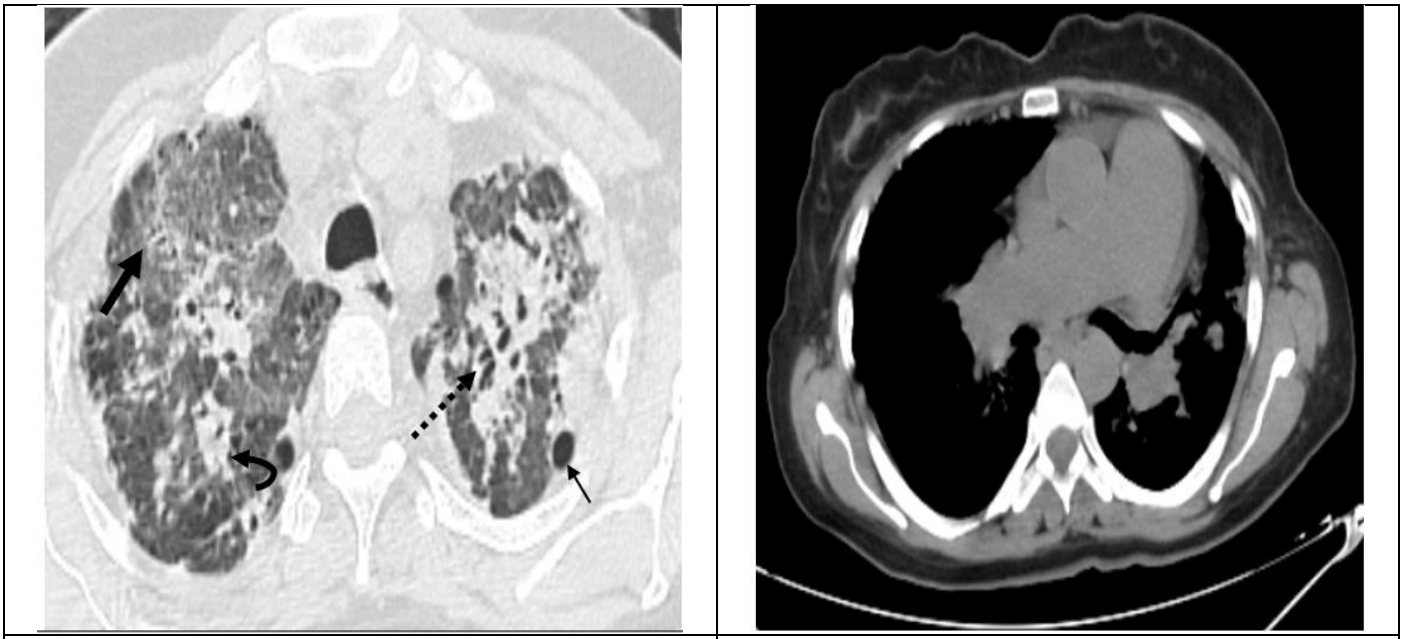


Figure (1): Bar graph of the ILD-RADS categories of the IPF and non-IPF patients.



(A) **(B)**

Figure (2): A 78-year-old male patient, a smoker, presented with gradual onset of progressive dyspnea and cough. **(A)** Axial and **(B)** coronal HRCT images, lung window, showing bilateral and diffuse distributions of pulmonary reticulations (thick arrows), traction bronchiectasis (dashed arrows), and honeycombing (curved arrows), with subpleural and basal predominance. This HRCT pattern is typical for UIP. The patient was categorized as ILD-RADS 1. The final diagnosis of the patient was IPF based on the multidisciplinary diagnosis.



(A) **(B)**

Figure (3): A 47-year-old female patient, non-smoker, diagnosed with rheumatoid arthritis, and presented with gradual onset of progressive dyspnea and cough. **(A)** Axial HRCT image at upper lung zones, lung window**,** showing bilateral and diffuse pulmonary reticulations with minor ground glass opacities (thick arrow), traction bronchiectasis, (dashed arrow), consolidation patches (curved arrow), and emphysematous bullae (thin arrow). The patient was categorized as ILD-RADS 4 (non-UIP). **(B)** Axial CT image, mediastinal window, shows dilated main pulmonary artery. The final diagnosis of the patient was CTD-ILD based on the multidisciplinary diagnosis.

DISCUSSION

Careful interpretation and reporting of the CT pattern, predominant location, extent, and distribution of the ILD features, is crucial to make an accurate diagnosis in ILD patients [10]. Using a standardized chest CT reporting template for ILDs, as recently proposed by **Berkowitz *et al.* [9],** may improve the recognition, description, and reporting of the different CT patterns of ILDs by radiologists and help them make accurate diagnoses.

This study was performed to assess the significance of introducing ILD-RADS in the diagnosis of ILDs at HRCT. The study included 42 patients with a median age of 57 years. The majority of the patients were between the ages ≥50- <60 years. The age distribution of the study patients is in accordance with clinical practice and previous studies of **Almeida *et al.* [11],** whose ILD patients had a mean age of 68 years, **Shih *et al.* [12],** whose study involved ILD patients with a mean age of 60.7, and **Alnaghy *et al.* [13],** whose study included ILD patients with a median age of 53 years.

Most of the study patients (57.1%) were females. This finding is different from studies by **Almeida *et al.* [11], Shih *et al.* [12] and Alnaghy *et al.* [13],** as the majority of ILDs patients were males.

Similar to the data of clinical practice and prior research [13], dyspnea and cough were the commonest presenting symptoms in this study. In the literature, there are various established risk factors for developing ILDs, including demographics, smoking history, occupational and environmental exposures, drugs, and infections [14].

Regarding the risk factors for developing ILDs, smoking was the most frequent risk factor in the current study. However, the frequency of smoking history is less common than that described in the prior studies. **Almeida *et al.* [11],** reported that 29.1% of their study patients had smoking history. While in **Shih *et al.* [12]** study 67% of the patients were smokers. This difference can be attributed to the small sample size and higher prevalence of female patients included in our study.

Regarding the prevalence of ILDs' final diagnoses, only eight patients (19.1%) were diagnosed with IPF, while 34 patients (80.9%) were diagnosed with non-IPF ILDs, with post-infection pulmonary fibrosis (19.1%), followed by CTD-ILD (14.2%) demonstrating the majority of non-IPF patients. This finding differs from the study of **Alnaghy *et al.* [13],** which reported that the majority of their patients (23.8%) had a diagnosis of CTD-ILD, and **Almeida *et al.* [11]** study, which stated that most of their patients (43%) had IPF.

In this study, in all ILD patients, the most prevalent ILDs HRCT pulmonary findings were pulmonary reticulations (100%) followed by traction bronchiectasis (73.8%), minor GGO (61.9%), and honeycombing (45.2%). Honeycombing was significantly more common in patients with IPF compared to those without IPF. This finding is important sincehoneycombing is a characteristic feature of UIP, and IPF is characterized by a typical UIP pattern on a chest HRCT scan [15]. On the contrary, a meta-analysis conducted by **Kim *et al.* [16],** concluded that the presence of honeycombing is not required for the HRCT diagnosis of IPF, since the presence of honeycombing denotes a late stage of IPF.

The majority of the study patients had bilateral lung involvement with diffuse zonal and peripheral axial distributions of the pulmonary features. ,Compared to our results**Alnaghy *et al.* [13],** reported a high prevalence of the diffuse axial and zonal distributions of the pulmonary features among their ILD patients.

Assessment of the extrapulmonary findings at HRCT in ILD patients is mandatory and may change patients' management and determine their prognosis [13]. In the current study, a low percentage (19.1%) of the patients had no extrapulmonary findings on HRCT scans. The most frequent extrapulmonary findings were hilar/mediastinal lymphadenopathy (47.6%) followed by pulmonary artery dilatation (28.6%). This finding is consistent with the published literature, as pulmonary hypertension (presented with dilated main pulmonary artery diameter ≥29 mm at CT) and mediastinal lymphadenopathy are common findings in ILDs patients [17-18].

Regarding the prevalence of ILD-RADS categories among the study patients, most of the study patients (36.1%) were categorized as ILD-RADS-4, followed by ILD-RADS-1 (35.7%). Similarly, **Alnaghy *et al.* [13]** study reported that the majority of the patients were assigned ILD-RADS-4, followed by ILD-RADS-1. Additionally, in this study, the majority of IPF patients (87.5%) were assigned ILD-RADS-1 versus eight (23.5%) non-IPF patients, and this difference was highly statistically significant. Most of the non-IPF patients were assigned ILD-RADS-4 (47.1%), while no IPF patients were assigned ILD-RADS category 4, and this difference was also statistically significant. Based on our findings, using the ILD-RADS can effectively help radiologists to differentiate between IPF and non-IPF ILDs, and make accurate diagnoses in view of the clinical and histopathological data.

The study has several limitations. First, this study included a small number of ILD patients and was performed at a single institution. Therefore, future larger multi-institutional studies are warranted. Second, all HRCT studies were supine and inspiratory, though, expiratory, or prone studies may have improved interpretation of HRCT pulmonary features in certain ILDs (expiratory images help to evaluate small airway disease and air trapping as in CHP, and prone images help to assess early or mild ILD) [19]. An expiratory or prone CT scan was not achieved in this study to minimize radiation dose. Third, in a considerable percentage of the study patients, the diagnoses of ILDs

were based on the multidisciplinary diagnosis in the absence of histopathological data. This can be explained by the fact that many patients either refused or were clinically unfit for lung biopsy. Fourth, we did not assess the intra- and inter-reader variability. Multi-reader studies are needed to assess ILD-RADS reproducibility.

CONCLUSION

It could be concluded that using the ILD-RADS for diagnosis of ILDs at chest HRCT can help differentiate between IPF and non-IPF ILDs. Future larger multi-institutional multi-reader studies are warranted to support its use in clinical practice.

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Competing interests: Nil.

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