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ORIGINAL ARTICLE

Role of High-Resolution Computed Tomography in Differentiating Post-COVID-19 Pulmonary Fibrosis from Fibrosing Interstitial Lung Diseases

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ABSTRACT

Background: It is important to distinguish between various causes of pulmonary fibrosis, including post-COVID-19 pulmonary fibrosis and fibrosing interstitial lung diseases (FILDs), such as idiopathic pulmonary fibrosis (IPF), sarcoidosis, connective tissue diseases as well as fibrotic hypersensitivity pneumonitis. The current study aimed for differentiation between post-COVID-19 pulmonary fibrosis and FILDs using high resolution computed tomography (HRCT).

Methods: We conducted this retrospective study on 36 patients, divided into two groups: group I: 18 patients diagnosed with post-COVID-19 pulmonary fibrosis and group II: 18 patients diagnosed with FILDs. All patients underwent HRCT of the chest. The following HRCT pulmonary features were recorded and compared between the two patients' groups: lung volume, reticulations, subpleural sparing sign, subpleural fibrosis, traction bronchiectasis, honeycombing, GGO, nodules, cysts, consolidation, mosaic attenuation, and emphysema.

Results: Mild fibrosis was more common in post-COVID-19 patients (66.7%) vs. FILDs (11.1%, P=0.002), while severe fibrosis predominated in FILDs (66.7% vs. 5.6%, P<0.001). Subpleural fibrosis was more frequent in FILDs (94.4% vs. 33.3%, P<0.001), whereas subpleural sparing was more common post-COVID-19 (66.7% vs. 5.6%, P<0.001). HRCT showed significant axial and zonal distribution differences (P<0.001), with lower zonal involvement more common post-COVID-19 (50% vs. 11.1%, P=0.03), and diffuse distribution more frequent in FILDs (77.8% vs. 38.9%, P=0.02). Subpleural fibrosis and diffuse axial distribution were independent predictors of post-COVID-19 fibrosis.

Conclusions: HRCT can efficiently differentiate between post-COVID-19 pulmonary fibrosis and FILDs. On HRCT, subpleural fibrosis and diffuse axial distribution of the pulmonary fibrosis can used as independent predictors of post-COVID-19 fibrosis.

Keywords:COVID-19 ;Pulmonary Fibrosis; HRCT ;FILD.

INTRODUCTION

Pulmonary fibrosis is considered a progressive and irreversible condition that requires early detection and accurate diagnosis [1]. With the emergence of COVID-19 pandemic, a large number of surviving patients world-wide are at risk of developing post-COVID-19 complications, Pulmonary fibrosis is likely to be one of the common complications [2,3].

It is important to distinguish between various causes of pulmonary fibrosis, including post-COVID-19 pulmonary fibrosis and other fibrosing interstitial lung diseases (FILDs), such as connective tissue diseases, idiopathic pulmonary fibrosis, sarcoidosis, as well as

fibrotic hypersensitivity pneumonitis [4]. HRCT scans could play a crucial role in evaluating and diagnosing these conditions [5].

The HRCT findings of pulmonary fibrosis involve reticular opacities, traction bronchiectasis, ground-glass opacities (GGO), honeycombing, consolidation, nodules, reticulations, in addition to the interlobular septal thickening [6]. However, the specific distribution and combination of these findings can vary depending on the underlying condition [7].

To ensure accurate diagnosis and appropriate treatment planning, HRCT scans must have adequate technical quality [8]. Additionally, radiologists must have a comprehensive knowledge of characteristic HRCT features and patterns associated with FILDs and post-COVID-19 pulmonary fibrosis [5].

In a recent study, researchers demonstrated that subpleural sparing sign on HRCT can differentiate post-COVID-19 pulmonary fibrosis from non-COVID fibrosing non-specific interstitial pneumonia [9].

Accurate differentiation between post-COVID-19 pulmonary fibrosis and other forms of fibrosing interstitial lung diseases (FILDs), such as idiopathic pulmonary fibrosis (IPF), connective tissue disease-associated ILD (CTD-ILD), and fibrotic hypersensitivity pneumonitis (fHP), is clinically crucial. These conditions differ significantly in their etiology, treatment strategies, and expected progression. For instance, IPF may require antifibrotic therapy such as pirfenidone or nintedanib, while CTD-ILD may respond to immunosuppressive agents. In contrast, post-COVID-19 fibrosis may be managed conservatively or with supportive care, as spontaneous improvement can occur in some patients. Misclassification could lead to inappropriate treatment or delayed intervention, underscoring the need for reliable diagnostic tools such as high-resolution computed tomography (HRCT)[9].

Moreover, the diagnostic significance of specific HRCT signs, such as subpleural sparing or the pattern of zonal involvement, remains underexplored in sufficiently powered cohorts. Thus, there is a critical need for targeted studies that elucidate HRCT-based differentiators and validate their diagnostic accuracy in distinguishing post-COVID-19 pulmonary fibrosis from non-COVID-related FILDs to inform timely and appropriate clinical management. So, the present work aimed for accurate differentiation between post-COVID-19 pulmonary fibrosis and fibrosing ILDs using HRCT.

METHODS

We carried out this single-institutional retrospective study after obtaining approval from Institutional Review Board (IRB#131/27-2-2024). The research was conducted under the World Medical Association's Code of Ethics (Helsinki Declaration) for humans.

The study included 36 patients who were referred from the Chest Department to the Radio-diagnosis Department of our university during the period from March 2024 to September 2024. We included patients who were diagnosed with post-COVID-19 pulmonary fibrosis for at least one year with available HRCT scans and patients diagnosed with FILDs for at least one year with available HRCT scans with no age predilection. Patients with inadequate HRCT images due to motion artifacts were excluded.

We recorded patients' clinical data (e.g., age, smoking status, occupational history, risk factors, comorbidities). All patients had non-contrast enhanced chest HRCT.

Chest HRCT protocol

All patients were examined using a 128-multidetector CT scanner (Philips Healthcare Ingenuity).

Patients were scanned in the supine position during full inspiration with no contrast administration. Thin-section HRCT images (1 mm slice thickness) were acquired using high spatial resolution reconstruction algorithms and reviewed on a dedicated PACS system in both lung and mediastinal windows.

HRCT image analysis

HRCT image analysis was performed on PACS system. In each HRCT scan, Pulmonary and extra-pulmonary findings were evaluated and

documented. Pulmonary features included lung volume (normal, hypo-inflated, or hyper-inflated), reticulations, traction bronchiectasis, honeycombing, GGO, nodules, cysts, consolidation, mosaic attenuation, and emphysema. Each pulmonary finding was recorded as either present or absent, with attention to its axial distribution (central, peripheral, or diffuse) and zonal involvement (upper, middle, or lower zones).

For characterization of the pulmonary fibrosis on HRCT, whether post-COVID-19 or non-COVID related fibrosis, we relied on the zonal and axial distributions of the pulmonary abnormalities, with detection of the predominant fibrotic features (e.g., GGO, reticulations, traction bronchiectasis, or honeycombing), and the presence or absence of subpleural sparing sign.

Extrapulmonary findings included enlarged hilar or mediastinal LNs, pulmonary artery dilatation, cardiomegaly, pericardial effusion, pleural effusion, pleural thickening, calcification of the trachea and main bronchi, hepatomegaly. Extra-pulmonary findings were interpreted as either present or absent.

Reference standard

The final diagnoses of pulmonary fibrosis patients were made by integrating patients' clinical data and HRCT findings. Based on the final diagnoses, the 36 patients were divided into two groups: Group I: patients with post-COVID 19 pulmonary fibrosis (n=18) and Group II: patients with FILDs (n=18).

Statistical analysis

Data was subsequently examined using SPSS version 23.1, the Statistical Package for the Social Sciences. Numbers and percentages were used to represent qualitative data in the analysis, whereas mean ± standard deviation (SD) was used to communicate quantitative data. To compare the two sets of patients, we employed t-tests, Fisher's exact test (f), and the Chi-square test (X^3) for qualitative variables. In order to find factors that can lead to pulmonary fibrosis after COVID-19, logistic regression analysis was used. For statistical significance, a p-value below 0.05 was used.

RESULTS

The study included 36 patients aged between 40 and 62 years, with a mean age of 51.9 ± 6.33 years. Among them, 15 (41.7%) were males and 21 (58.3%) were females. Group I (post-COVID-19 pulmonary fibrosis) included 18 patients (6 males and 12 females; mean age 52.2 ± 6.56 years), and Group II (FILDs) included 18 patients (9 males and 9 females; mean age 51.7 ± 6.27 years) (**Table 1**).

The clinical data of patients with post-COVID-19 pulmonary fibrosis and FILDs are presented in **Table 2**.

Table 3 shows a statistically significant variation between the two groups regarding the HRCT pulmonary findings, as 88.9% of the post-COVID-19 pulmonary fibrosis patients showed a normal lung volume versus 50% of the patients in the FILDs group (P=0.03).

Table 4 shows a statistically significant variation in the axial and zonal distribution of the HRCT pulmonary findings between the studied groups, as most of the patients in the FILD group (83.3%) showed a diffuse axial distribution, while most of the patients in the post-COVID fibrosis group (83.3%) showed a peripheral axial distribution (P<0.001). Also, 50% of the post-COVID-19 pulmonary fibrosis patients showed a lower zonal distribution in comparison to 11.1% of the patients in the FILD group (P=0.03). While 77.8% of the patients in the FILD group showed a diffuse zonal distribution compared to 38.9% of the patients in the post-COVID-19 pulmonary fibrosis group (P=0.02).

Table 5 shows the logistic regression analysis for predicting post-COVID-19 pulmonary fibrosis. Subpleural fibrosis and diffuse axial distribution can be used as independent factors for predicting post-COVID-19 pulmonary fibrosis.

A 48-year-old male patient, non-smoker presented with dyspnea and cough. The final diagnosis of the patient was IPF **(Fig. 1)**

A 49-year-old female patient, non-smoker, presented with a history of COVID-19 infection and complained of cough with dyspnea. The final diagnosis of the patient was post-COVID-19 pulmonary fibrosis **(Fig. 2)**

Table 1: Demographic data among the studied groups

Variables		Total (n=36)	Post-COVID-19 pulmonary fibrosis (n=18)	FILD group (n=18)	P Value
Age (years)	Mean ± SD	51.9 ± 6.33	52.2 ± 6.56	51.7 ± 6.27	0.821
	Range	(40 – 62)	(40 – 62)	(40 – 62)	
Sex (n. %)	Male	15 (41.7%)	6 (33.3%)	9 (50%)	0.312
	Female	21 (58.3%)	12 (66.7%)	9 (50%)	

Table 2: Clinical data among the post-COVID and non-COVID cases of pulmonary fibrosis (ILD group)

Variables (n. %)		Post-COVID-19 pulmonary fibrosis group (n=18)	FILD group (n=18)
Diagnosis	Idiopathic pulmonary fibrosis (IPF)	-	6 (33.3%)
	Post-infectious pulmonary fibrosis	Post-COVID 19 fibrosis 18 (100%)	2 (11.1%)
	CHP	-	5 (27.8%)
	Rheumatoid arthritis associated-ILD	-	1 (5.6%)
	Intravenous drug abuse induced ILD	-	1 (5.6%)
	Systemic lupus associated-ILD	-	1 (5.6%)
	Unclassified ILD	-	1 (5.6%)
	Respiratory bronchiolitis associated -ILD	-	1(5.6%)
Risk factors	None	-	9(50%)
	Pneumonia	18(100%)	2(11.1%)
	Environmental	-	5(27.8%)
	Rheumatoid arthritis	-	1(5.6%)
	Medications	-	1(5.6%)
Smoking status	Non-smoker	17(94.4%)	14(77.8%)

Variables (n. %)		Post-COVID-19 pulmonary fibrosis group (n=18)	FILD group (n=18)
	Ex-smoker	-	1(5.6%)
	Smoker	1(5.6%)	3(16.7%)
Comorbidities	None	9(50%)	10(55.6%)
	Diabetes mellitus	3(16.7%)	-
	Cardiac diseases	3(16.7%)	-
	Hepatic diseases	1(5.6%)	-
	Hypertension	6(33.3%)	4(22.2%)
	Chronic obstructive pulmonary disease (COPD)	-	4(22.2%)
	Bronchial asthma	-	1(5.6%)
*The same patient may have more than one associated comorbidity.			

Table 3: HRCT pulmonary findings among the studied groups

Pulmonary findings (n. %)		**Total (n=36)**	**Post-COVID (n=18)**	**ILD group (n=18)**	**P Value**
Lung volume	Normal	25 (69.4%)	16 (88.9%)	9 (50%)	0.032
	Hypo-inflated	1 (2.8%)	0 (0%)	1 (5.6%)	1.002
	Hyperinflated	10 (27.8%)	2 (11.1%)	8 (44.4%)	0.062
Reticulations	Absent	2 (5.6%)	2 (11.1%)	0 (0%)	0.492
	Present	34 (94.4%)	16 (88.9%)	18 (100%)	
Lung involvement by fibrosis	Mild (<25%)	14 (38.9%)	12 (66.7%)	2 (11.1%)	0.0022
	Moderate (26%- 50%)	9 (25%)	5 (27.8%)	4 (22.2%)	0.711
	Severe (>50%)	13 (36.1%)	1 (5.6%)	12 (66.7%)	<0.0012
Subpleural fibrosis	Absent	13 (36.1%)	12 (66.7%)	1 (5.6%)	<0.0011
	Present	23 (63.9%)	6 (33.3%)	17 (94.4%)	
Subpleural sparing sign	Absent	23 (63.9%)	6 (33.3%)	17 (94.4%)	<0.0012
	Present	13 (36.1%)	12 (66.7%)	1 (5.6%)	
Nodules	Absent	29 (80.6%)	18 (100%)	11 (61.1%)	0.0082
	Present	7 (19.4%)	0 (0%)	7 (38.9%)	

Pulmonary findings (n. %)		Total (n=36)	Post-COVID (n=18)	ILD group (n=18)	P Value
GGO	Absent	3 (8.3%)	2 (11.1%)	1 (5.6%)	1.002
	Minor	18 (50%)	12 (66.7%)	6 (33.3%)	0.051
	Extreme	15 (41.7%)	4 (22.2%)	11 (61.1%)	0.021
Crazy paving	Absent	22 (61.1%)	15 (83.3%)	7 (38.9%)	0.022
	Present	14 (38.9%)	3 (16.7%)	11 (61.1%)	
Consolidations	Absent	21 (58.3%)	15 (83.3%)	6 (33.3%)	0.0062
	Present	15 (41.7%)	3 (16.7%)	12 (66.7%)	
Mosaic attenuation	Absent	15 (41.7%)	10 (55.6%)	5 (27.8%)	0.091
	Present	21 (58.3%)	8 (44.4%)	13 (72.2%)	
Traction bronchiectasis	Absent	17 (47.2%)	15 (83.3%)	2 (11.1%)	<0.0012
	Present	19 (52.8%)	3 (16.7%)	16 (88.9%)	
Honeycombing	Absent	21 (58.3%)	13 (72.2%)	8 (44.4%)	0.091
	Present	15 (41.7%)	5 (27.8%)	10 (55.6%)	
Pulmonary cysts	Absent	25 (69.4%)	18 (100%)	7 (38.9%)	<0.0012
	Present	11 (30.6%)	0 (0%)	11 (61.1%)	
Emphysema	Absent	29 (82.9%)	15 (88.2%)	14 (77.8%)	0.662
	Present	6 (17.1%)	2 (11.8%)	4 (22.2%)	

Table 4: Distribution of HRCT pulmonary and extrapulmonary features among the studied groups

		Total (n=36)	Post-COVID (n=18)	ILD group (n=18)	P Value
Distribution (n. %)					
Axial distribution	Central	0 (0%)	0 (0%)	0 (0%)	<0.0012
	Peripheral	18 (50%)	15 (83.3%)	3 (16.7%)	
	Diffuse	18 (50%)	3 (16.7%)	15 (83.3%)	
Zonal distribution	Upper	2 (5.6%)	1 (5.6%)	1 (5.6%)	1.002
	Mid	2 (5.6%)	1 (5.6%)	1 (5.6%)	1.002
	Lower	11 (30.6%)	9 (50%)	2 (11.1%)	0.032
	Diffuse	21 (58.3%)	7 (38.9%)	14 (77.8%)	0.021
Laterality	Unilateral	0 (0%)	0 (0%)	0 (0%)	

	Bilateral	36 (100%)	18 (100%)	18 (100%)	1.002
Extrapulmonary findings (n. %)					
Extrapulmonary findings	None	13 (36.1%)	6 (33.3%)	7 (38.9%)	0.731
	Pleural effusion	10 (27.8%)	4 (22.2%)	6 (33.3%)	0.461
	Pleural thickening	1 (2.8%)	0 (0%)	1 (5.6%)	1.002
	Cardiomegaly	19 (52.8%)	10 (55.6%)	9 (50%)	0.741
	Mediastinal lymph nodes	1 (2.8%)	0 (0%)	1 (5.6%)	1.002

Table 5: Logistic regression analysis for predictors of post-COVID fibrosis among studied patients

Variables	**Univariate analysis**		**Multivariate analysis**	
	P value	**Odds (CI 95%)**	**P value**	**Odds (CI 95%)**
Hyperinflated lung volume	0.03	0..14 (0.02 – 0.81)	0.09	0.76 (0.55 – 1.04)
Reticulations	0.34	1.67 (0.59 – 4.74)	-	-
Severe lung involvement by fibrosis	<0.001	0.01 (0.001 – 0.17)	0.08	0.06 (0.002 – 1.45)
Subpleural fibrosis	0.002	0.29 (0.003 – 0.28)	0.01	0.03 (0.002 – 0.43)
Subpleural sparing sign	0.002	3.44(3.61-32.1)	0.59	1.91(0.89-15.28)
Nodules	0.09	0.76 (0.55 – 1.04)	-	-
Extreme GGO	0.03	0.18 (0.04 – 0.82)	0.87	1.52 (0.01 – 2.44)
Crazy paving	0.01	0.13 (0.03 – 0.61)	0.08	0.18 (0.02 – 1.23)
Consolidations	0.004	0.1 (0.02 – 0.49)	0.09	0.17 (0.02 – 1.37)
Mosaic attenuation	0.09	0.31 (0.08 – 1.23)	-	-
Traction bronchiectasis	<0.001	0.03 (0.004 – 0.17)	0.14	0.11 (0.01 – 2.12)
Honeycombing	0.09	0.31 (0.08 – 1.23)	-	-
Cysts	0.19	0.33 (0.07 – 1.71)	-	-
Emphysema	0.42	0.47 (0.07 – 2.96)	-	-
Diffuse axial distribution	<0.001	0.04 (0.01 – 0.23)	0.01	0.85 (0.17 – 0.83)
Diffuse zonal distribution	0.02	0.11 (0.02 – 0.66)	0.89	1.03 (0.69 – 1.51)

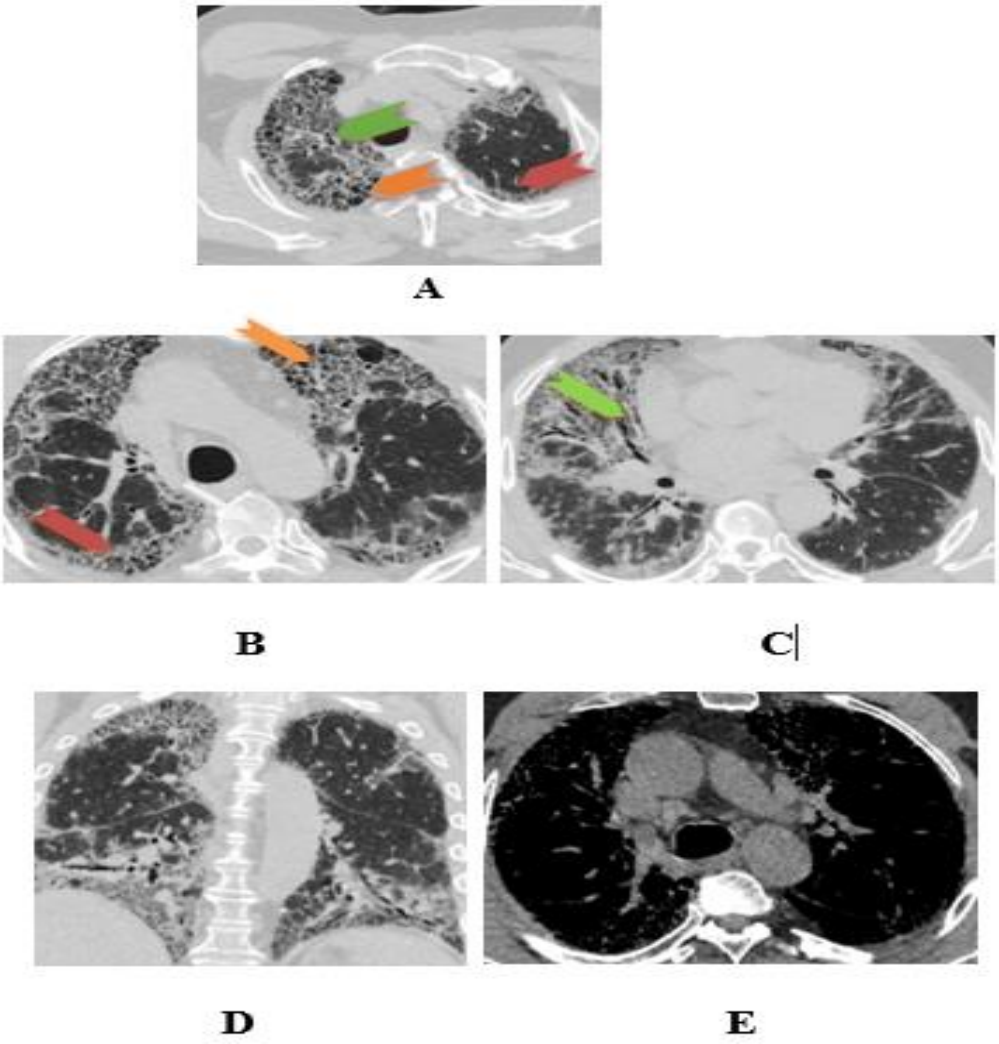

Fig. 1. (A, B, &C) Axial HRCT images (lung window) at level of the upper, middle and lower lung zones showing bilateral diffuse cenrtilobular and subpleural pulmonary reticulations (red arrows), traction bronchiectasis (green arrow), and honeycombing (orange arrow). (D) Coronal reformatted HRCT image at lung window showing the extent and diffuse distribution of the pulmonary findings. (E) Axial CT image (mediastinal window) showing enlarged mediastinal lymph nodes (white arrow).

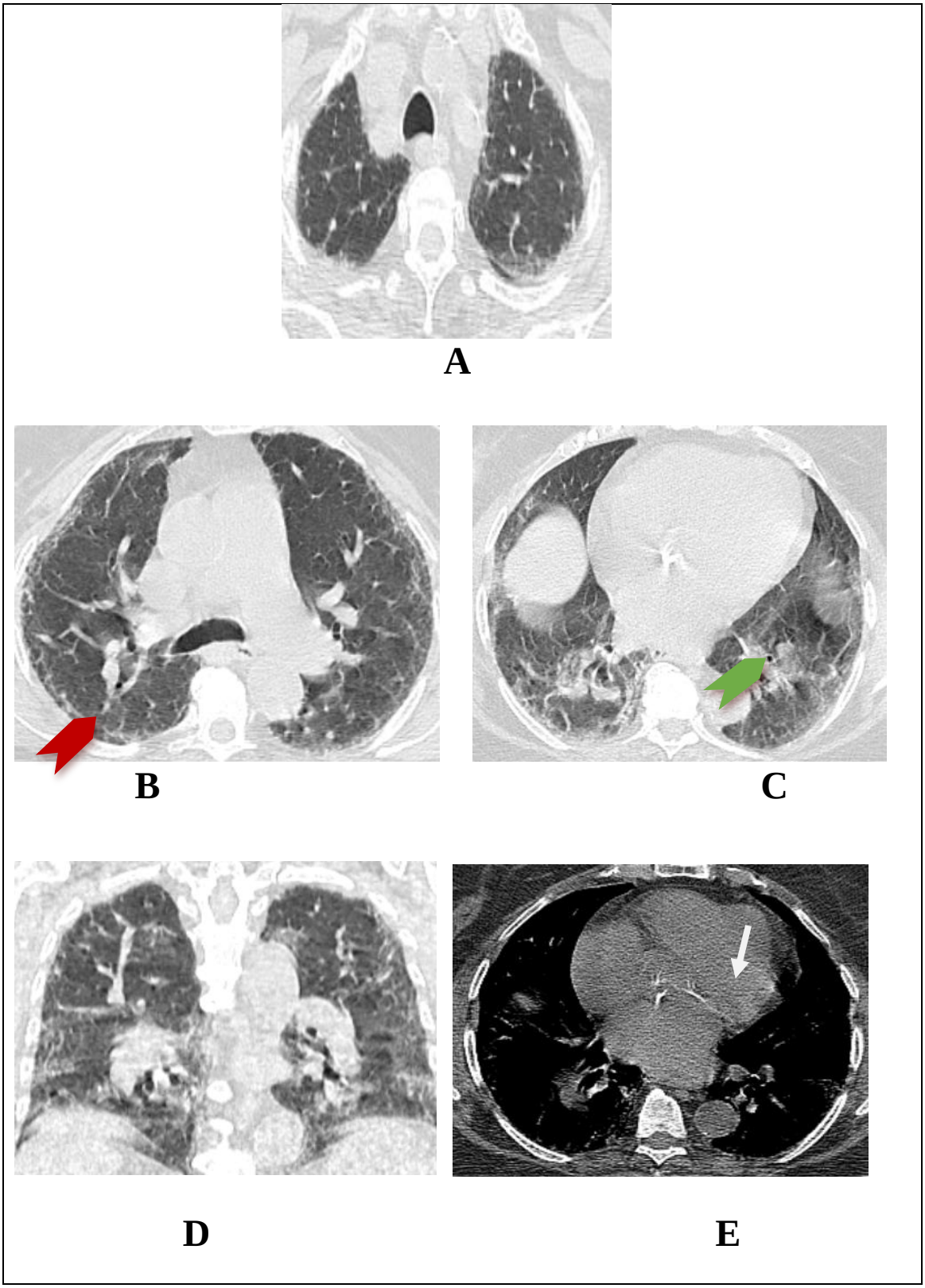

Figure 2: (A, B, &C) Axial HRCT images (lung window) at the level of upper, middle and lower lung zones showing bilateral predominantly basal peripherally located fine reticulations with subpleural space spared at some distance (red arrow) with GGO (green arrow). (D) Coronal reformatted HRCT image (lung window) showing the peripheral and predominantly basal distribution of the pulmonary findings. (E) Axial CT image (mediastinal window) showing cardiomegaly (white arrow).

DISCUSSION

Pulmonary fibrosis is considered a progressive and irreversible condition that requires early detection and accurate diagnosis [1]. It is important to distinguish between various causes of pulmonary fibrosis, including post-COVID-19 pulmonary fibrosis and other FILDs, such as IPF, sarcoidosis, connective tissue diseases, as well as fibrotic hypersensitivity pneumonitis [4]. HRCT scans play a crucial role in evaluating and diagnosing these conditions [5].

The current study was performed to assess the significance of HRCT in differentiating post-COVID-19 and non-COVID cases of pulmonary fibrosis. The study included 36 patients, divided into two groups: post-COVID-19 fibrosis group and FILDs group (n=18 for each group). The patients ages ranged from 40 to 62 years in both studied groups. The majority of the patients were between the ages ≥40-<60 years in the post-COVID-19 pulmonary fibrosis group and between the ages ≥45-<60 years in the FILDs group.

The age distribution of our study patients is in accordance with the previous study of Geringer et al., [9] study, whose post-COVID 19 pulmonary fibrosis patients had a mean age of 53 years and non-COVID patients of pulmonary fibrosis had a mean age of 52 years. Also, our findings align with Alnaghy et al. [10] study findings, since their ILD patients had a median age of 53 years. Most of our study patients in the post-COVID-19 fibrosis group (66.7%) were females while in the FILDs group, females and males had equal percentages. This finding is different from Geringer et al., [9] study, since in this study the majority of post-COVID-19 pulmonary fibrosis patients were males.

Similar to the data of clinical practice and prior research [11–14], dyspnea and cough were the commonest presenting symptoms in this study. In the literature, there are various established risk factors for developing post-COVID-19 pulmonary fibrosis, which are advanced age, male gender, and comorbidities such as diabetes and hypertension [14]. Similarly, developing non-COVID fibrosis can be due to host susceptibility, genetic factors, multi-factorial environmental factors, demographics, smoking history, occupational exposures, drugs, and infections [11].

Regarding the risk factors for developing post-COVID-19 pulmonary fibrosis, history of COVID-19 pneumonia was the risk factor in the current study in 100% of post-COVID-19 fibrosis patients. On the other hand, most patients in the FILDs group had no reported risk factors. Compared to Geringer et al. [9] study, most of the patients that developed post-COVID-19 pulmonary fibrosis had severe pneumonia as the most frequent risk factor and in non-COVID fibrosis cases, smoking (50%) was the most frequent risk factor.

All patients (100%) in the post-COVID-19 pulmonary fibrosis group had a history of COVID-19 infection. Regarding the prevalence of the final diagnoses in the FILD group, 6 patients (33.6%) were diagnosed with IPF, 12 patients (66.4%) were diagnosed with non-IPF ILDs. This finding matches the study of Geringer et al., [9], which reported that 100% of post-COVID-19 pulmonary fibrosis patients were diagnosed with post-infection pulmonary fibrosis and 40% of non-COVID cases of fibrosis were diagnosed with IPF.

In the current study, in the post-COVID-19 pulmonary fibrosis patients, the most prevalent HRCT pulmonary fibrosing features were pulmonary reticulations (88.9%), followed by subpleural sparing sign (66.7%), minor GGO (66.7%), mosaic attenuation (44.4%), honeycombing (27.8%), traction bronchiectasis, consolidation, crazy paving (16.7%) and severe lung involvement by fibrosis (5.6%).

While in the FILDs group, the most prevalent HRCT pulmonary fibrosing features were pulmonary reticulations (100%), subpleural fibrosis (94.4%), traction bronchiectasis (88.9%), mosaic attenuation (72.2%), consolidation (66.7%), severe lung involvement by fibrosis (66.7%), extreme GGO (61.1%), crazy paving (61.1%), cysts (61.1%), honeycombing (55.6%) and nodules (38.9%).

The results revealed significant differences between the studied groups as regards HRCT pulmonary findings, as 88.9% of the cases in the post-COVID-19 pulmonary fibrosis group showed a normal lung volume compared to 50% of the patients in the FILDs group (P=0.03).

Also, 66.7% of the patients in the post-COVID-19 pulmonary fibrosis group showed mild lung involvement by fibrosis compared to 11.1% of the patients in the FILDs group (P=0.002). Whereas, 66.7% of the patients in the FILDs group showed severe lung involvement by fibrosis in comparison to 5.6% of the patients in the post-COVID-19 pulmonary fibrosis group (P<0.001).

Furthermore, 94.4% of the patients in the FILDs group showed subpleural fibrosis versus 33.3% in the post-COVID-19 pulmonary fibrosis group (P<0.001). While 66.7% of patients in the post-COVID-19 pulmonary fibrosis group showed subpleural sparing sign in comparison to 5.6% of the patients in the FILD group (P<0.001). Also, 38.9% of the patients in the FILD group had nodules, while none of the patients in the post-COVID-19 pulmonary fibrosis group had nodules (P=0.008).

The post-COVID-19 pulmonary fibrosis and FILDs groups differed significantly as regards the prevalence of subpleural sparing sign and severity of lung involvement by fibrosis. This finding agrees with Geringer et al. [9] study, which showed a significant difference between the post-COVID-19 pulmonary fibrosis and FILDs groups regarding the prevalence of subpleural sparing sign.

Also, our study revealed a significant difference between the post-COVID-19 pulmonary fibrosis and FILDs groups regarding the prevalence of subpleural fibrosis. This finding is different from Geringer et al. [9] study in which there was no difference regarding subpleural fibrosis between both groups.

Regarding the prevalence of GGO, 66.7% of cases in the post-COVID-19 pulmonary fibrosis group showed minor GGO compared to 33.3% of the patients in the FILDs group (P=0.05). While 61.1% of patients in the FILDs group showed extreme GGO versus 22.2% of cases in the post-COVID-19 pulmonary fibrosis group (P=0.02).

As regards the prevalence of crazy paving, 61.1% of the patients in the FILDs group showed crazy paving in comparison to 16.7% of cases in the post-COVID-19 pulmonary fibrosis group (P=0.02). Also, 66.7% of the patients in the FILDs group showed consolidations in comparison to 16.7% of cases in the post-COVID-19 pulmonary fibrosis group (P=0.006).

In addition, 88.9% of the patients in the FILDs group showed traction bronchiectasis versus 16.7% of cases in the post-COVID-19 pulmonary fibrosis group (P<0.001). Also, 61.1% of the patients in the FILDs group had cysts, while none of cases in the post-COVID-19 pulmonary fibrosis group had cysts (P<0.001).

The axial and zonal distributions of the HRCT pulmonary features showed statistical significant difference between both groups, as most of the patients in the FILDs group (83.3%) showed a diffuse axial distribution, which matches results in Alnaghy et al. [10] study as they reported a high prevalence of the diffuse axial and zonal distributions of the pulmonary features among the FILDs patients. Whereas we demonstrated that most of the patients in the post-COVID-19 pulmonary fibrosis group (83.3%) showed a peripheral axial distribution (P<0.001). Also, 50% of cases in the post-COVID-19 pulmonary fibrosis group showed a lower zonal distribution in comparison to 11.1% of the patients in the FILD group (P=0.03). While 77.8% of the patients in the FILD group showed a diffuse zonal distribution versus 38.9% of cases in the post-COVID-19 pulmonary fibrosis group (P=0.02).

In the current study, a low percentage (33.3%) of the post-COVID-19 pulmonary fibrosis patients and (38.9%) of the FILDs patients had no extrapulmonary findings on HRCT scans. The most frequent extrapulmonary findings in the post-COVID-19 pulmonary fibrosis group

were cardiomegaly (55.6%) and pleural effusion (22.2%). While in ILDs group 50% of the patients had cardiomegaly, 33.3% had pleural effusion and 5.6% had pleural thickening.

Based on the logistic regression analysis for identifying HRCT features that can be used as predictors of post-COVID-19 pulmonary fibrosis, we found that subpleural fibrosis and diffuse axial distribution of the fibrosis can be considered independent factors for predicting post-COVID-19 fibrosis. This result is different from Geringer et al., [9] results, which suggest that subpleural sparing may distinguish post-COVID pulmonary fibrosis from non-COVID pulmonary fibrosis.

Recent studies have emphasized the utility of standardized reporting systems in the assessment of ILDs. The Interstitial Lung Disease Reporting and Data System (ILD-RADS) has been shown to enhance diagnostic accuracy and interobserver agreement among radiologists. Elshetry et al. [15] demonstrated the clinical utility, reproducibility, and radiologist acceptance of ILD-RADS in evaluating ILDs using HRCT. Similarly, Ebaid et al. [16] analyzed the reproducibility and validity of ILD-RADS, highlighting its effectiveness across varying levels of radiologist experience. Furthermore, Elshetry et al. [17] underscored the significance of employing ILD-RADS in the diagnosis of ILDs, advocating for its integration into routine clinical practice.

This study had few limitations. First, this study included a small number of pulmonary fibrosis patients and was performed at a single institution with short duration. Therefore, future larger and longer duration multi-institutional studies are warranted. Second, all HRCT studies were supine and inspiratory, though, expiratory, or prone studies might 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 fibrosing pulmonary insult). An expiratory or prone CT scan was not achieved in this study to minimize radiation dose. Third, the diagnoses of fibrosing lung disease either post-COVID or non-COVID19 were based on the multidisciplinary diagnosis in the absence of the histopathological data of the study patients. This can be explained by the fact that patients either refused or were clinically unfit for this invasive procedure. Additionally, in clinical practice, the diagnosis of post-COVID pulmonary fibrosis and FILDs does not depend exclusively on histopathology as the reference standard. Instead, multidisciplinary diagnosis integrating clinical, imaging, and pathological data is considered the reference standard in diagnosis.

Conclusions

HRCT can efficiently differentiate between post-COVID-19 pulmonary fibrosis and FILDs. On HRCT, subpleural fibrosis and diffuse axial distribution of the pulmonary fibrosis can used as independent predictors of post-COVID-19 fibrosis.

Conflict of Interest or financial disclosure:

No potential conflict of interest to be reported by the authors.

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