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Impact of antifibrotics on post-COVID-19 lung sequelae

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Abstract

Respiratory problems in acute COVID-19 and post-acute COVID-19 syndrome vary greatly, potentially leading to long-term functional difficulties. Off-label usage of antifibrotics, such as pirfenidone, has emerged as a promising treatment for post-COVID interstitial lung problems. Our study aims to assess clinical and radiological lung abnormalities post-COVID-19 and the effect of antifibrotics on the outcome. A retrospective observational study examined data from 90 COVID-19 patients who completed the follow-up period in the post-COVID clinic at the Chest Department, Kasr El Ainy Hospital, from August 2020 to August 2022. Demographic data, comorbidities, exercise tolerance, and chest computed tomography (CT) results were collected 1 and 6 months after the diagnosis. Initial CT scans (1 month following hospital admission) revealed diffuse ground-glass opacities (87.8%) and reticulations (43.3%). After 6 months, 33.3% were back to normal, 41% had persistent reticulations, 22.2% had ground glass opacities, and 3.3% had bronchiectasis. CT scores improved dramatically after 6 months. No significant link was detected between CT score change and off-label use of pirfenidone. Antifibrotic therapy has a modest effect on post-COVID lung problems. One-third of patients showed reticulations as persistent radiological abnormalities, which could guide future treatment choices.

Key words: post-COVID-19 lung abnormalities, antifibrotics, post-acute COVID-19 syndrome, interstitial abnormalities.

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Introduction

COVID-19, caused by a new virus (SARS-CoV-2), began in China in late 2019 and spread throughout the world before being declared a pandemic by World Health Organization in March 2020 [1]. Acute COVID-19 is characterized by respiratory symptoms, fever, and gastrointestinal difficulties [2]. Acute COVID-19 patients vary in the length and severity of the disease. Many individuals are asymptomatic, but others require hospitalization and ventilation [3]. However, worldwide, a percentage of patients with acute SARS-CoV-2 infection develop various persistent symptoms that do not resolve over several months [2]. These patients are diagnosed with "long COVID" or "post-acute sequelae of COVID-19" (PASC) [4]. Patients with a PASC diagnosis are likely to have diverse underlying biological mechanisms driving their symptoms due to SARS-CoV-2-induced organ or tissue harm, as well as related clotting or inflammatory processes during acute COVID-19 [3]. SARS-CoV-2's ability to infect a wide spectrum of human cell types may explain the diverse COVID-19 symptoms [5].

The spike subunit of SARS-CoV-2 interacts with the human angiotensin-converting enzyme 2 (ACE2) receptor to infect and enter host cells [5]. PASC symptoms include fatigue, muscle weakness, sleeplessness, palpitations, persistent rhinitis, dysgeusia, chills, a sore throat, and a headache [4]. Because PASC symptoms are so unique, several therapy techniques may be necessary to manage this complex disorder [6] effectively. Another early study of COVID-19 patients after hospital discharge discovered that more than a third develop lung fibrotic abnormalities, resulting in scarring of the lungs, which may impair gas exchange and exacerbate symptoms of fatigue, dyspnea, and exercise intolerance [7]. Fibrosis is not a typical complication of other viral pneumonia; nevertheless, it has been documented in around 8% of SARS patients and 20% of H7N9 influenza patients [8,9]. Fear of long-term consequences has led to the off-label use of antifibrotics in the hope of alleviating and eliminating post-covid interstitial lung problems. Multiple case series have shown that anti-fibrotic medications can improve post-covid lung sequelae [10]. This study aims to assess clinical and radiological lung abnormalities post-COVID-19 and the effect of anti-fibrotics on the outcome.

Materials and Methods

A retrospective observational study that examined data of 90 patients completed follow-up in a post-COVID clinic at the Chest Department, Kasr El Ainy Hospital, Cairo University, between August 2020 and August 2022. Ethical committee approval from the Faculty of Medicine, Cairo University, numbered MD-5-2022.

The inclusion criteria were patients aged 18 and older who

confirmed moderate to severe COVID-19 and had a positive reverse transcriptase-polymerase chain reaction nasopharyngeal swab. Patients got standard care therapy according to Egyptian recommendations for managing COVID-19 [11]. All patients were followed up after 6 months of COVID-19 diagnosis. Patients with any interstitial or chronic lung disease, hemodynamic instability, and/or heart failure were excluded. Patients with missing data were also excluded. Data gathered from the included were age, smoking history, comorbidities, oxygen saturation as assessed by pulse oximetry or arterial blood gases, length of hospitalization, and duration of oxygen therapy during active infection, if applicable. Data collected during follow-up included medications received, chest computed tomography (CT) and oxygen saturation. Steroids (prednisolone 20 mg once daily) and anti-fibrotics [pirfenidone 267 mg 3 times a day (TDS)] were used for at least 3 months in the previous 6 months in a group of patients; another group received steroids only.

CT chest, pulse oximetry for resting oxygen saturation, and stair climbing test for exercise desaturation were obtained 1 month after the active disease and 6 months later.

CT chest pattern [diffuse ground glass opacities (GGOs), reticulation, or severe organized pneumonia (OP) pattern] and quantitative assessment of illness severity using a semi-quantitative CT scoring technique were observed and documented.

CT chest score using the semi-quantitative scoring system: each of the five lung lobes was visually graded from 0 to 5, with 0 indicating no engagement, 1 suggesting less than 5% involvement, two indicating 5-25% involvement, 3 indicating 26-49% involvement, 4 indicating 50-75% involvement, and 5 indicating more than 75% involvement. The total CT score was calculated by adding the individual lobar scores and varied from 0 (no involvement) to 25 (highest engagement) [12].

Statistical analysis

Data were analyzed using the Statistical Program for Social Science (SPSS) version 24 (IBM, Armonk, NY, USA). Qualitative data were expressed as frequency and percentage. Quantitative data were expressed as median [interquartile range (IQR)], as the data was not normally distributed (the normality test and Kolmogorov-Smirnov and Shapiro-Wilk test were performed).

The following tests were done: the Mann-Whitney U test (MW) when comparing two groups (for abnormally distributed data), the Kruskal-Wallis test (KW) when comparing more than two groups (for abnormally distributed data), and the chi-square test was used when comparing non-parametric data and probability (p-value): $p<0.05$ was considered significant, $p<0.001$ was considered highly important, and $p>0.05$ was considered insignificant.

Results

The study comprised data of 90 patients with moderate to severe COVID-19 infection who completed 6 months for follow-up; the demographic and basic characteristics of all studied patients are shown in Table 1. Table 2 compares the patients' radiological data and oxygenation status collected after 1 month to data collected after 6 months of active illness.

Off-label use of anti-fibrotic medication was common throughout the post-covid period because of concerns about irreversible lung scarring. In the current study, steroids (prednisolone 20 mg once daily) and anti-fibrotics (pirfenidone 267 mg TDS) were used for at least 3 months in the previous 6 months in a group of patients 51.1% (n=46/90), another group received steroids only. Table 3 shows the correlation between CT score change (Δ CT score), Δ O_2 saturation (SO_2) (%) and pirfenidone. Table 4 shows the relation

Table 1. Demographic and basic characteristics of all studied patients.

		Studied patients (n=90)
Sex	Male	63 (70%)
	Female	27 (30%)
Age (years)	Mean ± standard deviation	57.2±13.07
	Min-Max	21-84
Smoking	No	73 (81.1%)
	Yes	17 (18.9%)
Comorbidities	DM	38 (42.2%)
	HTN	35 (38.9%)
O2 saturation (baseline)	Mean ± standard deviation	86.6±5.6
	Min-Max	65-96
Hospital stay (weeks)	Mean ± standard deviation	2.2±1.6
	Min-Max	1-8
Respiratory support	No	21 (23.3%)
	Yes	69 (76.7%)
Respiratory support measures	NIV	19 (27.5%)
	HNFC	9 (13%)
	O_2 mask	41 (59.4%)
Drugs received for >3 months	Steroids	84 (93.3%)
	Pirfenidone	46 (51.1%)
Severity of COVID	Moderate	49 (54.4%)
	Severe	34 (37.8%)
	Critical	7 (7.8%)

DM, diabetes mellitus; HTN, hypertension; NIV, noninvasive ventilation; HNFC, high flow nasal cannula.

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between smoking and CT score. This table presents various correlations and clinical outcomes. There was no statistically significant correlation between CT score at admission and smoking (p=0.776), as well as between Δ CT score and smoking (p=0.451).

Discussion

This retrospective observational study examined data of 90 patients previously diagnosed with COVID pneumonia who came for follow-up in the COVID clinic at the Chest Department, Kasr El Ainy Hospital, Cairo University, between August 2020 and August 2022. The studied patients included 49 patients (54.4%) with moderate disease, 34 patients (37.8%) with severe diseases, and 7 patients (7.8%) with critical disease.

Regarding demographics, all patients evaluated had a mean age of 57.2±13.07 years, with a 70:30 male-to-female ratio. The male predominance could be attributed to an androgen-driven pathophysiology of SARS-CoV-2, which leads to severe COVID-19 results. Multiple investigations support the hypothesis that estrogen has an immunologic protective effect in females [13]. These findings were comparable to other studies [14,15]. Diabetes was the most common comorbidity in our study. It was present in 42.2% of patients (n=38), with hypertension (HTN) accounting for 38.9% (n=35). It is unclear whether patients with diabetes are particularly vulnerable to COVID-19. However, multiple investigations have found a link between severe COVID-19 infection and diabetes mellitus [16,17]. It was proposed that the ACE2 could explain this connection [18]. Other studies found hypertension to be the most common comorbidity, followed by type II diabetes [14,19,20]. Hypertension is among the most common chronic disorders. It is hypothesized that hypertensive patients have increased ACE2 expression, which, while still controversial, may increase susceptibility and severity of COVID-19 [21]. This postulation explains all the research that identified HTN as the primary comorbidity.

The current study found that all patients had an average oxygen saturation of 86.6±5.6%, with a minimum of 65% and a maximum of 96%. The average hospital stay for all investigated

Table 2. Description of chest computed tomography, medication received and effort assessment in all studied patients.

Studied patients (n=90)				
Chest computed tomography pattern 1 month after active disease		Diffuse GGO patches Reticulations Extensive OP - crazy paving	79 (87.8%) 39 (43.3%) 11 (12.2%)	
Computed tomography score (1 month after active disease)		Mean±SD Min-Max	14.2±6.1 2-25	
Chest computed tomographypattern after 6 months		Reticulations GGOs Bronchiectasis Normal	37 (41.1%) 20 (22.2%) 3 (3.3%) 30 (33.3%)	
Computed tomography score, median (IQR) KW=141.2.		1 month after active disease After 6 months	14 (10-18) 3 (0.75-5)	p<0.001 HS
SO_2 saturation, median (IQR) (n=90)	1 month after active infection After 6 months	90 (89-92) 95 (93-96)	KW=150.7	p<0.001 HS
Stair climbing SO_2, median (IQR)	1 month after active infection After 6 months	88 (85-92.5) 95 (92-96)	KW=75.9	p<0.001 HS

GGO, diffuse ground glass opacities; OP, organized pneumonia; IQR, interquartile range; KW, Kruskal-Willis test; IQR, interquartile range; SO_2, O_2 saturation; HS, p<0.001 is considered highly significant; SD, standard deviation.

Table 3. Correlation between computed tomography (CT) score change (Δ CT score), Δ SO2 (%) and pirfenidone.

	Pirfenidone		Test	p
	Yes (n=46)	No (n=44)		
Δ CT score, median (IQR)	84.1 (74.1-100)	80 (56-93.75)	MW=831	0.191 NS
Δ SO_2 (%), median (IQR)	8 (4.17-10.4)	9.25 (5.3-13.4)	MW=866.5	0.240 NS

CT, computed tomography; SO_2, O_2 saturation; IQR, interquartile range; MW, Mann-Whitney U test; NS, not significant; SD, standard deviation; IQR, interquartile range.

Table 4. Relation between smoking and computed tomography score.

		Smoking		Test	p
		Yes (n=16)	No (n=73)		
CT score (1 month after active infection)	Median IQR	14.5 12.25-18	14 10-18	MW=593	0.776 NS
Δ CT score	Median IQR	84.5 77.1-100	82.3 65.4-94.09	MW=514	0.451 NS

CT, computed tomography; IQR, interquartile range; MW, Mann-Whitney U test; NS, non-significant.

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patients was 2.2±1.6 weeks, ranging from 1 week to 8 weeks. In all, 69 patients (76.7%) required respiratory assistance, with 2 (2.9%) on invasive mechanical ventilation, 19 (27.5%) on noninvasive ventilation, 7 (10.1%) on high-flow nasal cannula, and 41 (59.4%) on O_2 mask.

Núñez-Fernández *et al.* found that the average oxygen saturation at hospital admission was 92% (89-97%). The average length of stay for all analyzed patients was 7 (4-13.2) days; 26 patients (13.4%) required invasive mechanical ventilation [22]. COVID-19 hospital stay length varies based on disease severity, patient age, and comorbidities. While the median length of stay often ranges from 7 to 13 days, studies have documented cases with significantly longer hospitalizations, extending up to or beyond 8 weeks [23].

One of the most common long-term effects of COVID-19 pneumonia is the persistence of respiratory symptoms and/or radiological lung abnormalities [14]. The etiology of pulmonary fibrosis in COVID-19 patients comprises dysregulated immunological systems generating generalized epithelial and endothelial damage and an abnormal repair process that leads to pulmonary fibrosis [24-26].

In the present investigation, the baseline CT abnormalities at the time of active infection were 87.8% (n=79) with diffuse GGO patches, 43.3% (n=39) with reticulations, and 12.2% (n=11) with significant OP-crazy pavement. After 6 months, 30 patients (33.3%) recovered to normal, with reticulations being the most common anomaly in 37 patients (41.1%), followed by GGOs in 20 patients (22.2%), and bronchiectasis in three patients (3.3%). We found a decrease in ground-glass opacity but not in other abnormalities such as reticulations or bronchiectasis. These radiological findings were consistent with other studies [14,22].

Six months after hospital discharge, approximately (22%) of our patients continued to have some areas of ground-glass opacity, either reticular lesions (41%) or bronchiectasis (3%), as described by other studies [27], indicating that the mid-term radiological alterations tend to improve or remain unchanged without signs of progression to fibrosis in most patients. Comparison of CT scores throughout the trial revealed a statistically significant drop in CT scores at 6 months compared to those at 1 month after admission. This data indicates an improvement in the parenchymal affection of the lungs over 6 months after the active infection, as seen by an improvement in the median CT score. As a result, it is unclear whether this improvement is due to a specific treatment regimen.

At 6 months, SO_2 saturation was significantly higher ($p<0.001$) than at admission (median = 88, IQR=85-90). Similarly, Núñez-Fernández *et al.* showed considerable improvement in SO_2 at 3 and 12 months [22]. These could be explained by the improvement in lung CT with time. SO_2 levels were measured 1 and 6 months into the current trial while climbing stairs, with significant improvement observed ($p<0.001$). Early studies examining functional capacity provide information on the propensity to desaturate during field-based exercise testing. Daher *et al*. found that 60 days after discharge, no patients were severely desaturated on a 6-minute walking test [28]. However, 79% could not accomplish their projected walking distance, and 45% were below the lower limit of normal. Similar findings were observed 3 months after discharge; 16% of patients had desaturation, with 22% falling below the lower limit of normal walking distance [29].

The management of COVID-19 pulmonary fibrosis is fraught with ambiguity, mainly owing to the lack of available therapy options [24,25]. Anti-fibrotic drugs such as pirfenidone and nintedanib have a proven role in fibrotic disorders such as idiopathic pulmonary fibrosis (IPF). By analogy, they can treat post-COVID-19 fibrosis [27,30].

Prednisolone was administered to 84 patients (93.3%) and pirfenidone to 46 patients (51.1%) 3 to 6 months after discharge. The link between CT score change (Δ CT score), Δ SO_2 (%) and drug use (pirfenidone) was not statistically significant between both groups.

Several studies have explored the potential role of anti-fibrotic agents, such as nintedanib and pirfenidone, in managing hospitalized individuals with moderate to severe COVID-19 and those with pulmonary fibrosis following COVID-19 infection.

Vikas *et al.* described a case study of four individuals who responded effectively to nintedanib therapy for 1 month [31]. High-resolution CT (HRCT) scans confirmed the presence of lung fibrosis, prompting the start of anti-fibrotic therapy. The degree of pulmonary involvement varied across patients, but all had severe COVID-19 pneumonia and post-COVID pulmonary fibrosis. Jan Michael *et al*. reported a case of pulmonary fibrosis after severe COVID-19 pneumonia that demonstrated improvement in symptoms, pulmonary function, and HRCT after a 6-month course of nintedanib, steroids, and pulmonary rehabilitation [30]. Zhou *et al*. also reported a case report in which post-COVID pulmonary fibrosis symptoms, pulmonary function, and chest CT imaging improved following 2 years of pirfenidone treatment [32]. A Chinese experiment found that 4 weeks of pirfenidone did not significantly reduce lung interstitial lesions in people with severe COVID-19 (according to a CT scan). Pirfenidone therapy did, however, improve anti-inflammatory responses and reduce thrombotic consequences [33]. Ferrara *et al.* determined that pirfenidone may lessen or prevent the immune-inflammatory response that precedes lung fibrosis [34]. Furthermore, the customized timing of pirfenidone administration reflects its success in preventing pulmonary fibrosis; yet, due to its anti-fibrotic qualities, pirfenidone would cure residual pulmonary fibrotic alterations [35]. A retrospective cohort study examining data from multiple healthcare institutions found that COVID-19 patients with acute respiratory failure who received anti-fibrotic treatment had a notably lower 1-year mortality rate than those who did not receive such therapy. This suggests a potential therapeutic benefit, though further validation is needed [36]. Additionally, a review of anti-fibrotic applications in post-COVID-19 pulmonary fibrosis emphasized the need for randomized controlled trials to confirm their effectiveness [37].

In summary, anti-fibrotics's potential therapeutic value in the COVID-19 scenario is questionable for a variety of reasons. First, because there is currently no consensus on therapy selection criteria, the possibility of spontaneous illness resolution over time, reflecting inter-individual heterogeneity, cannot be ruled out. Furthermore, dose regimes and treatment durations have not been consistent throughout the data reported. Furthermore, the daily dose of anti-fibrotic medications may not always meet the required dose for the initial indication (IPF or non-IPF progressive pulmonary fibrosis).

Study limitations

Some limitations must be addressed. First, it was conducted at a single hospital, which, while potentially restricting its external validity, ensures consistency. Specific tests, such as the pulmonary function test, must be performed to produce more reliable results. Finally, the sample size is relatively small.

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Conclusions

This study shows that patients' CT findings, exercise ability, and oxygen saturation improved significantly between 1 and 6 months after COVID-19 pneumonia. Regardless of the anti-fibrotic medication, both CT scores and lung anomalies showed a constant reduction. After 6 months, one-third of the patients returned to normal CT findings, with persistent abnormalities primarily appearing as a reticular pattern. These findings help us understand the post-acute phase of COVID-19 and may guide future treatment options.

References

1. Jasper FW, Shuofeng Y, Kin-Hang K, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. Lancet 2020;395:514-23.
2. Alimohamadi Y, Sepandi M, Taghdir M, Hosamirudsari H. Determine the most common clinical symptoms in COVID-19 patients: a systematic review and meta-analysis. J Prev Med Hyg 2020;61:304-12.
3. Barboza J, Chambergo-Michilot D, Velasquez-Sotomayor M, et al. Assessment and management of asymptomatic COVID-19 infection: a systematic review. Travel Med Infect Dis 2021;41:102058.
4. Huang C, Huang L, Wang Y, et al. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet 2021;397:220-32. Expression of concern: Lancet 2023;401:90. Retracted and republished in: Lancet 2023;401: e21-33.
5. Walls A, Park Y, Tortorici M, et al. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. Cell 2020;181: 281-92.
6. Frontera J, Thorpe L, Simon N, et al. Post-acute sequelae of COVID-19 symptom phenotypes and therapeutic strategies: a prospective, observational study. Plos One 2022;17:e0275274.
7. Mylvaganam R, Bailey J, Sznajder J, Sala M. Recovering from a pandemic: pulmonary fibrosis after SARS-CoV-2 infection. Eur Respir Rev 2021;30:210194.
8. Lechowicz K, Drożdżal S, Machaj F, et al. COVID-19: the potential treatment of pulmonary fibrosis associated with SARS-CoV-2 infection. J Clin Med 2022;9:1917.
9. Zeng Z, Huang X, Lu P, et al. Imaging manifestations and pathological analysis of severe pneumonia caused by human infected avian influenza (H7N9). Radiol Infect Dis2015;1:64-9.
10. Dhooria S, Maturu VN, Talwar D, et al. A multicenter survey study of anti-fibrotic use for symptomatic patients with post-COVID-19 interstitial lung abnormalities. Lung India 2022;39: 254-60.
11. Masoud H, Elassal G, Hassany M, et al. Management protocol for COVID-19 patients version 1.4/30th May 2020. In: Coronavirus Disease 2019 (COVID-19), SARS COV2 Management Guideline. Egypt: Ministry of health and population (MOHP); 2020.
12. Li K, Fang Y, Li W, et al. CT image visual quantitative evaluation and clinical classification of coronavirus disease (COVID-19). Eur Radiol 2022;30:4407-16.
13. Twitchell D, Christensen M, Hackett G, et al. Examining male predominance of severe COVID-19 outcomes: a systematic review. Androg Clin Res Ther 2022;3:41-53.
14. Vijayakumar B, Tonkin J, Devaraj A, et al. CT lung abnormalities after COVID-19 at 3 months and 1 year after hospital discharge. Radiology 2022;30:444-54.
15. Jia F, Wang G, Xu J, et al. Role of tumor necrosis factor-α in the mortality of hospitalized patients with severe and critical COVID-19 pneumonia. Aging 2022;13:23895-912.
16. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet 2022;395:1054-62.
17. Guo W, Li M, Dong Y, et al. Diabetes is a risk factor for the progression and prognosis of COVID-19. Diabetes Metab Res Rev 2022;36:e3319.
18. Ma R, Holt R. COVID-19 and diabetes. Diabetic Med 2020;37: 723-5.
19. Magdy S, Elkorashy R, Elsebaie E, et al. Impact of comorbid pulmonary disease on COVID-19 disease severity and outcome: a retrospective cohort study. Egypt J Bronchol 2023;17:64.
20. Mardani R, Namavar M, Ghorbi E, et al. Association between serum inflammatory parameters and the disease severity in COVID-19 patients. J Clin Lab Anal 2022;36:e24162.
21. Fang L, Karakiulakis G, Roth M. Are patients with hypertension and diabetes mellitus at increased risk for COVID-19 infection? Lancet Respira Med 2020;8:e21.
22. Núñez-Fernández M, Ramos-Hernández C, García-Río F, et al. Evolution and long□term respiratory sequelae after severe COVID-19 pneumonia: nitric oxide diffusion measurement value. Respir Res 2023;24:48.
23. Rees EM, Nightingale ES, Jafari Y, et al. COVID-19 length of hospital stay: a systematic review and data synthesis. BMC Med 2020;18:270.
24. Seifirad S. Pirfenidone: a novel hypothetical treatment for COVID-19. Med Hypotheses 2020;144:110005.
25. Vasarmidi E, Tsitoura E, Spandidos DA, et al. Pulmonary fibrosis in the aftermath of the COVID-19 era (Review). Exp Ther Med 2020;20:2557-60.
26. Wu C, Chen X, Cai Y, et al. Risk factors associated with acute respiratory distress syndrome and death in patients with coronavirus disease 2019 pneumonia in Wuhan, China. JAMA Intern Med 2020;180:934-43.
27. Rivera-Ortega P, Hayton C, Blaikley J, et al. Nintedanib in the management of idiopathic pulmonary fibrosis: clinical trial evidence and real-world experience. Ther Adv Respir Dis 2018; 12:1753466618800618.
28. Daher A, Balfanz P, Cornelissen C, et al. Follow up of patients with severe coronavirus disease 2019 (COVID-19): pulmonary and extrapulmonary disease sequelae. Respir Med 2020;174: 106197.
29. Van den Borst B, Peters J, Brink M, et al. Comprehensive health assessment 3 months after recovery from acute coronavirus disease 2019 (COVID-19). Clin Infect Dis 2021;73:e1089-98.
30. Lomanta JMJ, Quinto ML, Urquiza SC, Santiaguel JM. Pulmonary function and chest computed tomography (CT) scan findings after antifibrotic treatment for COVID-19-related pulmonary fibrosis. Am J Case Rep 2022;23:e934830.
31. Marwah V, Choudhary R, Malik V, et al. Early experience of nintedanib in COVID-19 ARDS-related pulmonary fibrosis: a case series. Adv Respir Med 2021;89:589-96.

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32. Zhou X, Yang D, Kong X, et al. Case report: pirfenidone in the treatment of post-COVID-19 pulmonary fibrosis. Front Med 2022;9:925703.
33. Zhang F, Wei Y, He L, et al. A trial of pirfenidone in hospitalized adult patients with severe coronavirus disease 2019.Chin Med J 2022;135:368-70.
34. Ferrara F, La Porta R, Santilli P, et al. Are multiple sclerosis therapies safe in severe acute respiratory syndrome coronavirus 2 times? Indian J Pharmacol 2020;52:441-2.
35. Kayarat B, Khanna P& Sarkar S. Pulmonary fibrosis in COVID-19 recovered patients: problem and potential management. Indian Journal of Critical Care Medicine: Peer-reviewed, Official Publication of Indian Society of Critical Care Medicine 2021;25:242.
36. Wang HY, Tsai SC, Lin YC, et al. The effect of anti-fibrotic agents on acute respiratory failure in COVID-19 patients: a retrospective cohort study from TriNetX US collaborative networks. BMC Pulm Med 2024;24:160.
37. Lassan S, Tesar T, Tisonova J, Lassanova M. Pharmacological approaches to pulmonary fibrosis following COVID-19. Front Pharmacol 2023;14:1143158.

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