ORIGINAL ARTICLE

Assessment of respiratory function and exercise tolerance at 4–6 months after COVID-19 infection in patients with pneumonia of different severity

Laura Pini [iD],[1,2] Rossano Montori,[2] Jordan Giordani,[2] Michele Guerini,[1,2] Nicla Orzes,[2] Manuela Ciarfaglia,[2] Marianna Arici,[2] Carlo Cappelli,[2,3] Simone Piva,[4,5] Nicola Latronico,[4,5] Maria L. Muiesan[2,6] and Claudio Tantucci[1,2]

[1]Respiratory Medicine Unit, [3]Endocrine-Metabolic Medicine Unit, [4]Department of Anesthesia, Critical Care and Emergency Unit, and [6]Internal Medicine Unit, ASST-Spedali Civili, and Departments of [2]Clinical and Experimental Sciences, and [5]Medical and Surgical Specialties, Radiological Sciences and Public Health, University of Brescia, Brescia, Italy

Abstract

Background: The evaluation of COVID-19 systemic consequences is a wide research field in which respiratory function assessment has a pivotal role. However, the available data in the literature are still sparse and need further strengthening.

Aim: To assess respiratory function 4–6 months after hospital discharge based on lung disease severity in patients who overcome COVID-19 pneumonia.

Methods: Patients hospitalised either in the Internal Medicine Department (IMD) for moderate to severe disease or in the Intensive Care Unit (ICU) for critical disease underwent spirometry with maximal flow-volume curve, lung volumes, lung diffusion capacity (DL_{CO}) and six-minute walking test (6-MWT).

Results: Eighty-eight patients were analysed: 40 from the IMD and 48 from the ICU. In both cohorts, there was a greater prevalence of male patients. In the IMD cohort, 38% of patients showed at least one altered respiratory parameter, while 62% in the ICU cohort did so ($P < 0.05$). Total lung capacity (TLC) and DL_{CO} were the most frequently altered parameters: 15% and 33% from IMD versus 33% and 56% from ICU, respectively ($P < 0.05$). In IMD patients, 5% had only restrictive deficit, 22% had only lung diffusion impairment and 10% had both. In ICU patients, 6% had only restrictive deficit, 29% had only lung diffusion impairment and 27% had both ($P < 0.05$). ICU patients showed a higher frequency of abnormal 6-MWT ($P < 0.05$).

Conclusion: Lung function tests and 6-MWT are highly informative tools for monitoring the negative consequences of COVID-19 pneumonia, which were more frequent and more complex in patients discharged from ICU.

Introduction

Almost 2 years after the first recorded cases, the SARS-COV2 pandemic still represents a major problem for health systems worldwide. Alongside the need to research and adopt increasingly specific and effective preventive strategies and treatments, a new field of research is opening up: the characterisation of the medium- and long-term consequences of COVID-19 infection.[1,2]

Several multicentre and multidisciplinary studies demonstrated that individuals with previous SARS-COV2 infection had highly heterogeneous consequences. In fact, along with their progressive recovery process, patients are forced to live with new pathophysiological conditions, such as increased fatigue even for light effort, breathlessness, neurologic and sleep disorders, loss of control of previous respiratory and cardiovascular conditions and the onset of psychiatric disorders. The clinical relevance and impact in patients' everyday life of these conditions prompted the scientific community to define them as a unique pathological condition named long COVID.[3–10]

In this picture, assessing the medium- and long-term pulmonary consequences of COVID-19 pneumonia represents one of the most relevant research fields. The most frequently adopted patient follow-up strategy is based on clinical evaluation, respiratory function tests and imaging techniques. Although clinical and imaging evaluations provide a basis for a useful assessment of the patient's condition, they cannot offer specific quantitative data on respiratory function recovery. Therefore, to address the increasing need to track patients' respiratory function over time, considerable interest in applying respiratory function tests and assessing gas exchange dynamics is growing.[11–17]

Previous studies on this topic produced very interesting results. However, interpretation was difficult due to the high complexity of the pathophysiological background underlying the COVID-19 lung infection dynamics and the lack of a COVID-dedicated and standardised interpretative approach. Despite these limitations, initial studies documented how the respiratory consequences were associated with several factors, such as the severity of lung infection, hospitalisation time and the need to employ ventilation techniques. Similarly, the recovery time needed for their resolution follows the severity of the primary infection. Moreover, it was observed that in subjects who overcome mild to severe forms of lung infection, there was a tendency for a rapid respiratory function improvement followed by a progressive slower phase, often leading to its normalisation, while in subjects who faced critical forms of lung infection, the recovery process was slowed down and frequently incomplete. In these patients, it has been hypothesised that the massive inflammatory process downstream of the lung infection might lead to a permanent restrictive ventilatory defect caused by either fibrous alveolar consolidation or the deposition of fibrotic matrix on the pulmonary interstitium or both.[18–22]

On this basis, our study aimed to provide further insights on the medium- and long-term respiratory function and exercise tolerance consequences in patients who overcome COVID-19 pneumonia at different levels of severity and to evaluate the role of respiratory function tests as a routine follow-up tool.

Methods

Subjects and measurements

Respiratory function and exercise tolerance in a patient population discharged 4–6 months after hospitalisation have been assessed to observe possible medium- and long-term residual lung damage. According to the severity of COVID-19 infection, patients were recruited from the Internal Medicine Department (IMD) and the Intensive Care Unit (ICU) of the ASST-Spedali Civili di Brescia, Brescia, Italy, and divided into two cohorts. Enrolled patients met the following criteria: age over 18, a laboratory-confirmed SARS-COV2 infection documented through real-time reverse transcription-polymerase chain reaction (RT-PCR) and pulmonary involvement diagnosed with clinical evaluation and chest X-ray or high-resolution computed tomography (HRCT) imaging. Patients with a history of known obstructive, restrictive or mixed ventilatory defects caused by previous respiratory conditions were excluded from the study.

For each patient, physical examination, complete pulmonary function test with maximal flow-volume curve, lung volumes, lung diffusion capacity for carbon monoxide (DL_{CO}) measurements and six-minute walking test (6-MWT) were performed. Lung volumes were measured through the inert gas dilution technique using the helium closed-circuit multi-breath method, while DL_{CO} along with alveolar volume (V_A) and transfer coefficient for CO (K_{CO}) through a single-breath technique (BIO-MEDIN Instruments, Padua, Italy). DL_{CO} and K_{CO} were adjusted for patients' haemoglobin levels. Values of total lung capacity (TLC) < 80% predicted (pred.) and DL_{CO} < 80% pred. were chosen to identify the presence of a restrictive ventilatory defect and lung diffusion capacity reduction respectively.

Data were described according to the pulmonary function and 6-MWT results, and a dedicated database reporting demographic traits, body mass index (BMI) and relative percentages of the predicted respiratory and exercise tolerance values such as TLC, V_A, K_{CO}, DL_{CO}, SaO2 pre and post effort and walked distance was designed.

The study was performed in accordance with the Helsinki declaration and was approved by the University of Brescia's Department of Clinical and Experimental Science (DSCS) Ethics Committee. All participants signed written informed consent upon enrolling.

Statistics

Data were expressed as mean ± standard deviation (SD), and categorical variables were recorded as frequencies and percentages. Differences between grouped data were analysed with the chi-square test for categorical variables, while continuous variables were compared using the Student's *t*-test for paired data, and statistical significance was assessed for *P* values < 0.05. Analyses were performed using GraphPad Prism 6.0 (GraphPad Software, La Jolla, CA).

Results

A total of 88 patients with previous COVID-19 pneumonia were enrolled and divided into two cohorts: 40 patients were discharged from IMD for moderate to severe disease and 48 from ICU for critical disease. All the enrolled patients performed the proposed respiratory function tests. About 29 patients from the IMD and 47 from the ICU performed the 6-MWT.

A greater prevalence of male patients can be observed in both cohorts, with an overwhelming majority from the ICU ($P < 0.05$; $df = 1$; $V = 0.21$). Patients from the ICU cohort had higher mean weight ($P < 0.05$; $df = 86$; $d = 5.55$) but not significantly different BMI. On average, functional residual capacity (FRC), V_A and DL_{CO} (% pred.) came out to be significantly lower in the ICU cohort than in the IMD cohort ($P < 0.05$; $df = 86$; $d = 0.35$–5.84–4.71 respectively) (Table 1).

Most patients discharged from the IMD (62%) had their respiratory function within the normal limits compared to those discharged from the ICU (38%) after 4–6 months ($P < 0.05$; $df = 1$; $V = 0.24$) (Fig. 1). Only three (7%) patients discharged from IMD, and none discharged from ICU had an obstructive ventilatory defect (FEV_1/VC % < LLN). Six (15%) and 16 (33%) patients discharged from IMD and ICU, respectively, had a restrictive ventilatory defect. The percentages (and numbers) of patients with abnormal respiratory function parameters after hospital discharge following COVID-19 pneumonia at 4–6 months were simultaneously displayed for both cohorts in Fig. 2. Comparing the two cohorts, statistically significant differences between frequencies of normal and abnormal values were found for TLC, VA and DL_{CO} (all $P < 0.05$; $df = 1$; $V = 0.21$–0.26–0.23, respectively) (Fig. 2).

For the exercise tolerance assessment, we observed a significantly higher frequency of tests with a 6-min walked distance (% pred.) lower than normal in patients discharged from ICU (49%) compared with IMD patients (24%) ($P < 0.05$; $df = 1$; $V = 0.236$) (Fig. 3), although the average 6-min walked distance (% pred.) between the two cohorts showed no significant differences (Table 2).

Assessment of pattern of residual lung dysfunction between IMD and ICU cohorts

Patients were then divided into three groups for both IMD and ICU cohorts, according to the impairment of TLC and DL_{CO} parameters to detect specific residual lung damage. Patients with only reduction in lung volumes as documented by a TLC value <80% pred. (group A), patients with only interstitial lung damage as documented by a DL_{CO} value <80% pred. (group B) and patients with both TLC and DL_{CO} values <80% pred. (group C). Patients with TLC and DL_{CO} values higher than 80% pred. were considered to recover from any relevant SARS-COV2 pneumonia-related lung function impairment.

In the IMD cohort, nine (22%) patients showed a decreased DL_{CO} alone. Lung volume reduction alone (TLC < 80% pred.) was found only in two (5%) patients, while mixed damage (DL_{CO} and TLC < 80% pred.) was documented in four (10%) patients (Fig. 4).

In the ICU cohort, a decreased DL_{CO} alone was documented in 14 (29%) patients. Lung volume reduction alone (TLC < 80% pred.) was found in only 3 (6%) patients, and a decrease of both TLC and DL_{CO} (<80% pred.) was found in 13 (27%) patients (Fig. 4).

Comparing the patterns of residual lung dysfunction between the two cohorts, only mixed damage with TLC and DL_{CO} < 80% pred. was more often observed in ICU patients ($P < 0.05$; $df = 1$; $V = 0.21$).

Discussion

The findings of this study show that the severity of pneumonia due to COVID-19 infection, as inferred by the care setting, has not only more frequent and serious medium and long-term consequences on lung function and exercise tolerance, as expected, but a different pattern of residual lung functional damage.

Unfortunately, only one third of patients treated in ICU had all pulmonary function tests within the normal limits after 4–6 months from hospital discharge, in sharp contrast to patients treated in IMD.

Table 1 Demographic characteristics and respiratory function parameters of enrolled patients 4–6 months after hospital discharge

	IMD ($n = 40$)	ICU ($n = 48$)	P value
Sex (M/F)	26/14	40/8	0.048
Age (years)	63 ± 10	60 ± 9	0.254
Height (cm)	167 ± 11	169 ± 9	0.199
Weight (kg)	80 ± 15	87 ± 16	0.024
BMI (kg/m^2)	29 ± 5	30 ± 5	0.124
VC% pred.	108 ± 22	101 ± 19	0.109
FVC% pred.	109 ± 23	102 ± 20	0.120
FEV$_1$% pred.	106 ± 22	107 ± 20	0.975
FEV$_1$/FVC%	78 ± 7	84 ± 6	0.0003
FRC% pred.	87 ± 23	76 ± 21	0.029
RV% pred.	76 ± 17	71 ± 17	0.137
PEF% pred.	111 ± 15	115 ± 21	0.289
TLC% pred.	93 ± 14	87 ± 14	0.074
VA% pred.	89 ± 16	83 ± 12	0.025
DL$_{CO}$% pred.	85 ± 18	77 ± 14	0.019
K$_{CO}$% pred.	100 ± 21	96 ± 19	0.450

Data are mean ± SD. ICU, Intensive Care Unit; IMD, Internal Medicine Department.
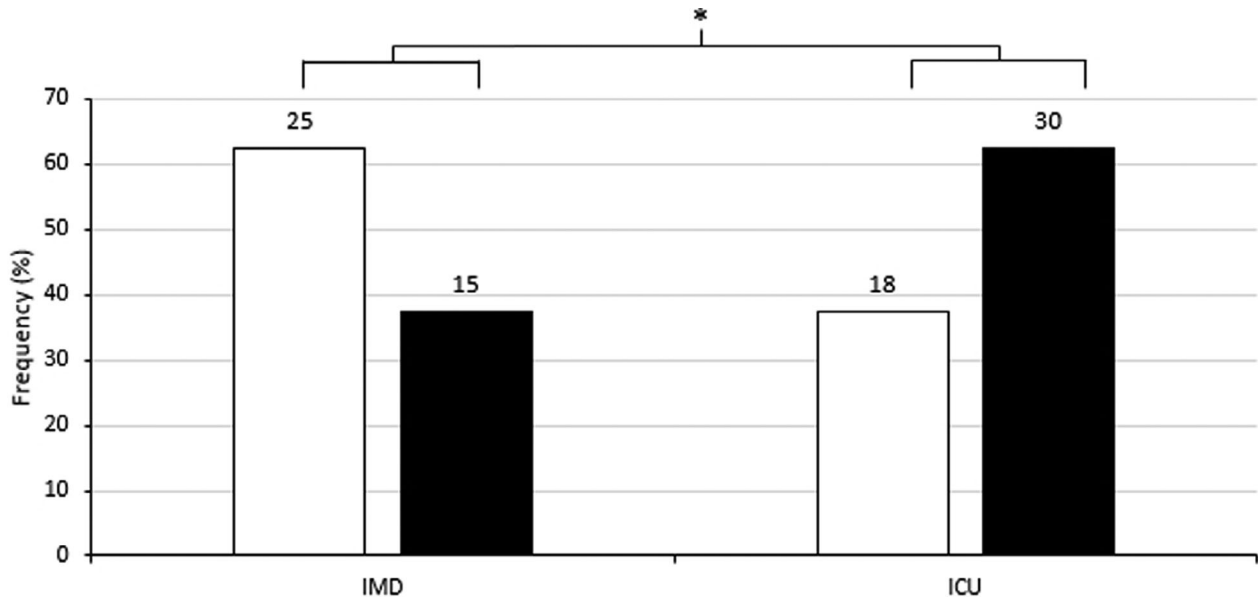
Figure 1 Frequency of normal and abnormal pulmonary function tests (PFTs) observed in patients discharged from the Internal Medicine Department (IMD) and Intensive Care Unit (ICU) after 4–6 months. On top of the columns, the numbers of patients are shown. More pathological PFR was found in ICU discharged patients (*=$P < 0.05$). (□) PFT NORMAL and (■) PFT NORMAL.
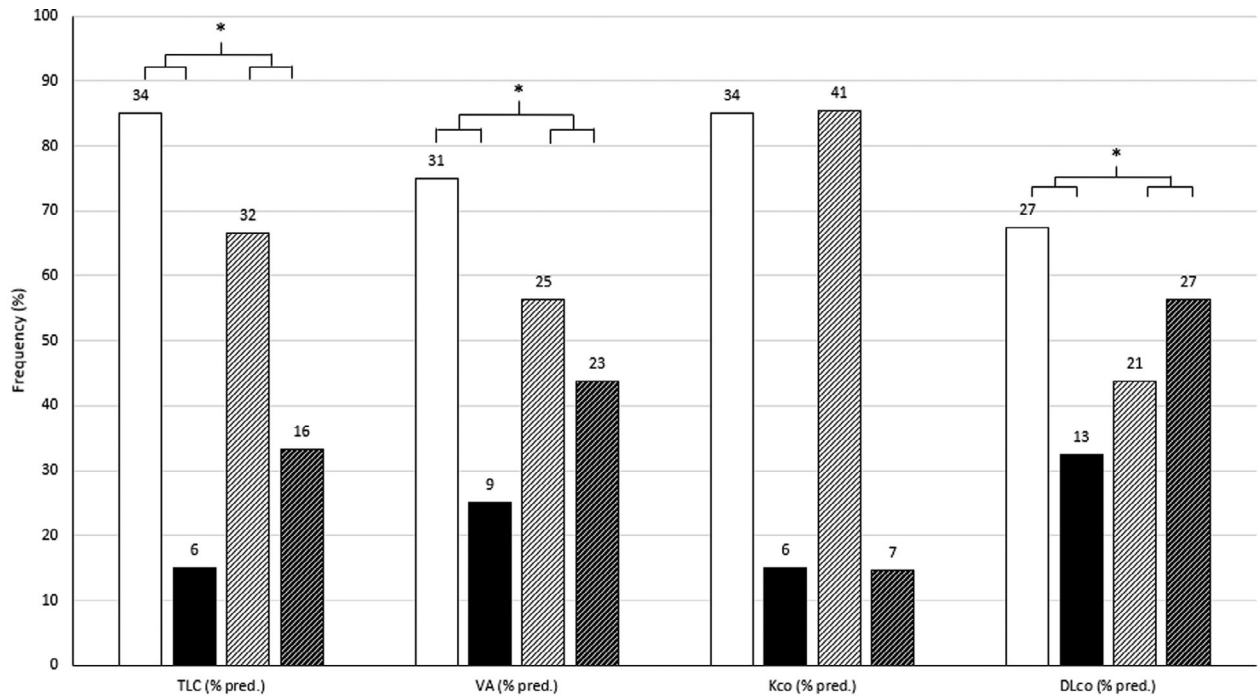

Figure 2 Comparison of frequency of normal and abnormal pulmonary function parameters, among those more compromised, between patients discharged from the Internal Medicine Department (IMD) and Intensive Care Unit (ICU) after 4–6 months. On top of the columns, the numbers of patients are shown. Abnormally reduced TLC, VA and DLco were found more frequently in ICU discharged patients (*=$P < 0.05$). DL_{CO}, Lung Diffusion capacity; TLC, Total Lung Capacity. (□) IMD > 80% pred., (■) IMD < 80% pred., (▨) ICU > 80% pred. and (▨) ICU < 80% pred.
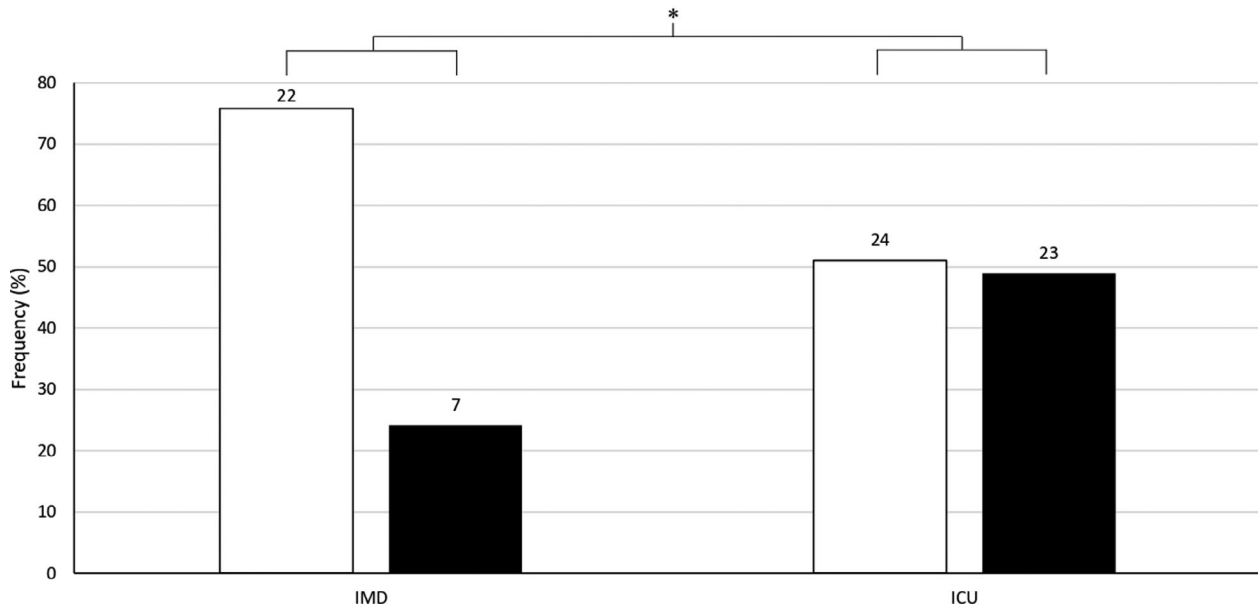
Figure 3 Frequency of normal and abnormal six-minute walking tests (6-MWTs) observed in patients discharged from the Internal Medicine Department (IMD) and Intensive Care Unit (ICU) after 4–6 months. On top of the columns, the numbers of patients are shown. More pathological 6-MWTs were found in ICU discharged patients (*=$P < 0.05$). (□) 6-MWT NORMAL and (■) 6-MWT ABNORMAL.

Table 2 Six-minute walking test parameters of enrolled patients 4–6 months after hospital discharge

	IMD ($n = 28$)	ICU ($n = 47$)	P value
SaO2%-pre	97 ± 1	98 ± 1	0.004
SaO2%-post	96 ± 2	96 ± 3	0.503
Distance %pred.	88 ± 16	82 ± 18	0.165

Data are mean ± SD. ICU, intensive care unit; IMD, internal medicine department.

In fact, more than 60% of patients discharged from ICU showed an impairment of lung function at 4–6 months. In this respect, the exaggerated inflammatory response of the host to viral pneumonia with severe gas exchange impairment (often configuring an ARDS condition) and excessive stress and strain on the lung parenchyma leading to self-inflicted lung injury are undoubtedly primary factors for such an outcome difference, but the ventilator-induced lung injury, due to unavoidable invasive mechanical ventilation, can likely contribute to the residual lung damage in survivors coming from intensive care.[23–27]

In both cohorts, the alveolar-capillary membrane damage caused by inflammatory-fibrotic thickening of alveolar septa (besides microvascular thrombosis) was the most common and persistent lung parenchyma dysfunction after COVID-19-related pneumonia, as documented by the DL_{CO} reduction. However, a concomitant restrictive ventilatory defect was found in the ICU cohort much more frequently than in the IMD cohort, suggesting a more widespread and marked development of lung tissue scar consolidation. Consequently, a greater occurrence of resting and mostly exertional dyspnoea is predictable as an unfavourable late clinical outcome in ICU discharged patients. This suspicion is supported by the higher frequency of abnormal 6-MWTs documented in the ICU cohort patients.

An isolated lung volume reduction was rarely observed, similarly in the two cohorts. The consolidation (i.e. organising pneumonia) and/or shrinkage (i.e. parenchymal bands) of a relevant amount of lung parenchyma, excluded from alveolar ventilation, was indeed a possible, although infrequent, consequence of COVID-19 pneumonia because, in the presence of a compensatory increase in K_{CO} in the other preserved regions of the lung, a VA reduction cannot cause a significant DL_{CO} decrease.[17,28]

The findings that emerged in this study are pretty similar to those reported in many other follow-up studies, although of different duration, underlying once again that lung diffusion capacity decrease and lung volume reduction, individually or together, are the main unfavourable consequences for lung function in survivors of COVID-19 pneumonia.[18,29,30] The novelty of our data lies in the fact that the severity of the viral lung infection may definitely influence not only the frequency but also the pattern of the residual lung damage. Indeed, in patients discharged from ICU, a more
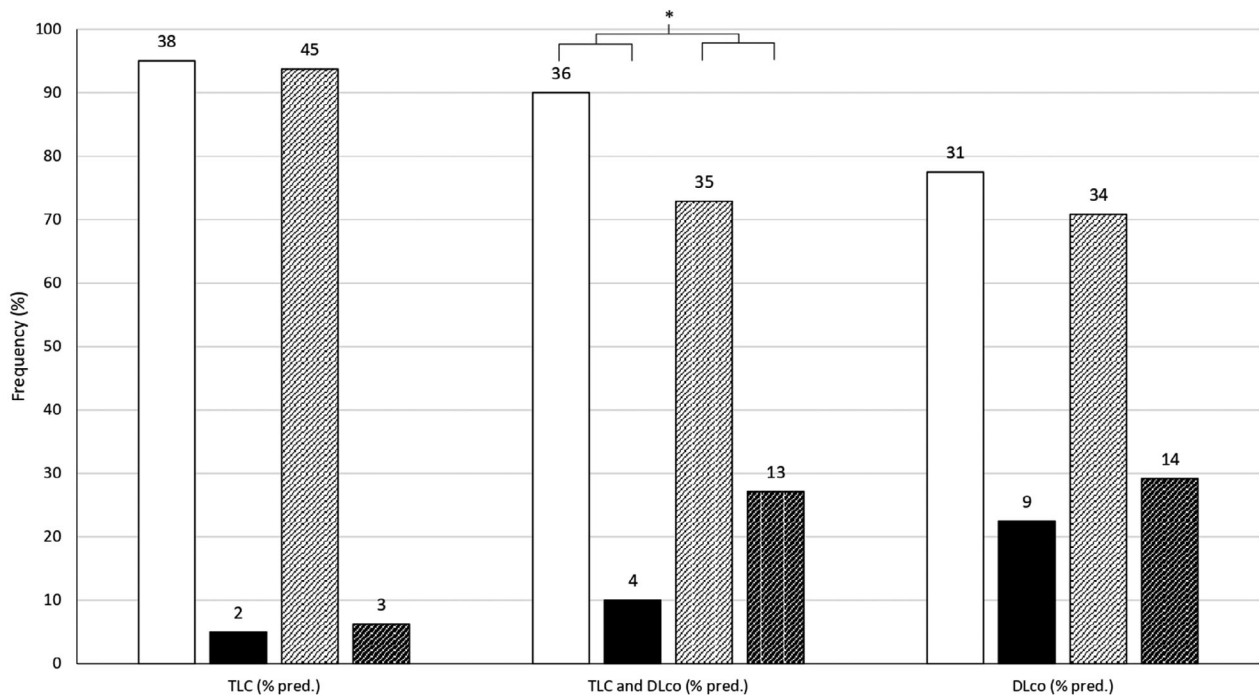
Figure 4 Comparison of frequency of residual lung disease patterns between patients discharged from the Internal Medicine Department (IMD) and the Intensive Care Unit (ICU) after 4–6 months. On top of the columns, the numbers of patients are shown. Only the coexistence of reduced TLC and DL_{CO} was the pathological pattern significantly more represented in patients discharged from ICU (*=$P < 0.05$), while reduced TLC alone and reduced DL_{CO} alone were similarly reported in both cohorts. DL_{CO}, Lung Diffusion capacity; TLC, Total Lung Capacity. (□) IMD > 80% pred., (■) IMD < 80% pred., (▨) ICU > 80% pred. and (▨) ICU < 80% pred.

complex pattern of disease in which lung volume reduction and lung diffusion capacity decrease coexist was more frequently observed than in patients discharged from IMD. These results agree with what was reported in one study, which limited the observation period in the early convalesce phase, showing that this pattern of pulmonary impairment may last for a long time in more severely affected patients.[19]

Finally, this work underlines once again that more comprehensive pulmonary function tests and 6-MWT performed as a follow-up strategy in patients hospitalised after COVID-19 infection leading to pneumonia may accurately describe the sequelae of the potential lung damage and represent an informative, reliable and cost-effective tool for monitoring the long-term respiratory dysfunction of these patients.

We recognise some limitations in our study, mainly related to the patients' lack of respiratory function tests before hospital admission. Therefore, theoretical values corrected for the anthropometric patients' characteristics were adopted to judge the collected results. Among other limitations, we acknowledge the lack of specifically gender-oriented comparisons and the lack of evaluation of enrolled subjects' smoking history and non-respiratory comorbidities.

Conclusion

In conclusion, the study shows that in patients hospitalised for COVID-19 infection leading to pneumonia, the severity of lung involvement is remarkably important for the medium- to long-term consequences for pulmonary function, not only because of the lower probability of full recovery but also for the more complex pattern of residual pulmonary dysfunction where the interstitial fibrotic thickening can be so marked and extensive leading to a significant restriction, often associated with and aggravated by fibrous shrinkage/consolidation of relevant portions of lung parenchyma.

Acknowledgements

Data Availability Statement

The data supporting the findings of this study are available from the corresponding author upon reasonable request.

References

1 Higgins V, Sohaei D, Diamandis EP, Prassas I. COVID-19: from an acute to chronic disease? Potential long-term health consequences. *Crit Rev Clin Lab Sci* 2021; **58**: 297–310.

2 Yelin D, Wirtheim E, Vetter P, Kalil AC, Bruchfeld J, Runold M *et al*. Long-term consequences of COVID-19: research needs. *Lancet Infect Dis* 2020; **20**: 1115–17.

3 Huang C, Huang L, Wang Y, Li X, Ren L, Gu X *et al*. 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 2021; **397**: 220–32.

4 Raveendran AV, Jayadevan R, Sashidharan S. Long COVID: an overview. *Diabetes Metab Syndr* 2021; **15**: 869–75.

5 Caminati M, Vultaggio A, Matucci A, Senna G, Almerigogna F, Bagnasco D *et al*. Asthma in a large COVID-19 cohort: prevalence, features, and determinants of COVID-19 disease severity. *Respir Med* 2021; **176**: 106261.

6 Crook H, Raza S, Nowell J, Young M, Edison P. Long covid-mechanisms, risk factors, and management. *BMJ* 2021; **26**: n1648.

7 Azim A, Pini L, Khakwani Z, Kumar S, Howarth P. Severe acute respiratory syndrome coronavirus 2 infection in those on mepolizumab therapy. *Ann Allergy Asthma Immunol* 2021; **126**: 438–40.

8 Yong SJ. Long COVID or post-COVID-19 syndrome: putative pathophysiology, risk factors, and treatments. *Infect Dis* 2021; **53**: 737–54.

9 Heffler E, Detoraki A, Contoli M, Papi A, Paoletti G, Malipiero G *et al*. Reply to: Kow CS et al. Are severe asthma patients at higher risk of developing severe outcomes from COVID-19? *Allergy* 2021; **76**: 961–2.

10 Latronico N, Peli E, Calza S, Rodella F, Novelli MP, Cella A *et al*. Physical, cognitive and mental health outcomes in 1-year survivors of COVID-19-associated ARDS. *Thorax* 2022; **77**: 300–3.

11 Boutou AK, Asimakos A, Kortianou E, Vogiatzis I, Tzouvelekis A. Long COVID-19 pulmonary sequelae and management considerations. *J Pers Med* 2021; **11**: 838.

12 Adeloye D, Elneima O, Daines L, Poinasamy K, Quint JK, Walker S *et al*. The long-term sequelae of COVID-19: an international consensus on research priorities for patients with pre-existing and new-onset airways disease. *Lancet Respir Med* 2021; **9**: 1467–78.

13 Tantucci C, Bottone D, Borghesi A, Guerini M, Quadri F, Pini L. Methods for measuring lung volumes: is there a better one? *Respiration* 2016; **91**: 273–80.

14 Tantucci C, Pini L. Tidal airway closure in asthma and COPD. *Monaldi Arch Chest Dis* 2016; **83**: 788.

15 Alqahtani JS, Alghamdi SM, Aldhahir AM, Althobiani M, Raya RP, Oyelade T. Thoracic imaging outcomes in COVID-19 survivors. *World J Radiol* 2021; **13**: 149–56.

16 Fratianni G, Malfatto G, Perger E, Facchetti L, Pini L, Bosco M *et al*. Lung ultrasound in patients with SARS-COV-2 pneumonia: correlations with chest computed tomography, respiratory impairment, and inflammatory cascade. *J Ultrasound Med* 2021; **41**: 1465–73.

17 Salehi S, Reddy S, Gholamrezanezhad A. Long-term pulmonary consequences of coronavirus disease 2019 (COVID-19): what we know and what to expect. *J Thorac Imaging* 2020; **35**: W87–9.

18 Orzes N, Pini L, Levi G, Uccelli S, Cettolo F, Tantucci C. A prospective evaluation of lung function at three and six months in patients with previous SARS-COV-2 pneumonia. *Respir Med* 2021; **186**: 106541.

19 Canonica, G. W., Blasi, F., Paggiaro, P., Senna, G., Passalacqua, G., Spanevello, A., Aliberti, S., Bagnasco, D., Bonavia, M., Bonini, M., Brussino, L., Bucca, C., Caiaffa, M. F., Calabrese, C., Camiciottoli, G., Caminati, M., Carpagnano, G. E., Caruso, C., Centanni, S., … Heffler, E. Oral CorticoSteroid sparing with biologics in severe asthma: A remark of the Severe Asthma Network in Italy (SANI). *World Allergy Organization Journal*, 2020; **13** (10): 100464. https://doi.org/10.1016/j.waojou.2020.100464

20 Mo X, Jian W, Su Z, Chen M, Peng H, Peng P *et al*. Abnormal pulmonary function in COVID-19 patients at time of hospital discharge. *Eur Respir J* 2020; **55**: 2001217.

21 Nusair S. Abnormal carbon monoxide diffusion capacity in COVID-19 patients at time of hospital discharge. *Eur Respir J* 2020; **56**: 2001832.

22 Ricard JD, Dreyfuss D, Saumon G. Ventilator-induced lung injury. *Eur Respir J Suppl* 2003; **42**: 2s–9s.

23 Batah SS, Fabro AT. Pulmonary pathology of ARDS in COVID-19: a pathological review for clinicians. *Respir Med* 2021; **176**: 106239.

24 Ñamendys-Silva SA. ECMO for ARDS due to COVID-19. *Heart Lung* 2020; **49**: 348–9.

25 Gibson PG, Qin L, Puah SH. COVID-19 acute respiratory distress syndrome (ARDS): clinical features and differences from typical pre-COVID-19 ARDS. *Med J Aust* 2020; **213**: 54–56.e1.

26 Ma X, Liang M, Ding M, Liu W, Ma H, Zhou X *et al*. Extracorporeal membrane oxygenation (ECMO) in critically ill patients with coronavirus disease 2019 (COVID-19) pneumonia and acute respiratory distress syndrome (ARDS). *Med Sci Monit* 2020; **6**: e925364.

27 Clay RD, Iyer VN, Reddy DR, Siontis B, Scanlon PD. The "complex restrictive" pulmonary function pattern: clinical and radiologic analysis of a common but previously undescribed restrictive pattern. *Chest* 2017; **152**: 1258–65.

28 Steinbeis F, Thibeault C, Doellinger F, Ring RM, Mittermaier M, Ruwwe-Glösenkamp C *et al*. Severity of respiratory failure and computed chest tomography in acute COVID-19 correlates with pulmonary function and respiratory symptoms after infection with SARS-CoV-2: an observational longitudinal study over 12 months. *Respir Med* 2021; **191**: 106709.

29 Wu X, Liu X, Zhou Y, Yu H, Li R, Zhan Q *et al*. 3-month, 6-month, 9-month, and 12-month respiratory outcomes in patients following COVID-19-related hospitalization: a prospective study. *Lancet Respir Med* 2021; **9**: 747–54.

30 Huang Y, Tan C, Wu J, Chen M, Wang Z, Luo L *et al*. Impact of coronavirus disease 2019 on pulmonary function in early convalescence phase. *Respir Res* 2020; **21**: 163.