


Cardiopulmonary Outcomes in Covid-19 Patients Discharged From a Tertiary Care Center: A Prospective Study

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Abstract To determine the cardiopulmonary changes in the survivors of acute COVID-19 infection at 3–6 month and 6–12 month. We followed up 53 patients out of which 28 (52%) had mild COVID-19 and 25 (48%) had severe COVID-19. The first follow-up was between 3 month after diagnosis up to 6 month and second follow-up between 6 and 12 month from the date of diagnosis of acute COVID-19. They were monitored using vital parameters, pulmonary function tests, echocardiography and a chest computed tomography (CT) scan. We found improvement in diffusing capacity for carbon monoxide (DLCO) with a median of 52% of predicted and 80% of predicted at the first and second follow-up, respectively. There was improvement in the CTSS in severe group from 22 (18–24) to 12 (10–18; $p < 0.001$). Multivariable logistic regression revealed increased odds of past severe disease with higher CTSS at follow-up (OR-1.7 [CI 1.14–2.77]; $P = 0.01$). Correlation was found between CTSS and DLCO at second follow-up ($r^2 = 0.36$; $p < 0.01$). Most of patients recovered from COVID-19 but a subgroup of patients continued to have persistent radiological and pulmonary function abnormalities necessitating a structured follow-up.

Keywords Pulmonary function test · Echocardiography · DLCO · COVID-19 · CT severity score

Introduction

SARS-CoV-2 infection continues to lay enormous pressure on healthcare system globally. The survivor pool continues to increase, many continue to experience symptoms long after acute illness. COVID-19 is a multisystemic disease, in which symptoms range from mild-to-severe life-threatening complications like pneumonia, acute respiratory distress syndrome, myocarditis and pulmonary embolism [1].

Till date more than 100 million people worldwide have recovered from COVID-19, but some organ systems like lung and heart continue to experience long-term impairment. Majority of evidence worldwide regarding post-viral syndromes was concluded from experience in severe acute respiratory virus syndrome (SARS) and middle east respiratory syndrome (MERS) survivors. One third of MERS survivors were found to have persisting chest abnormalities at 6-week follow-up. Similarly, in a subgroup of SARS, survivors around 30% of patients had persisting pulmonary fibrosis at 3- and 6-month of follow-up [2–5].

Based on the duration of symptoms, long COVID includes an ongoing symptomatic phase which lasts for 4–12 weeks and any symptoms lasting for more than 12 weeks fall under the spectrum of post-COVID-19 syndrome [6]. Post-COVID-19 sequelae can encompass diverse manifestations like pulmonary fibrosis, pulmonary and systemic vascular disease, bronchiectasis, chronic fatigue, and psychosocial disorders. Cardiovascular involvement may occur in about 20 to 30% of patients hospitalized with severe COVID-19. These may manifest as elevated troponin levels, venous thromboembolism, heart failure and arrhythmias.

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The long-term sequelae which are initiated with this inflammatory process include myocardial fibrosis or scarring, persisting left ventricular dysfunction, inappropriate sinus tachycardias and autonomic dysfunction [7–17].

The pathophysiology is poorly understood, and treatment options are minimal. Therefore, these patients should be followed up to detect and manage the sequelae which can cause functional impairment of varying degree. So far, there is paucity prospective data on the long-term follow-up of cardiopulmonary changes over one year after acute COVID-19 infection from India. This prospective observational study aims to follow-up on cardiopulmonary changes in the survivors of acute COVID-19 infection at 3–6 month and 6–12 month.

Material and Methods

Study Design and Participants

In this prospective observational study, patients were recruited from outpatient and inpatient services of All India Institute of Medical Sciences, New Delhi, from Oct 2020 to Oct 2022. Since ours was one of the first studies from India, considering the current setting, time constraints, resources, and feasibility, an arbitrary sample size of 45 patients was chosen. The inclusion criteria were age between 18 and 65 year; confirmed cases of COVID-19 with either cartridge-based nucleic amplification tests or real-time polymerase chain reaction (RT-PCR). We excluded cases who refused consent, had a known cardiopulmonary disease, or were pregnant. The study was approved by the Institutional Ethics Committee of AIIMS, New Delhi, and was performed in accordance with the Declaration of Helsinki. Informed consent was obtained from all participants before collecting the data.

Procedure

Based on the severity of acute COVID-19 illness as per the Indian Council of Medical Research COVID-19 task force guidelines, patients were categorized as mild or severe [18]. Patients were characterized as having mild disease if they had symptoms of upper respiratory tract and/or fever without shortness of breath or hypoxia, and as a severe disease if respiratory rate > 30/min or breathlessness or oxygen saturation (SpO_2) < 90% on room air.

Data were collected using a structured questionnaire which included baseline parameters like age, sex, date of diagnosis, duration of symptoms (cough, fever, and shortness of breath), comorbidities, vitals (pulse rate (PR), respiratory rate (RR), mean arterial pressure (MAP), and ratio of oxygen saturation on pulse oximetry and fraction of inspired

oxygen [$\text{SpO}_2/\text{FiO}_2$]), need for supplemental oxygen, drugs received, computed tomography severity score (CTSS) and left ventricular ejection fraction (LVEF). A computed tomography of the chest was done at the second follow-up visit.

Pulmonary Function Variables

Spirometry was performed using MIR Spirolab III as per the ATS/ERS guidelines. Pulmonary function tests (Forced expiratory volume at 1 s (FEV_1), forced vital capacity (FVC), ratio of FEV_1/FVC , forced expiratory flow between 25 and 75% of vital capacity ($\text{FEF}_{25-75\%}$), and diffusion capacity of lung for carbon monoxide (DLCO)) were recorded as percentage predicted values, and z-scores at both the follow-ups.

Echocardiographic Variables

Standard echocardiography was performed using a 1.7–3.4 MHz tissue harmonic transducer by an experienced cardiologist. For cardiac evaluation, parameters suggesting systolic and diastolic dysfunction (peak velocity of blood flow in early diastole (E), ratio of peak velocity in early diastole and peak velocity in late diastole (transmitral E/A), velocity of the mitral annulus by pulsed tissue Doppler at lateral side (lateral e'), velocity of the mitral annulus by pulsed tissue Doppler at septal side (medial e'), ratio of peak early mitral inflow velocity and average early diastolic mitral annulus velocity (E/e'), left ventricular ejection fraction (LVEF), tricuspid regurgitation velocity (TRV) and regional wall motion abnormalities) were recorded at both the follow-ups.

CT Variables

CT scans were acquired on a 1280-slice multidetector CT with a 128×0.6 mm collimation and spiral pitch factor of 1.1 (SOMATOM Definition Flash, Siemens Healthineers). Scans were obtained in the craniocaudal direction without an iodine contrast agent and in a low-dose setting (100 kVp tube potential). Axial reconstructions were performed with a slice thickness of 1 mm. CT images were evaluated for the presence of ground-glass opacities (GGOs), consolidations, bronchial dilatation, and reticulations as defined by the glossary of terms of the Fleischner Society. They were reported as either present or absent. The CTSS was calculated at baseline and second follow-up. A score was given depending on the percentage of involvement of each of the five lobes—1 for < 5%, 2 for 5–25%, 3 for 26–49%, 4 for 50–75% and 5 for > 75% involvement. The total CT severity score is the sum of individual lobar scores and

ranges from 0 (no involvement) to 25 (Maximum involvement) when all lobes show more than 75% involvement.

For imaging assessments, two radiologists with 5 year and 25 year of thoracic radiology experience, reviewed the images independently, with a final finding reached by consensus when a discrepancy was found. The radiologists were masked to the clinical information or clinical progress of the patients, except for the knowledge that these images were of patients with COVID-19.

Statistical Analysis

A descriptive statistical analysis was done. The normality of variables was checked with the use of the Shapiro–Wilk test. If variables were normally distributed, they were expressed as mean \pm SD, otherwise median with inter-quartile range. We used the Wilcoxon rank sum test to compare unpaired quantitative variables (vitals, pulmonary function test parameters [PFT] and echocardiographic parameters) in both groups (mild and severe) and Wilcoxon signed-rank test to compare paired quantitative variables (vitals, PFTs, and echocardiographic parameters) between first and second follow-up. Chi-square test/Fisher's exact test was used to assess the association between categorical data. The McNemar test was used to compare paired categorical data. Predictors of DLCO less than 80% at the second follow-up were determined using univariable and multivariable logistic regression analysis. Predictors of disease severity at baseline were determined using univariable and multivariable logistic regression analysis. Linear correlation was assessed between DLCO and CTSS at the second follow-up using Pearson's correlation coefficient. All the statistical analysis was performed using STATA 15.0 version software. The results were considered statistically significant at a p -value less than 0.05.

Results

For this study, 113 patients with confirmed acute COVID-19 infection were screened. Sixty patients were excluded; twenty-eight had known cardiopulmonary disease, ten patients did not give consent, 20 patients did not have baseline CT scans, and two patients did not have persistent symptoms. Of the 53 patients included in the study, 28 (52%) had mild COVID-19, and 25 (47%) had severe COVID-19 illness (Fig. 1).

The median (IQR) age of the overall study population was 43 year (31–61). There were significantly older individuals in the severe group compared to the mild group [53 year (IQR 37–63) versus 34 year (IQR 27–52); ($p=0.03$)]. There was no difference in gender between the two groups ($p=0.72$). There was a significantly longer duration of acute symptoms like cough and fever in the severe group (13 ± 8 days) compared to the mild group (4 ± 2.3 days). Comorbid diseases were seen in 23 (44%) of the study population, common comorbidities being hypertension [$n=16$ (30%)], diabetes [$n=18$ (34%)] and hypothyroidism [$n=2$ (3.77%)]. There was no significant difference in the two groups in terms of the presence of comorbidities ($p=0.08$). Median CTSS in the overall population was 4 (IQR 3–22). Baseline CTSS was higher in the severe group (22 [IQR 18–24]) compared to the mild group (3 [IQR 2–4]) ($p=0.001$). Baseline LVEF was 55% (IQR 55–60), and there was no significant difference between groups (Table 1).

The median pulse rate was higher in the severe group [100 beats/min (IQR 90–110)] as compared to the mild group [90 beats/min (IQR 88–105)] ($p=0.02$) at baseline. MAP was higher in the severe group [98 mmHg (IQR 93–106)] compared to the mild group [90 mmHg (IQR 85–96)] ($p=0.01$) at baseline. There was significantly lower SpO_2/FiO_2 in the severe group [116 (IQR 100–146)] compared to the mild group [466 (IQR 457–467)] ($p=0.001$) at baseline. There was no significant change in median pulse rate, MAP and

Fig. 1 Study flow diagram

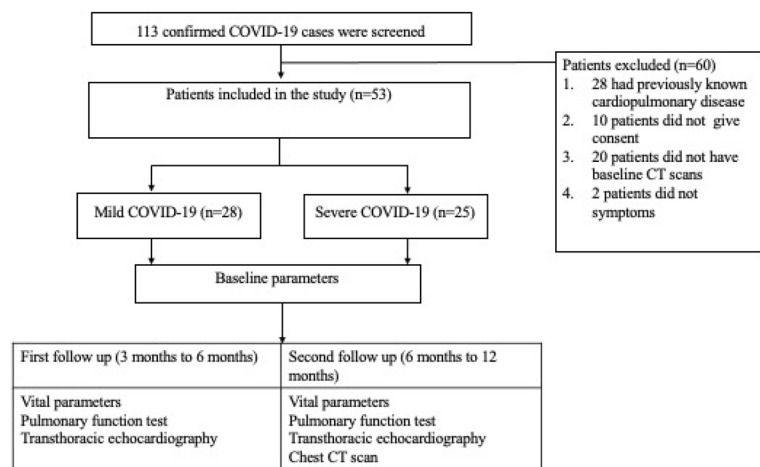


Table 1 Demography and baseline parameters of mild and severe COVID-19 groups

| Baseline variables | Mild (n=28) | Severe (n=25) | P-Value* |
|---|---------------|---------------|----------|
| Age (year) | 34 (27–52) | 53 (37–63) | 0.03 |
| Male (%) | 11 (50) | 11 (50) | 0.72 |
| Duration of symptoms (Days) | 3.5 (2–5) | 10 (7–20) | 0.001 |
| Diagnosis to first follow-up (month) | 3.4 ± 0.7 | 3.6 ± 0.5 | |
| Diagnosis to second follow-up (month) | 8.7 ± 1.5 | 9 ± 1 | |
| Cough (Days) | 3 (0–4) | 10 (4–10) | 0.001 |
| Fever (Days) | 3 (2–4) | 10 (7–12) | 0.01 |
| Shortness of breath (Days) | – | 10 (7–12) | – |
| Mean Pulse rate (beats/min) | 90 (88–105) | 100 (90–110) | 0.02 |
| Mean MAP (mmHg) | 90 (85–96) | 98 (93–106) | 0.01 |
| Mean SpO ₂ /FiO ₂ ratio | 466 (457–467) | 116 (100–146) | 0.001 |
| Comorbidities n (%) | 9 (40) | 14 (60) | 0.08 |
| Hypertension n (%) | 8 (50) | 8 (50) | 0.78 |
| Diabetes n (%) | 8 (45) | 10 (55) | 0.38 |
| Thyroid disease n (%) | 0 | 2 (100) | 0.12 |
| Remdesivir n (%) | 1(5) | 18 (95) | 0.01 |
| Steroids n (%) | – | 25 (100) | 0.01 |
| Base line CTSS | 3 (2–4) | 22 (18–24) | 0.001 |
| Baseline LVEF | 55 (55–60) | 55 (50–60) | 0.06 |

*All values are Median (IQR) or n (%); Wilcoxon rank sum tests were used for unpaired continuous data and Chi-square for unpaired categorical data

Abbreviation IQR Inter-quartile Range, MAP Mean arterial pressure, SpO₂ Oxygen saturation, FiO₂ Fractionated inspired oxygen, CTSS CT severity index, LVEF left ventricular ejection fraction

SpO₂/FiO₂ ratio from baseline to first follow-up and from first to second follow-up in the mild group. However, in the severe group, there was a significant change in SpO₂/FiO₂ ratio from baseline [146 (IQR 116–188)] to first follow-up [457 (IQR 447–466)] ($p < 0.01$) and from first follow-up [447 (IQR 438–448)] to second follow-up [457 (IQR 452–461)] ($p < 0.01$).

At first follow-up, FEV₁/FVC was 99% of predicted (IQR 93–108) in the mild as compared to 111% predicted (IQR 98–117) in the severe group ($p < 0.01$). Median DLCO was lower in the severe (52% of predicted, IQR 39–71) compared to the mild group (81% of predicted, IQR 70–88) ($p < 0.01$). Similarly, during the second follow-up, the median FEV₁/FVC was 98% of the predicted (IQR 95–107) in the mild compared to 105% of the predicted (IQR 96–117) in the severe group ($p = 0.08$). DLCO was significantly lower in the severe group (62% of predicted, [IQR 56–72]) compared to the mild group (86% of predicted, [IQR 79–91]) ($p < 0.01$) at second follow-up (Table 2).

DLCO showed significant improvement from the first (52% of predicted [IQR 20–71]) to the second follow-up (80% of predicted [IQR 60–87]) ($p < 0.01$). A similar trend was reflected in the z-scores. DLCO showed consistent improvement across all the groups. In the mild group, it was 81% of predicted (IQR 70–88) to 86% of predicted (IQR 79–91) ($p < 0.01$). Among the severe group, it

improved from 52% of predicted (IQR 39–72) to 62% of predicted (IQR 56–72) ($p < 0.01$). There was an improvement in diffusion restriction over time in both groups (Fig. 2).

In the overall population at the second follow-up, 26 (49%) patients had DLCO less than 80% of predicted. 26% were from the mild group, and 74% were from the severe group. Seven (25%) patients in the mild and 19 (76%) in severe had DLCO less than 80% at the second follow-up. Univariable logistic regression analysis showed increased odds of impaired DLCO with duration of fever (OR-1.14 [95% CI 1.00–1.29]; $p = 0.04$), duration of cough (OR-1.13 [95% CI 1.00–1.27]; $p = 0.03$), duration of shortness of breath (OR-1.18 [95% CI 1.05–1.33]; $p = 0.005$), baseline pulse rate (OR-1.04 [95% CI 0.99–1.09]; $p = 0.05$), baseline SpO₂/FiO₂ ratio (OR-0.99 [95% CI 0.99–0.99]; $p = 0.04$), baseline CTSS (OR-1.11 [95% CI 1.04–1.18]; $p = 0.002$), need for oxygen supplementation (OR-9.5 [95% CI 2.7–33.3]; $p = 0.001$), steroid (OR-9.5 [95% CI 2.7–33.3]; $p = 0.01$), and remdesivir (OR-5.13 [95% CI 1.48–17.73]; $p = 0.01$). However, these variables did not show any independent association on multivariable analysis.

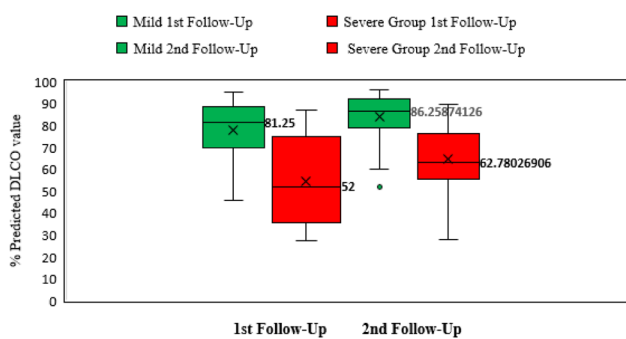
No difference was seen in the echocardiographic parameters between the mild and severe groups at either of the follow-up. Similarly, there was no difference in the echocardiographic parameters (RV dysfunction, TRV, E, E/e', E/A,

Table 2 Trend of pulmonary function and echocardiographic variables at first and second follow-up in the study population (n=53)

| | First follow-up | Second follow-up | p-value |
|-------------------------------------|----------------------|---------------------|---------|
| <i>Pulmonary function variables</i> | | | |
| FEV ₁ (z score) | -0.95(-1.77, -0.01) | -0.98(-1.81, -0.03) | 0.47 |
| FVC | 83(76, 89) | 84 (72, 91) | 0.83 |
| FVC (z score) | -1.34 (-2.01, -0.91) | -1.5(-2.2, -0.8) | 0.01 |
| FEV ₁ /FVC | 94 (102, 113) | 101 (96, 111) | 0.33 |
| FEV ₁ /FVC (z score) | 0.3 (-0.28, 1.8) | 0.22(-0.34, 1.8) | 0.21 |
| FEF _{25-75%} | 92(79, 143) | 90 (76, 116) | 0.14 |
| FEF _{25-75%} (z score) | -0.9 (-2.5, 1.5) | 1.4 (-2.55, 1.4) | 0.46 |
| DLCO | 52 (20, 71) | 80 (60, 87) | 0.001 |
| DLCO (z score) | -2.07(-3.1, -1.23) | -1.5 (-2.8--0.98) | 0.001 |
| <i>Echocardiographic variables</i> | | | |
| E | 90 (84-100) | 80 (74-84) | 0.001 |
| E/A | 1.2 (0.8-1.2) | 1 (0.95-1.2) | 0.21 |
| Med e' | 9 (8-9) | 8.4 (8-9) | 0.33 |
| Lat e' | 11 (11-12) | 11.2 (11-13) | 0.82 |
| E/e | 8.4 (8-9) | 8 (7.2-8.2) | 0.005 |
| LVEF | 60 (55-65) | 60 (55-60) | 0.31 |

Median (IQR) have been used for all above parameters, and Wilcoxon signed-rank was used to analyze time-related differences

Abbreviations IQR Inter-quartile range, FEV₁ Forced expiratory volume at 1 s, FVC Forced vital capacity, FEF_{25-75%} forced expiratory flow between 25 and 75% of vital capacity, DLCO diffusion capacity of lung for carbon monoxide, E peak velocity of blood flow in early diastole, E/A ratio of peak velocity in early diastole and peak velocity in late diastole, lat e' velocity of the mitral annulus by pulsed tissue Doppler at lateral side, med e' velocity of the mitral annulus by pulsed tissue Doppler at septal side, E/e' ratio of peak early mitral inflow velocity and average early diastolic mitral annulus velocity, LVEF left ventricular ejection fraction

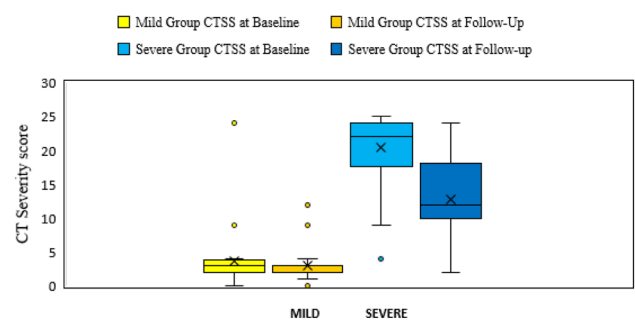


Abbreviation: DLCO, Diffusion capacity of lung for carbon monoxide

Fig. 2 Box whisker plot depicting the comparison of DLCO between first and second follow-up. *Abbreviation* DLCO, Diffusion capacity of lung for carbon monoxide

Lateral e', Medial e', LVEF) between the first and second follow-up in either group.

At the baseline, CTSS was significantly higher in the severe group (22 [IQR 18-24]) compared to the mild group (3 [IQR 2-3.5] (p=0.001). At follow-up, CTSS was higher in the severe group (12 [IQR 10-18]) compared to the mild group (3 [IQR 2-3]) (p<0.01). There was an improvement of CTSS from baseline (4 [IQR 3-22]) to the second



Abbreviation: CTSS; CT Severity Score.

Fig. 3 Box whisker plot depicting the comparison of CTSS in mild and severe group at baseline and second follow-up. *Abbreviation* CTSS; CT Severity Score

follow-up (4 [IQR 3-12]) (p=0.001) in the overall study population. In the severe group, there was a significant improvement in the CTSS from baseline (22 [IQR 18-24]) to follow-up (12 [IQR 10-18]) (p=0.001) (Fig. 3).

At least one radiological abnormality was seen in 70% of patients at baseline. At follow-up, 62% had at least one radiological abnormality. At baseline, ground-glass opacities (GGO) were seen in 60%, reticulation in 51%, consolidations

in 54%, and bronchial dilatations in 22%. At follow-up, GGOs were seen in 50%, reticulation in 50%, consolidations in 10%, and bronchial dilatations in 14%. There was a maximum reduction in the consolidation from baseline to follow-up (Fig. 4). There was a correlation between CTSS and the DLCO. The higher the CTSS, the greater the DLCO at second follow-up ($r^2=0.36$; $p<0.01$).

On univariable logistic regression analysis, the odds of severe disease at baseline were associated with age (OR 1.03 [95% CI 1.00–1.072], $p=0.03$), CTSS at follow-up (OR 1.07 [95% CI 1.32–2.20], $p=0.001$) and DLCO (OR 0.90 [95% CI 0.85–0.95], $p=0.001$). We also identified CTSS at follow-up (OR 1.7 [95% CI 1.14–2.77], $p=0.01$) as an independent risk factor to predict severe disease, including in the multivariable analysis with age and DLCO (Table 2).

Discussion

Many prospective observational studies have revealed cardiopulmonary sequelae in patients recovering from COVID-19 infection.

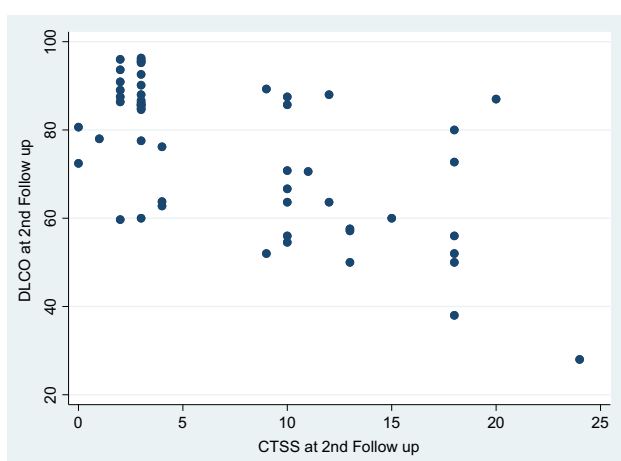
The median age in our study was 43 year which is comparable to a study done by Naik et al., in which the median age was 41 year [19]. In the study by Guler, patients who survived severe/critical COVID-19 were older than patients who were followed up after mild/moderate disease (60 ± 12 versus 52 ± 11 year) and had equal sex distribution. In our study, patients with severe COVID-19 were older than patients with mild COVID-19. There was no difference in sex distribution between the mild and severe groups. Our study also supports that older age was a risk factor for severe

illness due to associated comorbidities and compromised immunity in older age [11].

We recorded fever, cough, and shortness of breath, as these were the common symptoms reported in multiple studies worldwide in acute COVID-19 patients [20]. In our study, the duration of fever and cough were longer in the severe group compared to the mild group, which can be attributed to extensive tissue injury, cytokine storm, and pathophysiological process seen in severe COVID-19. There was a significant improvement in the SpO_2/FiO_2 ratio in the severe group on follow-up, suggesting the recovery of underlying lung injury over time.

In line with other studies, our study revealed that severe COVID-19 patients had higher CTSS at baseline. There was an improvement in the CTSS from baseline to follow-up in the overall study population, especially in the severe group. At the second follow-up, 62% of patients had at least one pathological finding on CT scans. GGOs were the most common pathological finding seen in our study. There was a reduction in all the pathological findings on CT on follow-up with maximum reduction in consolidation. A similar study done by Sonnweber et al. studied cardiopulmonary recovery after COVID-19 revealed lung abnormalities in 77% at 60 days and 63% at 100 days [8]. The main findings on CT scan like GGOs, consolidation, and reticulation were similar to our study. Consolidations and bronchial dilation resolved completely, similar to our study population. There was a weak correlation between CT severity score and DLCO, supporting the findings of our study. To date, it is still unclear whether such subclinical structural changes justify the routine use of CT scan for follow-up after acute COVID-19. In a study by Vijaykumar, 41 of them had GGOs and fibrotic bands at 3 month; only 16% had residual lung abnormalities at 1 year, with none of the patients showing the progression of imaging abnormalities [21]. Liu et al. also found 42 and 75% radiological resolution at 1 month and 6 month, respectively [22]. This is consistent with our imaging findings suggesting the reversibility of COVID-19-associated pulmonary damage, and till now, no clear signs of progressive ILD have been observed.

Our cohort demonstrated lower lung volumes (FVC and FEV_1) in patients with severe COVID-19 and a higher FEV_1/FVC ratio in the severe group, suggesting restrictive physiology. The most significant finding in our patients was a reduction in diffusion capacity. In addition, DLCO was significantly lower in the severe group, suggesting a higher degree of interstitial and pulmonary vascular involvement. These findings were in line with other studies, which revealed that a higher percentage of severe patients had diffusion restriction [22]. Several studies have shown DLCO impairment suggestive of interstitial or pulmonary vascular abnormalities in COVID-19 infections [10, 11, 23–25]. DLCO showed significant improvement in both mild and severe groups of



Abbreviation: DLCO; Diffusion capacity of lung for carbon monoxide, CTSS; CT Severity Score.

Fig. 4 Scatterplot depicting the correlation of DLCO and CTSS in study population at second follow-up. *Abbreviation:* DLCO; Diffusion capacity of lung for carbon monoxide, CTSS; CT severity score

our study population from the first to second follow-up, suggesting recovery of interstitial and structural changes in the lung. Our results are consistent with other follow-up studies on COVID-19 patients [8, 26].

Though there was a significant improvement in diffusion capacity on follow-up, 49% of our study population had DLCO less than 80% of predicted at the second follow-up, like the study by Gambernini [26]. This indicates that some patients, who recover from acute COVID-19, still had persisting pulmonary function abnormalities at 6–12 month. There is a need for long-term follow-up studies to know the natural history of pulmonary function.

Risk factors for diffusion and restriction impairment on PFTs at 1 year after recovery were female sex, chronic kidney disease, mechanical ventilation, smoking status, residual CT abnormalities, and length of hospital stay [27]. We also found that duration of symptoms, CT abnormality and need for oxygenation as risk factors for diffusion impairment, however, did not reach statistical significance due to the smaller sample size.

Few studies have reported the association between diffusion restriction capacity and the presence of fibrotic sequelae on chest CT [28–30]. In our study, lower DLCO was associated with higher CTSS indicative of underlying lung injury. Given its expense and radiation risk, chest CT cannot be performed for every symptomatic COVID-19 survivor. Considering all these factors, patients with persisting symptoms following recovery from COVID-19 can be followed up with regular PFT with DLCO measurements. We can reserve CT scan for more selective patients who show abnormalities on PFTs.

It is evident from the pathogenesis of COVID-19 that there is myocardial injury even in patients without severe disease, raising concerns regarding cardiac sequelae. Lassen et al. have found that RV function and biomarkers improve during follow-up, but LVEF was not different from matched controls [28]. Similarly, Catena et al. concluded that there was no evidence of cardiac dysfunction on ECHO at 41 days follow-up [29]. These were similar to our study, which showed no difference in RV and LV function in both groups on follow-up. Several studies have shown that MRI was a more sensitive tool to detect subclinical changes in myocardium associated with worse prognosis [30]. So, there is a need for studies evaluating cardiac involvement and myocardial inflammation in patients recovering from COVID-19 using sensitive tools.

This was one of the first prospective observational study to assess cardiopulmonary sequelae following recovery from acute COVID-19 in the Indian population. The trend of pulmonary function and echocardiographic parameters was reported at two follow-ups in the mild and severe groups. This study also tried to correlate DLCO and CTSS and compare CTSS at follow-up with baseline in both the groups.

This study is not free from limitations. Inherent selection bias in the form of patients who were discharged alive and willing for follow-up were recruited from a single center. Cases were recruited in all three waves of the COVID-19 pandemic. Each wave was caused by a different variant and could have an impact on the cardiopulmonary sequelae. The absence of PFTs and ECHO parameters prior to COVID-19 illness was lacking for comparison.

Conclusion

In post-COVID-19 patients, there was significant change in the SpO_2/FiO_2 ratio and DLCO from first to second follow-up suggesting improvement in lung function. However, in some of the patients still had less than 80% of predicted DLCO at the second follow-up, indicating persisting lung function abnormalities.

There was a significant improvement in the CTSS from baseline to follow-up in the overall study population, especially in the severe group. Among the radiological findings, consolidation showed marked improvement on sequential follow-up. However, there was no difference in the transthoracic echocardiographic parameters between the mild and severe groups over 1 year indicating the necessity of more sensitive tools for following up cardiac sequelae. We conclude that follow-up for cardiopulmonary sequelae is necessary for those with persisting clinical symptoms after recovery from acute COVID-19 infection.

Acknowledgements We would like to express our thanks to the pulmonary function test laboratory staff and nursing staff involved in the management and follow-up of all the patients.

Authors' contributions Sanjeev Sinha and Lakshmi Prasanna Vaishnavi Kattamuri conceptualized the study and determined the methodology. Lakshmi Prasanna Vaishnavi Kattamuri, Vibhav Sharma, Radhika Sarda, Kunal Sharma, Anuj Ajayababu, Gaurav Gupta, Arvind Kumar and Sanjeev Sinha contributed to participant recruitment and data collection. Surabhi Vyas reviewed the radiological images and cross-verified the radiological findings. Rajeew Narang performed and verified echocardiographic evaluation of the subjects. Shivam Pandey performed the data analysis. Sanjeev Sinha, Surabhi Vyas, Arvind Kumar, Naveet Wig and Rajiv Narang performed roles as overall team leaders for the study. Sanjeev Sinha and Lakshmi Prasanna Vaishnavi Kattamuri accessed, verified the data and wrote the manuscript. All authors read and approved the final draft for the manuscript.

Funding We did not receive funding from any source as part of this study.

Declarations

Conflict of interest No conflict of interest reported by any of the authors.

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