Persistant post-covid 19 interstitial lung disease

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Abstract

The follow-up of the sequelae of patients declared cured of severe COVID lung disease has been organized in many hospitals, in particular at the Mohammed VI University Hospital in Marrakech, Morocco. The objective of this study is to evaluate the clinical, scannographic and respiratory functional sequelae at 3 months according to the severity of the initial damage. It is a monocentric prospective observational study using data from computerized medical records. We organized the 3-month follow-up of patients of the 3rd wave cured of severe COVID: clinical evaluation, lung scans, respiratory function tests (RFTs). This study includes five patients with persistant inflammatory interstitial lung disease (ILD) following SARS-CoV-2 when treated with prednisolone.

Categories: Radiology, Pulmonology
Keywords: "emergency visit" "spirometry" "biologic" "long term follow up", thoracic ct scan, severe acute respiratory syndrome coronavirus-2 (sars-cov-2), fibrotic lung disease, long-term symptoms of covid-19

Introduction

Although there are extensive data regarding the clinical manifestations, case fatality rate, and risk factors associated with mortality in severe coronavirus disease 2019 (COVID-19), the long-term respiratory, functional sequelae in COVID-19 survivors and thoracic CT scan modifications are still poorly understood.

The follow-up of the sequelae of patients cured of severe COVID has been organized in many centers. The population that has been followed up had a 77.6% rate of a comorbidity.

The monitoring was systematically proposed between the third and the sixth month for all patients (ambulatory, hospitalization without or with oxygen therapy, resuscitation). It included clinical, radiological and respiratory reassessment. Respiratory exploration covers plethysmography (Pulmonary function testing) with carbon monoxide diffusion measurement (DLCO) and, if necessary, a chest CT scan. In our article, we summarize the achievements by an illustration of 5 cases of SARS-CoV-2 infected patients having different initial degrees of severity.

The aim of this study is to assess wether the clinical, scannographic and respiratory sequelae at the third and the sixth month according to the severity of the initial damage are similar to those found in the literature.

Case Presentation

The therapeutic conduct consisted of an hospitalization, national therapeutic protocol of covid-19: Azithromycin 500 mg D1 then 250 mg for 6 days, Vit C 1000 mgx2, Zinc 45 mg, Vit D 100.000 IU, Hemostatic treatment 0.4 IU one inj/dr and corticosteroid therapy 40 mg/dr with adjuvant treatment. The follow up of COVID-19 recovered patients consisted on chest CT scan and spirometry.

Case 1 :

35-year-old hospital staff patient hospitalized in an intensive care unit for Covid-19, without
any particular pathological history, presented to the hospital with cough, dyspnea stage II of Modified Medical Research Council and anosmia in a context of fever. The CT scan showed peripheral ground glass opacities compatible with a sars-cov pneumonia with an estimated initial involvement of 25% and a positive PCR test for COVID-19. Follow-up CT scan after 1 month showed a radiological cleaning.(Figure1)

![CT scan](image)

**FIGURE 1: Chest non contrasted CT scan at one month interval**

A : Peripheral ground glass opacities

B : Radiological cleaning

Spirometry, plethysmography, and DLCO measurement were performed 3 months after discharge according to ERS-ATS recommendations. DLCO was measured on a single respiratory cycle to minimize the risk of cross-infection.

The spirometry results of this patient showed flow-volume curve at the limit of normal with small airways involvement and the plethysmography a CPT at 91%; DEMS 25: 57%; FVC: 87%; FEV1: 80%; FEV1/FVC: 79 and DLCO: 74%. (Table 1)

**TABLE 1: Spirometry results of this patient showed flow-volume curve at the limit of normal**

<table>
<thead>
<tr>
<th></th>
<th>FVC</th>
<th>FEV1</th>
<th>FEV1/FVC</th>
<th>DEMS 25</th>
<th>CPT</th>
<th>DLCO</th>
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<tr>
<td></td>
<td>87%</td>
<td>80%</td>
<td>79%</td>
<td>57%</td>
<td>91%</td>
<td>74%</td>
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small airways involvement DEMS 25: 57% and DLCO : 74%.

**Case 2 :**

60-year-old patient, hypertensive patient, hospitalized in intensive care unit unit for 15 days for severe Covid-19 CORADS 5 pneumopathy, put on OLD and transferred to inpatient unit after completion of his treatment, the patient kept a respiratory difficulty at discharge. The initial CT scan showed consolidation marked in inferior lobes associated with a crazy paving
pattern in the left superior lobe control and control CT scan at 3 months showing a tinted sign with diffuse ground glass opacities. (Figure2)

![FIGURE 2: Non contrasted chest CT scans at 3-month interval](image)

A : Consolidation marked in inferior lobes associated with a crazy paving pattern in the left superior lobe
B : Control CT scan at 3 months showing a tinted sign with diffuse ground glass opacities

The spirometry results of this patient showed mild restrictive syndrome : CPT at 78 and DLCO : 70% mild diffusion disorder. (Table 2)

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<tr>
<th>FVC</th>
<th>FEV1</th>
<th>FEV1/FVC</th>
<th>CPT</th>
<th>DLCO</th>
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<tr>
<td>81%</td>
<td>88%</td>
<td>77%</td>
<td>78%</td>
<td>70%</td>
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CPT at 78 and DLCO : 70% mild diffusion disorder.

**Case 3 :**

Mrs G.V, 58 years old, occasional smoker, with high blood pressure under amlodipine 5mg and cardioaspirine 100 mg, stayed 5 days in intensive care for covid pneumopathy confirmed on PCR and evocative aspect of the thoracic CT with an estimated initial involvement of 75%. The patient retained dyspnea after the end of her treatment and OVT after three months on oral corticosteroid therapy with improvement of her clinical symptomatology. The initial CT scan showed 50-75% involvement, condensation area and some foci of organized pneumonia (Figure 4)
FIGURE 4: Non contrasted chest CT scans at 1,3 and 6 months interval of covid 19 pneumonia infection.

marked decrease in the attenuation of GGO, with a slightly increased extension of the GGO (“tinted” sign or “melting sugar” sign, which is defined as an imaging appearance of increased extension of the GGO or consolidation and decreased attenuation).

A Initial CT scan with 50-75% involvement, condensation area and some foci of organized pneumonia.

B a significant reduction in ground glass opacification, with a slightly increased extension of the GGO "tinted sign" or "melting sugar" sign

C CT scan at 3 months showing expiratory trapping

D After 6 months of treatment by prednisolone therapy 0,5 mg/kg/jr with degression scheme, CT scan at 6 months showing architectural distortion with traction bronchiectasis compatible with fibrosis images.

The spirometry results of this patient showed: DEMS 25: 51%; FVC: 66%; FEV1: 59%; FEV1/FVC post: 52%. Results: Moderately severe irreversible TVO after bronchodilator. (Table 3)
TABLE 3: Spirometry showed an obstructive ventilation disorder

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<th>DEM 25</th>
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<tr>
<td></td>
<td>66 %</td>
<td>59 %</td>
<td>52 %</td>
<td>51 %</td>
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Moderately severe irreversible TVO FEV1/FCV : 52% after bronchodilator.

Trans-thoracic ultrasound : LV size and systolic function preserved LVEF 68, no valvulopathies, good DV and no htp

Arterial gasometry:

PH: 7.53 PCO2: 34.1 mmHg Po2: 38mmHg HCO3--: 28.5 Sa02: 78% AA

IR type I severe requiring OLD.

Case 4:

65-year-old patient, who was hospitalized for Covid-19 in the intensive care unit with an initial 75% involvement, who presented one year later with dyspnea, chest pain with suspected pulmonary embolism. After 6 months of treatment by prednisolone therapy 0,5 mg/kg/jr with degression scheme, CT scan at 6 months showing fibrosis-like changes (Figure7)

![CT scan](image)

**FIGURE 8: CT scan without injection at 6 months showing fibrosis-like changes**

A : sub pleural reticulations and ground glass opacities

B : traction bronchiectasis

C : architectural distorsion

D : pneumatoceles related to architectural distortion
The plethysmography: results of this patient showed: tiffeneau 90% CV 49% CPT 57, moderately severe TVR and moderate diffusion disorder: DLCO at 47% (Figure9)

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<tr>
<th>FVC</th>
<th>FEV1</th>
<th>FEV1/FVC</th>
<th>CPT</th>
<th>DLCO</th>
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<tr>
<td>45%</td>
<td>50%</td>
<td>90%</td>
<td>55%</td>
<td>47%</td>
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**Discussion**

The long-term effects of COVID-19 on patients have been explored in recent studies, leading to the description of Long-COVID. Follow-up was provided to all COVID-19 pneumonia patients discharged from major educational hospital. [1]

In our study, the most common symptoms persisting after acute coronavirus were dyspnea, dry cough in 60%, and asthenia in 86% of all patients. Anxiety was noted in most patients. In context, these results are similar to those reported by Dominic L. Sykes. [2]

The presence of symptoms at follow-up was not associated with acute COVID-19 disease severity. The presence of long-term symptoms is common in people with COVID-19. We propose that the Long-COVID phenomenon cannot be directly related to the action of SARS-CoV-2, and we believe that the biopsychosocial impact of COVID-19 may play a large role in its pathogenesis. [3]

Current recommendations say that patients with severe COVID-19 pneumonia should receive a clinical and radiological screening 12 weeks after discharge in order to detect and promptly manage respiratory consequences from the virus. [4]

In the current research, CT follow-up showed persistent abnormalities in 80% of patients, including ground-glass images and pulmonary fibrosis images. Among the scannographic patterns found: melting sugar sign, tinted sign, mosaic appearance with expiratory trapping, mosaic perfusion of vascular and radiological clean-up.

Previous research has described GGO as a common persistent finding, a progressive increase in linear and reticular opacities during illness, and the frequency of consolidation significantly decreasing after the acute phase of the disease. These findings appear to mirror organization, with parenchymal bands possibly indicating OP or atelectasis and reticulation combined with architectural distortion possibly indicating fibrosis progression. [5]

The most common CT pattern (46/74, 62%) was a combination of ground-glass opacity and
reticular pattern, followed by architectural distortion (68/74, 92%) and bronchial dilatation (66/74, 89%) [6].

Respiratory function tests (RFTs) can be divided into those that evaluate pulmonary mechanics, i.e., the mechanisms for moving air in and out of the airway, as well as lung volumes. They included spirometry, plethysmography and DLCO.

As mentioned, the main tests studied and which appear to be useful for the evaluation of patients recovered from COVID-19 are spirometry, DLCO, PC6M and measurement of maximum respiratory pressures;

Pulmonary function tests were performed 6 months after discharge using the Master Screen Body (Jaeger ms-pft analysis unit, W14rzburg, Germany) and according to the American Thoracic Society standards on the following items: forced vital capacity (FVC), forced expiratory volume in one second (FEV1), FEV1/FVC ratio, maximum expiratory flow at 50% FVC (FEF50), maximum expiratory flow at 75% FVC (FEF75), maximum midexpiration flow (MMEF75/25), and diffusing capacity for carbon monoxide (DLCO) corrected for hemoglobin. [7]

In our study, EFR was performed for all the patients with DLCO measurement for 10 of them. There were 19 (79%) restrictive syndromes (all had CT abnormalities), 3 (12.5%) obstructive ventilatory disorders and 5 (20.8%) had CO2 diffusion disorders.

These results are similar to those of Qian Wu and all reported that in a group of 54 patients, 41.5% of the remaining had pulmonary dysfunction. 7.5% had restrictive ventilatory dysfunction (forced vital capacity 80% of predicted value), 18.9% had small airway dysfunction, and 32.1% had pulmonary diffusion impairment (diffusing capacity for carbon monoxide 80% of predicted value). Six of the 54 patients enrolled dropped out of the chest CT tests. [8]

**Conclusions**

Lung dysfunction due to SARS-CoV-2 infection improved over time, but affected patients did not fully recover even after 6 months of discharge. Even after 6 months of recovery, some COVID-19 patients still showed abnormal lung CT findings and impaired lung function, with imaging abnormalities being more frequent, especially in critically ill patients. These observations suggest that COVID-19 patients may experience permanent lung damage after
viral infection and require long-term follow-up.

**Additional Information**

**Disclosures**

**Human subjects:** All authors have confirmed that this study did not involve human participants or tissue. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services info:** All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

**References**


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