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# Post COVID-19 Pulmonary Fibrosis

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#### ABSTRACT

**Introduction:** Pulmonary fibrosis is a progressive, incurable disease with a lower survival rate than most cancers. Due to the rapid increase in deaths following SARS-CoV-2 infection, evidence of a link between viral infection and the development of pulmonary fibrosis in patients with Covid-19 present with degrees of fibrotic change ranging from fibrosis, to disseminated fibrotic disease after severe acute lung injury.

**Objective:** The purpose of the study is the management of patients with post-Covid-19 pulmonary fibrosis, with the aim of early treatment of these complications, so that patients can return to their previous lives.

Materials and Methods: This is an observational study. Data were collected from the medical records of 60 patients hospitalized in "Shefqet Ndroqi" hospital, Tirana, in the internal pathology ward, where post-Covid 19 patients are treated, were reviewed. Their demographic, clinical, physiological, laboratory and imaging data were collected. These patients were followed in the period, March 2022-June 2022.

**Results:** From the 60 patients who were clinically followed for 10 weeks, it was found that at the end of the 10th week, 25.6% of the patients had a significant improvement, 64% of the patients had a slight improvement, and 10.4% of these patients had no improvement. no improvement, compared to their previous condition.

**Conclusion:** The elderly and those with severe symptoms during the acute phase are at greater risk of moderate and severe sequelae, which require multidisciplinary management, according to the patient's condition.

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#### Introduction

Pulmonary fibrosis is a progressive, incurable disease with a lower survival rate than most cancers. Due to the rapid increase in deaths following SARS-CoV-2 infection, evidence of a link between viral infection and the development of pulmonary fibrosis in patients with Covid-19 present with degrees of fibrotic change ranging from fibrosis, to disseminated fibrotic disease after severe acute lung injury [1]. This set of symptoms, originally called Long-Covid, is now called PASC (Post-Acute Consequences of Covid-19, Post-Acute Consequences of Covid-19). One of the main differential diagnoses on CT due to infection by Covid-19 is a pattern of non-specific interstitial pneumonia, both in the cellular and fibrotic phases of the disease [2]. The term fibrosis is often used to include post-Covid findings, such as parenchymal and subpleural bands that may represent only areas of focal atelectasis, abnormalities and reticular thickening, rather than diffuse fibrosis [3]. In post-Covid-19 patients, cardiac complications are observed in response to the release of cytokines secondary to systemic inflammation, Macrophages play an important role in the process of inflammation and regeneration [4]. In cardiac tissue samples from patients with Covid-19, increased phagocytosis and the presence of cellular antigens on T lymphocytes have been observed

[5]. Quantitative study of the cellular immune response, done in samples from patients with this disease, shows a significant increase in CD68+ cells [6]. Beyond lung damage, we have systemic involvement, with central nervous system involvement and clinical manifestations, such as cognitive impairment [7]. Among the manifestations associated with prolonged Covid-19 syndrome are fatigue, weight loss, headache and arterial hypotension [8]. Other conditions that may persist after recovery from COVID-19 may include: kidney damage, liver lesions, endocrine disorders, diabetes, kidney failure), gastrointestinal symptoms (diarrhea, weight loss, malnutrition), dermatological (alopecia, lesions of the skin, decubitus ulcers), and sleep disorders [9].

## **Materials and Methods**

The medical records of 60 patients, hospitalized at the "Shefqet Ndroqi" hospital, in the internal pathology ward, where post-Covid 19 patients were treated, were observed. Their demographic, clinical, physiological, laboratory and imaging data were collected. Of the patients who were observed, 6 patients were on respirators, 14 patients were on 3 sources of oxygen, 20 patients were on 2 sources of oxygen, 8 patients were on 1 source of oxygen and 12 patients were without oxygen. The participants in the study are patients who are hospitalized to be treated for post-Covid 19 complications.

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Statistical analysis. The data were entered into Excel and then analyzed statistically, using the Ch Square program. The statistical analysis of the data is presented in the form of graphs. The variables are presented in %, deriving the results, based on the data obtained.

Results
Tabel 1: The Progress of these Patients who were followed up

Patients who were followed clinically	Their progress after 2 weeks of hospital stay	Their progress after 3 weeks of hospital stay	Their progress after 4 weeks of hospital stay	Their progress after 5 weeks of hospital stay
6 patients with ventilators	4- of them switched to 3 O2 sources 2- in endotracheal intubation. Ferritin, PCR, D-Dimer, Fibrinogen, glucose, are in high values. Altered hematopoietic function and elevated cytokines.	4 - patients with 2 sources of O2, with cardiac complications - arterial fibrillation - heart failure. 2 patients-endotracheal intubation-hemoptysisloss of life.	4- patients with 1 O2 source, with pulse disorders, HTA, dyspnea, respiratory insufficiency of the 1st degree.	4- patients with 5 liters of O2, with pulse disorders, HTA, dyspnea, respiratory insufficiency of the 1st degree. Ferritin, CRP, D-Dimer, Fibrinogen, glucose, are in high values. With, Alteration of hematopoietic function: of blood counts and erythropoietin, high cytokines. The laboratory picture improved, compared to their condition in the first week, but the test values continued to be high.
14 patients with 3 O2 sources	10 patients with 2 O2 sources, 4 - with 3 O2 sources Ferritin, PCR, D-Dimer, Fibrinogen, glucose, creatinine, are in high values, with changes in hematopoietic function and high cytokines.	14 patients with 2 O2 sources	8 - patients with 1 O2 source, 6 - continued with 2 O2 sources.	8 patients with 1 O2 source, 2 - with 2 O2 sources. Ferritin, CRP, D-Dimer, Fibrinogen, glucose, creatinine, are in high values, with changes in hematopoietic function and high cytokines. The laboratory picture improved, compared to their condition in the first week, but the values of laboratory analyzes continued to be high.
20 patients with 2 O2 sources	18 - patients with 2 O2 sources, 2 - with 1 O2 source. Ferritin, PCR, D-Dimer, Fibrinogen, glucose, creatinine, are in high values. With changes in hematopoietic function and high cytokines.	16 patients with 2 O2 sources, 4-with pulmonary complications-respiratory insufficiency grade 2-persistent coughhemoptysis-endotracheal intubation.	14 patients with 2 O2 sources, with pulse disorders and HTA. Ferritin, PCR, D-Dimer, Fibrinogen, glucose, creatinine, are in high values. With changes in hematopoietic function.	12 of them continued with 2 sources of O2. 8 passed with 1 O2 source. The laboratory picture improved, compared to their condition in the first week, but the test values continued to be high.
8- patients with 1 O2 source	8 - patients with 1 O2 source, 4 of them with persistent cough, dyspnea, HTA. Ferritin, PCR, D-Dimer, Fibrinogen, glucose, creatinine, are in high values. With changes in hematopoietic function.	4 -patients with 5 liters of O2, and 4- with 3 liters of O2.	4- with 3 liters of O2 4-with 1 liter of O2.	4 with 1 liter of O2, - home oxygen therapy. 4 without O2. PCR, D-Dimer, Fibrinogen, glucose, creatinine are in high values.

According to the data in the table, ventilator patients and those with 3 sources of oxygen present greater pulmonary damage and cardiovascular complications such as arterial fibrillation and heart failure are more frequent in these patients, compared to others. In addition, it was observed that even patients with 2 sources of oxygen and those with 1 source of oxygen can suffer complications such as sudden hemoptysis, especially when the patients exert themselves a lot and from the cough that can be dry, characteristic of fibrosis, or even with secretions, especially in patients with overlapping bacterial infections.

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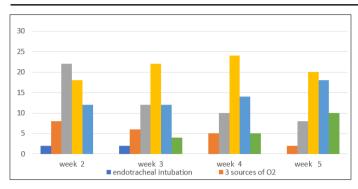


Figure 1: Oxygen needs and Related Complications

This chart presents a general assessment of these patients included in the study, assessing their oxygenation needs and related complications.

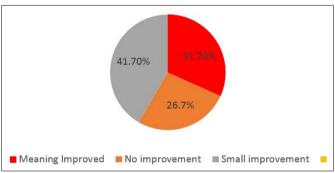


Figure 2: Improvement of Patients

According to the above data, at the end of the 5th week, 31.7% of these patients had a significant improvement, 41.7% of these patients had little improvement and 26.7% of these patients had no improvement, in the report with their previous state.

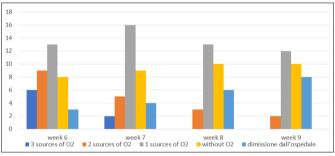


Figure 3: Sources of O2

This figure shows the patients' progress over the next 5 weeks and their gradual improvement in reducing oxygen needs. At the end of the 5th week, of the 60 patients who were enrolled in the study, 2 patients died in the 2nd week, 19 patients were discharged from the hospital, (exactly 10 of them no longer needed oxygen and 9 with oxygen therapy in home). 39 patients who were still hospitalized at the end of the 5th week, we continued to follow clinically for the next 5 weeks.



Figure 4: Improvement during the Weeks

At the end of the 10th week, we observe that 25.6% of patients have had a significant improvement, 64% of patients have had small improvements and 10.4% of these patients have not had any improvement, compared to their previous condition.

#### Discussion

According to our study, there is a direct relationship with the increased oxygen needs of these patients and the complications they present. This is confirmed in other studies, which also show the importance of timely management of these complications, according to it is said that: cardiac complications are more frequent in patients with respiratory and with 3 sources of oxygen [10]. Even according to it turns out that patients with ventilators and those with 3 sources of oxygen present greater pulmonary damage and cardiovascular complications such as arterial fibrillation and heart failure are more frequent in these patients, compared to others [11]. In our study, it was observed that even patients with 2 oxygen sources and those with 1 oxygen source may suffer complications such as sudden hemoptysis. These occur especially when patients are very stressed by a cough that can be dry, characteristic of fibrosis, or even with secretions, especially in patients with overlapping bacterial infections, this is also stated in the study [10]. Numerous studies have proven that the development of pulmonary fibrosis occurs as a result of the "cytokine storm" from the immune system's response against the SARS-CoV-2 virus. In particular, the most frequent cytokines are IL-1 $\beta$ , IL-6, IL-7, IL-8, tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) and TGF- $\beta$ , a cytokine considered crucial in the initiation and progression of fibrosis [12]. In the study of it is said that in this case it is not so much about "pulmonary fibrosis" as about "fibrotic tissue" after pneumonia, according to the authors [13]. The essential difference between them lies in the fact that, while pulmonary fibrosis, whether idiopathic or non-idiopathic, represents an interstitial pathology, which often leads to a progressive deterioration of the patient's respiratory condition, according to the study [14]. Based on other studies [13]. scarred fibrotic tissue, on the other hand, represents simple lung scarring, often non-evolving and therefore without the possibility of causing a progressive damage to pulmonary.

### Conclusion

To reduce the risk of developing PCPF (Pulmonary Fibrosis post covid), it would be advisable to identify patients with the most severe respiratory symptoms, in order to continue with effective drug therapy (minimizing the factors implicated in persistent lung injury and prolonged inflammatory response [15]. Thus, avoiding a worsening of the clinical condition and consequently the development of pulmonary fibrosis [16-20].

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