
PULMONARY FUNCTION EXAMINATION IN PATIENTS AFTER SEVERE COVID-19 PNEUMONIA

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Abstract: Covid-19 virus (SARS-CoV-2) came unexpectedly to the world population and affected more than 644 million people (confirmed cases) as of November 24th, 2022. Bulgaria is also among the affected countries with nearly 1,300,000 people of which 38,000 have resulted in death. In the coming years, Covid-19 is expected to have a major impact on the physical, cognitive, mental and social health of those affected, even with a mild form of the disease. A large proportion of patients develop Covid-19-associated pneumonia, which is usually bilateral, interstitial pneumonia, characterized with typical "ground-glass" appearance on CT scan. Autopsies performed on patients who died of severe Covid-19 infection showed the presence of diffuse alveolar damage (present in ARDS), but with a significant prevalence of thrombus formation in the pulmonary capillaries. A significant number of hospitalized patients develop severe Covid-19 pneumonia (evidence of pneumonia, plus one of the following: respiratory rate >30 breaths/min; severe distress syndrome; or saturation (SpO₂) ≤93% at rest). They have the need for supplemental oxygen. All these data raise interest about the long-term consequences of this disease.

The aim of the study is to determine the changes in lung function indicators in patients who experienced a severe form of Covid-19 pneumonia.

A total of 35 patients between the ages of 44 and 67, examined between the second and sixth month of the acute illness, took part in the study. All patients were hospitalized with severe Covid-19 pneumonia without evidence of previous lung disease. A low saturation value (SpO₂<90%) was reported during the hospital stay and a normal saturation at discharge. In this regard, we performed blood gas analysis of the patients, which showed normal pO₂ values.

An objective assessment of lung function can be given by tests such as spirometry and lung diffusion capacity. The largest percentage of patients had disturbances related to damage in the diffusion capacity of the lung. The indicator that undergoes the most serious change after the Covid-19 infection is DL_{co}. It measures the ability of the lungs to transport gas from inhaled air to the erythrocytes in the pulmonary capillaries. The performed spirometry of these patients did not show significant changes of restrictive or obstructive type. A subset of patients underwent a six-minute walk test (6MWT), in which slight desaturation was observed with rapid recovery.

In conclusion, the diffusion capacity of the lungs is severely altered after severe infection with Covid-19 and may serve as an indicator for pulmonary parenchymal recovery.

Keywords: Covid-19, Lung function, Diffusion capacity

1. INTRODUCTION

Covid-19 virus (SARS-CoV-2) came unexpectedly to the world population and affected more than 644 million people (confirmed cases) as of November 24th, 2022. Bulgaria is also among the affected countries with nearly 1,300,000 people of which 38,000 have resulted in death. In the coming years, Covid-19 is expected to have a major impact on the physical, cognitive, mental and social health of those affected, even with a mild form of the disease. A large proportion of patients develop Covid-19-associated pneumonia, which is usually bilateral, interstitial pneumonia, characterized with typical "ground-glass" appearance on CT scan. (1,2) Autopsies performed on patients who died of severe Covid-19 infection showed the presence of diffuse alveolar damage (present in ARDS), but with a significant prevalence of thrombus formation in the pulmonary capillaries. A significant number of hospitalized patients develop severe Covid-19 pneumonia which requires supplemental oxygen. (3) All these data raise interest about the long-term consequences of this disease.

Although there are studies that demonstrate the changes in lung function and in CT in the short term, data on the duration of these changes are scarce. An objective assessment of lung function can be obtained by examinations such as spirometry and diffusion capacity. The disorders in the largest percentage are related to damage in the diffusion capacity, followed by restrictive disorders and in the smallest percentage - obstructive disorders. (4) The British Thoracic Society recommends pulmonary function assessment three months after discharge in patients who

survived Covid-19 pneumonia with persistent respiratory symptoms and Chest X-Ray abnormalities. (5) Hence the need to follow up patients who have survived Covid-19 in order to receive prompt treatment and rehabilitation.

2. METHODS

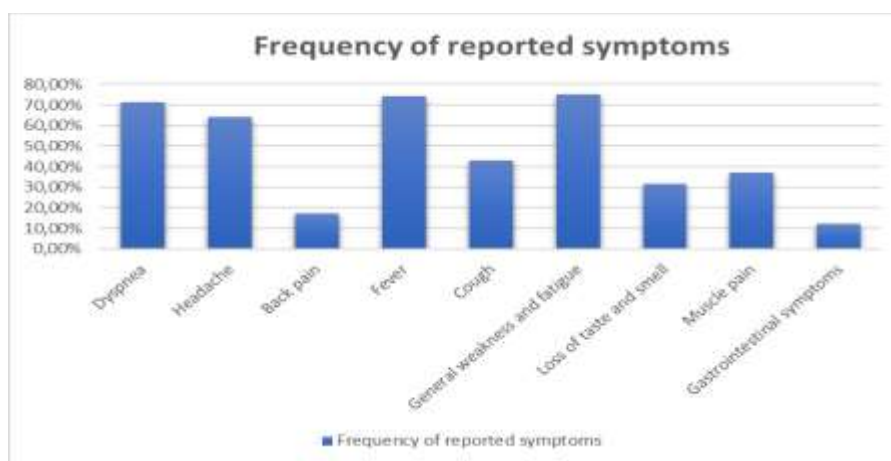
The present study included patients between 44 and 67 years of age who were admitted to St. George Hospital, Plovdiv, Bulgaria between November 2021 and May 2022. All procedures used were approved by the Institutional Ethics Committee at the Medical University – Plovdiv. All patients had evidence of a positive RT-PCR test for Covid-19, the presence of pneumonia on chest X-Ray, and were classified with severe form of the disease (evidence of pneumonia, plus one of the following: respiratory rate >30 breaths/min; severe distress syndrome; or saturation (SpO₂) ≤93% at rest).

Patients underwent the following examinations between the second and sixth month after discharge: pulmonary function tests (spirometry and lung diffusion capacity), blood gas analysis, and 6MWT (six minute walking test). Anthropometric data such as height, weight and BMI were analyzed. Pulmonary function testing was performed in the department of Pathophysiology at the Medical University - Plovdiv with "Vyntus™ BODY Plethysmograph" (Vyair Medical) diagnostic device. The gas mixture used for the diffusion capacity evaluation contained 0.3% CO, 0.3% CH₄, 0.3% C₂H₂, 21% O₂, N₂-rest. The following indicators were reported: DLco, TLC, slow vital capacity (VC), FVC, FEV₁, and FEV₁/FVC ratio. An ABL800 FLEX blood gas analyzer (Radiometer) was used for blood gas analysis, and hemoglobin and PaO₂ values were recorded.

The 6MWT was performed in a 30-meter corridor with a portable pulse oximeter (Nonin, Pulse Oximeter 2500A) and the following parameters were recorded: SpO₂, heart rate, 6-min distance walked, and the modified Borg dyspnea scale score.

3. RESULTS

35 patients participated in the study, out of a total of 100 invited (withdrawn from the study due to thromboembolic complications, disability or unwillingness). Their average age was 56.20 years, and 54.3% of them were male. The most frequently observed comorbidities were arterial hypertension (20 patients, 57%), diabetes (12%), cerebrovascular disease (12%). 71.4% of the patients were non-smokers and the mean BMI was 34.06. Inclusion criteria for participation were: severe Covid-19 pneumonia (data of pneumonia, plus one of the following: respiratory rate >30 breaths/min; severe distress syndrome; or saturation (SpO₂) ≤93% at rest), positive RT-PCR test for Covid-19, presence of pneumonia on X-ray and need for oxygen administration during hospitalization. Patients most often report the following symptoms: shortness of breath and heavy breathing (71.4%), fever (74.2%), general weakness and fatigue (75%), headache (64.2%), cough (42,8%), loss of taste and smell (31.4%), muscle pain (37.1%), back pain (17%), gastrointestinal complaints (12%). Dyspnea occurs on average on the 6.6th day from the initial symptoms, and part of the patients (28.6%) do not have a subjective feeling of shortness of breath, despite the low saturation measured with a pulse oximeter and the need for oxygen administration. (6,7)



The entire group of patients was overweight (9 patients) and obese (26 patients, 74.3%). There was no significant difference between the mean SaO₂ of those who were overweight (78.7%) and those who were obese (78.8%). The obese patients showed greater variability in saturation values ranging from 50% to 91%.

All patients underwent spirometry and lung diffusion capacity testing. One patient was unable to perform the spirometry maneuver due to psychiatric disorder (schizophrenia). Of the remaining 34 patients, 9 had VC<80% (26.4%), FVC<80% had 7 patients (20.5%), FEV1<80% - 8 patients (23.5%).

The most significant deviations were observed in the diffusion capacity of the patients with the main parameter - DLco. Out of 35 patients, one did not perform the maneuver correctly. Decreased DLco values <80% were observed in 25 patients (73.5%). Subjectively, after submaximal effort, patients scored a mean value on the modified Borg scale of 2.61 (SD of 2.44), corresponding to mild to moderate dyspnea. However 25.7% of patients still had severe dyspnea after exercise (Modified Borg Score >4). No significant correlation was found between DLco values and Borg scale score.

Table 1 Data summary of the patients divided by gender

Parameters	Studied group of patients	
	Males n=19	Females n=16
Age (years)	53.9±8.18	58.8±6.59
Height (centimeters)	176.5±5.57	165.5±6.16
BMI (kg/m ²)	33.1±6.16	35.1±8.28
sO ₂ after discharge (%)	96.1±1.72	94.1±2.79
sO ₂ at rest (on the 3th month after discharge) (%)	95.0±1.68	95.7±1.69
FVC (L)	3.82±0.76	2.67±0.74
FEV ₁ (L)	3.15±0.67	2.21±0.60
MEF ₅₀ (L/s)	4.66±1.85	3.11±1.03
DL _{co}	7.8±2.59	5.39±2.18
DL _{co} %predicted	75.3±19.8	66.7±20.8
KCO	1.40±0.34	1.34±0.28
KCO %predicted	97.7±23.2	88.1±19.0

The lowest sO₂ values during the hospital stay were 78.0±11.9% and at discharge 95.3±1.7%. A 6-minute walking test (6MWD) was performed to assess functional capacity and dyspnea in these patients. The average values of this parameter at rest were 95.0±2.5%, and after 6MWD sO₂ decreased to 89.5±3.3%, without significant desaturation and with subsequent rapid recovery.

However, the blood gas analysis of 30 patients shows no changes in the pH and PCO₂ but there was a significant decrease in the PaO₂ (below 75mmHg) in 50% them.

4. DISCUSSION

The SARS-CoV-2 virus has caused much discussion about the course and consequences of this disease. A large number of studies have proven the importance of DLco as an parameter determining lung function after surviving Covid-19 infection. According to a retrospective multi-center cohort study in China, 17% of patients who recovered from SARS, regardless of disease severity, had abnormalities in DLco and CT scan of the lungs 6 months after recovery. (8) Another SARS study of a total of 97 patients that assessed lung function at 3, 6, and 12th month after symptom onset concluded that 23% of the survivors still had a significant decrease in DLco 1 year after symptom onset. (9) Our study confirms the results of all global studies and shows a significant reduction in DLco in the first months after discharge in patients who survived severe Covid-19 pneumonia. The percentage of abnormalities in spirometry is lower (26.4%). Other studies and meta-analyses have reported similar results. R. Torres-Castro et al. (2021) in a meta-analysis found that the main lung function disorders are reduced diffusion capacity, restrictive and obstructive ventilatory disorders, with a significant prevalence of diffusion capacity disorders - 66% of patients after severe infection (4,10,11). In comparison, our study reported a decrease in DLco in 73.5% of patients.

In the present study, no significant correlation was reported between DLco reduction and the modified Borg scale score, but this may be due to the small number of patients included in the study. (12) However, a large percentage of patients still had evidence of severe dyspnea after submaximal exercise (25,7%). This is in support of Fabio Anastasio's study, which evaluated the relationship between the degree of lung damage, lung function parameters and residual symptoms. (13)

The relationship between obesity and the severe course of Covid-19 pneumonia is interesting and important. 74.3% of patients included in our study had a BMI > 30, which shows the significance of this risk factor for the severity of the infection and mortality. This is also confirmed by a meta-analysis from June 3, 2022. including 3,140,413

patients from 167 studies. Obese patients were 1.5 times more likely to be seriously ill and 1.09 times more likely to die than non-obese individuals. (6, 14, 15, 16)

The comorbidities are also a significant factor in the development of Covid-19 infection, with arterial hypertension and diabetes being the most significant. (15, 16)

Our patients required oxygen administration during hospitalization due to the severity of the disease and sO₂ below the acceptable minimum (mean values in the range of 78.0±11.9%). At discharge, however, all patients recovered normal sO₂ values, which ranged between 95.0±2.5%. In the follow-up of these patients, subsequent measurements of sO₂ at rest were within the normal range but after the 6-minute walking test (6MWD), a decrease was reported, that quickly recovered to normal. However, when examining PaO₂ through blood gas analysis, a significant decrease in this parameter (values below 75 mmHg) was observed in 15 patients (50%) out of 30 examined.

A publication by Antoniou KM et al. (2022) emphasizes the recommendations based on current sources that encourage respiratory function testing to be done up to 3 months after severe COVID-19. The testing should include static and dynamic pulmonary function parameters, expiratory debits and lung diffusion capacity. DLco has the main role for assessing long-term effects on the respiratory system. (17)

Pulmonary function parameters are a sensitive predictor of patients' long-term status, but should always be considered with caution due to the possibility of comorbidities or damaging effects caused by smoking and atmospheric pollution.

5. CONCLUSION

In conclusion, saturation is a valid indicator for oxygen administration during the acute stage of severe Covid-19 pneumonia, but at follow-up its role is variable. From the lung function tests, the most significant are the dynamics of the lung diffusion capacity parameters, which reveals their potential as a predictor at follow-up.

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