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An assessment of post–COVID-19 infection pulmonary functions in healthcare professionals

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Key Words: Pulmonary function tests Diffusing capacity of the lungs for carbon monoxide Healthcare professional COVID-19 infection 6-minute walk test

ABSTRACT

Background: The medium- and long-term effects of COVID-19 infection on pulmonary function are still unknown. The present study aimed to investigate the pulmonary functions in healthcare professionals who had persistent complaints after contracting COVID-19 and returning to work.

Methods: The study included COVID-19-infected healthcare professionals from the Duzce University Medical Faculty Hospital who volunteered to participate. Medical histories, medical records, pulmonary function tests, the diffusing capacity of the lungs for carbon monoxide (DLCO) test, and the 6-minute walk test (6MW) were used to collect data from all participants.

Results: The study included 53 healthcare professionals, with an average age of 38 ± 10 years (min: 24 years and max: 71 years), including 29 female (54.7%) and 24 male (45.3%) participants. Of the participants, 22.6% were smokers, 35.8% (19 individuals) had comorbidities, and 17% (9 individuals) were hospitalized. The mean length of stay was 9 ± 4 days (mean ± standard deviation). The most prevalent symptoms were weakness (88.7%), muscle aches (67.9%), inability to smell/taste (60.4%), headache (54.7%), fever (45.3%), cough (41.5%), and shortness of breath (37.7%). The mean time to return to work after a positive polymerase chain reaction (PCR) test for COVID-19 was 18 ± 13 days. The average time among post-disease pulmonary function tests, 6MW, and DLCO tests was 89 ± 36 days (min: 15 and max: 205). The DLCO level decreased in 39.6% (21) of the participants. Female participants had a significantly higher rate of decreased DLCO levels than male participants (25% vs. 55.2%, P = .026). DLCO levels were significantly higher in participants with long-term persistent complaints (P = .043). The later the time to return to work, the lower the DLCO value (r = −.290 and P = .035). The 6MW distance was positively correlated with hemoglobin and lymphocyte levels at the time of the disease onset and negatively correlated with D-dimer levels. The most prevalent symptoms during the control visits were shortness of breath/effort dyspnea (24.6%), weakness (9.5%), and muscle aches (7.6%).

Conclusion: Significant persistent complaints (47.2%) and low DLCO levels (39.6%) were observed in healthcare professionals during control visits at a mean time of 3 months after the COVID-19 infection. Symptoms and spirometry measurements, including DLCO, may be helpful in the follow-up of healthcare professionals who contracted COVID-19. Further comprehensive studies with long-term follow-up periods are required.

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INTRODUCTION

The coronavirus disease 2019 (COVID-19) is caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which first appeared in Wuhan, China in December 2019, and was officially declared a global pandemic by the World Health Organization on March 11, 2020.1 As of 13 March 2022, over 455 million confirmed cases and over 6 million deaths have been reported globally (https://www.who.int/publications/m/item/weekly-epidemiological-update-on-covid-19—15-march-2022).
The COVID-19 pandemic adversely affected health care professionals, inflicting a heavy burden on the health care systems of countries. In particular, health care professionals at epidemic centers were exposed to an elevated infection risk. Health care professionals were at risk from patient contact and affected by community-induced transmission. In the absence of their colleagues who were sick or were quarantined during the pandemic, health care workers had to work extra shifts to sustain the health care system. They also had to quickly adapt to a various spectrum of medical interventions, as they were required to work outside of their medical specialty. In the meantime, health care workers had to adapt to newly published guidelines during the pandemic to treat patients diagnosed with COVID-19. They also had to make unprecedented clinical and ethical decisions determining their patients’ mortality.

During the COVID-19 pandemic, frontline health care workers are more likely to encounter COVID-19 infection at the time of their return to work. The fear of being re-infected with the virus and re-infecting family members continues to affect health care workers who return to work after recovering from the infection. Knowing the long-term effects of COVID-19 on health care workers, who will be back at work and continue to be on the front line during the pandemic, is important for the healthy management of the pandemic. For this reason, various countries publish guidelines that determine the return to work criteria of health care workers and update these guidelines according to the course of the pandemic. For example, the guideline published by the British Columbia Ministry of Health for health care professionals to return to work after COVID-19 infection (http://www.bccdc.ca/Health-Professionals-Site/Documents/COVID19_HCW_ReturnToWorkGuidance.pdf) summarized the criteria that must be met for a health care worker to return to work. If the health care worker has mild respiratory symptoms after the isolation period is completed, it was suggested that the decision to return to work should be made on a case-by-case basis through a risk assessment by the individual health care worker and their leader. In general, it has been recommended that returning to work while being still symptomatic should be considered an exception, not the rule.

The long-term outcomes of people infected with SARS-CoV-2 have not yet been fully understood. Whilst a series of longitudinal investigations are underway to increase the knowledge and understanding, reports highlight that sustained transmission and emerging variants continue to cause global challenges to health care providers. Currently, it is estimated that of those infected with COVID-19 in the UK, one in ten people will experience prolonged symptoms lasting months to years including fatigue, breathlessness, neurological deconditioning. In addition to these symptoms; health care workers may continue to experience numerous symptoms (such as severe fatigue, shortness of breath, anxiety, depression, pain, persistent cough, difficulty swallowing, change in voice, incontinence, diarrhea, and dysphagia). This broad spectrum of symptoms, covering the recovery period after COVID-19 infection, shows that COVID-19 infection is not just a respiratory disorder, but a multisystem disease, therefore, the decision to return to work should be evaluated multidisciplinary.

The present study aimed to investigate the pulmonary functions of health care professionals with persistent complaints who contracted COVID-19 and returned to work using pulmonary function tests, the 6-minute walk test (6MWT), and the diffusing capacity of the lungs for carbon monoxide (DLCO) test.

METHODS

Study population

Health care professionals from the Düzce University Medical Faculty Hospital who contracted COVID-19 and volunteered to participate in the study between August 2020 and April 2021 were included in the study. Medical histories, medical records, pulmonary function tests, the DLCO test, and the 6MWT were used to collect data from all participants. The characteristics of the study population shown in Figure 1.

The permission was obtained from our institutional ethics committee for the use of patient data for publication purposes (Date of Approval: 15.03.2021; Reference number/Protocol No:2021/71).

Assessments

The tests were performed by using a standard spirometer (Care Fusion Germany 234 GmbH/ SentrySuite Software version 2.7) according to American Thoracic Society criteria, while the patients were at rest and seated in the upright position. A minimum of 3 satisfactory forced expiratory manoeuvres was required for each subject. Forced vital capacity (FVC), forced expiratory volume in the first
second (FEV1), FEV1/FVC (%) and Forced expiratory flow between 25% and 75% of vital capacity, DLCO were measured. Results were expressed as absolute values and as percentages of predictive values.

**Statistical analysis**

Data were entered into the SPSS 21.0 Program (Statistical Package for Social Sciences for Windows). For the paired comparison numerical data, the Student’s t-test was used. Chi square was used in the comparison of categorical data. Pearson correlation test was used for correlation analysis. A P value less than 0.05 was considered to be the statistically significant.

**RESULTS**

**Demographic and clinical characteristics**

A total of 53 health care professionals, 29 female (54.7%) and 24 male (45.3%), were included in the study. Of the participants, 22% were smokers and 35.8% (19 patients) had comorbidities. The most prevalent symptoms were weakness (88.7%), muscle aches (67.9%), inability to smell/taste (60.4%), headache (54.7%), fever (45.3%), cough (41.5%), and shortness of breath (37.7%). The demographic and clinical characteristics of the health care professionals are shown in Table 1.

Of the participants, 14 (26.4%) were classified as moderate/severe and 39 (73.6%) as mild cases, and 9 (17%) were hospitalized. Decreased DLCO levels (<80%) were reported in 21 participants (39.6%). The most common treatments included favipiravir (92.5%), low-molecular-weight heparin (LMWH) (66%), antibiotic therapy (41.5%), and corticosteroids (18.9%). During the control visits, 47.2% of the participants had persistent symptoms. The most common persistent symptoms were shortness of breath/effort dyspnea (25%), weakness (88.7%), muscle aches (67.9%), inability to breathe/effort dyspnea (24.6%), weakness (9.5%), and muscle aches (7.5%) (Table 2).

The mean length of stay of the 9 hospitalized patients was 9 ± 4 days (mean ± standard deviation). The mean age of the participants was 38 ± 10 years (min: 24 years and max: 71 years). The average time among post-diagnosis pulmonary function, 6MW, and DLCO tests was 89 ± 36 days (min: 15 days and max: 205 days). The mean time to return to work after a positive PCR test result for COVID-19 was 18 ± 13 days (Table 3). The health care professionals’ pulmonary function test and 6MWT results are shown in Table 4.

**Table 1**

Demographic and clinical characteristics of health care professionals who contracted COVID-19

| Gender       | Male         | 24 (45.3) |
|--------------|--------------|-----------|
| Female       | 29 (54.7)    |
| Smoker       | 12 (22.6)    |
| Comorbidity  | 19 (35.8)    |
| Comorbidities| None         | 42 (79.2) |
|              | Hypertension | 4 (7.5)   |
|              | Asthma       | 4 (7.5)   |
|              | Other        | 11 (20.8) |
| Symptoms     | Weakness     | 47 (88.7) |
|              | Muscle pain  | 36 (67.9) |
|              | Odor-taste loss | 59 (60.4) |
|              | Headache     | 29 (54.7) |
|              | Fever        | 24 (45.3) |
|              | Cough        | 22 (41.5) |
|              | Dyspnea      | 20 (37.7) |
|              | Sore throat  | 10 (18.9) |
|              | Diarrhea     | 9 (17.0)  |

**Table 2**

Disease severity, treatment, prolonged symptoms, and DLCO values of the health care professionals who had COVID-19

| COVID-19 disease severity | N (%)      |
|---------------------------|------------|
| Mild                      | 39 (73.6)  |
| Moderate/Severe           | 14 (26.4)  |
| Treatment                 |            |
| Outpatient                | 44 (83.0)  |
| Inpatient                 | 9 (17.0)   |
| Treatment Features        |            |
| Favipiravir               | 49 (92.5)  |
| LMWH                      | 35 (66.0)  |
| Antibiotic                | 22 (41.5)  |
| Steroid therapy           | 10 (18.9)  |
| Oxygen support            | 7 (13.2)   |
| Tocilizumab               | 3 (5.7)    |
| NIMV                      | 2 (3.8)    |
| Prolonged ongoing symptoms| 25 (47.2)  |
| Dyspnea                   | 13 (24.6)  |
| Weakness                  | 5 (9.5)    |
| Muscle pains              | 4 (7.5)    |
| Other                     | 3 (5.7)    |
| DLCO (low<80)             | 21 (39.6)  |

**Table 3**

Age laboratory parameters and time to return to work in health care professionals who had COVID-19

| Mean ± SD (min-max) |        |
|---------------------|--------|
| Age (year)          | 38±10  (24-71) |
| Hospitalization (day)| 9±4 (3-18) |
| Ferritin (ng/mL)    | 204±312 (8-1789) |
| D-dimer (µg/mL)     | 0.30±0.30 (0.08-2.05) |
| CRP (mg/dL)         | 1.66±2.93 (0.06-12.40) |
| SPO2 (%)            | 96±1 (90-98) |
| LDH (IU/L)          | 215±89 (118-471) |
| Hemoglobin (g/dL)   | 13.7±1.4 (8.4-16.8) |
| Leukocyte (10^3/µL) | 6.525±1.985 (2300-10900) |
| Lymphocyte (10^3/µL) | 1.850±0.690 (0.540-3.23) |
| Control time (day)  | 89±35 (15-205) |
| Back to work (day)  | 18±13 (10-60) |

**Table 4**

Pulmonary function tests and 6-minute walk test of health care professionals who had COVID-19

| Spirometry            |                           |
|-----------------------|----------------------------|
| FVC (%)               | 102±13 (73-130)            |
| FEV1 (%)              | 99±12 (74-129)             |
| FEV1/FVC              | 81±5 (63-92)               |
| FEF25-75 (%)          | 88±20 (40-144)             |
| DLCO (%)              | 82.7±13.7 (52.0-116.0)     |

6 minutes walking test

| Walking distance (m) | 538±57 (378-648) |
|----------------------|-----------------|
| Pre-oxygen Saturation (%) | 97±4 (91-98) |
| Post-oxygen Saturation (%) | 97±2 (87-99) |
| Pre-systolic blood pressure (mmHg) | 110±10 (90-140) |
| Post-systolic blood pressure (mmHg) | 115±20 (80-160) |
| Pre-pulse rate/min | 82±11 (62-110) |
| Post-pulse rate/min | 115±16 (85-160) |

± SD = standard deviation; min-max = minimum-maximum; FVC = Forced vital capacity; FEV1 = Forced expiratory volume in the first second; FEF25-75 = Forced expiratory flow between 25% and 75% of vital capacity.
The rate of decreased DLCO was significantly higher in women than in men (25% vs. 55.2%, \( P = .026 \)). There was no significant difference among the participants in terms of smoking status, comorbidities, severity of disease, and treatment location (Table 5).

There was no significant difference between the participants with and without decreased DLCO levels at the control visit in terms of the initial symptoms, including weakness, muscle pain, loss of smell/taste, headache, fever, cough, dyspnea, and sore throat. Although participants with shortness of breath had a higher incidence of low DLCO levels than those without this symptom, the difference was not statistically significant (35% vs. 45%, \( P = .156 \)). The proportion of participants who reported diarrhea and had lower DLCO levels was significantly higher than that of those who did not report diarrhea (77.8% vs. 22.2%, \( P = .025 \)) (Table 6).

A comparison of the initial symptoms of the cases with and without decreased DLCO levels at the control visit (Table 5).

A comparison of cases with and without lower DLCO levels at the control visit (Table 6).

A comparison of the laboratory parameters revealed no significant difference between the participants with and without lower DLCO levels at the control visit (Table 7).

A comparison of the treatment parameters revealed no significant difference between the participants with and without lower DLCO levels at the control visit (Table 8).

A comparison of laboratory and pulmonary function test parameters of the cases with and without decreased DLCO levels at the control visit (Table 8).
A comparison of the time to return to work and DLCO values indicated that the later the return to work, the lower the DLCO value ($r = -0.290, P = .035$) (Fig 2).

The 6MWT distance was positive correlated with hemoglobin ($r = 0.299, P = .039$) and lymphocyte ($r = 0.352, P = .014$) levels when patients tested positive for SARS-CoV-2 but negatively correlated with D-dimer levels ($r = -0.391, P = .010$) (Fig 3).

**DISCUSSION**

Significant persistent complaints (47.2%) in health care professionals at control visits at a mean period of 3 months after COVID-19 infection included shortness of breath/effort dyspnea (24.6%), weakness (9.5%), and muscle aches (7.6%). Decreased DLCO levels were observed in 40% of the cases. The FEF$_{25\%-75\%}$ and FEV1 (%) levels were significantly lower in participants with decreased DLCO levels than in those with normal DLCO levels.

Health care professionals who care for patients are the most vulnerable to COVID-19 transmission. Therefore, to ensure uninterrupted health care services, one of the top priorities in the fight against the pandemic is to protect health care professionals.9

The present study aimed to investigate whether the effects of COVID-19 infection persisted in health care professionals who returned to work after being isolated and those who were assigned to priority duty during the pandemic.

At the beginning of the pandemic, the only information available about the potential damage of the infection was based on the long-term consequences of SARS-CoV-2 infection in 2003 and Middle East respiratory syndrome (MERS) in 2012. Further studies are required to determine the long-term effects of SARS-CoV-2 infection.

In a study by Jenny et al.10 that reported the results of 55 patients who were followed up for 2 years, it was shown that 52% of the SARS survivors had impaired DLCO levels. Even 24 months after the disease, exercise capacity and health status were significantly lower than in the control group. In that study, 27 of the individuals included in the patient group were health care professionals. In addition, 29.6% of the health care professionals and 7.1% of the non-health care professionals could not return to work 2 years after the onset of the disease. The study suggested that the deep psychological trauma because of the SARS outbreak, which affected a substantial number of employees in the study's institution, accounted for the lower percentage of health care professionals returning to work when compared to non-health care professionals. Another study on the permanent pulmonary effects of surviving health care professionals 15 years after SARS-CoV infection assessed the pulmonary function tests and lung tomography results of 58 health care professionals. More than 30% of the SARS survivors had impaired DLCO levels, and more than 30% had small airway dysfunction 15 years after the onset of SARS. Abnormalities in CT scans persisted in more than 20% of the patients with SARS. It was reported that SARS infection could cause permanent damage, and health authorities should provide further support for early pulmonary rehabilitation.11 Although 14 (26.4%) participants had moderate/mild infection in the present study, decreased DLCO levels were observed in 39% of the cases, and small airway functions and FEV1 (%) were significantly lower in participants with decreased DLCO levels. Based on the study that reported permanent abnormalities in pulmonary function even 15 years after the onset of SARS infection, health care professionals can be scheduled to undergo pulmonary function tests when they return to work after being infected with SARS-CoV-2, and the same can be repeated at certain intervals in those with lower rates.
Although many studies have been conducted on the pathogenesis and treatment of acute SARS-CoV-2 disease, the medium- and long-term outcomes have not yet been fully understood, especially in survivors who had a severe prognosis. Güler et al. included 113 patients in their study, which was the first in Europe to report post-SARS-CoV-2 infection follow-up results. There were 66 severe/critical and 47 mild/moderate cases. They assessed the pulmonary functions 4 months after the onset of the COVID-19 infection. In patients with severe/critical disease, the DLCO level was impaired and significantly lower than in those with mild/moderate disease. As a result, they suggested that the lower DLCO levels (%) at month 4 was the most important factor associated with severe/critical COVID-19 infection. 

Fig 3. Correlation between 6MWT and hemoglobin, lymphocyte, and D-dimer levels.
A study by Liang et al. with 76 participants, which investigated the sequelae in patients discharged in the third month after COVID infection, included 65 health care professionals. During follow-up in the 3 months after hospital discharge, 15 (20%) patients had fever, 45 (60%) patients complained of cough, 33 (43%) had increased sputum production, 47 (62%) had chest tightness and palpitations during activity, 45 (60%) complained of fatigue and 20 (26%) patients had diarrhea. Similarly, in the present study, the most common persistent symptom was shortness of breath. The frequency of cough was not as high as in the aforementioned study because most of our followed-up patients were mild outpatients. Liang et al. demonstrated that lymphocyte count was significantly correlated with symptoms of chest tightness and palpitations after patients were discharged from the hospital. In the present study, the 6MWT value had a positive correlation with lymphocyte count and hemoglobin levels. Liang et al. identified 21 patients (27%) with impaired pulmonary function at 3 months following discharge. In the present study, 21 (39.6%) patients had decreased DLCO levels and the rate of decrease was significantly higher in female participants than in male participants. Low DLCO levels were also significantly associated with participants who had persistent complaints and returned to work at a later time.

Zhao et al. investigated 55 patients who recovered from COVID-19 infection in the third month after COVID and reported that 25% of them had abnormal findings on pulmonary function tests, although most patients did not have any respiratory symptoms. They reported anomalies in total lung capacity (TLC) in 7% of patients, FEV1 in 11%, FVC in 10%, DLCO in 16%, and small airway function in 13%. In the present study, there was a decrease in pulmonary function (DLCO). Although the majority of patients did not have respiratory symptoms, lower DLCO levels suggested that a pulmonary function screening be performed upon return to work and at regular intervals.

Wu et al. investigated pulmonary functions at 3, 6, 9, and 12 months after discharge in 83 patients with severe COVID-19 who did not require mechanical ventilation. After 1 year, 9 (11%) patients had low FVC levels and 27 (33%) had impaired DLCO values. Although most of our participants had mild infections, the rate of decreased DLCO level was similar in the present study.

At 6 months after recovery from infection, George et al. screened health care professionals with mild COVID-19 infection for cardiovascular anomalies. The study included 74 seropositive and 75 seronegative cases that were compatible in terms of age, gender, and ethnicity. There was no difference in terms of cardiovascular complications, and they suggested that cardiac screening was not indicated in asymptomatic patients after mild COVID-19 infection. The present study found a decrease in DLCO levels but did not screen the participants for cardiac anomalies.

The present study had certain limitations. Firstly, the study included 53 patients with only confirmed SARS-CoV-2 infection. A larger sample size would be ideal for further studies. Secondly, we could not measure pulmonary function tests in critically ill patients because such patients were not included in this study. This was a single-center study. The control period of the patients we included in the study was not standardized and it included a wide range. Further studies should be planned to investigate long-term pulmonary status (impairment or improvement) based on a larger sample size and groups involving an equal number of patients.

**CONCLUSION**

Significant persistent complaints (47.2%) and low DLCO (39.6%) levels were observed in health care professionals during the control visits at a mean time of 3 months after COVID-19 infection.
Symptoms and spirometry measurements, including DLCO, may be useful in the follow-up of health care professionals with COVID-19 infection. In particular, 6MWT and DLCO measurements may aid in the decision to return to work for health care professionals with persistent complaints after COVID-19 infection. Health care professionals with impaired pulmonary function should be evaluated on a regular basis. Further comprehensive studies with long-term follow-up periods are required.

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