SCIE DOI: 10.14744/scie.2021.48344
South. Clin. Ist. Euras. 2022;33(2):142-149 Original Article

Effect of COVID-19 Infection on the Functional Exercise Capacity and Echocardiographic Findings of Healthcare Workers

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Submitted: 14.10.2021
Accepted: 02.12.2021

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Keywords: COVID-19; exercise capacity; healthcare workers; six-minute walk test.

ABSTRACT

Objective: COVID-19 disease has affected all segments of society, especially healthcare workers. We aimed to evaluate the exercise capacity and cardiac functions of healthcare workers who had COVID-19 infection.

Methods: Forty healthcare workers with COVID-19 infection (21 females, 19 males), who have completed their treatment, were assessed on the 30th day of recovery. Twenty healthy volunteers were matched as a control group. Exercise capacity was measured using the six-minute walk test (6MWT). The results of 6MWT were given as an absolute value in meters. Cardiac functions were evaluated by echocardiography.

Results: Walking distances were similar in both healthcare workers with COVID-19 and healthy controls. 0′ pulse and 6′ pulse were significantly high in healthcare workers, whereas 0′ SpO_2 was low in 6MWT. The thorax CT findings showed a positive correlation with the total number of symptoms and clinical severity. Ejection fraction (EF) showed a negative correlation with 6′ pulse, and the right atrial area revealed a negative correlation with 6′ SO_2. The mean distance in 6MWT performed by inpatients and outpatients was 546.9±36.8 m vs 511.8±54.0 m, respectively. The walking distance and EF of outpatients were lower than inpatients. Enoxaparin treatment was independently associated with walking distance and EF.

Conclusion: COVID-19 infection and hospitalization status affect cardiac functions and physical functional capacity. In our study, we showed that prophylactic enoxaparin use was the strongest independent factor affecting EF and walking distance in healthcare workers with mild to moderate COVID-19 infection. We think that it is important to follow up with healthcare professionals in terms of possible impairments in cardiac function and exercise capacity after COVID-19 infection.

INTRODUCTION

Recently, an epidemic affecting the whole world has emerged, and a new type of coronavirus was discovered. It was later named severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and first identified in Wuhan, China, on January 7, 2020.[1] In a very short time, SARS-CoV-2 rapidly spread throughout the world and the disease, COVID-19, was characterized as a pandemic by the World Health Organization (WHO).

Coronavirus disease has directly or indirectly affected all segments of society, especially health workers. Health workers are at high risk of infection with SARS-CoV-2. The WHO has announced that over 10% of global infections are accounted for by healthcare workers. Therefore, healthcare workers with COVID-19 total over 1.4 million cases around the world, while overall 13.8 million people were infected by the coronavirus by July.

Clinical findings of COVID-19 vary from asymptomatic carriage to acute respiratory failure.[2] Studies about the course of the disease have still been proceeding throughout the world. The most accepted mechanism is the downregulation of angiotensin-converting enzyme (ACE) receptors, particularly ACE-2, by the SARS-CoV-2.[3] These receptors are found at high rates in the vascular endothelium and type 2 alveolar cells of the lungs. The balance of renin-angiotensin system is provided according to the ratio of ACE and ACE-2, which work opposite to each other. ACE stimulates inflammation, causing vasoconstriction, bronchoconstriction, and fibrosis, whereas ACE-2 has the opposite effects. It is thought that the breakdown of this balance may have a role in COVID-19 pathophysiology.[4]

Besides this mechanism, uncontrolled coronavirus infection leads to cytokine storm and overproduction of proinflammatory cytokines such as tumor necrosis factor-α, IL-1β, and IL-6 by the immune system which results in multiple organ injuries.[5] Although the pathophysiology of SARS-CoV-2 infection is not fully clear yet, the major concern is cardiac and pulmonary system deterioration. Recent studies suggested that cardiac involvement may be a late phenomenon of the viral respiratory infection and can be subclinical with few inflammatory cells or present with overt manifestations even absence of respiratory symptoms.[6,7] In the evidence of mentioned data, we aimed to assess the physical functional capacity by six-minute walk test (6MWT) and the echocardiography findings in a group of healthcare workers who experienced COVID-19 infection in the early period.

MATERIALS AND METHODS

Study design and participants

In this cross-sectional study, 40 healthcare workers who completed their treatment for COVID-19 infection (21 females and 19 males) and 20 healthy volunteers (10 females and 10 males) were assessed after an average of about 30 days after the isolation period (range 40–50 days of COVID-19 infection). All patients underwent transthoracic echocardiography (TTE) and 6MWT to assess cardiac functions and exercise capacity. Demographic and clinical information was obtained by a structured questionnaire. Laboratory and radiologic information was collected from electronic medical records. Clinical severity was assessed according to symptoms, radiologic findings, and clinical findings. Asymptomatic, mild, moderate, and severe disease definitions were based on interim guidance of the WHO definition.[8] Patients with severe disease according to WHO definition were excluded. Other than patients with severe COVID-19 infection, those who had uncontrolled hypertension on admission, history of coronary artery disease and heart failure, multisystem diseases that require corticosteroid usage or immunosuppressive agents, and renal failure were excluded from the study. All patients had resting 12-lead electrocardiograms (ECGs). Patients with ECG abnormalities such as ST-T changes, QTc and PR interval, and tachy-bradycardia were excluded. Informed consent was taken from all participants. The study was conducted following the approval of the local ethics committee in accordance with the Ministry of Health and Declaration of Helsinki.

Physical and laboratory measurements

Anthropometric data (weight, height) and systemic blood pressure were obtained by physical examination according to standard procedures. Body mass index was calculated by dividing weight (kg) by height (m^2). Resting systolic and diastolic blood pressures were measured three times at 1-min intervals using a standard mercury sphygmomanometer after 5-min rest. The average of the second and the third readings were used in the analyses. A confirmed case was defined as a patient with positive results according to real-time reverse transcription-polymerase chain reaction (RT-PCR) assay for SARS-CoV-2 in upper respiratory specimens (nasopharyngeal and oropharyngeal swab). CT was acquired using one machine: Philips Ingenuity (128 slices). CT scans were performed in caudocranial scanning direction without intravenous contrast injection. Thorax CT examination was read first by one radiologist, and the report was then checked by another radiologist. CT results were determined by consensus discussion for diagnostic performance analysis. Routine biochemical tests were completed with an AU 5800 analyzer. The whole blood count was determined on LH 750 Hematology Analyzers (Beckman Coulter Inc., USA).

Six-minute walk test

The exercise capacities of the participants were assessed with 6MWT. The 6MWT for this study included the method recommended by the American Thoracic Society.[9] We measured the 6-minute walk distance at baseline. Following a standardized protocol, participants walked up and down a 30-m hallway for 6 min after instructions to cover as much distance as possible. The total distance completed during the 6 min was recorded. The oxygen saturation (SpO_2) and pulse rate at the start and end of the test were collected in the data file. SpO_2 was measured via a finger probe using a Masimo Rad 5 with Adult Sensor (Masimo, Irvine, CA, USA) while standing at the beginning of the 6MWT and then again while standing at the end of the test after 6 min walking.

Transthoracic echocardiography

TTE was done with the subject positioned in left lateral decubitus, using available ultrasound equipment (Vivid S5, GE Vingmed Ultrasound, with a 3.5 MHz transducer). All examinations were performed by one physician to minimize interobserver variability. Standard views were used to obtain parasternal, apical, and subcostal views. All parameters were recorded according to the American Society of Echocardiography standards and recommendations of the European Association of Cardiovascular Imaging. Left atrial size, right atrial (RA) area, and both left and right ventricular (RV) dimensions were measured. RV diameter >42 mm at the base was described as RV dilatation, and RA area >18 cm^2 was described as RA enlargement. RV systolic function was evaluated using tricuspid annular plane systolic excursion (TAPSE). TAPSE cut-off value <16 mm was accepted as RV systolic dysfunction.

Statistical analysis

All statistical analyses were performed using SPSS version 22 software (SPSS Inc., Chicago, IL, USA). Continuous variables are expressed as mean and (standard deviation, SD), and categorical variables are reported as a number and (percentages). Skewness and kurtosis were used to evaluate the distribution of data. Patient characteristics between each group were compared using the Chi-square test or Fisher's exact test for categorical variables and the Mann–Whitney U or Student's t-test for continuous variables according to whether data were distributed normally or not. Pearson correlation analysis was employed to assess correlations between parametric variables, and Spearman correlation analysis was used for nonparametric variables. Univariate and multivariate logistic regression analyses were conducted to evaluate the effective factors regarding treatment methods on ejection fraction (EF) and linear regression analysis was performed to evaluate effective factors on walking distance. P-values of <0.05 were considered statistically significant.

RESULTS

The demographic, clinical, and laboratory characteristics of the healthcare workers with COVID-19 are shown in Table 1. The patients consisted of 19 males and 21 females, which includes 16 physicians, 9 nurses, and 15 others. Overall mean age was 36±8 years (ranges between 25 and 57). Clinical symptoms of these patients were fever, headache, fatigue, myalgia, loss of smell or taste, dry cough, dyspnea, chest pain, diarrhea, nausea, runny nose, sore throat, anorexia, and cough with sputum. The most frequently seen symptoms are shown in Figure 1. Routine blood tests did not show statistical significance between COVID-19 patients and healthy controls (Table 1). According to thorax CT, 3 patients (8.3%) showed ground-glass opacity, 1 patient (2.8%) showed unilateral pneumonia, and 8 patients (22.2%) showed bilateral pneumonia, but 24 patients (66.7%) did not show any signs. Asymptomatic healthcare workers included 12.5% of the total patient group (5 out of 40). Most of them experienced mild disease at rates of 80% (32 out of 40), and only 7.5% (3 out of 40) of patients had a moderate disease. Twelve subjects had comorbidities: mild asthma (3), hypertension (2), hypothyroidism (3), and chronic gastritis (4). The cigarette smoking history of participants was questioned and 30% of the participants were smokers (Table 1).

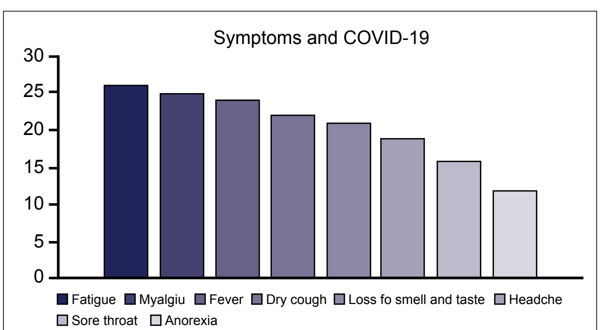

Figure 1. Frequency of symptoms in patients with COVID-19 infection.

Compared with the control group, 0′ pulse and 6′ pulse were significantly higher in healthcare patients, while 0′

Table 1. Baseline characteristics of health workers with COVID-19

	Health workers with Covid-19 (n=40) Mean±SD
Age (years)	36.4±8.9
Gender, n (%)	
Male	19 (47.5)
Female	21 (52.5)
Smoking history, n (%)	
No	28 (70.0)
Yes	12 (30.0)
Comorbidities, n (%)	
No	27 (67.5)
Yes	13 (32.5)
Clinic presentation, n (%)	
Asymptomatic	5 (12.5)
Mild	32 (80.0)
Moderate	3 (7.5)
Laboratory	
Hb (g/L)	13.1±1.2
WBC ($\times 10^9$/L)	6019.0±2553.2
Neutrophil ($\times 10^9$/L)	3647.5±1868.0
Lymphocyte ($\times 10^9$/L)	1920.0±902.6
Platelet ($\times 10^9$/L)	231666.7±55388.0
Serum creatinine (mg/L)	0.6±0.1
Albumin (g/L)	10.8±16.3
ALT (U/L)	20.8±12.6
AST (U/L)	23,1±10,4
LDH (U/L)	250.3±168.0
CRP (mg/L)	8.9±7.2
D-dimer (mg/L)	467.7±354.8
Ferritin (µg/L)	99.5±65.5
Thorax CT findings, n (%)	
Ground glass opacity	3 (8.3)
Unilateral pneumonia	1 (2.8)
Bilateral pneumonia	9 (22.2)
None	27 (66.7)
Oseltamivir	23 (59.0)
Medical therapy, n (%)	
Azithromycin	22 (56.4)
Hydroxychloroquine	40 (100.0)
Favipiravir	3 (7.7)
Enoxaparin	13 (32.5)
Hospitalization status, n (%)	
Outpatient	27 (67.5)
Inpatient	13 (32.5)
After treatment symptoms, n (%)	
No	26 (65.0)
Yes	14 (35.0)

Hb: hemoglobin; WBC: White blood cell; ALT: alanine transaminase; AST: aspartate transaminase; LDH: lactate dehydrogenase; CRP: C-reactive protein.

SpO_2 was lower. On the other hand, the walking distance of the participants was similar. There were no significant differences in age, gender, anthropometric measurements, blood pressure, and TTE findings between the healthcare workers with COVID-19 and control subjects (Table 2).

The thorax CT findings were positively correlated with the total number of symptoms (r=0.370, p=0.026) and clinical severity (r=0.352, p=0.036). The clinical severity of the patients did not show any correlation with the echocardiographic findings and 6MWT (not shown in the table). Additionally, EF showed a negative correlation with 6′ pulse (r=–0.264, p=0.044), and RA area had a negative correlation with 6′ SpO_2 (r=–0.389, p<0.015), as shown in Table 3. When walking test and TTE findings were compared according to the treatment method of healthcare workers with COVID-19, it was observed that walking distance and EF were significantly lower among outpatients than inpatients (p<0.05) (Table 4).

The univariate and multivariate comparisons of variables regarding EF are reported in Table 5. Enoxaparin treatment was independently associated with the EF both in univariate and multivariate regression (p=0.048). Furthermore, enoxaparin treatment has an effect on the walking

Table 2. Clinical and laboratory characteristics of controls and health workers with COVID-19

	Health Workers (n=40) Mean±SD	Controls (n=20) Mean±SD	p-value
Age (years)	36.4±8.9	38.2±6.4	0.46
Gender, n (%)			
Female	19 (47.5)	10 (50)	0.855
Male	21 (52.2)	10 (50)	
Medical profession, n (%)			
Medical doctor	16 (40)	14 (70.0)	0.052**
Nurse	9 (22.5)	2 (10.0)	
Other health worker	15 (37.5)	4 (20.0)	
Smoking history, n (%)	12 (30)	0 (0)	0.005*
Body mass index (kg/m²)	26.3±4.7	24.7±3.6	0.194
Systolic blood pressures (mmHg)	113.0±9.1	114.5±8.9	0.547
Diastolic blood pressures (mmHg)	73.5±7.4	72.5±5.5	0.557***
6 minutes walking test			
0’ SpO_2	97.9±1.0	98.5±0.9	0.040
0’ pulse	83.7±11.9	76.0±1.3	0.020
6’ SpO_2	97.4±1.5	97.8±1.2	0.304
6’ pulse	116.6±17.1	103.0±11.5	0.002
Walking distance (m)	523.2±51.4	534.8±33.4	0.366
Echocardiography findings			
Ejection fraction %	58.1±2.5	58.5±2.9	0.557
Left atrium area (cm²)	3.2±0.4	3.0±0.3	0.200
Right ventricle (cm)	3.1±0.3	3.1±03	0.909
Right atrium area (cm²)	11.2±2.0	11.1±1.9	0.939
Tricuspid annular plane systolic excursion (mm)	23.1±3.3	24.4±3.0	0.139

*Fisher’s exact test. **Linear-by-linear association, pearson chi-square. ***Mann-Whitney U, student t-test. Statistical significance: p<0.05, p<0.001. SpO_2: Peripheral oxygen saturation.

Table 3. Correlation between ECHO-Thorax CT findings and, 6MWT, clinical characteristics in patients with COVID-19

	Total number of symptoms		Clinical severity		6’ Pulse		6’ SpO_2	
	r	p	r	p	r	p	r	p
Thorax CT findings	0.370*	0.026	0.351*	0.036				
Ejection fraction	0.080	0.628	-0.086	0.601	-0.264*	0.044		
Right atrium area	0.280	0.088	0.248	0.133	-0.007	0.961	-0.389*	0.016

Statistical Significance: *p<0.05, **p<0.001. ECHO: Echocardiography; CT: computerized tomography; 6MWT: 6 minute walking test; SpO_2: peripheral oxygen saturation.

distance (β=0.325, p=0.041). Azithromycin treatment has no effect on both EF and walking distance (Table 5).

Subgroup analysis according to cigarette smoking status of COVID-19 patients revealed that 0′ pulse (p=0.032) and left atrial area (p=0.02) of smoking patients were significantly higher than the nonsmoking patients. However, there was no significant difference in EF and walking distance according to the smoking status of the participants (Table E1). Comparative analysis of the patient group according to the presence of comorbidities did not show any statistical significance regarding TTE findings and 6MWT results (Table E2).

Table 4. Comparison of walking test and echo findings according to the hospitalization status of the health workers with COVID-19

	Outpatient (n=27) Mean±SD	Inpatient (n=13) Mean±SD	p-value
Age (years)	36.1±8.9	37.0±9.1	0.780
Height (m)	168.4±8.3	168.6±9.2	0.933
Weight (kg)	72.9±15.9	77.6±13.3	0.360
BMI (kg/m^2)	25.8±4.9	27.3±4.5	0.351
Systolic BP (mmHg)	111.5±9.5	116.2±7.7	0.131
Diastolic BP (mmHg)	72.6±7.6	75.4±6.6	0.266
0' SpO_2	98.1±1.0	97.6±1.0	0.198
0' Pulse	83.3±12.4	84.4±11.1	0.790
6' SpO_2	97.2±1.5	97.7±1.5	0.327
6' Pulse	118.7±18.2	112.3±14.1	0.275
Walking distance (m)	511.8±54.0	546.9±36.8	0.041
EF (%)	57.5±2.5	59.2±1.9	0.023
LA area (cm^2)	3.2±0.5	3.2±0.3	0.901
RV (cm)	3.0±0.4	3.1±0.2	0.549
RA area (cm^2)	11.4±2.0	10.7±1.9	0.268
TAPSE (mm)	23.2±3.8	22.9±2.0	0.837

Statistical significance: p<0.05, p<0.001. BMI: Body mass index; BP: Blood pressure; SpO_2: Peripheral oxygen saturation; EF: Ejection fraction; LA: Left atrium; RV: Right ventricle; RA: Right atrium; TAPSE: Tricuspid annular plane systolic excursion.

DISCUSSION

Healthcare workers are known to be at significant risk even when they are protected against COVID-19. It is important to recognize the disease at an early stage and take necessary measures. Therefore, in this study, we evaluated the respiratory and cardiac functions of healthcare workers with COVID-19 infection whose treatments were completed. The major symptoms of COVID-19 are fever, cough, dyspnea, myalgia, anorexia, fatigue, sore throat, headache, and loss of smell or taste. These symptoms may appear between 2 days and 14 days after exposure.[10] In our study, the questionnaire covered all symptoms and was completed by 40 healthcare workers. The most common symptoms were fatigue (65%), myalgia (62.5%), fever (60%), dry cough (55%), and loss of smell or taste (52.5%). The median time from illness onset to symptoms currently used to screen for COVID-19 was 3 days. Wei et al.[11] reported that fever and cough were early symptoms in mild COVID-19 cases. A Chinese study found that the first three symptoms were fever (41.8%), lethargy (33.0%), and muscle pain (30.1%) before the diagnosis of COVID-19.[12] While most people hospitalized for COVID-19 had a fever in the study,[13] another study reported anosmia for 47% of test positives, and it was found to be strongly associated with SARS-CoV-2 positivity.[14]

Comprehensive healthcare worker screening with minimal or no symptoms can be helpful to protect patients and personnel. In a study with 592 healthcare workers, the initial symptoms and their relationship to the SARS-CoV-2 RT-PCR assays were investigated, and a total of 16% of these healthcare workers were diagnosed with clinical COVID-19.[15] An Italian study indicated that almost one-third (29%) of COVID-19 cases were asymptomatic.[16] Rivett et al.[17] reported that 3% of healthcare workers tested positive for SARS-CoV-2 in the absence of symptoms. In our study, all patients were SARS-CoV-2 RT-PCR positive, 12.5% of healthcare workers with COVID-19 were asymptomatic, most (80%) of them had mild–severe clinics. Recent studies have suggested that the transmis-

Table 5. Regression analysis of effective factors on ejection fraction and walking distance

	Univariate regression					Multivariate regression			
Ejection fraction*	**ß**	**Std. Error**	**p**	**Exp (B)**		**ß**	**Std. Error**	**p**	**Exp (B)**
Age	-0.019	0.037	0.607	0.981	Age	-0.030	0.041	0.474	0.971
Enoxaparin	1.705	0.863	0.048	5.500	Enoxaparin	1.716	0.893	0.045	5.561
Azithromycin	-0.143	0.674	0.832	0.867	Azithromycin	-0.260	0.735	0.724	0.771
Smoking	0.124	0.737	0.866	1.132	Smoking	0.394	0.831	0.636	1.482
Walking distance**	**ß**	**Std. Error**	**p**	**Beta**		**ß**	**Std. Error**	**p**	**Beta**
Age	-0.049	0.940	0.959	-0.008	Age	-0.063	0.918	0.946	-0.011
Enoxaparin	35.145	16.613	0.041	0.325	Enoxaparin	43.388	17.456	0.018	0.392
Azithromycin	-15.551	16.739	0.359	-0.151	Azithromycin	-19.921	16.581	0.238	0.392
Smoking	7.690	17.908	0.670	0.069	Smoking	6.116	17.926	0.735	0.055

*Logistic regression analysis. **Linear regression analysis, Statistical Significance: p<0.05.

sion in COVID-19 is primarily person-to-person by direct contact, droplets, and fomites.[18] After exposure, SARS-CoV-2 invades the lung parenchyma and results in severe interstitial inflammation.[6,19] The histological assessment of lung biopsy samples obtained from COVID-19-infected patients showed diffuse alveolar epithelium destruction, capillary damage/bleeding, hyaline membrane formation, alveolar septal fibrous proliferation, and pulmonary consolidation.[20] These lesions are seen as ground-glass opacity images and then appear as unilateral and/or bilateral pneumonia in the lungs on thorax CT.[21] Of our patients, 66.7% did not have any finding of pneumonia on the thorax CT. However, our findings revealed that the thorax CT results are associated with the total number of symptoms in the rest of the patients.

6MWT is a valuable measurement that provides information regarding all systems during physical activity, including pulmonary and cardiovascular systems, blood circulation, neuromuscular units, body metabolism, and peripheral circulation.[9] The purpose of the 6MWT is to assess the functional capacity of patients with cardiopulmonary disease. In our study, the functional capacity of healthcare workers with COVID-19 was significantly lower than healthy controls. In a previous study, which included healthcare workers who were discharged with SARS coronavirus pneumonia, significant impairment of pulmonary functions was shown at 6 months after illness onset.[22] In another study, which examined lung function tests and 6MWT after 2 years, the exercise capacity and health status of patients were significantly lower than the general population, and 30% of healthcare workers were unable to return to work.[23] Huang et al.[24] conducted a retrospective study involving 57 COVID-19 patients. Serial lung function, lung imaging examination, and exercise capacity were examined 30 days after discharge. They found impaired diffusion capacity, decreased respiratory muscle strength, and lung imaging abnormalities in more than half of COVID-19 patients in the early recovery period. A study on COVID-19 patients revealed that impairment of diffusion capacity is the most common abnormality of lung function, followed by restrictive ventilator defects, which are both associated with the severity of the disease.[25]

COVID-19 infection mainly disrupts the lungs, causing interstitial pneumonitis and severe acute respiratory distress syndrome. Besides the pulmonary system, it affects multiple organs, especially the cardiovascular system. Although the relationship between COVID-19–associated cardiac injury and risk of mortality remains unclear, known cardiovascular manifestations are acute cardiac injury, acute coronary event, left ventricular systolic dysfunction, heart failure, arrhythmia, and venous thromboembolism.[26,27] Huang et al.[28] reported that 12% of the patients had COVID-19-associated acute cardiac injury, and these patients had elevated cardiac troponin I levels. The common cardiac complications of COVID-19 emerge with an increase in plasma levels of cardiac troponins and N-terminal pro-brain natriuretic peptide and the presence of echo-/electrocardiographic abnormalities. TTE of our patients does not show a statistically significant difference from the healthy group. The findings of echocardiography of our patient group were in the normal range, which can be explained by the absence of clinical cardiovascular disease history. However, when we compared the relationship between the echocardiographic parameters and 6MWT results, we found a negative correlation between EF and the pulse rate at 6 min. This condition may give clues about the relation between subclinical cardiac injury, systemic inflammation, and myocardial wall stress. Furthermore, the RA area demonstrated a negative linear correlation with oxygen saturation at the sixth minute. In severe cases of COVID-19 infection, pneumonia can be complicated by acute myocardial injury with or without an existing cardiac disease. Several factors such as acute respiratory distress syndrome, pulmonary vascular thrombosis, viral myocardial damage, inflammatory response, and autoimmune damage may be responsible for myocardial damage.[29] Multiple mechanisms may be responsible for the cardiovascular complications of COVID-19.

One-third of healthcare workers with COVID-19 were treated as inpatients. We found that inpatients had better walking distance and EF levels than outpatients. Inpatients had received a routine regimen of prophylactic enoxaparin treatment. While all of the patients had received the hydroxychloroquine treatment, three of the diagnosed patients had received favipiravir treatment in accordance with health ministry treatment guidelines.[30] In regression analysis, enoxaparin treatment independently affects EF and walking distance in 6MWT. We suggest that better walking distance and EF values of inpatients may be the result of more intensive treatment regarding prophylactic enoxaparin treatment. It has been demonstrated that prophylactic enoxaparin treatment is associated with decreased mortality via both anti-inflammatory and antithrombotic effects in severe COVID-19 disease.[31,32] However, there are limited data for enoxaparin treatment on cardiac functions and exercise capacity in COVID-19 patients. Our current study suggests prophylactic enoxaparin treatment results in better exercise capacity even in mild–moderate disease. On the other hand, studies regarding favipiravir on COVID-19 patients revealed that early recovery and less inflammatory response is more likely in favipiravir-treated patients.[33,34] However, the low number of patients who received favipiravir limits the interpretation of data to assess the effect of favipiravir treatment on EF and walking distance in our study. Clinical severity of both inpatient and outpatient groups did not associate with 6MWT- and TTE-related parameters. It was stated that myocardial injury and low EF may be associated with high levels of cytokines both as a part of hemophagocytic lymphohistiocytosis and stress cardiomyopathy.[35] Our study group does not contain critically ill patients who have a history of ARDS, septic shock, and multiorgan failure during the COVID-19 disease course. Therefore, myocardial involvement may be part of critical COVID-19 disease.

It is already known that smoking increases the severity of the inflammatory response associated with COVID-19 through various mechanisms such as promoting mucosal inflammation, inflammatory cytokines, TNF-α expression, increased permeability in epithelial cells, and impaired mucociliary clearance.[36] Besides COVID-19 associated morbidities, long-term smoking has been linked to structural and functional alterations in both LV and RV consistent with hypertrophic cardiomyopathy.[37] A recent study by Surme et al.[38] suggested that cigarette smoking is not associated with disease severity. Among our patient group, cigarette smokers only had increased LA area but not RV and LV. These results may be explained by the young age of our patient group as hypertrophic cardiomyopathy is a long-term effect of cigarette smoking. However, the results, together with the increased LA area on TTE and increased 0′ pulse on 6MWT, suggest a prothrombotic and pro-arrhythmogenic state in COVID-19 patients with cigarette smoking habits.

There are several limitations to our study. One of them is the small sample size, which can serve as a pilot study. In addition, studies hypothesize that the clinical spectrum of COVID-19 is a consequence of the variable immune response of the host. Therefore, the measurement of cytokines like interleukin-1 receptor antagonists, IL-10, IL-6, and TNF-α can provide more accurate information about the clinical severity and immune response of the patients.[39] Because we excluded severe illness, the data of troponin-t and brain natriuretic peptide, which could strengthen TTE findings, were not present. We used 6MWT for the assessment of functional capacity, and to provide objective results, a single trained healthcare professional carried out the test. However, individuals' performance could be affected by both physical and psychological factors. Finally, this cross-sectional analysis provides only a short follow-up, and the long-term dynamic variation of pulmonary and cardiac function still requires further investigation.

CONCLUSION

The study showed that there may be a deterioration in the pulmonary functional capacity of healthcare workers with COVID-19 infection. The higher EF on TTE and walking distance in the hospitalized patient group compared to the outpatient group suggested that the use of enoxaparin may help to maintain exercise capacity even in mild–moderate COVID-19 infection. Although there are no accurate data about the effect of treatment strategies on physical functional capacity and echocardiography findings, our study may give an insight in this regard. Our results suggest that medium and long-term follow-up of patients with COVID-19 is important in terms of possible deterioration of physical functional capacity.

Ethics Committee Approval

This study approved by the Kartal Dr. Lütfi Kirdar Training and Research Hospital Clinical Research Ethics Committee (Date: 27.05.2020, Decision No: 2020/514/178/12).

Informed Consent

Prospective study.

Peer-review

Internally peer-reviewed.

Authorship Contributions

Concept: B.B., S.A.; Design: B.B., S.A.; Supervision: Ö.K.; Materials: N.P.T.; Data: B.B., H.E.; Analysis: B.B., S.A.; Literature search: H.E., Ö.K.; Writing: H.E.; Critical revision: B.B., S.A.

Conflict of Interest

None declared.

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Sağlık Çalışanlarında COVID-19 Enfeksiyonunun Fonksiyonel Egzersiz Kapasitesi ve Ekokardiyografi Bulgularına Etkisi

Amaç: COVID-19 enfeksiyonu, başta sağlık çalışanları olmak üzere toplumun tüm kesimlerini etkilemiştir. COVID-19 enfeksiyonu olan sağlık çalışanlarının egzersiz kapasitesini ve kalp fonksiyonlarını değerlendirmeyi amaçladık.

Gereç ve Yöntem: COVID-19 enfeksiyonlu (21 kadın, 19 erkek) tedavilerini tamamlayan 40 sağlık çalışanı, iyileşmelerinin otuzuncu gününde değerlendirildi. Yirmi sağlıklı gönüllü kontrol grubu olarak eşleştirildi. Egzersiz kapasitesi altı dakika yürüme testi (6DYT) ile ölçüldü. 6DYT sonuçları metre cinsinden mutlak değer olarak verildi. Kalp fonksiyonları ekokardiyografi ile değerlendirildi.

Bulgular: COVID-19 enfeksiyonu geçirmiş sağlık çalışanları ve sağlıklı kontrollerde yürüme mesafesi benzerdi. Sağlık çalışanlarında 0' nabız ve 6' nabız anlamlı olarak yüksek, 6DYT'de 0' SpO_2 düşüktü. Toraks BT bulguları, toplam semptom sayısı ve klinik şiddet ile pozitif korelasyon gösterdi. Ejeksiyon fraksiyonu (EF) 6' nabız ile negatif korelasyon ve RA alanı 6' SO_2 ile negatif korelasyon bulundu. Yatan hastalar ve ayaktan hastalar tarafından yapılan 6DYT'de ortalama mesafe sırasıyla 546.9±36.8m ve 511.8±54.0m idi. Ayaktan hastaların yürüme mesafesi ve EF'si yatan hastalara göre daha düşüktü. Enoksaparin tedavisi bağımsız olarak yürüme mesafesi ve EF ile ilişkiliydi.

Sonuç: COVID-19 enfeksiyonu ve hastanede yatış durumu, kardiyak fonksiyonları ve fiziksel fonksiyonel kapasiteyi etkilemektedir. Çalışmamızda, hafif ve orta dereceli COVID-19 enfeksiyonu geçirmiş sağlık çalışanlarında, EF ve yürüme mesafesini etkileyen en güçlü bağımsız faktörün profilaktik enoksaparin kullanımı olduğunu gösterdik. Sağlık çalışanlarının COVID-19 enfeksiyonu sonrası kardiyak fonksiyon ve egzersiz kapasitesinde olası sorunlar açısından takibinin önemli olduğu düşünmekteyiz.

Anahtar Sözcükler: Altı dakika yürüme testi; COVID-19; egzersiz kapasitesi; sağlık çalışanları.