Evaluation of the relationship between the disease severity and the level of physical activity in patients followed up with COVID-19 diagnosis

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ABSTRACT

Objectives: To investigate the relationship between physical activity level and disease severity, anxiety level, sleep quality, and fatigue in patients followed up with COVID-19 diagnosis.

Methods: This was a cross-sectional study of 111 volunteer patients who were receiving treatment with COVID-19 diagnosis at the Chest Diseases Polyclinic, Sanko University, Sani Konukoğlu Practice and Research Hospital, Gaziantep, Turkey. Between May 2021 and July 2021 were included in the study and classified clinically and radiologically. They were evaluated on the basis of demographic characteristics, International Physical Activity Questionnaire, Beck Anxiety Inventory, Pittsburgh Sleep Quality Index, and Fatigue Severity Scale.

Results: Approximately 63% of the patients did not have a habit of exercise, while 52.3% of our patients were clinically mild cases, and 33.3% had normal lung tomography. While clinical disease severity was not associated with exercise habits, sleep quality was impaired in clinically severe patients.

Conclusion: The results of our study suggested that physical inactivity is common. Anxiety is a frequent symptom in COVID-19 cases and also COVID-19 negatively affects sleep quality.

Keywords: disease severity, level of physical activity, COVID-19 diagnosis

Original Article

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Coronavirus disease (COVID-19) is one form of severe acute respiratory syndrome which was first appeared in Wuhan, China in December 2019. Coronavirus disease-19 spread rapidly around the world and it was accepted as a pandemic in April 2020. The symptoms of COVID-19 is typically pneumonia and it progresses as an acute respiratory failure in severe cases. The virus also affects many organs and systems such as the cardiovascular and urinary systems. Fever, cough, chest tightness, and dyspnea were most common symptoms.
It has been shown that the host’s immunity plays a critical role in the response against the virus in patients with COVID-19. It was suggested that the patients who had healthy immune system responses, the disease severity decreased and the recovery time shortened. It is well known that regular physical activity plays important role to supporting the components of the immune system. In addition, physical activity is recognized as a non-pharmacological, inexpensive, and readily available method of coping with COVID-19 risk factors. A current issue of concern is the lack of physical activity on the general population, particularly on the elderly people and people with cardiovascular disease.

During the pandemic, sleep quality is another important component for a healthy life. Early research has shown that in individuals isolated during the COVID-19 outbreak in China their sleep quality has decreased. The World Health Organization indicated that, fatigue is one of the general symptoms, as well as fever and dry cough, among COVID-19 cases. Recent evidence suggested that regular exercise habit increases the endurance of the cardiorespiratory system, and strengthens the immune system by activating lymphocytes and may reduce the disease severity in COVID-19. It is not clear that regular exercise improves response of immune system to respiratory virus susceptibility in humans. On the other hand, limited information is available on how physical activity affects the immune system response associated with COVID-19 susceptibility. It is emphasized that as the pandemic continues, retrospective studies are of utmost importance to determine if physical activity status has any impact on the COVID-19 condition. In this study, we aimed to investigate the relationship between physical activity level and disease severity, anxiety level, sleep quality, and fatigue in patients followed up with COVID-19 diagnosis.

**Methods.** This cross-sectional study was carried out at Sanko University, Gaziantep, Turkey. Prior to the study, Sanko University Ethics Committee for Non-Invasive Research approved the study. This study was carried out in accordance with the Helsinki Declaration principles. No sample size justification during the 2 months study period due to the pandemic difficulties, therefore all the patients who volunteered to participate the study were included. The study carried out 111 volunteer patients who were receiving treatment with COVID-19 diagnosis in the Chest Diseases Polyclinic, Sanko University Sani Konukoğlu Practice and Research Hospital between May 2021 and July 2021. The inclusion criteria were ≥18 years of age, positive nasopharyngeal or oropharyngeal swab samples, or confirmed lung infection on computed tomography (CT) scan. Patients who were treated in the intensive care unit, had a previous cerebrovascular accident, psychiatric disease, obstructive sleep apnea syndrome, congestive heart failure, using sleeping pills, and had cooperation problems were excluded.

All patients were evaluated clinically and by radiologically methods. Based on the CT findings; a pulmonologist classified the patients as normal lung image, mild lung involvement (20% ground glass), moderate lung involvement (20-50% ground glass), and severe lung involvement (more than 50% ground glass). After the tomography classification, patients were grouped as; clinically mild, moderate, severe, and critical COVID-19 cases. Cases were included in one of the groups; mild - if mild symptoms and no findings on imaging; moderate - if fever and respiratory tract infection symptoms and pneumonia findings on imaging; severe- if respiratory frequency ≥30/min or oxygen saturation ≤93% or partial pressure of oxygen/ fractional inspired oxygen ≤300 mmHg or lesions seen to be progressing more than half within 1-2 days on lung imaging; and critical - if shock, respiratory failure severe enough to require mechanical ventilation, and other organ failures requiring intensive care follow-up. As there are only 3 severe cases, medium and sever groups were combined in the statistical calculations.

Within the scope of socio-demographic evaluation, age, gender, height, weight, education level, occupation, smoking status, exercise habits, medications, and so on were recorded.

Physical activity level was determined by using the International Physical Activity Questionnaire (IPAQ) short form’s Turkish version. The validity and reliability study of the questionnaire in Turkey was carried out by Öztürk in 2005. The questionnaire includes 7 questions on the time spent sitting, walking, doing moderate activities, and doing vigorous activities in the past 7 days. The metabolic equivalents (MET) method was used to determine the level of physical activity. Metabolic equivalent is the energy consumption per unit of any physical activity. It corresponds to 3.5 mL/kg/min oxygen uptake. Physical activity score is calculated by multiplying 8 to calculate the

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IPAQ vigorous physical activity score, 4 to calculate the moderate-intensity physical activity score, and 3.3 to calculate the walking score, by multiplying the number of days and minutes of activity. The total score is obtained by summing each component. Apart from this continuous scoring, classification can also be made according to the numerical data obtained. Physical activity levels were classified as those physically inactive (<600 MET-min/week), those with low physical activity (600-3000 MET-min/week), and those with adequate physical activity (beneficial for health) (>3000 MET-min/week).

Patients’ anxiety levels were measured with the Turkish version of the Beck Anxiety Inventory. The validity and reliability study of the questionnaire was completed by Ulusoy et al. Based on the scores of the inventory; patients were classified as normal (<10), mild (10-18), moderate (19-29), and severe (30-63).

The patients’ sleep quality was evaluated by the Turkish version of Pittsburgh Sleep Quality Index (PSQI). The Turkish version of the questionnaire has validity and reliability. The scale classified the sleep quality as good sleep and bad sleep, and contains 24 questions. Of these, 19 are self-evaluation questions while 5 are answered by the individual’s spouse or roommate. These 5 questions answered by the individual’s spouse or roommate are not included while calculating the index score. The said 19 questions assess 7 different components (subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbance, medication use, and daytime function evaluation). Some of the components relate to a single question, while others are linked to several questions. Each question is scored from 0 to 3. The sum of the sub-scores of these 7 components gives the total index score ranging from 0 to 21. High scores indicate poor sleep quality. The index does not demonstrate the presence of sleep disturbance or the prevalence of sleep disturbances. However, a total PSQI score equal to or higher than 5 suggests poor sleep quality.

Turkish version of the Fatigue Severity Scale was used to assess fatigue level. The scale consists of 9 items that patients can apply on their own, and the total score is calculated by averaging the scores of 9 items. The lower the total score, the less fatigue.

**Statistical analysis.** The Number Cruncher Statistical System, 2007 (Kaysville, Utah, USA) was used for data analysis. While evaluating the study data, we checked the distribution of the data with the Shapiro-Wilk test, in addition to using descriptive statistical methods (mean, standard deviation, median, frequency, ratio, minimum, maximum). The Kruskal-Wallis test was used for the comparison of quantitative data of three or more groups without normal distribution and the Mann-Whitney U-test for the comparison of 2 groups without normal distribution. The Chi-square analysis was utilized to determine the relationship between qualitative data. The relationship between the questionnaire scores used in the evaluation and the patient's age and body mass index was clarified with the results of the correlation analysis. We used Spearman’s correlation analysis to determine the relationship between quantitative data. Significance level was set at 0.01 and 0.05.

**Results.** The study was carried out between January-April 2021 after the ethics committee approval. We completed the study with 111 COVID-19 patients who had the inclusion criteria. The patients were aged between 19-79 years, and their mean age was 47.21 years (SD 14.65). Their body mass index mean was 28.49 kg/m² (SD 5.22) and only 30% was adequate weight. It is noteworthy that only 16% of the individuals were smoking, and 63% of participants was inactive (did not have regular exercise habits). Table 1 shows the general demographic and clinical characteristics of the patients.

Table 2 summarizes the results of correlation analysis. We detected a weak positive correlation between age and body mass index and a strong positive correlation between age and IPAQ total score (p<0.05). There was a moderate positive correlation between Beck Anxiety Inventory score and Fatigue Severity Scale score, PSQI subjective sleep quality, sleep disturbance, and daytime dysfunction, and a weak positive correlation between Beck Anxiety Inventory score and sleep latency, use of sleeping medication, and PSQI total score (p<0.05). There was a weekly positive correlation between Fatigue Severity Scale score and PSQI subjective sleep quality. Also it was found that a very weekly positive correlation between Fatigue Severity Scale score and PSQI total score (p<0.05).

The CT results showed that the patients were equally distributed among the groups. Table 3 summarizes the changes in the evaluation parameters based on the CT results. Age and body mass index values were significantly different between patients with mild or moderate lung involvement and patients with normal lung image (Table 3) (p<0.05). The mean age of individuals with normal lung image was significantly lower than those with mild or moderate lung involvement (p<0.05). On the other hand, the mean body mass index of individuals with moderate lung involvement was significantly higher than those with normal lung image or mild lung involvement (p<0.05).
The patients were divided into groups as mild, moderate, or severe COVID-19 cases according to their clinical symptoms. Table 4 summarizes the change in evaluation parameters based on clinical classification. We observed a significant difference in age, body mass index, and PSQI total scores between clinically mild and moderate or severe patients (p<0.05) (Table 4). Clinically moderate or severe patients had significantly higher age, body mass index, and PSQI scores.

Discussion. The study was planned to evaluate the relationship between physical activity level and disease severity, anxiety level, sleep quality, and fatigue in COVID-19 patients. We observed a strong positive correlation between patient age and IPAQ total score. Additionally, we determined a moderately positive correlation between Beck Anxiety Inventory score and Fatigue Severity Scale score, PSQI subjective sleep quality, sleep disturbance, and daytime dysfunction.

After the first year of the COVID-19 pandemic, the results of research on the effects of COVID-19 on the prognosis, health and wellness behaviors have begun to be published.20-24 We interpreted the results of our research in the light of previous research findings.

In our study, observed positive correlation between patient age and physical activity level is not surprising. According to the World Health Organization’s classification, middle age is 44-60, elderly age is 60-75, senile age is 75-90.25 The majority (40.5%) of our patients in the study were in the young adult group, and the number of elderly and senile age patients were low. Therefore, we did not determine a correlation as to the decrease in physical activity level with age.

One of the important findings of our study was the relationship between sleep disorders and anxiety. Several restrictions and lifestyle changes aimed to prevent the spread of different viruses have been reported to deteriorate the psychological well-being of individuals.26 The quarantine practice has been shown to have negative psychological impacts during previous outbreaks.22 It was thought that general psychological problems related to the pandemic process may increase the susceptibility of patients to anxiety during Covid 19 treatment. It has been noted that psychological symptoms such as stress, anxiety, and depression increase in relation to the time spent in quarantine.23 Sleep is also negatively affected in people impacted by the COVID-19 outbreak. Early research has shown that individuals isolated during the COVID-19 outbreak in China demonstrated poor sleep quality.27-28 Lopez-Bueno et al29 suggested that decreased psychological well-being and mental health during the COVID-19 quarantine are associated with health habits such as alcohol consumption, diet, physical activity, and sleep. Similarly, Ingram et al25 showed that negative mood states such as anxiety, tension, and depression were associated with poor sleep. A comprehensive study including review and meta-analysis emphasized the high level of correlation between sleep problems and anxiety and depression.30 In our study, anxiety has been revealed to be a crucial parameter negatively affecting sleep quality in patients. It is possible that increased anxiety during the inpatient treatment period, and the need to stay away from family members play a role in worsening sleep health of the patients.
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Table 2 - Correlation analysis results. The relationship between the questionnaire scores used in the evaluation and the patient’s age and body mass index was clarified with the results of the correlation analysis.

| Variables               | Age (year) | BMI (kg/m²) | IPAQ Total score (MET) | Beck anxiety inventory score | Fatigue severity scale score | PSQI Subjective sleep quality |
|-------------------------|------------|-------------|------------------------|-----------------------------|----------------------------|-------------------------------|
| Age (year)              | 1          |             |                        |                             |                            |                               |
| BMI (kg/m²)             | 0.000**    | 0.374(t)    |                        |                             |                            |                               |
| IPAQ total score (MET)  | 0.003**    | 0.398       | 0.972(t)               |                             |                            |                               |
| Beck anxiety inventory score | -0.024(t)  | -0.077(t) | -0.054(t) | 1                        |                             |                               |
| Fatigue severity scale score | 0.054      | 0.784       | 0.296                  | 0.000**                     | 1                           |                               |
| PSQI subjective sleep quality | 0.184(t)  | -0.026(t)  | -0.164(t)             | 0.445(t)                    | 0.000**                     |                               |
| PSQI sleep onset latency | 0.663      | 0.394       | 0.498                  | 0.000**                     | 0.347(t)                    | 0.384(t)                      |
| PSQI sleep duration     | 0.039(t)   | 0.000(t)    | -0.065(t)             | 0.396(t)                    | 0.119(t)                    | 0.384(t)                      |
| PSQI sleep efficiency   | 0.547      | 0.158       | 0.731                  | 0.863                       | 0.186                       | 0.364                        |
| PSQI sleep disturbances | 0.058(t)   | 0.135(t)    | 0.033(t)               | -0.017(t)                   | -0.127(t)                   | 0.087(t)                      |
| PSQI subjective sleep quality | 0.514      | 0.512       | 0.139                  | 0.686                       | 0.817                       | 0.265                        |
| PSQI sleep disturbances | 0.063(t)   | 0.063(t)    | -0.141(t)             | 0.039(t)                    | -0.022(t)                   | 0.107(t)                      |
| PSQI sleep efficiency   | 0.428      | 0.533       | 0.538                  | 0.000**                     | 0.054                       | 0.001**                      |
| PSQI sleep onset latency | 0.076(t)   | 0.060(t)    | -0.059(t)             | 0.487(t)                    | 0.183(t)                    | 0.319(t)                      |
| PSQI use of sleeping medication | 0.652      | 0.613       | 0.613                  | 0.025*                      | 0.495                       | 0.030*                        |
| PSQI daytime dysfunction | -0.043(t)  | -0.049(t)  | 0.048(t)               | 0.212(t)                    | 0.065(t)                    | 0.206(t)                      |
| PSQI total score        | 0.259      | 0.507(t)    | 0.537(t)               | 0.576(t)                    | 0.452(t)                    | 0.647(t)                      |

*Correlation is significant at the 0.05 level (2-tailed).  **Correlation is significant at the 0.01 level (2-tailed). r: correlation efficient, BMI: body mass index, PSQI: Pittsburgh Sleep Quality Index, MET: metabolic equivalent

Table 2 - Correlation analysis results. The relationship between the questionnaire scores used in the evaluation and the patient’s age and body mass index was clarified with the results of the correlation analysis (continuation).

| Variables               | PSQI Sleep onset latency | PSQI Sleep duration | PSQI Sleep efficiency | PSQI Sleep disturbances | PSQI Use of sleeping medication | PSQI Daytime dysfunction | PSQI total score |
|-------------------------|--------------------------|---------------------|-----------------------|-------------------------|---------------------------------|-------------------------|-----------------|
| Age (year)              | 0.383                    | 0.084(t)            | 1                     |                         |                                 |                         |                 |
| Body mass index (kg/m²) | 0.383                    | 0.000**             | 0.084(t)              | 0.000**                 |                                 |                         |                 |
| IPAQ total score (MET)  | 0.000**                  | 0.713               | 0.003(t)              | 0.594                   |                                 |                         |                 |
| Beck anxiety inventory score | 0.360(t)  | -0.035(t) | 0.051(t) | 1                        |                                 |                         |                 |
| Fatigue severity scale score | 0.004** | 0.218     | 0.419               | 0.441                   | 0.274(t)                      | 0.078(t)                | 0.074(t)        |
| PSQI daytime dysfunction | 0.000**                  | 0.345               | 0.055                 | 0.000**                  | 0.000**                       | 0.009**                 |                 |
| PSQI total score        | 0.000**                  | 0.090(t)            | 0.183(t)              | 0.414(t)                 | 0.249(t)                       | 0.447(t)                 |                 |

*Correlation is significant at the 0.05 level (2-tailed).  **Correlation is significant at the 0.01 level (2-tailed). r: correlation efficient, BMI: body mass index, PSQI: Pittsburgh Sleep Quality Index, MET: metabolic equivalent
Previous studies reported that in patients with COVID-19 the incidence of fatigue was 44 to 69.6%.30-33 We also observed a positive correlation between depression levels and sleep problems in our patients. Townsend et al34 concluded that there was a correlation between pre-existing depression and fatigue in patients with COVID-19 diagnosis. This is similar to the result of our research.

In order to better understand the impact of age, body mass index, and physical activity level variables on the disease severity in COVID-19, we compared the individuals with normal lung image and mild and moderate lung involvement based on their CT results. The 3 groups showed no difference in terms of physical activity level according to IPAQ results.

The results of our research could not provide an idea on the relationship between physical activity level and COVID-19 prognosis or severity. It is stated that the immune system can be modulated with regular physical activity; however, no scientific relationship has been established between physical activity and COVID-19 currently.35 A study carried out in Brazil36 concluded that among hospitalized COVID-19 patients who were physically active and inactive, there was no difference in terms of intubation prevalence, oxygen therapy, symptoms, and length of stay in hospital. The similarity of the physical activity level evaluated with the IPAQ in our study supports the result of this research.

Tavakol et al37 evaluated the relationship between physical activity, healthy lifestyle, and COVID-19 severity in the elderly. Contrary to the results of our study, Tavakol et al37 found a correlation between weekly energy expenditure level and disease severity. On average, our study included middle-aged individuals, and they are likely to be slightly more active than the elderly. In our study, this fact may have resulted in a finding different than the mentioned research. The absence of serious cases among our patients and the fact that all patients had similar activity levels seem to explain this different result.
Age has been highlighted as a crucial variable determining disease severity in COVID-19 patients. A meta-analysis study demonstrated that while mortality by age was 1% lower in patients under 50 years of age, it increased exponentially in those over 50. The mean age of the patients included in our study is 47 years. No patient showed severe lung involvement and was not evaluated as a clinically severe COVID-19 case. The mean age of individuals with normal lung image was significantly lower than those with mild or moderate lung involvement. Another observation consistent with this finding was that the patients clinically in the moderate or severe group were older. All these results are in line with the literature.

It is assumed that there may be a correlation between obesity and COVID-19 severity since respiratory tract infections display a worse course in obese individuals. Considering that obesity is a common risk factor increasing disease severity in influenza and COVID-19, it is important to investigate the relationship between obesity and COVID-19 severity. Lifelong regular exercise has been reported to help maintain a sufficient balance between pro-inflammatory cytokines such as interleukin (IL)-8 and IL-1β and anti-inflammatory cytokines such as IL-1ra and IL-4. A sedentary, excess-calorie lifestyle also results in proinflammatory ACE1 bias. A study with more than 5200 hospitalized COVID-19 patients demonstrated a strong correlation between obesity and critical disease. It has been observed that obese patients under the age of 60 are 3 times more likely to need intensive care than those who are slim.

Our results relating to body mass index were in support of the current literature. The mean body mass index of individuals with moderate lung involvement was significantly higher than those with normal lung image or mild lung involvement. Similarly, the body mass index of clinically moderate or severe cases was higher than those with mild symptoms.

**Study limitation.** Our study provided an idea on the effect of age, body mass index, and physical activity level on disease severity in patients diagnosed with COVID-19. However, our study presents some limitations. The first is the lack of generalizability since our sample was not large enough. The second is the exclusion of patients in the intensive care unit. The fact that these patients could not be evaluated when their condition was stable after their discharge from the intensive care unit prevented us from obtaining clearer information on the relationship between the clinical manifestation of COVID-19 and age, body mass index, and physical activity level. Lastly, because of the cross-sectional design of the study; the results did not clearly show a cause-effect relationship between body mass index and physical activity level on disease severity in patients diagnosed with COVID-19. This is an important limitation of the study and must be clearly stated in the discussion section.

In conclusion, our study could not show a relationship between the level of physical activity and the severity of the COVID-19 clinic. The results of our study suggested that physical inactivity is common, anxiety is frequent symptom in COVID-19 cases and also that COVID-19 negatively affects sleep quality.

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