# **Original Article**

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Website: https://eurasianjpulmonol.org DOI: 10.14744/ejp.2023.9003

# The effect of strengthening and relaxation exercises on musculoskeletal pain, anxiety, and sleep quality in COVID-19 survivors

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#### Abstract:

**BACKGROUND AND AIM:** Musculoskeletal pain, anxiety, and sleep problems may persist in people after Coronavirus Disease 2019 (COVID-19). The aim of this study was to examine the effects of strengthening and relaxation exercises on musculoskeletal pain, anxiety, and sleep quality in COVID-19 survivors.

**METHODS:** The study was conducted at Gaziosmanpaşa Training and Research Hospital and included outpatients aged between 18 and 65 who were diagnosed with COVID-19 in the last 3 months. Subjects were randomly assigned to either experimental or control groups. The experimental group participated in a home-based strengthening and relaxation exercises program 3 times a week for 8 weeks, while control group participants did not receive any exercise program. McGill Pain Scale Short Form (SF-MPQ), Short-Form 36 (SF-36), Beck Anxiety Scale, and Pittsburgh Sleep Quality Index (PSQI) were conducted on all patients before and after the study.

**RESULTS:** A total of 117 COVID-19 survivors were screened for eligibility, and 76 eligible subjects were randomized into groups. Baseline characteristics and assessment results were similar between the groups (p>0.05). After the study, a significant difference was found in the experimental group in terms of all outcome results (p<0.05). In the control group, there was a statistically significant difference in all assessments except McGill-Current score, SF-36-Physical Role Difficulty, SF-36-Social Functioning, and SF-36-Pain sub-dimension scores (p<0.05). The improvement was significantly higher in the experimental group than in the control group except for the SF-36-Emotional Role Difficulty sub-dimension (p<0.05).

**CONCLUSIONS:** In conclusion, strengthening and relaxation exercises had a significantly positive effect on post-COVID-19 musculoskeletal pain, anxiety, and sleep quality.

#### Keywords:

Anxiety, COVID-19, pain, relaxation exercises, sleep quality, strengthening exercises

This study was presented at National Lung Health Congress 2021 and the European Respiratory Society 2022 Congress.

**How to cite this article:** Keskin B, Saka S. The effect of strengthening and relaxation exercises on musculoskeletal pain, anxiety, and sleep quality in COVID-19 survivors. Eurasian J Pulmonol 2023;25:125-132.

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> Received: 26-09-2022 Revised: 28-11-2022 Accepted: 28-12-2022 Published: 17-05-2023

# Introduction

The most common symptoms of the Coronavirus Disease 2019 (COVID-19) are cough, fever, shortness of breath, and musculoskeletal and gastrointestinal symptoms. COVID-19 also causes health problems such as insomnia, depressive symptoms, anxiety, and fear in patients.<sup>[1]</sup> Pain, anxiety, and sleep disorders have been observed in many patients after isolation treatment, triggering a series of physiological events that can cause a decrease in immunity.<sup>[2]</sup>

In the study conducted by Carfi et al.,<sup>[3]</sup> only 12.6% of participants were completely symptom-free, 32% had one or two symptoms, and 55% had three or more symptoms on average two months after the onset of COVID-19 symptoms. No signs or symptoms of fever or acute illness were observed in any of the patients. Quality of life was decreased in 44.1% of the patients. The percentage of fatigue, shortness of breath, joint pain, and chest pain was 53.1%, 43.4%, 27.3%, and 21.7%, respectively. The literature has shown the beneficial effects of moderate-intensity exercise, which is performed at least 150 minutes per week, especially in older adults and people with chronic diseases in host immune defense.<sup>[4]</sup> Moderate-intensity exercise increases leukocyte function, and low-to-moderate-intensity exercise is an important method in improving immune responses against the progression of COVID-19 infection.<sup>[5]</sup>

Muscle tension is assumed to be a sign of the physiological response of the human body to disturbing thoughts, and with the application of progressive muscle relaxation, deep muscles are getting relaxed in line with this definition.<sup>[6]</sup> By reducing the activity of the sympathetic nervous system, the negative effects of psychological situations can be prevented, and physical and mental relaxation can be increased.<sup>[7]</sup> Progressive muscle relaxation is easy to learn and does not require a specific place, special technology, or equipment. Additionally, Seyedi et al.<sup>[8]</sup> showed that progressive relaxation exercise (PRE) can reduce fatigue and improve sleep quality in patients with Chronic Obstructive Pulmonary Disease (COPD). Liu et al.<sup>[9]</sup> stated that PRE is effective in improving sleep quality and reducing anxiety in COVID-19 patients.

Based on the literature, many studies have demonstrated the benefits of strengthening and PRE exercises in different populations.<sup>[4,5,8,9]</sup> Meanwhile, pain, anxiety, and sleep problems are widely known to persist after COVID-19.<sup>[2,3]</sup> Although there are a limited number of studies examining the effects of strengthening and PRE exercises on these problems, no study has been found in which both exercise types are used, and these problems are discussed together. Therefore, our study aimed to examine the effects of home-based moderate-intensity strengthening and relaxation exercises on musculoskeletal pain, anxiety, and sleep quality in COVID-19 survivors.

# **Materials and Methods**

# Study design

This was a prospective, randomized clinical, controlled trial performed on COVID-19 survivors referred to the Gaziosmanpaşa Training and Research Hospital. The study was approved by the Halic University Ethics Committee (Reference number: 202; December 24, 2020), and the protocol was in accordance with the guidelines of the Declaration of Helsinki. Written informed consent was obtained from all participants. A total of 117 COVID-19 survivors were screened for eligibility, and 76 outpatient COVID-19 survivors who met the inclusion and exclusion criteria and agreed to participate in the study were randomized into two groups: the experimental and control groups. Moderate-intensity strengthening exercises and relaxation exercises were applied to the participants in the experimental group, while no application or suggestion was made to the control group.

#### **Subjects**

The inclusion criteria were as follows: aged between 18–65 years, not having severe mental retardation that would prevent communication, being diagnosed with COVID-19 in the last three months, having a negative PCR test or completing the 14-day isolation period, and not having undergone surgery in the last six months. Individuals who could not cooperate, could not continue to study regularly, had chronic pain for at least four months, and used sleeping or psychiatric drugs were excluded from the study.

Subjects were initially evaluated for basic characteristics, and eligible subjects were randomized into two groups using a computer-generated sequence: the experimental group and the control group [Fig. 1].

#### Keskin and Saka: Effect of exercises for Covid-19 survivors



Figure 1: Flow diagram

# **Outcome measurements**

The McGill Pain Scale Short Form (SF-MPQ), Short-Form 36 (SF-36), Beck Anxiety Scale, and Pittsburgh Sleep Quality Index (PSQI) were conducted on all patients before and after the study.

The SF-MPQ provides information about the sensory characteristics, severity, and effect of pain. SF-MPQ consists of three parts. In the first part, 15 descriptive words measure the sensory and perceptual dimensions of pain. In the second part [Visual Analogue Scale (VAS)], the current pain intensity of the patient is evaluated using visuals. Volunteers are expected to give a score between 0 and 10 for the severity of their pain. The third part has six expressions to determine the severity of the patient's pain.<sup>[10,11]</sup>

The quality of life was examined with SF-36, which consists of 36 items with eight dimensions. These dimensions are physical functioning, physical role, emotional role, vitality, mental health, social functioning, bodily pain, and general health.<sup>[12]</sup> SF-36 is evaluated considering the last four weeks. SF-36 gives total scores for each dimension separately. It evaluates health between 0 and 100, with 0 points indicating poor health and 100 points indicating good health.<sup>[13]</sup>

The Beck Anxiety Scale is used to measure anxiety-related symptoms in the last week. There are 21 items on the scale, and they are scored as 0 (never), 1 (mild), 2 (moderate), and 3 (severe). Anxiety levels of individuals can be categorized according to the score obtained:  $\leq$ 17 points for low anxiety, 18–24 points for moderate anxiety, and  $\geq$ 25 points for high-level anxiety.<sup>[14,15]</sup>

The PSQI, which is used to evaluate sleep quality, is a 19-item self-report scale that is scored between 0 and 3 points. It is accepted that a total scale score of 5 and above indicates poor sleep quality.<sup>[16,17]</sup>

#### Intervention

The exercise program, which consisted of strengthening and PRE, was taught to the experimental group in the first session by a physiotherapist, and a training brochure was given to the patient. The patients were asked to do 45-minutes program three days a week for eight weeks at home. The continuity of the exercises was checked every week by telephone communication.

The strengthening exercises included calisthenics and progressively increasing free weights resistance exercises for upper and lower extremity major muscle groups and trunk muscles. The exercises were done as three sets of ten repetitions.

The relaxation exercises were applied systematically in a quiet environment with comfortable clothing and grad-

#### Table 1: Demographic data of patients

|   | Expe<br>g | rimental<br>roup | C<br>ç | ontrol<br>group | р     |
|---|-----------|------------------|--------|-----------------|-------|
|   | n         | %                | n      | %               |       |
| Age (year) (mean±SD)  | 38.6      | 5±11.56          | 36.3   | 36±10.97        | 0.352 |
| Gender  |           |                  |        |                 |       |
| Female  | 15        | 39.47            | 15     | 39.47           | 1.000 |
| Male  | 23        | 60.53            | 23     | 60.53           |       |
| BMI (kg/m <sup>2</sup> ) (mean±SD)                          | 26.6      | 67±3.84          | 26.    | 14±3.97         | 0.556 |
| Chronic disease   | 1         | 2.63             | 1      | 2.63            | 1.000 |
| Drug usage  | 1         | 2.63             | 1      | 2.63            | 1.000 |
| COVID-19 symptoms   |           |                  |        |                 |       |
| Fever   | 0         | 0                | 0      | 0               | -     |
| Cough   | 0         | 0                | 0      | 0               | -     |
| Headache  | 3         | 7.89             | 0      | 0               | 0.240 |
| Diarrhea  | 0         | 0                | 0      | 0               | -     |
| Back pain   | 20        | 52.63            | 15     | 39.47           | 0.250 |
| Dyspnea   | 4         | 10.52            | 6      | 15.78           | 0.497 |
| Musculoskeletal pain  | 29        | 76.31            | 32     | 84.21           | 0.387 |
| Cigarette usage   |           |                  |        |                 |       |
| Yes   | 9         | 23.68            | 16     | 42.10           | 0.053 |
| No  | 29        | 76.32            | 22     | 57.90           |       |
| Alcohol usage   |           |                  |        |                 |       |
| Yes   | 14        | 36.84            | 10     | 26.32           | 0.324 |
| No  | 24        | 63.16            | 28     | 73.68           |       |
| Time between acute COVID-19 and assessment (days) (mean±SD) | 46.5      | 2±23.68          | 49.4   | 14±27.99        | 0.704 |

SD: Standart deviation, BMI: Body Mass Index

ual contraction and relaxation of each muscle. Subjects were asked to maintain the contraction for ten seconds and then relax for 30 seconds. The relaxation exercises were studied in combination with breathing.

#### Statistical analysis

The sample size was calculated using the G-power v3.1 program (Universitat Kiel, Germany). According to similar literature with a 0.58 effect size, with a 95% confidence level and 80% power, a sample size of 38 subjects was estimated for each group.<sup>[18]</sup> The statistical analysis was performed using the SPSS 22 (SPSS Inc., Chicago, USA) statistical software. Mean±standard deviation (Mean±SD) and percentage (%) were used for the descriptive variables. The normality of data was tested using the Kolmogorov-Smirnov test. For comparison, Chi-squared tests, independent samples t-test, paired t-test, or Analysis of Variance (ANOVA) were used where applicable. Statistical significance was accepted for p values <0.05.

# Results

A hundred seventeen COVID-19 survivors were screened for eligibility; 76 eligible subjects randomized into the

experimental group (38 subjects) and control group (38 subjects) and participated in the study [Fig. 1]. The sociodemographic characteristics of the groups were presented in Table 1. No significant differences were found in age, gender, body mass index, chronic disease, drug usage, smoking history, COVID-19 symptoms, and the elapsed day after acute COVID-19. Regarding comorbidities, one participant in the experimental group had a diagnosis of asthma but was not using any related medication, and another patient was using levocetirizine dihydrochloride for skin problems. In the control group, only one patient had a diagnosis of hypertension and used bisoprolol fumarate as a medication. There were no significant differences between the groups in baseline values of all parameters (Table 2).

At the end of the eight weeks, all outcome measures were significantly changed in the experimental group. On the other hand, all outcome measures except McGill's current pain and SF-36 physical role-social functioning-bodily pain scores were significantly changed in the control group. The improvement was significantly higher in the experimental group than the control group except for the SF-36-emotional role difficulty sub-dimension (Table 3).

Table 3: Effects of the exercise program on outcome measures

|  | Table 2. Com | parison c | of baseline | outcome | measures | results |
|--|--------------|-----------|-------------|---------|----------|---------|
|--|--------------|-----------|-------------|---------|----------|---------|

|                      | Experimental group | Control<br>group | р     |
|----------------------|--------------------|------------------|-------|
| McGill total         | 9.39±5.45          | 9.39±5.61        | 0.815 |
| McGill VAS           | 4.23±1.28          | 4.50±1.62        | 0.285 |
| McGill current score | 1.92±0.58          | 2.05±0.65        | 0.359 |
| SF-36                |                    |                  |       |
| Physical functioning | 78.00±16.00        | 75.00±16.37      | 0.303 |
| Physical role        | 77.00±25.00        | 76.00±25.69      | 0.600 |
| Emotional role       | 89.81±17.51        | 83.00±27.70      | 0.442 |
| Vitality             | 62.00±11.00        | 58.00±14.94      | 0.374 |
| Mental health        | 69.00±12.00        | 68.00±12.50      | 0.830 |
| Social functioning   | 73.36±12.39        | 70.39±14.94      | 0.436 |
| Bodily pain          | 63.22±14.91        | 61.58±15.38      | 0.536 |
| General health       | 64.00±14.00        | 65.00±13.83      | 0.971 |
| Beck anxiety scale   | 9.39±4.09          | 11.31±6.32       | 0.265 |
| PSQI                 | 6.15±2.89          | 6.94±3.19        | 0.254 |

VAS: Visual Analog Scale, SF-36: Short-Form 36, PSQI: Pittsburg Sleep Quality Index

# Discussion

This study investigated the effects of strengthening and relaxation exercises on musculoskeletal pain, anxiety, and sleep quality in COVID-19 survivors. The results indicate that both musculoskeletal pain and anxiety decreased, while sleep quality and quality of life improved. Therefore, it has been demonstrated that the application of strengthening and PRE can be effective in reducing pain and anxiety, and increasing sleep quality and quality of life in COVID-19 survivors.

Based on the baseline McGill pain scores, musculoskeletal pain was prominent in our sample of COVID-19 survivors. When COVID-19 patients return to their physically active lives after the isolation period is over, they may experience difficulties due to pain-related symptoms and decreased general well-being.<sup>[19,20]</sup> In our study, the rate of musculoskeletal pain was over 75% for both groups, and the severity of pain was above 4, which supports this situation. At the end of the study, pain scores improved in both groups, with greater improvement observed in the experimental group. In a review examining the clinical characteristics of musculoskeletal muscle pain in Long COVID-19, it was noted that pain symptoms did not consistently decrease or increase over time.<sup>[21]</sup> In a clinical study, patients were followed up at three and six months post-discharge and reported a decline in the prevalence of pain.<sup>[22]</sup> Therefore, the observed change in pain perception during the eight-week period of our study is normal, and this change was in the direction of improvement in the

|                            |               | Experimenta | l group     |         |                | Control gro | dn         |         | Δ between<br>groups p |
|----------------------------|---------------|-------------|-------------|---------|----------------|-------------|------------|---------|-----------------------|
|                            | Before        | After       | Δ           | ٩       | Before         | After       | Δ          | ٩       |                       |
| McGill total               | 4.23±1.28     | 3.26±0.97   | -2.34±2.25  | <0.001* | 9.39±5.61      | 8.52±4.71   | -0.87±1.09 | <0.001* | 0.001*                |
| McGill VAS                 | $1.92\pm0.58$ | 1.31±0.47   | -0.97±0.68  | <0.001* | 4.50±1.62      | 4.18±1.39   | -0.32±0.57 | 0.003*  | <0.001*               |
| McGill current score       | 78.29±15.69   | 89.21±11.24 | -0.61±0.55  | <0.001* | 2.05±0.65      | 1.97±0.63   | -0.08±0.27 | 0.083   | <0.001*               |
| SF36- physical functioning | 77.63±24.52   | 90.13±16.99 | 10.92±7.52  | <0.001* | 74.61±16.37    | 79.60±13.42 | 5.00±6.37  | <0.001* | <0.001*               |
| SF36- physical role        | 88.28±19.61   | 96.49±10.36 | 12.50±13.94 | 0.005*  | 75.00.29±25.33 | 78.29±20.26 | 3.29±10.35 | 0.059   | 0.001*                |
| SF36- emotional role       | 61.62±10.54   | 71.05±7.90  | 8.11±14.51  | <0.001* | 83.32±27.70    | 87.70±21.15 | 4.38±11.41 | 0.039*  | 0.200                 |
| SF36- vitality             | 69.08±11.88   | 76.74±5.08  | 9.32±5.42   | <0.001* | 58.29±14.94    | 63.02±11.24 | 4.74±6.97  | <0.001* | <0.001*               |
| SF36- mental health        | 73.36±12.39   | 82.24±6.90  | 7.57±7.82   | <0.001* | 68.42±12.50    | 70.94±11.45 | 2.53±4.69  | 0.001*  | 0.002*                |
| SF36- social functioning   | 63.22±14.91   | 71.38±8.33  | 8.88±9.15   | <0.001* | 70.39±14.94    | 71.38±13.90 | 0.99±4.48  | 0.180   | <0.001*               |
| SF36- bodily pain          | 64.34±14.01   | 75.92±9.64  | 8.16±9.47   | <0.001* | 61.58±15.38    | 63.42±14.76 | 1.84±4.01  | 0.165   | <0.001*               |
| SF36- general health       | 9.39±4.09     | 6.71±2.75   | 11.58±6.16  | <0.001* | 64.87±13.83    | 68.94±12.47 | 4.08±4.91  | <0.001* | <0.001*               |
| Beck anxiety scale         | 6.15±2.89     | 4.42±1.68   | -2.681.61   | <0.001* | 11.31±6.32     | 9.76±5.26   | -1.55±1.54 | <0.001* | 0.002*                |
| PSQI                       | 4.23±1.28     | 3.26±0.97   | -1.74±1.45  | <0.001* | 6.94±3.19      | 6.57±2.71   | −0.37±0.71 | 0.004*  | <0.001*               |
|                            |               |             |             |         |                |             |            |         |                       |

\*: p<0.05. VAS: Visual Analog Scale; SF-36: Short-Form 36, PSQI: Pittsburg Sleep Quality Index

control group. In the literature, it is well documented that exercise is an effective therapeutic modality for reducing pain and improving sleep quality, cognitive function, and physical function in painful conditions. <sup>[23]</sup> Increasing evidence supports the beneficial effects of physical activity for many conditions, including cancer, diabetes, obesity, and cardiovascular problems.<sup>[24]</sup> Even small amounts of activity can provide significant benefits, especially in patients transitioning from a sedentary state to an active state. Therefore, the application of strengthening exercises in the program was effective for reducing pain and improving general well-being in COVID-19 survivors. On the other hand, it is known that relaxation exercises can relieve pain by reducing skeletal muscle tension, releasing endorphins, reducing tissue oxygen demand, and lowering the levels of chemicals such as lactic acid, which can trigger pain.<sup>[25]</sup>

In our study, quality of life improved at the end, with a greater improvement observed in the experimental group than in the control group, except for the emotional role parameter. To the best of our knowledge, no study has examined the effects of strengthening and relaxation exercises on the quality of life in COVID-19 survivors. However, in comparison to studies on other diseases that can cause musculoskeletal pain, Saza and Cevik found that relaxation exercises have a significant effect on the quality of life in COPD.<sup>[26]</sup> In a study of elderly people by Dehkordi and Jalili, relaxation exercises made a significant difference in all SF-36 sub-scores in the experimental group, while no improvement was achieved in the control group.<sup>[27]</sup> Akmese and Oran examined the effect of relaxation exercises on pregnant women and found a significant increase in quality of life scores and a decrease in pain.<sup>[28]</sup> Social distancing is a crucial measure in reducing the rate of COVID-19 transmission and related deaths. However, leading a sedentary life is a consequence of social isolation. Therefore, while social isolation is one of the main strategies against COVID-19, it brings with it many behavioral and physiological changes that can have negative consequences for health, including decreased physical activity levels, weight gain, an increase in fatty body mass, insulin resistance, and loss of muscle tissue. Adopting a healthy lifestyle, including an exercise routine, can help protect health by avoiding these negative consequences and by supporting the immune system.<sup>[29]</sup> Therefore, as in our study, it is accepted that strengthening exercises and progressive relaxation exercises have positive effects on the quality of life.

Based on the SF-36 scores of the experimental and control groups before the study, it was determined that all parameters of quality of life were lower compared to the study that examined the population norm values of SF-36,<sup>[30]</sup> with the most affected parameters being pain and social functionality sub-parameters.

At the end of the study, both groups showed an improvement in anxiety levels, with a significantly greater improvement in the experimental group. PRE has an influence on the sympathetic nervous system, promoting physical and mental relaxation, and reducing anxiety.<sup>[7]</sup> In a study by Liu et al.,<sup>[9]</sup> 51 patients received PRE training for 30 minutes a day, five days a week, and anxiety levels decreased in the experimental group compared to the control group. In a study by Xiao et al., [18] 79 COVID-19 patients were randomized into a control and an experimental (PRE) group, and a significant improvement in anxiety levels was observed in the experimental group compared to the control group. By sequentially tensing and relaxing the muscles, PRE allows patients to experience two different emotional states, promoting muscle relaxation and alleviating negative emotions such as tension and anxiety, and leaving the whole body in a relaxed state.<sup>[18,31]</sup> Although the effect of emotional state on the immune system is known, the benefits obtained with PRE may support recovery by supporting the immune system.<sup>[32]</sup> This finding is consistent with our study, which suggests that PRE and strengthening exercises are effective methods in reducing anxiety, one of the symptoms of COVID-19.

Furthermore, the anxiety level of the control group decreased at the end of the study, which is an expected result in parallel with the decrease in COVID-19 effects as time passes after the disease. In a meta-analysis study, it was indicated that anxiety and depression problems were most severe during acute COVID-19 infections and declined significantly during the first 12 months. However, it was indicated that average symptom levels remained above healthy norms even at 12 months and continued to improve.<sup>[33]</sup>

After the study, it was observed that sleep quality improved in both groups, but significantly more in the experimental group. The improvement in both groups was expected in accordance with the literature. A study aimed at evaluating sleep quality after acute COVID-19 infection stated that sleep disturbances improved over time.<sup>[34]</sup> However, the significant difference in favor of the exercise group coincides with the effects of strengthening and PRE exercises. Studies show that PRE can reduce fatigue and improve sleep quality in patients with COPD.<sup>[8]</sup> In a randomized controlled trial conducted by Aksu et al.,[31] it was shown that PRE can improve the sleep and quality of life of patients after pneumonectomy. A PRE intervention was performed in 45 patients with COPD, and the results showed that PRE was an effective method for improving sleep quality.<sup>[8]</sup> In this study, patients reported that they focused on the contraction and relaxation of the skeletal muscle groups during training, temporarily losing attention to emotional stress. They also achieved physical relaxation by relaxing their bodies, successfully calming down and falling asleep. A study on sleep quality showed significant improvements following a 16-week physical activity program.[35] Conditions like anxiety and depressive symptoms, problems with self-efficacy, negative thoughts, and inactivity can reduce sleep quality. However, the positive effects of exercise and PRE on these conditions can improve sleep quality.<sup>[36]</sup> Our study and this knowledge show that PRE and strengthening exercises can effectively improve the sleep quality of COVID-19 patients.

Furthermore, the sleep quality scores of the control group also significantly improved in our study. In addition to improvement in sleep disturbances over time, this improvement may be related to the patient's exposure to chronobiotic light after isolation, increased physical activity level, and psychosocial involvement. However, the sleep quality scores of all participants in our study initially had poor sleep quality scores.

The limitations of our study include the lack of information on the social differences of participants and their psychological status before COVID-19, and not recording the length of stay in the hospital. The length of hospital stay can be considered a factor in anxiety and sleep quality. On the other hand, the fact that the social isolation conditions at the time the first participants were evaluated were more severe than the dates of our last evaluation may have had a positive effect on the patients' quality of life, anxiety, and sleep quality.

In conclusion, the results of our study showed that strengthening and relaxation exercises may provide positive effects on musculoskeletal pain, anxiety, and sleep quality in post-COVID-19 survivors. Based on our findings, PRE and strengthening training should be considered as an effective method against the ongoing symptoms of COVID-19 and similar conditions that may arise in the future.

# **Conflicts of interest**

There are no conflicts of interest.

# **Ethics Committee Approval**

The study was approved by the Haliç University Noninterventional Clinical Research Ethics Committee (No: 202, Date: 24/12/2020).

# **Financial support and sponsorship** Nil.

#### Peer-review

Externally peer-reviewed.

# **Authorship Contributions**

Concept – B.K., S.S.; Design – B.K., S.S.; Supervision – S.S.; Funding – B.K.; Materials – B.K.; Data collection &/ or processing – B.K.; Analysis and/or interpretation – B.K., S.S.; Literature search – B.K., S.S.; Writing – B.K., S.S.; Critical review – S.S.

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