ORIGINAL ARTICLE

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A New Beginning After Severe COVID-19: Long-Term Quality of Life Study

Şiddetli COVID-19 Sonrası Yeni Bir Başlangıç: Uzun Dönem Hayat Kalitesi Çalışması

ABSTRACT

Objective:

The pandemic caused by coronavirus (2019-nCoV) overwhelmed the health systems and became an important cause of morbidity and mortality. It reduces health-related quality of life by causing long-term physical, mental and cognitive disorders. Our aim is to evaluate the long-term effects of COVID-19 on patients by assessing quality of life and respiratory functions of the patients with severe COVID-19 during hospital follow-up and one year after discharge.

Material and Methods:

This is a retrospective cross-sectional study. Data from the Nothingam Health Profile (NSP) questionnaire and the Modified Medical Research Council Scale (mMRC), which were administered to patients in person on the first day of their ICU discharge and again in person and via telemedicine at month 12, were scanned from the files. Wilcoxon Signed-Rank test was used for statistical analyses, $p < .05$ value was considered significant.

Results:

The patients' mean scores according to the NHP scale were 29.5±37.6 for pain, 23.4±25.5 for emotional variables, 39±36.1 for sleep, 25±33.2 for social isolation, 65±33.7 for physical activity, 98.2±9.1 for energy, and the total score for part 1 was 280.3±95.1 ($p < .001$). Although a statistically significant decrease was detected in the mean scores of the NHP scale at the 12th month, the increase remained.

Conclusion:

It is of great importance for public health that patients with COVID-19 are followed up and treated in terms of post-COVID syndrome.

Key Words:

Post COVID-19 syndrome, Nottingham Health Profile Questionnaire, Public Health

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ÖZ

Amaç:

Koronavirüs (2019-nCoV) sebep olduğu pandemi ile önemli bir morbidite ve mortalite nedeni olarak sağlık sistemini ele geçirmiştir. Uzun dönem fiziksel, mental ve kognitif bozukluklar oluşturarak sağlık ilişkili hayat kalitesini düşürmektedir. Amacımız, ağır dereceli COVID-19 tanısı almış hastaların hastanede takipleri esnasında ve taburculuktan bir yıl sonrasındaki süreçte hayat kalitesi ve solunum fonksiyonu açısından değerlendirilmesi ile COVID-19'un uzun dönemde hastalar üzerindeki etkisini araştırmaktır.

Gereç ve Yöntemler:

Bu çalışma, retrospektif kesitsel tiptedir. Hastalara yoğun bakım taburculuklarının birinci günü yüz yüze ve on ikinci ayında yüz yüze ve teletıp uygulaması ile uygulanan Nothingam Sağlık Profili (NSP) anketi ve Modifiye Medikal Araştırma Kurulu Skalası (mMRC) verileri dosyalardan tarandı. İstatiksel analizlerde Wilcoxon Signed-Rank testi kullanıldı, $p < ,05$ değeri anlamlı kabul edildi.

Bulgular:

Hastaların ilk NSP skalasına göre ortalamaları, ağrı; 29,5±37,6, duygusal reaksiyon; 23,4±25,5, uyku; 39±36,1, sosyal izolasyon; 25±33,2, fiziksel aktivite; 65±33,7, enerji: 98,2±9,1, birinci bölüm toplam puanı; 280,3±95,1 ($p < .001$) olarak bulunmuştur. On ikinci ay yapılan NSP skalası ortalama puanlarında istatistiksel olarak anlamlı düşüş saptanmasına rağmen yükseklik devam etmektedir.

Sonuç:

COVID-19 geçiren hastaların post-COVID sendromu açısından takiplerinin yapılıp, gerekli önlemlerin alınması toplum sağlığı açısından büyük öneme sahiptir.

Anahtar Kelimeler:

Post COVID-19 sendromu, Nottingham Sağlık Profili Anketi, Halk Sağlığı

INTRODUCTION

Since November 2019, the severe acute respiratory syndrome-coronavirus 2 (SARS-CoV-2) has overwhelmed the healthcare systems and is a significant cause of mortality and morbidity globally. Unfortunately, after three years of the pandemic, it left approximately 600 million infected cases and six million deaths (1).

The disease has wide spectrum of clinical signs and symptoms ranging from asymptomatic clinical disease to multi-organ failure necessitating intensive care follow-up. Various complications such as respiratory failure, acute respiratory distress syndrome (ARDS), and multi-organ failure have been observed in approximately 20% of hospitalized patients (2). Patients with severe coronavirus disease may need rehabilitation after discharge as a result of prolonged mechanical ventilation, intensive care unit stays and physical limitations (3). Long COVID-19 (post-COVID-19 syndrome) is the term for symptoms that persist or appear three months after the first SARS-CoV-2 infection and last for at least two months without any other known cause (4). At least three quarters of the patients followed in the intensive care unit due to COVID-19 have one or more of the post-intensive care syndrome symptoms (5). These conditions reduce the health-related quality of life of the patients by creating physical, mental and cognitive disorders (6). The World Health Organization (WHO) defines quality of life as "individuals' perceptions of their position in life in relation to their goals, expectations, standards, and concerns in the context of the culture and value systems in which they live" (7).

This study aims to investigate the long-term effects of COVID-19 on patients who had severe COVID-19 and stayed in critical care units by evaluating quality of life and respiratory functions during hospital follow-up and one year after discharge.

MATERIAL and METHODS

Study design and participants

This is a retrospective, cross-sectional study carried out between January 2021 and December 2022 at the Adana City Education and Research Hospital.

In total, 176 patients with confirmed severe SARS-CoV-2 infection by positive result on real time polymerase chain reaction (Real time-PCR) testing of a nasal or nasopharyngeal sample, followed up in the intensive care unit with the diagnosis of severe COVID-19 pneumonia and respiratory failure and discharged after completion of treatment were included in our study. Of the 30 patients excluded from the study, 21 patients died before 12th month control and 9 patients could not be reached. Additionally, individuals who had a history of lung disease or cancer, were pregnant, under the age of 18, did not satisfy the criteria for severe COVID-19 pneumonia, and whose data were incomplete were excluded from the trial. The study was completed with a total of 146 patients who met the inclusion criteria (Figure 1.Flowchart).

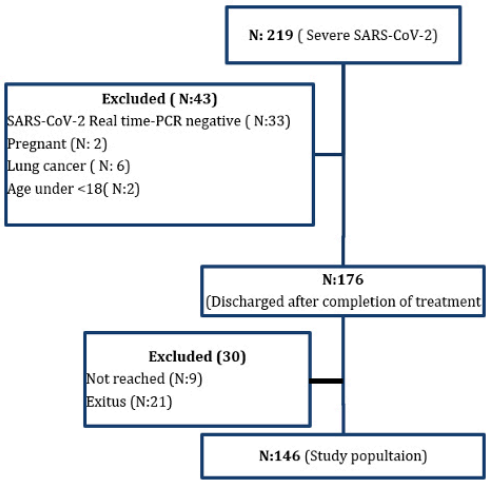

Figure 1. Patient Flowchart

The demographic data of the patients, such as age and gender, body mass index and comorbidities were recorded in standard data forms.

Data collection tools

Data from the Nothingam Health Profile (NSP) questionnaire and the Modified Medical Research Council Scale (mMRC), which were administered to patients in person on the first day of their ICU discharge and again in person and via telemedicine at month 12, were scanned from the files.

The Nothingam Health Profile Questionnaire (NHP)

NHP evaluates the perception of issues with one's emotional, social, and physical health as well as how much they affect with daily activities (8). NHP composes of 38 items divided into six domains: Energy, pain, emotional reactions, sleep, social isolation and physical activity. Each item uses Yes/No answer format and weighted differently. NHP scores are calculated by averaging domain scores between 0-100. The higher the total score, the greater the severity of the health problems (9).

Modified Medical Research Board Scale (mMRC)

Fletcher was the first to utilize the mMRC to examine the degree of exercise-induced breathlessness in individuals with and without pulmonary pathology (10). Later, it was revised by the British Medical Research Council (MRC) in order to track the disease's prognosis (11). The mMRC is a five-item scale that requires patients to indicate the amount of exercise that generates dyspnea. It is based on different physical activities that make people feel like they are having problem breathing. There are numerous studies validated its use in the evaluation of dyspnea using arterial blood gas and pulmonary function tests (12-14).

Statistical analysis

Statistical analyses were performed using SPSS version 25 (SPSS, Chicago, IL, USA). Mean±SD, median (IQR), number and percentage (%) values were used for descriptive statistics. Normality distributions were measured by Kolmogorov-Smirnov and Shapiro-Wilk tests. Wilcoxon Signed-Rank test was used in the analysis as the data did not fit the normal distribution. p-value < .05 was considered statistically significant.

RESULTS

A total of 146 patients were included in the study. The mean age was 53.24±14.10, and mean body mass index was 28.45±5.50, and 61% (n:89) of the patients were male and 39% (n:57) were female. Demographic characteristics and comorbidities of the patients are shown in Table I.

Table I. Demographic and disease characteristics of the patients.

Features		x̄±SD	Median (IQR)
Age		53.24±14.10	53 (22)
Height		1.68±0.10	1.70 (0.16)
Weight		80.77±15.58	80 (21)
BMI		28.45±5.50	27.75 (6)
		n	**%**
Sex	Female	57	39
	Male	89	61
Additional diseases	None	83	56.8
	HT	41	28.1
	DM	5	3.4
	CAD	3	2.1
	HT + DM	8	5.5
	DM + CAD	3	2.1
	COPD	3	2.1
Total		**146**	**100**

BMI: Body mass index, **CAD:** Coronary artery disease, **COPD:** Chronic obstructive pulmonary disease, **DM:** Diabetes mellitus, **HT:** Hypertension, **IQR:** Interquartile Range, **SD:** Standard deviation, **x̄:** Mean

The patients' mean scores according to the first day NHP scale were; 29.5±37.6 for pain, 23.4±25.5 for emotional variables, 39±36.1 for sleep, 25±33.2 for social isolation, 65±33.7 for physical activity, 98.2±9.1 for energy, and the total score for part 1 was 280.3±95.1 (p < .001). Although a statistically significant decrease was detected in the mean scores of the NHP scale at the 12th month, the increase still continued (p < .001). Table II shows the comparison of the NHP scores of the patients on the 1st day and 12th month of their intensive care discharge.

Table II. Comparison of patients' NHP scores on the 1st day and 12th month of their intensive care discharge.

			x̄±SD	Median (IQR)	z score	*P*-value*
Nottingham Health Profile	Pain	First Test	29.5±37.6	0 (59.4)		**<.001**
		Last Test	9.6±17.7	0 (12.9)	7.118	
	Emotional Reactions	First Test	23.4±25.5	17.5 (31.5)		
		Last Test	6.3±9.6	0 (10.4)	8.042	**<.001**
	Sleep	First Test	39±36.1	27.2 (77.6)		
		Last Test	21±22.5	16.1 (27.2)	7.267	**<.001**
	Social Isolation	First Test	25±33.2	0 (42.6)		
		Last Test	4.4±10.5	0 (0)	7.235	**<.001**
	Physical Activity	First Test	65±33.7	78.7 (65.4)		
		Last Test	17.3±18.2	11.5 (23.8)	10.017	**<.001**
	Energy	First Test	98.2±9.1	100 (0)		
		Last Test	28.5±19.2	24 (12.8)	10.580	**<.001**
	1st Part Total Score	First Test	280.3±95.1	289.2 (126.6)		
		Last Test	87.4±70.6	69.6 (80)	10.482	**<.001**
	2nd Part	First Test	6.5±0.8	7 (1)		
		Last Test	1.6±1.3	2 (2)	10.569	**<.001**

IQR: Interquartile Range, **NHP:** Nottingham health profile questionnaire, **SD:** Standard deviation, **x̄:** Mean
*Wilcoxon Signed-Rank Test.

The mean mMRC scores of the patients were 4 on the 1st day of their intensive care discharge and 1 at the 12th month follow-up, and difference was statistically significant (p < .001). The comparison of mMRC scores is shown in Table III.

Table III. Comparison of patients' mMRC scores.

		Median (IQR)	*z* score	*P*-value*
mMRC	First Test	5 (0)		
	Last Test	1 (1)	10.685	**< .001**

mMRC: Modified medical research board scale, **IQR:** Interquartile Range
*Wilcoxon Signed-Rank Test.

DISCUSSION

The National Institute for Health and Clinical Excellence defines long COVID-19 as the persistance of COVID-19 infection signs and symptoms for more than four weeks (15). In this study, although a significant improvement was observed in the mean physical activity, sleep quality and fatigue index, after 12 months of follow-up, the limitation continued.

In long COVID-19, musculoskeletal pain was reported at a rate of at least 0.3% and at most 65.2% (16, 17). Inflammatory cytokine increase, immune cell hyperactivation, direct virus entry into neurological and musculoskeletal system via angiotensin-converting enzyme 2 receptor (ACE2), and psychological factors were accused mechanisms (18). In our study, the mean score of pain due to COVID-19 was 29.5 (0-100) on the first day of discharge, and despite a significant decrease at the end of the 1st year, it continued with an average score of 9.6 (0-100). The development of analgesia by opioids released by stress stimulation and inflammation may be responsible for the low pain score in patients with severe COVID-19 (19, 20).

Recent investigations showed that at one, three, six, and 12-month follow-ups after COVID-19 infection, 30-40% of patients had clinically severe depressive psychopathology (21). Depression manifested by impaired mood, decreased interest and cognitive impairment, negatively affects the daily life of patients. The result of SARS-CoV-2 infection, including greater infection rates, increased hospitalization and intensive care unit admission, and higher mortality rate, has been reported to be influenced by depressive symptoms associated with COVID-19 as well as pre-existing depression (22). A study by Vlake et al. showed that ICU patients reported probable depression less frequently compared to the patients followed up in the service, but no differences were found in post-traumatic stress disorder (PTSD), anxiety, or overall health-related quality of life scores. In the 3rd month controls, PTSD and anxiety severity were related with being Caucasian, and depression with education (23). In our study, emotional reaction score of our patients scored an average of 23.4 points (0-100) on the first day and 6.3 (0-100) points at 12th moth control, showing significant improvement. The decrease in emotional reaction scores may be due to patients' increased social support and physical well-being.

Sleep is one of the important physiological activities performed by all animal species. It is necessary for a healthy life such as enhancing memory, modulating immune function, and regulating hormonal secretions (24). Sleep disturbances have been widely observed during the COVID-19 pandemic. Four out of ten people reported sleep problems, and the main complaint was insomnia (25). In our study, the sleep quality index of our patients continued to be low at the 12th month control. Stress, depression, lack of physical activity due to quarantine, increased daytime sleepiness and circadian rhythm disorder may be responsible for prolonged sleep disorders.

The COVID-19 epidemic has prompted the use of currently unheard-of "social distancing" tactics that are essential to prevent the virus's spread (26). During the course of the pandemic, the prevalence of social isolation increased by 6.7% (6.3-7.0) points. Elderly people and men experienced the greatest increase in the prevalence of social isolation (27). In our study, social isolation index, which was high immediately after intensive care discharge, decreased during our follow-ups and regressed to similar averages with the community.

According to a recent study, the majority of COVID-19 survivors sustained good physical and functional recoveries and returned to their regular professions and lifestyles during the one-year follow-up. However, the follow-up cohorts still had inferior health quality than the control population (28). In our study, although a significant improvement was observed in the mean physical activity index after 12 months of follow-up, the limitation continued. This may be due to the increase in the chance of physical activity with the end of quarantines and the development of exercise capacities over time.

Fatigue is the most common symptom in long COVID-19 disease, and its etiology is attributed to post-viral conditions (29, 30). A meta-analysis of 81 studies showed that approximately one-third of the participants experienced chronic fatigue (31). Pain inquiries in our study revealed that an intense fatigue continued at 12th month. Dyspnea is the second most common complaint with long COVID-19 (32). A study by Brugge et al. showed a significant decrease in lung diffusing capacity after severe COVID-19 pneumonia and found a significant correlation between carbon monoxide diffusion capacity (DLCO Test) and forced expiratory volume in the first second (fev1) measurements and physical function part of mMMRC and Short Form-36 (SF-36) questionnaire scores (33). However, a significant decrease was detected in control mMMRC in our study and participants generally described dyspnea only during heavy exertion. Deconditioning, restrictive/obstructive airflow limitation or systemic inflammation have been proposed for explaining the presence of fatigue and effort dyspnoea at 12th month (34).

The long-lasting symptoms of COVID-19 lead to loss of physical and mental health functions as well as quality of life (35). Even two years after severe COVID-19, the health-related quality of life index may still be low in pa-

tients (36). In a 12 month follow up study conducted in the post-COVID patients by Betschart et al., 12 of 41 patients continued to have moderate-to-severe pain that impairs their quality of life (37). Another study showed that post-COVID-19 patients' decreased quality of life was influenced by demographic and socioeconomic characteristics (38). In our study, although it showed improvement in the 12th month controls, quality of life index was still remained low ın line with the literature.

The main limitations of our study are that; it is a questionnaire study based on the subjective responses of the patients and objective evaluation of pulmonary capacities like pulmonary function tests and carbon monoxide diffusion tests were not performed.

CONCLUSION

Definition and recognition of the post-COVID syndrome constitute the first step in the transition to the treatment of patients. In addition to its devastating effects in the acute period, COVID-19 will continue to exist in our lives with its contribution to low quality of life in the long term. We suggest that follow up of the patients with COVID-19 in terms of post-COVID syndrome and taking the necessary precautions are important for public health and the country's economy.

Ethics Committee Approval:
This research complies with all the relevant national regulations, institutional policies and is in accordance the tenets of the Helsinki Declaration, and has been approved by the Adana City Education and Research Hospital, Medical Faculty Ethical Committee, (approval number: 2023/2389).

Informed Consent:
All the participants' rights were protected and written informed consents were obtained before the procedures according to the Helsinki Declaration.

Author Contributions:
Concept – S.B.S., G.Y.Ö.; Design - S.B.S., G.Y.Ö.; Supervision - S.B.S., G.Y.Ö.; Resources - S.B.S., G.Y.Ö.; Materials - S.B.S., G.Y.Ö.; Data Collection and/or Processing - S.B.S., G.Y.Ö,T.S. ;Analysis and/ or Interpretation - S.B.S., G.Y.Ö,T.S.; Literature Search - S.B.S., G.Y.Ö,T.S.; Writing Manuscript - S.B.S., G.Y.Ö,T.S.; Critical Review - S.B.S., G.Y.Ö,T.S.

Conflict of Interest:
The authors have no conflict of interest to declare.

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