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RESEARCH ARTICLE

Post-COVID-19 functional limitations in hospitalized patients and associated risk factors: A 3-month follow-up study

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Abstract

Background and Purpose: Many patients experience post-COVID-19 functional limitations. This study aimed to monitor the functional improvement of patients over 3 months of follow-up and determine the risk factors.

Methods: This prospective cohort study evaluated 100 hospitalized patients who recovered from COVID-19 infection. The mean age was 53.2 ± 13.1 years. Fifty-nine had at least one comorbid condition. The mean lengths of the hospital and ICU stays were 7.8 ± 3.3 and 5.3 ± 2.5 days, respectively. The functional status of the patients was evaluated using functional independence measure (FIM) and post-COVID-19 functional status (PCFS) questionnaires at four time-points of discharge, 1 week, 1 month, and 3 months after discharge.

Results: Mean FIM score was 107.2 ± 17.4 at the time of discharge, 113.3 ± 14.9 at 1 week, 120.3 ± 10.2 at 1 month, and 124.3 ± 6.4 at 3 months after discharge ($p < 0.001$). The PCFS score was 2.71 ± 1.25 at discharge, 2.09 ± 1.3 at 1 week, 1.14 ± 1.1 at 1 month, and 0.64 ± 0.59 at 3 months after discharge ($p < 0.001$). Female sex, older age, and the lengths of hospital and ICU stays were negatively correlated with the functional status score.

Discussion: Post-COVID-19 functional limitations are observed in hospitalized patients and improve over 3 months after discharge. Female sex, older age, longer hospital, and ICU stays are risk factors that negatively impact functional status.

KEYWORDS
COVID-19, functional status, rehabilitation, risk factor

1 | INTRODUCTION

COVID-19 pandemic, caused by SARS-CoV-2, has posed a global health challenge and forced world-leading health organizations to expand scientific knowledge on different aspects of the condition to provide timely interventions in order to minimize virus transmission and impact (Crain et al., 2021). It is acknowledged that COVID-19 is a multi-organ disorder, and other than respiratory symptoms, several other symptoms develop, including cardiovascular, gastrointestinal, neurologic, and musculoskeletal complications (Thakur et al., 2021; Zaim et al., 2020).

Some symptoms are prolonged and persistent, not only in the elderly and patients with comorbidities but also in young and active patients with no prior history of comorbidities (Tenforde et al., 2020).

Therefore, the impact of COVID-19 goes beyond its clinical outcomes and affects health-related quality of life (HRQoL) in the post-COVID-19 period (Poudel et al., 2021).

According to the cumulative body of evidence, 11%–24% of COVID-19 patients experience long-term symptoms even 3 months after disease onset ("Understanding the long-term health effects of COVID-19," 2020). Persistent fatigue and musculoskeletal weakness, dyspnea, headache, and attention disorder are among the most common long-term symptoms (Salamanna et al., 2021). The significance of post-COVID-19 complications demands the development of rehabilitation programs to reduce the impacts on the patients' daily activities.

In order to manage the chronic effects of COVID-19, longitudinal evaluation of the patient function and impacting factors is of utmost importance. In this study, we aimed to evaluate the impact of COVID-19 on the post-discharge functional status of the patients and monitor changes over 3 months. We also investigated the risk factors of poor functional outcomes.

2 | METHODS

This prospective cohort was approved by the Ethics Committee of Shahid Beheshti University of Medical Sciences under code IR.SBMU.MSP.REC.1400.266. Inclusion criteria comprised a definitive diagnosis of COVID-19 based on a positive PCR test and the need for hospitalization. Exclusion criteria included physical disabilities and underlying conditions affecting the personal function of patients, such as fibromyalgia, osteoarthritis, and multiple sclerosis. Overall, 417 COVID-19 patients were evaluated for eligibility, and eventually, 103 were recruited. Three patients were lost to follow-up and excluded from the analysis. Ultimately, data for 100 patients (51 males and 49 females) were analyzed (Figure 1).

2.1 | Function evaluation

The functional status of the patients was evaluated using functional independence measure (FIM) and post-COVID-19 functional status (PCFS) questionnaires. The FIM questionnaire includes 18 questions in motor and cognitive function subscales. Motor function is further divided into the subscales of self-care, sphincter control, transfers, and locomotion. Cognitive function is categorized into communication and social cognition subscales. Each FIM question is scored on a 1–7 ordinal scale, leading to a total score ranging from 18 to 126. A higher score is indicative of a better function. The validity and reliability of the Persian translation of FIM have been demonstrated (Naghdi et al., 2016).

PCFS is comprised of a series of consecutive questions that focuses on different aspects of daily activities during the follow-up period of COVID-19. Accordingly, personal post-COVID-19 status is categorized into five grades from 0 to 4, respectively indicating no functional limitation, negligible functional limitation, slight functional limitation, moderate functional limitation, and severe functional limitation (Klok et al., 2020).

Questionnaires were filled out at four time-points of discharge, 1 week, 1 month, and 3 months after discharge by an investigator who was not involved in the study design. The first evaluation was in person, while the next three were performed through phone calls.

2.2 | Statistical analysis

Statistical analyses were made using SPSS for Windows version 16 (SPSS Inc.). Descriptive data are presented by mean ± standard deviation (SD) or number and percentage. Kolmogorov–Smirnov test was used to check the normal distribution of data. ANOVA assessed changes in scores over time. Comparison of mean values between

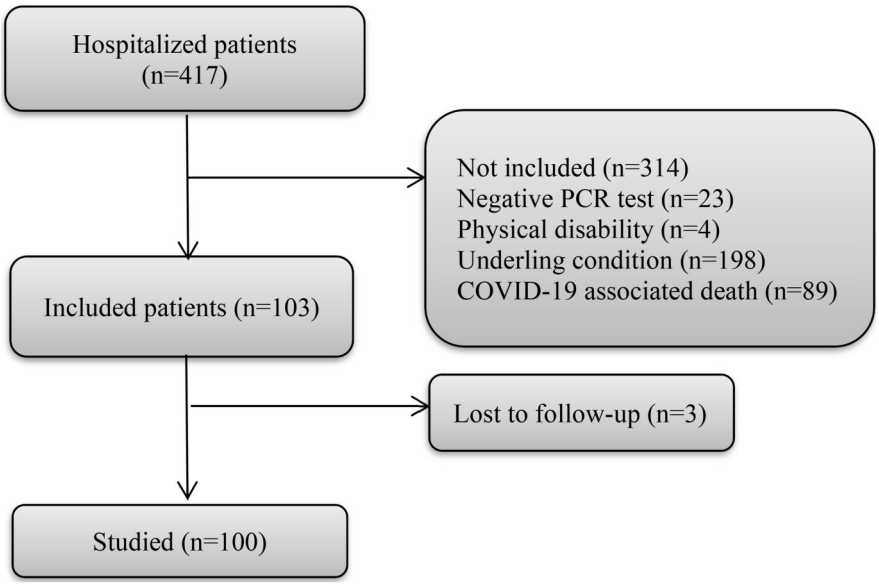

FIGURE 1 Flow diagram of the study inclusion and exclusion

different groups was undertaken using an independent *t*-test or its nonparametric counterpart, the Mann–Whitney *U*-test. The chi-square test was used to compare the qualitative variables. Pearson's correlation coefficient test was applied to evaluate the potential correlations. A multiple linear regression test was used to omit the effect of confounding factors on the association of post-COVID-19 functions and its risk factors. A *p*-value of <0.05 was considered significant.

TABLE 1 Characteristic features of the hospitalized COVID-19 patients

Variable	Patients (n = 100)
Age (year)	53.2 (13.1)
Sex	
Male	49
Female	51
Education	
Illiterate	23
Low education level	47
High education level	30
Occupation	
Housewife	39
Retired	12
Employed	49
Comorbidities	59
Body mass index	24.6 (3.1)
Length of hospital stay (days)	7.8 (3.3)
Length of ICU stay (days)	5.3 (2.5)
Intubation period (days)	2.8 (1.3)

Note: Quantitative data are presented as mean (SD).

3 | RESULTS

A total of 100 patients, including 51 males and 49 females with a mean age of 53.2 ± 13.1, ranging from 29 to 85 years, were studied. Fifty-nine patients had at least one comorbidity, including hypertension, diabetes, and cardiovascular disorders. The patients were hospitalized for 2–21 days. Seventeen patients needed ICU admission for a range of 1–10 days. The duration of intubation of the patients ranged from one to 5 days. The three groups of patients included illiterate, low educational level (less than an associate's degree), and high educational level (associate degree and higher). Demographic data are listed in Table 1. Changes in the FIM score over time were statistically significant ($p < 0.001$). Also, motor and cognitive function subscales showed significant improvement (both $p < 0.001$). In the motor subscale, sphincter control did not significantly change. In the cognitive subscale, both communication and social cognition scores significantly improved over time ($p = 0.03$ and $p = 0.009$, respectively) (Table 2 and Figure 2).

PCFS grade was 2.71 ± 1.25 at discharge, 2.09 ± 1.3 1 week, 1.14 ± 1.14 1 month, and 0.64 ± 0.89 3 months after discharge. Accordingly, PCFS grade significantly improved over time ($p < 0.001$) (Figure 3).

Regarding underlying and predisposing conditions, a significant negative correlation was found between improvement of FIM score and age ($r = -0.412$, $p < 0.001$), and lengths of hospital ($r = -0.365$, $p = 0.008$), and of ICU stays ($r = -0.588$, $p < 0.001$). Considering sex, the FIM score improved more significantly in male patients ($p = 0.02$). Regarding PCFS changes, improvements were negatively correlated with age ($r = -0.408$, $p < 0.001$), and lengths of hospital ($r = -0.282$, $p = 0.015$), and ICU stays ($r = -0.549$, $p < 0.001$). No significant difference was found between PCFS scale improvement in males and females ($p = 0.89$). Moreover, no significant association was found between functional measurements and occupation, education, BMI, or intubation length. The same associations were demonstrated in multivariate analysis (Tables 3 and 4).

TABLE 2 Changes in FIM score and its subscales up to 3 months after hospitalization for COVID-19

Score	At discharge	One week after discharge	One month after discharge	Three months after discharge	*p* -value
Total FIM	107.2 (17.4)	113.3 (14.9)	120.3 (10.2)	124.3 (6.4)	< 0.001
Motor function	73.4 (16.5)	78.9 (14.1)	85.4 (10.1)	88.3 (6.4)	< 0.001
Self-care	33.2 (9.2)	35.9 (7.6)	39.3 (5.3)	40.5 (3.5)	< 0.001
Sphincter control	14.0 (0.2)	13.9 (1.0)	13.9 (0.6)	14.0 (0.1)	0.32
Transfers	16.7 (4.8)	18 (3.9)	19.6 (3.1)	20.3 (2.1)	< 0.001
Locomotion	9.5 (3.4)	11.1 (2.7)	12.5 (2.2)	13.4 (1.4)	< 0.001
Cognitive function	33.8 (2.2)	34.4 (1.7)	34.8 (0.6)	35.0 (0)	< 0.001
Communication	13.5 (1.1)	13.8 (0.7)	13.9 (0.2)	14.0 (0)	0.03
Social cognition	20.3 (1.4)	20.6 (1.2)	20.8 (0.6)	21.0 (0)	0.01

Note: Data are demonstrated as mean (SD). $p < 0.05$ is considered significant.

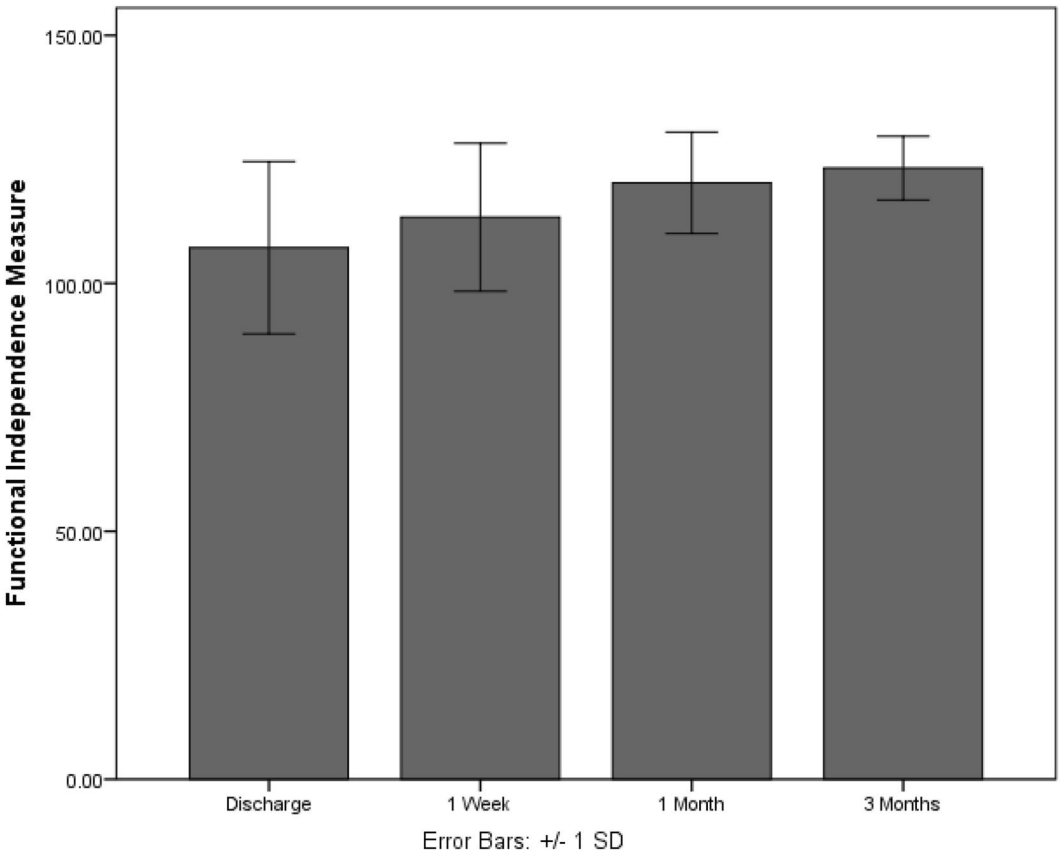

FIGURE 2 Continuous improvement of functional independence score over 3 months

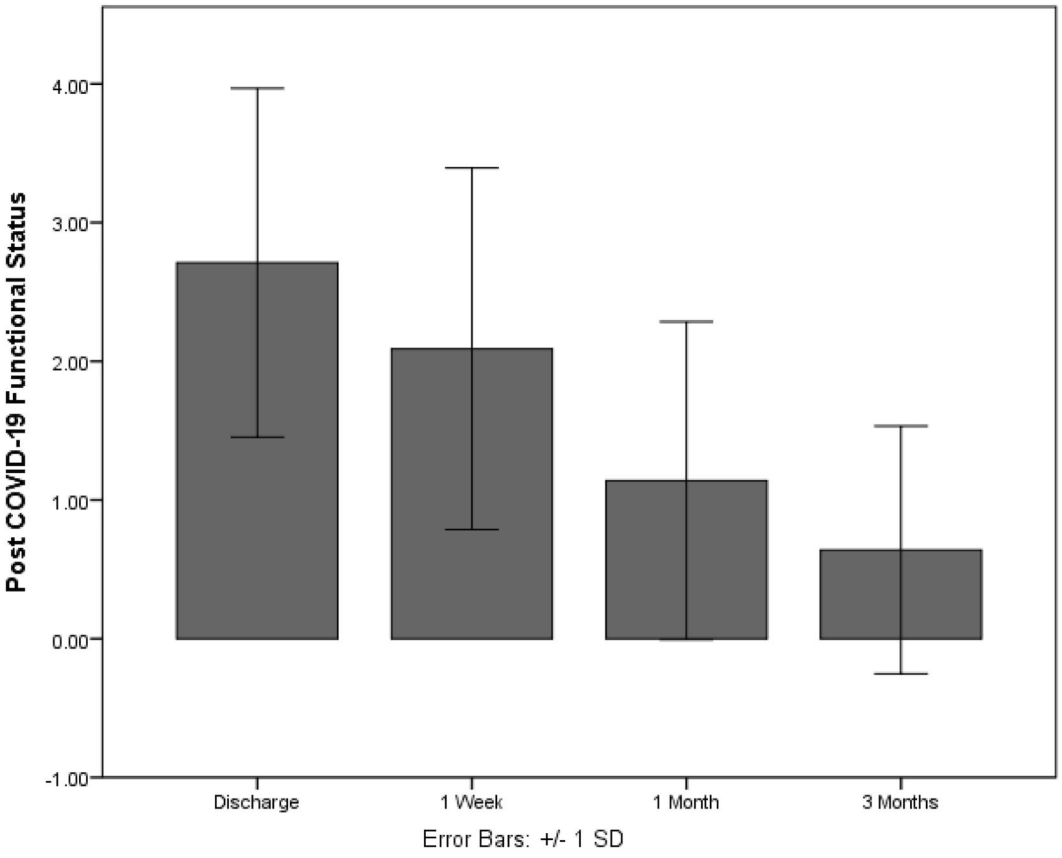

FIGURE 3 Continuous improvement of post-COVID-19 functional status over 3 months

TABLE 3 Multiple regression analysis shows the predictive value of demographic and hospitalization factors on the functional independence measure (FIM) score

Variable	Odds ratio	*p*-value	95% CI	
			Lower	Upper
Age	1.923	0.031	1.143	3.129
Sex	1.671	0.048	0.117	1.99
BMI	1.228	0.28	0.765	2.113
Education	1.056	0.82	0.701	1.229
Occupation	0.998	0.85	0.654	1.091
Comorbidity	1.202	0.09	0.872	0.1651
Length of hospital stay	1.439	0.04	1.303	2.533
Length of ICU stay	2.131	0.01	1.245	3.389
Intubation period	1.287	0.11	0.897	2.432

TABLE 4 Multiple regression analysis shows the predictive value of demographic and hospitalization factors on the post-COVID-19 function (PCFS) score

Variable	Odds ratio	*p*-value	95% CI	
			Lower	Upper
Age	1.727	0.027	1.221	2.996
Sex	1.084	0.41	0.569	1.345
BMI	1.102	0.36	0.689	1.187
Education	1.002	0.78	0.839	1.441
Occupation	1.091	0.77	0.692	1.501
Comorbidity	1.192	0.11	0.826	1.721
Length of hospital stay	1.648	0.032	0.1421	2.845
Length of ICU stay	2.321	0.023	1.456	3.578
Intubation period	1.199	0.21	0.882	1.983

4 | DISCUSSION

In this study, we evaluated the personal function of COVID-19 patients over 3 months after discharge. The impact of various demographic and hospitalization factors on post-COVID-19 function was also evaluated. According to the results, the functional status of patients continuously improved during the 3 months and almost reached an optimal level at the end of follow-up. Sex, age, lengths of the hospital, and ICU stays were important predictors of post-COVID-19 function. In this respect, female sex, older age, longer hospital, and ICU stays were associated with inferior functional outcomes.

After evaluating the functional status of 242 hospitalized COVID-19 patients 6 months after the infection, Taboada et al. found that 44 (18.2%) patients required ICU admission, and the median length of ICU stay was 13 days. Mechanical ventilation was needed for 31 (12.8%) patients, and the overall median hospital stay was 10 days. In total, 183 patients (32 of whom required ICU admission) completed the questionnaires. Improvement in the PCFS was noticed in 87 (47.5%) patients. Female sex, older age, longer hospitalization, and the need for mechanical ventilation and ICU admission were associated with more functional limitations (Taboada et al., 2021). In the present study, we found that 17 (17%) patients needed ICU admission, and the lengths of the hospital and ICU stays were considerably lower than their findings (7.8 and 5.3 days, respectively). Similar to the abovementioned study, female sex, older age, and longer hospital and ICU stays were associated with more functional limitations. However, mechanical ventilation was not a risk factor for worse functional outcomes.

A multicenter study evaluated the post-COVID-19 functional limitations in the daily living activities of 2000 hospitalized patients with a mean follow-up of 8.4 months, and 20%–30% of patients reported limitations in at least one daily activity. Also, the severity of COVID-19 symptoms at the time of hospitalization and the need for ICU admission were significantly associated with worse functional outcomes. Similar to our study, female sex and older age were associated with more functional limitations (Fernández-de-Las-Peñas et al., 2021).

Another multicenter study reported long-term post-COVID-19 symptoms and associated risk factors in 1142 previously hospitalized patients. Only 212 (18.6%) patients were symptom-free in the 7 months of follow-up. Female sex, ICU admission, more hospitalization days, more medical comorbidities, and more acute COVID-19 symptoms at admission were associated with more post-COVID-19 symptoms. Fatigue, alopecia, and dyspnea were the most frequent post-COVID-19 symptoms (60.8%, 26.3%, and 23.5%, respectively) (Fernández-de-Las-Peñas et al., 2021). In our study, comorbidities were not associated with long-term functional limitations. This discrepancy can be attributed to the small sample size compared to this study.

Du et al. evaluated the post-COVID-19 functional status of 95 discharged patients with a median age of 62 years. At 6 months follow-up, complete functional status (PCFS grade 0) was recorded in 67 (70.5%) patients. Myalgia or arthralgia at the disease onset was associated with the worse post-COVID-19 functional outcomes (Du et al., 2021). We did not evaluate the onset symptoms of the patients and their impact on post-COVID-19 functional status.

Mohamed Hussein et al. evaluated the post-COVID-19 functional status in 444 recovered patients and found post-COVID-19 functional limitations in 80% of the patients. Older age, female sex, need for oxygen supplementation, ICU admission, smoking, and comorbid conditions were associated with more functional limitations (Mohamed Hussein et al., 2021). In the present study, most patients achieved an almost complete functional status (mean PCFS grade of 0.64) at the end of 3 months of follow-up.

The long-term impacts of COVID-19 on functional status, and other HRQoL indicators, have been evaluated in several other investigations (Leigh et al., 2021; Moreno-Pérez et al., 2021; Madhavan & Pandurangan, 2021; Sanchez-Ramirez et al., 2021). The majority of these studies reported the significance of long-term COVID-19 functional impacts and the need for early rehabilitative

interventions to reduce disease's health and economic burdens. Risk factors of poor functional status such as female sex, older age, ICU admission, and the length of hospitalization are characteristic factors that help identify at-risk patients to undertake appropriate and timely interventions.

The present study was not without limitations, the main limitation being a small sample size. Moreover, we only included hospitalized patients. Therefore, the results of this study cannot be generalized to nonhospitalized COVID-19 patients, who probably have different characteristics. On the other hand, we did not evaluate the number and severity of symptoms at the time of hospitalization. Several studies have shown it to be of importance in predicting functional outcomes.

5 | IMPLICATIONS ON PHYSIOTHERAPY PRACTICE

Post-COVID-19 functional limitations are observed in hospitalized patients and continuously improve over 3 months after discharge to reach an almost optimal status after 3 months in most patients. Female sex, older age, longer hospital, and ICU stays are associated with inferior post-COVID-19 functional outcomes and can be used as indicators to identify patients at higher risk of post-COVID-19 functional limitations.

ACKNOWLEDGMENTS

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ETHICS STATEMENT

In this prospective cohort, eligible COVID-19 patients admitted to Shohada-Tajrish Educational Hospital were recruited. The ethics committee of Shahid Beheshti University of Medical Sciences approved this research under the code IR.SBMU.MSP.REC.1400.266.

PATIENT CONSENT STATEMENT

All patients provided written informed consent prior to their participation in the study.

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