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Long-term functioning status of COVID-19 survivors: a prospective observational evaluation of a cohort of patients surviving hospitalisation

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ABSTRACT

Objectives The study investigated the long-term functional status of hospitalised COVID-19 survivors to explore and document their functional situation.

Design This prospective observational study assessed 801 COVID-19 survivors at 3–11 months after hospital discharge. It analyses participants' sociodemographic background, COVID-19 clinical manifestations, and clinical and functional evaluations.

Setting Tertiary-level university hospital in São Paulo, Brazil.

Participants Study participants are COVID-19 survivors admitted to hospital care for at least 24 hours to treat acute SARS-CoV-2 infection.

Outcome measures Epworth Sleepiness Scale, EuroQoL-5 Dimensions-5 Levels, Functional Assessment of Chronic Illness Therapy–Fatigue, Functional Independence Measure, Functional Oral Intake Scale, Handgrip Strength, Insomnia Severity Index, Medical Research Council (MRC) Dyspnea Scale, MRC sum score, Modified Borg Dyspnea Scale, pain Visual Analogue Scale, Post-COVID-19 Functional Status, Timed Up and Go, WHO Disability Assessment Schedule 2.0, 1-Minute Sit to Stand Test.

Results Many participants required invasive mechanical ventilation (41.57%, 333 of 801). Mean age was 55.35±14.58 years. With a mean of 6.56 (SD: 1.58; 95% CI: 6.45 to 6.67) months after hospital discharge, 70.86% (567 of 800) reported limited daily activities, which were severe in 5.62% (45 of 800). They also reported pain and discomfort (64.50%, 516 of 800), breathlessness (64.66%, 514 of 795), and anxiety and depression (57.27%, 457 of 798). Daytime sleepiness and insomnia evaluations showed subthreshold results. Most (92.85%, 727 of 783) participants reported unrestricted oral intake. Data indicated no generalised fatigue (mean score: 39.18, SD: 9.77; 95% CI: 38.50 to 39.86). Assessments showed poor handgrip strength (52.20%, 379 of 726) and abnormal Timed Up and Go results (mean 13.07 s, SD: 6.49). The invasive mechanical ventilation group seemed to have a better handgrip strength however. We found no clear trends of change in their functional status during months passed since hospital discharge.

Conclusions Muscle weakness, pain, anxiety, depression, breathlessness, reduced mobility, insomnia and daytime sleepiness were the most prevalent long-term conditions identified among previously hospitalised COVID-19 survivors.

STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ The same test battery was applied in person to all study participants. Minor discrepancies in the number of participants assessed in each evaluation occurred due to non-assessment for various reasons.
⇒ The study test battery used both self-reported, clinical assessments and quantifiable measures.
⇒ It lacks a control group, which was not feasible in the study setting during the time it was conducted, when most wards were converted to admit COVID-19 cases.
⇒ Evaluations were conducted by a multidisciplinary team of numerous health and rehabilitation professionals, which was due to the short time window we had to conduct all assessments.

INTRODUCTION

Data on the global outbreak of COVID-19 show that the vast majority of people infected by the SARS-CoV-2 do not die from the disease.[1 2] The long-term functional status of COVID-19 survivors remains poorly explored and documented. Disabling consequences may impact the individual, who despite being classified as recovered, could benefit from multidisciplinary rehabilitation to restore function in all aspects of life. Given

the diversity of clinical manifestations in patients with COVID-19 and the short period since the occurrence of the first cases, little is known about the long-term impact of COVID-19 on functioning, including the repercussions at different stages of recovery.

Information regarding post-acute sequelae of SARS-CoV-2 (PASC) is emerging. Despite some heterogeneity in evaluation and follow-up methods, there are recurrent and interesting findings in recent literature. Self-reported fatigue is the main long-term symptom after hospital discharge.[3–7] Huang *et al* report increased fatigue or muscle weakness in 63% of 1655 patients 6 months after symptoms onset.[8] Breathlessness, defined as the unpleasant sensation of uncomfortable, rapid or difficult breathing, has also been reported as a persistent symptom.[5–10] Pain (myalgia, arthralgia and headaches) is a frequent persisting long-term complaint of COVID-19 survivors.[3–5 7–9 11 12] Other self-reported symptoms include anxiety and depression,[6–8 12] memory[5 7] concentration[5] and sleep disorders.[5 7–9] Objective assessments including the Short Physical Performance Battery Test and the 2-Minute Walking Test detected a prevalence of 32%[13] to 53.8%[11] of long-term physical impairments after hospital discharge. Different levels of fatigue, muscle weakness, pain and discomfort may require different models of rehabilitation service delivery. However, there is still a knowledge gap on objective evaluation and classification criteria for the several functional domains affected by COVID-19 to guide more effective rehabilitation needs assessments and interventions. Thus, a better understanding of functional disorders that may arise in the long term after hospitalisation to treat COVID-19 will contribute to better health outcomes.

Therefore, this is a prospective observational evaluation of a cohort of COVID-19 survivors managed at the University of São Paulo Medical School General Hospital (HCFMUSP) during the acute phase of the disease after 3–11 months of hospital discharge, aiming at identifying their long-term functioning status and rehabilitation needs.

MATERIALS AND METHODS

Study population

The study population consists of 801 COVID-19 survivors, 18 years or older, who were admitted at HCFMUSP for more than 24 hours between March and August 2020, with a diagnosis of COVID-19 confirmed by either PCR or serology testing for SARS-CoV-2.

Patient and public involvement

Study participants did not take part in the design or conduct of the work. Nevertheless, study results and guidance are shared with participants and patients attending post-COVID-19 rehabilitation in the study setting through informative and educational leaflets.

Study design

This prospective observational evaluation of a cohort of COVID-19 survivors is based on a follow-up test battery conducted 3–11 months after hospital discharge with people previously admitted to treat acute COVID-19. Participants were recruited between 7 October 2020 and 8 April 2021. Study assessments were completed between 20 October 2020 and 16 April 2021. Data were registered using the Research Electronic Data Capture platform. Further details about the study protocol are available elsewhere.[14 15] To accommodate for limitations in recruitment, the study included participants 3–11 months after hospital discharge. The reporting of this cohort study followed the principles of the Strengthening the Reporting of Observational Studies in Epidemiology statement.

Assessments

All data were collected at HCFMUSP premises. When possible, questionnaires were administered by teleconsultation prior to in-person assessments, which were conducted by a multidisciplinary team of 16 evaluators.

Sociodemographic and COVID-19 clinical manifestation data include age, sex, race, comorbidities and symptoms upon hospital admission, length of hospital stay (LoS) and time since hospital discharge. Clinical and functional evaluations used a large set of tools and scales, as per the study protocol (see online supplemental table 1).[14]

Handgrip strength measurement used a Jamar hydraulic hand dynamometer (Sammons Preston, Bolingbrook, Illinois, USA). Participants were seated with their elbows by their sides and bent at right angle, and a neutral wrist position. Each hand was tested three times and mean scores recorded. The mean score from the side with the highest results was included for data analysis.

A G-Walk inertial sensor (BTS Bioengineering and LetSense Group, Padova, Italy) measured and informed Timed Up and Go (TUG) results.

Data analysis

All continuous study data related to participants' characteristics or results are presented as arithmetic means±SDs. Intervals at 95% CI for the means were estimated with Student's t-distribution at the proper df. When appropriate, the range between minimum and maximum values is included. Categorical and binary data are shown as number of positive occurrences along with the percentage relative to the total study population. The total number of participants included (n) may vary across attributes due to data availability and evaluations applicability. As missing data were uncommon for the variables of interest, we dismissed any data imputation method.

Results are shown for the full dataset of participants as well as three subgroups classified according to the WHO definitions of illness severity for COVID-19[16]: those who did not receive oxygen support, those who did and those who received invasive mechanical ventilation. When analysing handgrip strength and TUG results, participants were further divided into age groups. Handgrip strength data were stratified by sex and age groups for

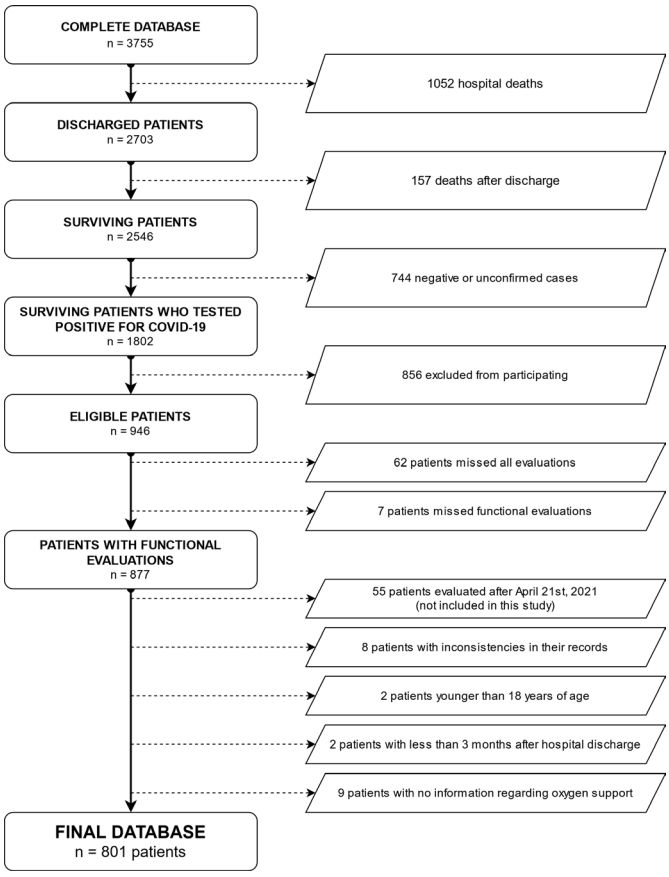

Figure 1 Flow diagram of study participants.

classification. For these two variables, we investigated differences among the three subgroups using factorial analysis of variance (ANOVA) tests with additional confounders of age (elder participants ≥60 years of age; younger participants <60 years of age), race (white/Asian; mixed/black/Indigenous/other), sex, total number of comorbidities (0–1 comorbidity; 2–3 comorbidities; 4+ comorbidities) and time since hospital discharge. Two-way interactions were also accounted for. Tukey's honestly significant difference (HSD) test was used as a post-hoc test for multiple comparisons. Homoscedasticity was verified by residuals versus fitted plots. G-test for homogeneity was used for comparing differences in proportions. The family-wise error rate was controlled with the Holm-Bonferroni approach. The null hypothesis is rejected for $p<0.05$.

Additionally, for pain Visual Analogue Scale (VAS), anxiety and depression (EuroQoL-5 Dimensions-5 Levels, EQ-5D-5L), dyspnoea (Medical Research Council (MRC) Dyspnea Scale), fatigue (Functional Assessment of Chronic Illness Therapy (FACIT)–Fatigue) and muscle strength (handgrip strength measurement), participants were divided into nine groups, according to the time elapsed since hospital discharge; the groups for 3 and 11 months (both extremes of our range) had less than 10 participants each and were not included in the analyses.

Finally, we have conducted supplementary analysis to understand whether variables related to acute COVID-19 (such as the need for intubation) were associated with post-COVID-19 functional outcomes such as sleep, pain, motor strength and dyspnoea. Linear regression models, also adjusted for confounders, were conducted to this end, and those results can be found in the online supplemental tables.

All data analyses were performed with IBM SPSS V.27.0, Python and related libraries,[17–19] except for the additional multivariate linear regression analysis which was performed with STATA V.17.0 BE. P values were only calculated for continuous variables. Because this is a new condition, of which many aspects are yet unknown, possible predictors or effect modifiers were not described, and subgroup and sensitivity analyses were not performed.

RESULTS

Figure 1 shows a flow diagram of study participants. As per the study protocol,[14 15] all patients with COVID-19 discharged in the period covered by the study were consecutively invited to take part. Reasons for exclusion included the lack of confirmatory PCR or serology tests, age (<18 years), time since hospital discharge (<3 months) and lack of information on the type of oxygen support received during treatment, or any other data inconsistency.

The majority of the study population (n=719) received some form of oxygen support, with non-invasive support (n=386) being more frequent than invasive mechanical ventilation (n=333). Only approximately 10% of participants did not require any oxygen support (n=82). Participants' age ranged from 18.4 to 101.3 years, with an average of 55.35±14.58 years (95% CI: 54.34 to 56.36). Age distribution is similar between groups. LoS is markedly longer for those who received invasive support, averaging at 30.19±21.05 days (95% CI: 27.92 to 32.46) compared with 6.50±6.17 (95% CI: 5.14 to 7.86) for the group with no oxygen support, and 11.63±10.16 (95% CI: 10.61 to 12.65) for the non-invasive support group. A large proportion of participants was admitted to intensive care (n=497), with an average LoS in intensive care of 8.39±12.00 days (95% CI: 7.56 to 9.22). Overall, the study population consisted of 421 men (52.56%) and 380 women (47.44%). The most common comorbidities among all participants were hypertension (462 of 801, 57.68%) and diabetes (292 of 801, 36.45%). Details on other participants' characteristics are shown in table 1 and in the online supplemental table 2.

Post-COVID-19 Functional Status (PCFS) scale results revealed that 70.86% of participants (567 of 800) reported limitations in daily activities, which were severe for 5.62% (45 of 800) of them. The invasive mechanical ventilation group presented a slightly larger proportion of participants referring some form of limitation, reaching 78.08% (260 of 333). EQ-5D-5L results showed that 64.50% (516 of 800) still suffered from pain and discomfort, while 57.27% (457 of 798) reported anxiety and depression. Pain VAS results corroborated it by showing that 45.93%

Table 1 Sociodemographic and clinical data presented as n participants (%), mean (SD), alongside 95% CI and range

	All participants (n=801)			No oxygen support (n=82)			Oxygen support (n=386)			Intubation (n=333)		
Sex												
Male	421 (52.56%)			38 (46.34%)			213 (55.18%)			170 (51.05%)		
Female	380 (47.44%)			44 (53.66%)			173 (44.82%)			163 (48.95%)		
Race												
White	370 (46.19%)			36 (43.90%)			188 (48.70%)			146 (43.84%)		
Mixed	288 (35.96%)			30 (36.59%)			132 (34.20%)			126 (37.84%)		
Black	107 (13.36%)			10 (12.20%)			49 (12.69%)			48 (14.41%)		
Asian	11 (1.37%)			4 (4.88%)			6 (1.55%)			1 (0.30%)		
Indigenous	7 (0.87%)			0 (0.00%)			4 (1.04%)			3 (0.90%)		
Not informed	18 (2.25%)			2 (2.44%)			7 (1.81%)			9 (2.70%)		
The most common symptoms upon hospital admission												
Cough	309 (39.62%, total=780)			28 (34.57%, total=81)			129 (34.04%, total=379)			152 (47.50%, total=320)		
Rheumatic joint disease	215 (27.78%, total=774)			15 (18.52%, total=81)			110 (29.02%, total=379)			90 (28.66%, total=314)		
Chest pain	203 (26.06%, total=779)			14 (17.50%, total=80)			109 (28.68%, total=380)			80 (25.08%, total=319)		
The most common comorbidities												
Hypertension	462 (57.68%, total=801)			37 (45.12%, total=82)			231 (59.84%, total=386)			194 (58.26%, total=333)		
Diabetes	292 (36.45%, total=801)			26 (31.71%, total=82)			139 (36.01%, total=386)			127 (38.14%, total=333)		
	Mean (SD)	**95% CI**	**Range**	**Mean (SD)**	**95% CI**	**Range**	**Mean (SD)**	**95% CI**	**Range**	**Mean (SD)**	**95% CI**	**Range**
Age (in years)	55.35 (14.58)	54.34 to 56.36	18.40–101.30	50.90 (17.08)	47.15 to 54.66	18.40–88.30	56.59 (14.71)	55.12 to 58.06	21.10–101.30	55.00 (13.55)	53.54 to 56.46	18.60–86.30
Length of hospital stay (in days)	18.82 (18.22)	17.56 to 20.08	1.00–154.00	6.50 (6.17)	5.14 to 7.86	1.00–32.00	11.63 (10.16)	10.61 to 12.65	1.00–96.00	30.19 (21.05)	27.92 to 32.46	1.00–154.00
Length of ward stay (in days)	10.43 (10.01)	9.74 to 11.13	0.00–82.00	5.66 (5.59)	4.43 to 6.89	1.00–32.00	9.15 (7.35)	8.41 to 9.88	0.00–70.00	13.10 (12.51)	11.75 to 14.45	0.00–82.00
Length of ICU stay (in days)	8.39 (12.00)	7.56 to 9.22	0.00–76.00	0.84 (2.76)	0.24 to 1.45	0.00–14.00	2.48 (5.32)	1.95 to 3.01	0.00–43.00	17.09 (13.49)	15.64 to 18.55	0.00–76.00
Time since hospital discharge (in months)	6.56 (1.58)	6.45 to 6.67	3.00–11.00	6.49 (1.29)	6.20 to 6.77	5.00–11.00	6.51 (1.47)	6.36 to 6.66	3.00–11.00	6.63 (1.75)	6.45 to 6.82	3.00–11.00

.ICU, intensive care unit; n, number.

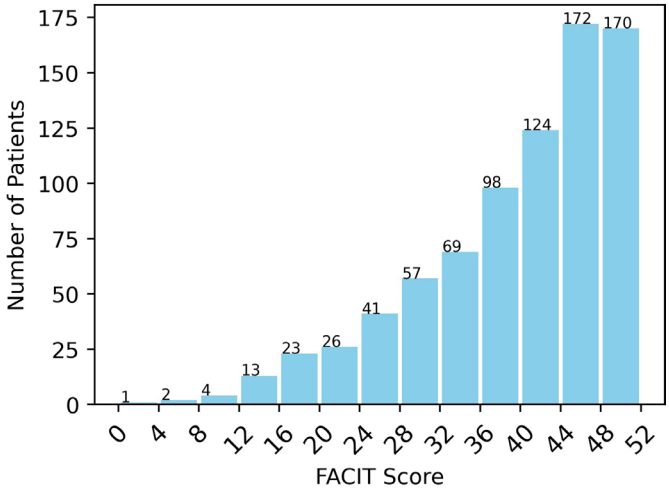

Figure 2 Histogram for the FACIT–Fatigue scale. FACIT, Functional Assessment of Chronic Illness Therapy.

(333 of 725) of participants scored 60 or higher, on a scale from 0 to 100. Still, Functional Independence Measure (FIM) results showed a high level of independence (86.53%, 636 of 735), as with the Functional Oral Intake Scale (FOIS), in which 92.85% (727 of 783) of participants reported no restrictions.

Many participants (64.66%, 514 of 795) reported some breathlessness (modified MRC (mMRC) Dyspnea Scale ≥1). Results from the FACIT–Fatigue scale indicated low fatigue scores, as shown in figure 2. All groups performed similarly in the 1-Minute Sit to Stand Test (1MSTST), with averages close to 19 repetitions. Accounting for the 95% CI, the variation in oxygen saturation before and after the test was also similar, with an overall average of −0.85±2.53% (95% CI: −1.06% to −0.63%), where the negative value indicates a worst score after the test. Additional functional assessments are available in tables 2 and 3.

The Epworth Sleepiness Scale and Insomnia Severity Index showed that participants, on average, may feel excessive sleepiness or have subthreshold insomnia, markedly on the group that received no oxygen support (tables 2 and 3).

Tables 2 and 3 and online supplemental tables 3 and 4 present additional details on qualitative evaluations. All groups presented similar results across evaluations. Minor discrepancies in the number of participants assessed in each evaluation occurred due to non-assessment for various reasons.

The handgrip strength measurement showed many participants (52.20%, 379 of 726) had 'poor' results when compared with normative values for the Brazilian population.[20 21] Although the group of participants who required invasive mechanical ventilation tends to outperform other groups on every age subset, the majority of them still performed poorly (40.40%, 120 of 297). These results can be seen in figure 3 and online supplemental table 5, along other quantitative results. Similarly, TUG results revealed that, on average and for all age groups, participants did not reach normative results.

Factorial ANOVA tests were conducted with handgrip strength and TUG results as dependent variables. For TUG, as expected, age (elder/younger) presented a significant main effect on participants' performance ($f(1)=19.888$, $p<0.001$), as well as sex ($f(1)=4.910$, $p=0.027$). Estimated marginal means suggest worst scores (longer TUG times) for elder patients and for women. The number of comorbidities also had a significant effect ($f(2)=3.570$, $p=0.029$), with statistically significant difference between all three groups (0–1 comorbidities; 2–3 comorbidities and 4+ comorbidities), and worst estimated marginal means for patients with more comorbidities. Still, there was no significant main effect related neither to the type of oxygen support received nor to the number of months since hospital discharge. Race was not a significant factor. There were also no significant two-way interaction effects between the variables. For the handgrip strength measurement, age and sex had, once again, a significant main effect on performance (respectively, $f(1)=18.946$, $p<0.001$ and $f(1)=262.056$, $p<0.001$), which was to be expected, since those factors are also taken into account when classifying the results. Once again, estimated marginal means indicate worst scores (lower handgrip strength) for elder and female patients. The number of comorbidities had a significant main effect on the handgrip test ($f(2)=4.065$, $p=0.018$), with significant differences across all groups and worst estimated marginal mean scores for patients with more comorbidities, similarly to TUG. However, this time the level of oxygen support also presented a significant main effect ($f(2)=22.199$, $p<0.001$). Tukey's HSD revealed that the invasive mechanical ventilation group was significantly different from the other two ($p<0.001$), but there was no difference between the group without oxygen support and with non-invasive oxygen support. The estimated marginal mean for the invasive mechanical ventilation group suggests a better handgrip score, when compared with the other two, corroborating our findings in figure 3. The number of months since hospital discharge did not present a significant effect, nor did race. No significant two-way interactions were found.

As shown in online supplemental table 4, the analysis of the five selected variables (participants' classification on handgrip strength, pain VAS, EQ-5D-5L anxiety and depression dimension, mMRC Dyspnea Scale and average scores on FACIT–Fatigue) demonstrates no clear trend nor statistically significant difference ($p>0.05$) between the distribution of participants' scores and classifications according to the time elapsed since hospital discharge.

Finally, through our linear regression models, we found that intubation had no significant effect on VAS for pain and dyspnoea, but presented significant effects on Epworth Sleepiness Scale and handgrip. Similar to our ANOVA findings, the beta coefficients show that patients who were intubated had better results in the handgrip

Table 2 Functional assessments

	All participants (n=801)	No oxygen support (n=82)	Oxygen support (n=386)	Intubation (n=333)
PCFS				
0	233 (29.12%, n=800)	34 (41.98%, n=81)	126 (32.64%, n=386)	73 (21.92%, n=333)
1	317 (39.62%, n=800)	26 (32.10%, n=81)	124 (32.12%, n=386)	167 (50.15%, n=333)
2	136 (17.00%, n=800)	12 (14.81%, n=81)	76 (19.69%, n=386)	48 (14.41%, n=333)
3	69 (8.62%, n=800)	5 (6.17%, n=81)	39 (10.10%, n=386)	25 (7.51%), n=333
4	45 (5.62%, n=800)	4 (4.94%, n=81)	21 (5.44%, n=386)	20 (6.01%, n=333)
EQ-5D-5L (mobility)				
1	448 (56.00%, n=800)	56 (69.14%, n=81)	221 (57.25%, n=386)	171 (51.35%, n=333)
2	150 (18.75%, n=800)	10 (12.35%, n=81)	67 (17.36%, n=386)	73 (21.92%, n=333)
3	126 (15.75%, n=800)	11 (13.58%, n=81)	60 (15.54%, n=386)	55 (16.52%, n=333)
4	62 (7.75%, n=800)	3 (3.70%, n=81)	31 (8.03%, n=386)	28 (8.41%, n=333)
5	14 (1.75%, n=800)	1 (1.23%, n=81)	7 (1.81%, n=386)	6 (1.80%, n=333)
EQ-5D-5L (self-care)				
1	617 (77.12%, n=800)	72 (88.89%, n=81)	304 (78.76%, n=386)	241 (72.37%, n=333)
2	95 (11.88%, n=800)	5 (6.17%, n=81)	39 (10.10%, n=386)	51 (15.32%, n=333)
3	51 (6.38%, n=800)	3 (3.70%, n=81)	23 (5.96%, n=386)	25 (7.51%, n=333)
4	18 (2.25%, n=800)	0 (0.00%, n=81)	9 (2.33%, n=386)	9 (2.70%, n=333)
5	19 (2.38%, n=800)	1 (1.23%, n=81)	11 (2.85%, n=386)	7 (2.10%, n=333)
EQ-5D-5L (daily routine)				
1	499 (62.38%, n=800)	57 (70.37%, n=81)	252 (65.28%, n=386)	190 (57.06%, n=333)
2	127 (15.88%, n=800)	8 (9.88%, n=81)	50 (12.95%, n=386)	69 (20.72%, n=333)
3	104 (13.00%, n=800)	10 (12.35%, n=81)	49 (12.69%, n=386)	45 (13.51%, n=333)
4	44 (5.50%, n=800)	4 (4.94%, n=81)	22 (5.70%, n=386)	18 (5.41%, n=333)
5	26 (3.25%, n=800)	2 (2.47%, n=81)	13 (3.37%, n=386)	11 (3.30%, n=333)
EQ-5D-5L (pain and discomfort)				
1	284 (35.50%, n=800)	37 (45.68%, n=81)	134 (34.72%, n=386)	113 (33.93%, n=333)
2	185 (23.12%, n=800)	19 (23.46%, n=81)	96 (24.87%, n=386)	70 (21.02%, n=333)
3	187 (23.38%, n=800)	14 (17.28%, n=81)	93 (24.09%, n=386)	80 (24.02%, n=333)
4	131 (16.38%, n=800)	10 (12.35%, n=81)	54 (13.99%, n=386)	67 (20.12%, n=333)
5	13 (1.62%, n=800)	1 (1.23%, n=81)	9 (2.33%, n=386)	3 (0.90%, n=333)
EQ-5D-5L (anxiety and depression)				
1	341 (42.73%, n=798)	41 (50.62%, n=81)	171 (44.30%, n=386)	129 (38.97%, n=331)
2	194 (24.31%, n=798)	13 (16.05%, n=81)	93 (24.09%, n=386)	88 (26.59%, n=331)
3	121 (15.16%, n=798)	14 (17.28%, n=81)	63 (16.32%, n=386)	44 (13.29%, n=331)
4	124 (15.54%, n=798)	11 (13.58%, n=81)	46 (11.92%, n=386)	67 (20.24%, n=331)
5	18 (2.26%, n=798)	2 (2.47%, n=81)	13 (3.37%, n=386)	3 (0.91%, n=331)
mMRC Dyspnea Scale				
0	281 (35.35%, n=795)	29 (36.25%, n=80)	137 (35.58%, n=385)	115 (34.85%, n=330)
1	276 (34.72%, n=795)	32 (40.00%, n=80)	121 (31.43%, n=385)	123 (37.27%, n=330)
2	142 (17.86%, n=795)	12 (15.00%, n=80)	74 (19.22%, n=385)	56 (16.97%, n=330)
3	74 (9.31%, n=795)	6 (7.50%, n=80)	47 (12.21%, n=385)	21 (6.36%, n=330)
4	22 (2.77%, n=795)	1 (1.25%, n=80)	6 (1.56%, n=385)	15 (4.55%, n=330)
FOIS				
1	1 (0.13%, n=783)	0 (0.00%, n=80)	1 (0.26%, n=379)	0 (0.00%, n=324)
2	2 (0.26%, n=783)	1 (1.25%, n=80)	1 (0.26%, n=379)	0 (0.00%, n=324)

Continued

Table 2 Continued

	All participants (n=801)	No oxygen support (n=82)	Oxygen support (n=386)	Intubation (n=333)
3	1 (0.13%, n=783)	0 (0.00%, n=80)	0 (0.00%, n=379)	1 (0.31%, n=324)
4	1 (0.13%, n=783)	0 (0.00%, n=80)	0 (0.00%, n=379)	1 (0.31%, n=324)
5	13 (1.66%, n=783)	0 (0.00%, n=80)	9 (2.37%, n=379)	4 (1.23%, n=324)
6	38 (4.85%, n=783)	7 (8.75%, n=80)	26 (6.86%, n=379)	5 (1.54%, n=324)
7	727 (92.85%, n=783)	72 (90.00%, n=80)	342 (90.24%, n=379)	313 (96.60%, n=324)
Pain VAS				
0–39	249 (34.34%, n=725)	25 (33.33%, n=75)	119 (33.33%, n=357)	105 (35.84%, n=293)
40–59	143 (19.72%, n=725)	13 (17.33%, n=75)	69 (19.33%, n=357)	61 (20.82%, n=293)
60–100	333 (45.93%, n=725)	37 (49.33%, n=75)	169 (47.34%, n=357)	127 (43.34%, n=293)
FIM				
18	2 (0.27%, n=735)	1 (1.32%, n=76)	0 (0.00%, n=359)	1 (0.33%, n=300)
19–60	11 (1.50%, n=735)	0 (0.00%, n=76)	7 (1.95%, n=359)	4 (1.33%, n=300)
61–103	86 (11.70%, n=735)	9 (11.84%, n=76)	30 (8.36%, n=359)	47 (15.67%, n=300)
104–126	636 (86.53%, n=735)	66 (86.84%, n=76)	322 (89.69%, n=359)	248 (82.67%, n=300)
ESS				
0–7	355 (44.38%, n=800)	28 (34.57%, n=81)	164 (42.49%, n=386)	163 (48.95%, n=333)
8–9	90 (11.25%, n=800)	13 (16.05%, n=81)	38 (9.84%, n=386)	39 (11.71%, n=333)
10–15	224 (28.00%, n=800)	15 (18.52%, n=81)	116 (30.05%, n=386)	93 (27.93%, n=333)
16–24	131 (16.38%, n=800)	25 (30.86%, n=81)	68 (17.62%, n=386)	38 (11.41%, n=333)
ISI				
0–7	479 (59.95%, n=799)	41 (50.62%, n=81)	225 (58.29%, n=386)	213 (64.16%, n=332)
8–14	203 (25.41%, n=799)	25 (30.86%, n=81)	97 (25.13%, n=386)	81 (24.40%, n=332)
15–21	94 (11.76%, n=799)	10 (12.35%, n=81)	50 (12.95%, n=386)	34 (10.24%, n=332)
22–28	23 (2.88%, n=799)	5 (6.17%, n=81)	14 (3.63%, n=386)	4 (1.20%, n=332)
MRC sum score				
0–35	15 (2.05%, n=733)	0 (0.00%, n=75)	10 (2.79%, n=359)	5 (1.67%, n=299)
36–47	130 (17.74%, n=733)	11 (14.67%, n=75)	59 (16.43%, n=359)	60 (20.07%, n=299)
48–60	588 (80.22%, n=733)	64 (85.33%, n=75)	290 (80.78%, n=359)	234 (78.26%, n=299)

Categorical data presented as n participants (%).
EQ-5D-5L, EuroQoL-5 Dimensions-5 Levels; ESS, Epworth Sleepiness Scale; FIM, Functional Independence Measure; FOIS, Functional Oral Intake Scale; ISI, Insomnia Severity Index; mMRC, modified Medical Research Council; PCFS, Post-COVID-19 Functional Status; VAS, Visual Analogue Scale.

test. The full results may be found in online supplemental table 6.

DISCUSSION

PCFS scores revealed that COVID-19 survivors presented different levels of long-term functioning limitations in their daily activities. More than two of every three study participants reported some functional limitations, whereas only 5.62% reported being dependent on another person due to COVID-19 persistent symptoms, pain, and depression and anxiety. Likewise, FIM scores also detected complete or moderate dependence in only 1.77% of them. WHO Disability Assessment Schedule 2.0 simple summary scoring showed that the vast part of the study population presented none to mild levels of compromised functioning in cognition, mobility, self-care and getting along. Other findings include the significant prevalence of pain, depression and anxiety, muscular weakness, breathlessness and impaired mobility. There is also evidence of insomnia, daytime sleepiness and fatigue, despite their smaller relevance.

Participants reported higher levels of pain and discomfort (64.50%), as well as anxiety and depression (57.27%), compared with a previous publication of long-term consequences of COVID-19 in patients after hospital discharge.[8] Huang *et al*[8] report a large cohort study of hospitalised patients with COVID-19 of whom 27% reported pain and discomfort. Despite being hospitalised, only 4% were ventilated during hospitalisation. We hypothesise that the higher number of participants admitted to intensive

Table 3 Functional assessments

	All participants (n=801)				No oxygen support (n=82)				Oxygen support (n=386)				Intubation (n=333)			
	Mean (SD)	95% CI	n	Range	Mean (SD)	95% CI	n	Range	Mean (SD)	95% CI	n	Range	Mean (SD)	95% CI	n	Range
Basal oxygen saturation (in %)	96.34 (2.37)	96.16 to 96.52	664	79.00–99.00	97.19 (1.70)	96.78 to 97.61	67	90.00–99.00	96.46 (2.37)	96.20 to 96.72	320	79.00–99.00	96.00 (2.46)	95.71 to 96.29	277	82.00–99.00
Final oxygen saturation (in %)	95.71 (2.96)	95.46 to 95.96	533	68.00–99.00	96.79 (1.83)	96.29 to 97.30	53	92.00–99.00	95.52 (3.48)	95.09 to 95.95	252	68.00–99.00	95.67 (2.46)	95.35 to 95.99	228	84.00–99.00
Oxygen saturation variation	–0.85 (2.53)	–1.06 to –0.63	533	–25.00 to 6.00	–0.36 (1.95)	–0.90 to 0.18	53	–7.00 to 6.00	–1.10 (2.94)	–1.47 to –0.74	252	–25.00 to 5.00	–0.68 (2.12)	–0.96 to –0.40	228	–14.00 to 5.00
FACIT-F	39.18 (9.77)	38.50 to 39.86	800	1.00–52.00	39.16 (10.51)	36.83 to 41.48	81	6.00–52.00	38.62 (10.06)	37.62 to 39.63	386	6.00–52.00	39.83 (9.22)	38.84 to 40.82	333	1.00–52.00
ISI	7.30 (6.11)	6.88 to 7.73	799	0.00–28.00	8.33 (6.77)	6.84 to 9.83	81	0.00–26.00	7.79 (6.43)	7.14 to 8.43	386	0.00–28.00	6.49 (5.46)	5.90 to 7.08	332	0.00–27.00
WHODAS 2.0	20.78 (9.37)	20.13 to 21.43	800	12.00–60.00	20.11 (9.59)	17.99 to 22.23	81	12.00–56.00	21.14 (9.67)	20.17 to 22.10	386	12.00–60.00	20.53 (8.96)	19.56 to 21.49	333	12.00–60.00
Number of sit to stand repetitions	18.96 (6.42)	18.42 to 19.51	533	4.00–45.00	18.57 (5.12)	17.15 to 19.98	53	11.00–32.00	19.08 (6.84)	18.23 to 19.93	252	5.00–45.00	18.93 (6.23)	18.11 to 19.74	228	4.00–36.00
Handgrip strength (all participants)																
All ages	21.22 (12.70)	20.30 to 22.15	726	0.00–68.67	16.50 (10.79)	14.00 to 19.00	74	0.00–44.00	18.80 (12.32)	17.51 to 20.08	355	0.00–58.67	25.29 (12.48)	23.87 to 26.72	297	0.00–68.67
Handgrip strength (male participants)																
All ages	27.96 (11.83)	26.78 to 29.15	386	0.00–68.67	23.74 (9.84)	20.36 to 27.12	35	1.70–44.00	25.01 (11.52)	23.40 to 26.63	198	0.00–58.67	32.74 (11.07)	30.98 to 34.51	153	1.30–68.67
Handgrip strength (female participants)																
All ages	13.57 (8.70)	12.64 to 14.50	340	0.00–44.30	10.01 (6.75)	7.82 to 12.20	39	0.00–24.00	10.96 (8.14)	9.68 to 12.24	157	0.00–38.70	17.38 (8.34)	16.01 to 18.75	144	0.00–44.30
Timed Up and Go duration (in seconds)																
All ages	13.07 (6.49)	12.59 to 13.55	696	5.47–91.11	12.37 (3.49)	11.57 to 13.18	75	6.88–32.65	13.19 (6.89)	12.46 to 13.93	340	5.47–91.11	13.11 (6.61)	12.33 to 13.88	281	6.05–64.74

Continuous data presented as mean (SD), alongside 95% CI and number of participants (n).
FACIT-F, Functional Assessment of Chronic Illness Therapy–Fatigue; ISI, Insomnia Severity Index; WHODAS, WHO Disability Assessment Schedule.

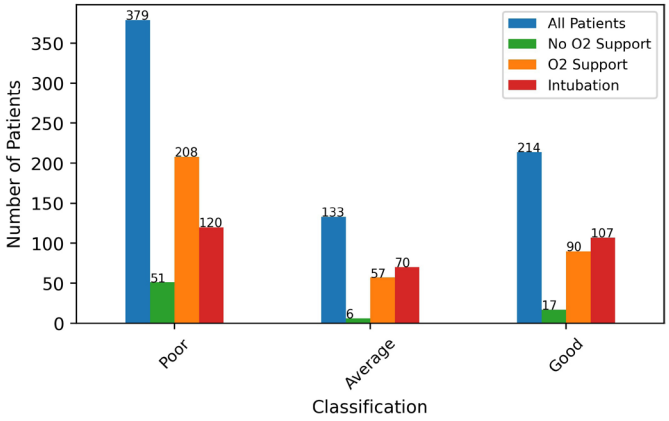

Figure 3 Handgrip strength measurement results distribution.

care may have influenced our results. Similar to other authors,[8 22–24] we also stratified our patients on the basis of respiratory support methods during hospitalisation. Our VAS for pain results corroborated other studies showing it as a relevant PASC result.[3–5 7–9 11 12] In the identified literature, pain has been reported using heterogeneous assessment methods in different publications. According to Xiong *et al*,[3] hospitalised patients with COVID-19 reported persisting symptoms of chest pain (12.3%), myalgia (4.5%) and arthralgia (7.6%) 97.0 days (95.0–102.0) after discharge, compared with 0% of patients reporting pain-related symptoms in a control group (p<0.01). Having a higher number of patients admitted to the intensive care unit (ICU) might have influenced a higher prevalence of pain and discomfort. Besides the effects of COVID-19, patients hospitalised in ICUs may develop pain due to critical illness polyneuropathy and neuropathic pain, repeated proning (with consequent brachial plexopathy, joint subluxation) and are also at greater risk of procedural pain. Nonetheless, pain and discomfort can be a possible symptom to be assessed in all hospitalised COVID-19 survivors. Managing chronic pain seems to be needed throughout the observed period. We suggest that EQ-5D-5L is used as a triage tool for further comprehensive assessments.

Ours is also a large cohort of COVID-19 survivors treated in intensive care who were mechanically ventilated. Our findings remain unchanged despite several months been passed after discharge, suggesting no spontaneous recovery over time.

Results also showed that 64.66% of study participants reported mMRC Dyspnea Scale ≥1, and only 29.94% reported mMRC Dyspnea Scale ≥2. We observed similar distributions between the three groups. Considering that most participants in intensive care required mechanical ventilation, we think that proper intensive care during the acute infection period plays a vital role in recovering lung functions.

Similarly to our results, previous reports also evidenced high prevalence of breathlessness,[5–10] ranging between 5% and 42.7%.[3 5 7 9 11] Only 26% of the population investigated by Huang *et al* scored 1 or higher on the mMRC Dyspnea Scale.[8] We suspect it can be attributed to the fact that in that study, 6–8 months after symptoms onset, only 4% of the population were under intensive care, and therefore a quite different population. Anastasio *et al* found mMRC Dyspnea Scale results ≥2 in 15.8% of its 379 hospitalised and non-hospitalised participants, of which 34 were admitted to intensive care.[9] In another population of 120 patients, of which 20% were treated in intensive care, 29.2% showed an mMRC Dyspnea Scale results of 2 or higher and 53.3% of 1 or higher.[5] As such, we speculate that being under intensive care is possibly influencing breathlessness. Furthermore, patients with an mMRC Dyspnea Scale result higher or equal to 2 might be a good candidate for quantitative pulmonary assessments.

Literature shows muscle weakness has been identified as a common self-reported PASC symptom,[8] but lacking further quantification. Low handgrip strength for all ages and sex groups has also been identified in COVID-19 hospitalised patients,[25] but to our knowledge, not at the long term. Even though general self-reported disability and quality of life tools were not able to capture mobility limitations, we detected increased duration for the TUG. For the younger age groups (18–50 years old), our participants presented longer testing times than the worst reported results of healthy subjects,[26 27] demonstrating that this population also shows the effects of PASC. Similarly, we found abnormal results for the elderly (71+ years old),[28–30] including a systematic review spanning 34 studies from different populations.[31] We also note that less than 25% of our population was fully able to move around independently.[32] Results of 1MSTST also seem to be lower than normative data found in the literature.[33] These findings highlight the need for instrumentalised measures to capture individual rehabilitation needs.

Previous publications identified fatigue as an important PASC finding.[3–5 7 8 34] Our data do not confirm this finding. This discrepancy is an argument for the use of validated and reliable scales to assess fatigue. Furthermore, the association, correlation, and possible causality between fatigue, breathlessness, and muscle weakness, and their effect on functioning in PASC patients, should be explored further. It seems that daytime sleepiness and insomnia might be an issue for this population.[5 7–9] However, there were no marked alterations in our population. Given our results of fatigue levels, a possible relationship between fatigue, insomnia and daytime sleepiness should be considered.

FOIS results did not show any lasting issues with oral intake 3–11 months after COVID-19. This is an interesting finding, different from patients admitted to an intensive and comprehensive inpatient rehabilitation treatment, immediately after hospital discharge.[35]

Different from symptoms' prevalence, as previously published, objective quantification of the level of fatigue, muscle weakness, pain and breathlessness will inform most appropriate rehabilitation service delivery models. For example, patients reporting low PCFS scores could be adequately monitored and managed by rehabilitation

interventions delivered at the community and primary care settings, including remote monitoring, task shifting and educational programmes. On the other hand, the more severely impaired patients may require an integrated and comprehensive rehabilitation approach. Our results suggest only 5.62% would benefit from hospital-based specialised multidisciplinary rehabilitation interventions.

This observational study had some limitations. First, the absence of a control group for comparison, which was not feasible in the study setting during the time it was conducted, as previously reported.[15] Second, due to the large number of participants assessed during the pandemic and the limited time window for evaluations, several evaluators were involved in data collection. Third, our missing data derived from participants' inability to perform some of the tests for a myriad of reasons. Fourth, we have not addressed the influence of other relevant factors such as the impact of the socioeconomic status, exposure to ambient air pollution and other environmental data on the levels of breathlessness, fatigue, pain and overall functional status of study participants after returning home from hospitalisation. Finally, we accounted for common confounders in this study; however, since many aspects of COVID-19 are still unknown, there may be significant confounders that were not addressed. We demonstrated that even 3–11 months after hospital discharge for COVID-19 acute treatment, a high percentage of study participants presented with different needs and would benefit from rehabilitation interventions to restore their functioning status.

CONCLUSION

Three to eleven months after hospital discharge to treat acute infection, COVID-19 survivors presented with their functioning status compromised mainly due to muscle weakness, reduced mobility, pain, anxiety, depression, breathlessness, insomnia and daytime sleepiness. Except for poorer handgrip strength among those who did not receive invasive oxygen support, there are no significant differences in the functioning status between them and those who required mechanical ventilation.

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Patient and public involvement Patients and/or the public were involved in the design, or conduct, or reporting, or dissemination plans of this research. Refer to the Methods section for further details.

Patient consent for publication Not required.

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Data availability statement Data are available upon reasonable request. De-identified individual participant data that underlie the results reported in this article, including data dictionaries, are available upon request. Researchers interested in exploring our data are invited to contact the corresponding author (at marta.imamura@fm.usp.br) who will forward any request for data access to the committee at HCFMUSP responsible for ensuring proposals are methodologically sound and aligned. To gain access, data requestors will need to sign a data access agreement, as per HCFMUSP policies on data sharing. Data will be available for 5 years following article publication. The study protocol and statistical analysis plan used here are publicly available on our institutional website.

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REFERENCES

1 World Health Organization. Who coronavirus (COVID-19) Dashboard. Available: https://covid19.who.int [Accessed 05 May 2021].
2 Worldometers. COVID-19 coronavirus pandemic. Available: https://www.worldometers.info/coronavirus/ [Accessed 05 May 2021].
3 Xiong Q, Xu M, Li J, *et al*. Clinical sequelae of COVID-19 survivors in Wuhan, China: a single-centre longitudinal study. *Clin Microbiol Infect* 2021;27:89–95.
4 Petersen MS, Kristiansen MF, Hanusson KD, *et al*. Long COVID in the faroe Islands: a longitudinal study among nonhospitalized patients. *Clin Infect Dis* 2021;73:e4058-e4063.
5 Garrigues E, Janvier P, Kherabi Y, *et al*. Post-discharge persistent symptoms and health-related quality of life after hospitalization for COVID-19. *J Infect* 2020;81:e4–6.

6 González J, Benítez ID, Carmona P. Pulmonary function and radiological features in survivors of critical covid-19: a 3-month prospective cohort. *Chest* 2021.
7 Writing Committee for the COMEBAC Study Group, Morin L, Savale L, *et al*. Four-month clinical status of a cohort of patients after hospitalization for COVID-19. *JAMA* 2021;325:1525-1534.
8 Huang C, Huang L, Wang Y, *et al*. 6-Month consequences of COVID-19 in patients discharged from hospital: a cohort study. *Lancet* 2021;397:220–32.
9 Anastasio F, Barbuto S, Scarnecchia E, *et al*. Medium-term impact of COVID-19 on pulmonary function, functional capacity and quality of life. *Eur Respir J* 2021;58. doi:10.1183/13993003.04015-2020. [Epub ahead of print: 16 09 2021].
10 Debeaumont D, Boujibar F, Ferrand-Devouge E, *et al*. Cardiopulmonary exercise testing to assess persistent symptoms at 6 months in people with COVID-19 who survived hospitalization: a pilot study. *Phys Ther* 2021;101. doi:10.1093/ptj/pzab099. [Epub ahead of print: 01 06 2021].
11 Bellan M, Soddu D, Balbo PE, *et al*. Respiratory and psychophysical sequelae among patients with COVID-19 four months after hospital discharge. *JAMA Netw Open* 2021;4:e2036142.
12 Walle-Hansen MM, Ranhoff AH, Mellingsæter M, *et al*. Health-related quality of life, functional decline, and long-term mortality in older patients following hospitalisation due to COVID-19. *BMC Geriatr* 2021;21:1–10.
13 Baricich A, Borg MB, Cuneo D, *et al*. Midterm functional sequelae and implications in rehabilitation after COVID-19: a cross-sectional study. *Eur J Phys Rehabil Med* 2021;57.
14 IMREA Conducts Res. Proj. COVID-19 Surviv. Mid- and long-term complications affecting functioning after COVID-19 (Abbreviated Research Protocol). Available: http://www.pesquisaimrea.fm.usp.br/index.php/noticias-cpc/503-imrea-conducts-research-project-with-covid-19-survivors
15 Busatto GF, de Araújo AL, Duarte AJdaS, *et al*. Post-acute sequelae of SARS-CoV-2 infection (PASC): a protocol for a multidisciplinary prospective observational evaluation of a cohort of patients surviving hospitalisation in Sao Paulo, Brazil. *BMJ Open* 2021;11:e051706.
16 Agarwal A, Rochwerg B, Lamontagne F, *et al*. A living WHO guideline on drugs for covid-19. *BMJ* 2020;370:m3379.
17 Virtanen P, Gommers R, Oliphant TE, *et al*. SciPy 1.0: fundamental algorithms for scientific computing in python. *Nat Methods* 2020;17:261–72.
18 Harris CR, Millman KJ, van der Walt SJ, *et al*. Array programming with NumPy. *Nature* 2020;585:357–62.
19 McKinney W. 9th Python in Science Conference. In: *Data structures for statistical computing in python*. Austin, USA, 2010: 56–61.
20 Vianna LC, Oliveira RB, Araújo CGS. Age-related decline in handgrip strength differs according to gender. *J Strength Cond Res* 2007;21:1310–4.
21 Rodrigues-Barbosa A, de Miranda LM, Vieira-Guimarães A, *et al*. Age and gender differences regarding physical performance in the elderly from barbados and cuba. *Rev Salud Publica* 2011;13:54–66.
22 Cao B, Wang Y, Wen D, *et al*. A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. *N Engl J Med* 2020;382:1787–99.
23 Kadri SS, Sun J, Lawandi A, *et al*. Association between caseload surge and COVID-19 survival in 558 U.S. hospitals, March to August 2020. *Ann Intern Med* 2021;174:1240–51.
24 Whitfield GP, Harris AM, Kadri SS, *et al*. Trends in clinical severity of hospitalized patients with coronavirus disease 2019-premier hospital dataset, April 2020-April 2021. *Open Forum Infect Dis* 2022;9:ofab599.
25 Tuzun S, Keles A, Okutan D, *et al*. Assessment of musculoskeletal pain, fatigue and grip strength in hospitalized patients with COVID-19. *Eur J Phys Rehabil Med* 2021;57:653-662.
26 Sivakumar VPR, Doraisami B, Prabhu V. Age related timed up and go test values and its analysis among elderly kanchipuram district population. *J Clin Diagnostic Res* 2018;12:YC06–8.
27 Kear BM, Guck TP, McGaha AL. Timed up and go (TUG) test: normative reference values for ages 20 to 59 years and relationships with physical and mental health risk factors. *J Prim Care Community Health* 2017;8:9–13.
28 Pondal M, del Ser T. Normative data and determinants for the timed "up and go" test in a population-based sample of elderly individuals without gait disturbances. *J Geriatr Phys Ther* 2008;31:57–63.
29 Bohannon RW. Reference values for the timed up and go test: a descriptive meta-analysis. *J Geriatr Phys Ther* 2006;29:64–8.
30 Ibrahim A, Singh DKA, Shahar S. 'Timed up and go' test: age, gender and cognitive impairment stratified normative values of older adults. *PLoS One* 2017;12:e0185641.
31 Long J, Cai T, Huang X, *et al*. Reference value for the TUGT in healthy older people: a systematic review and meta-analysis. *Geriatr Nurs* 2020;41:325–30.
32 Podsiadlo D, Richardson S. The timed "Up & Go": a test of basic functional mobility for frail elderly persons. *J Am Geriatr Soc* 1991;39:142–8.
33 Strassmann A, Steurer-Stey C, Lana KD, *et al*. Population-based reference values for the 1-min sit-to-stand test. *Int J Public Health* 2013;58:949–53.
34 Lopez-Leon S, Wegman-Ostrosky T, Perelman C, *et al*. More than 50 long-term effects of COVID-19: a systematic review and meta-analysis. *medRxiv* 2021. doi:10.1101/2021.01.27.21250617. [Epub ahead of print: 30 Jan 2021].
35 Imamura M, Mirisola AR, Ribeiro FdeQ, *et al*. Rehabilitation of patients after COVID-19 recovery: an experience at the physical and rehabilitation medicine institute and lucy montoro rehabilitation institute. *Clinics* 2021;76:e2804.