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

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

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

ABSTRACT

Objectives: The study investigated the long-term functional status of hospitalized COVID-19 survivors to explore and document their functional situation. Design: This prospective observational study assessed 801 COVID-19 survivors at three to eleven months after hospital discharge. It uses data on participants' sociodemographic background, COVID-19 clinical manifestations, and additional clinical and functional evaluations. Setting: Tertiary-level university hospital in Sao Paulo, Brazil. Participants: Study participants are COVID-19 survivors admitted to hospital care for at least 24h to treat acute SARS-CoV-2 infection. Main 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 Measurement, Insomnia Severity Index, MRC Dyspnea Scale, MRC Sum Score, Modified Borg Dyspnea Scale, Pain Visual Analogue Scale, Post-COVID-19 Functional Status scale, Timed Up and Go, World Health Organization Disability Assessment Schedule 2.0, 01-minute Sit to Stand Test. Results: Many participants required invasive mechanical ventilation (41.57%, 333/801). Their mean age was 55.35 ± 14.58 years. With a mean of 6.56 (S.D: 1.58; 95% C.I: 6.45 to 6.67) months after hospital discharge, 70.86% (567/800) reported limited daily activities, which were severe in 5.62% (45/800). They also reported pain and discomfort (64.50%, 516/800), breathlessness (64.66%, 514/795), and anxiety and depression (57.27%, 457/798). Daytime sleepiness and insomnia evaluations showed borderline results. Most (92.85%, 727/783) participants reported unrestricted oral intake. Data indicated no generalized fatigue (mean score: 39.18, S.D: 9.77; C.I: 95% 38.50 to 39.86). Assessments showed poor handgrip strength (52.20%, 379/726) and abnormal timed up and go results (mean 13.07s, S.D 6.49). 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 hospitalized COVID-19 survivors.
ARTICLE SUMMARY

Strengths and limitations of this study

1. 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.

2. The study test battery used both self-reported, clinical assessments and quantifiable measures.

3. 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.

4. 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 Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) does 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 COVID-19 patients 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 six months after symptoms onset.[8] Breathlessness 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] and memory[5,7] concentration[5] and sleep disorders.[5,7-9] Objective assessments including the Short Physical Performance Battery Test and the 2-Minutes 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 most effective rehabilitation needs assessments and interventions. Thus, a better understanding of functional disorders that may arise in the long-term after hospitalization 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 three to eleven months of hospital discharge, aiming at identifying their long-term functioning status and rehabilitation needs.
MATERIALS & 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 Polymerase Chain Reaction (PCR) or serology testing for SARS-CoV-2. Written informed consent was obtained from all participants included.

STUDY DESIGN

This prospective observational evaluation of a cohort of COVID-19 survivors is based on a follow-up test battery conducted three to eleven months after hospital discharge with people previously admitted to treat acute COVID-19. Participants were recruited between October 7, 2020 and April 8, 2021. Study assessments were completed between October 20, 2020 and April 16, 2021. Data was registered using the Research Electronic Data Capture (REDCap) platform. The study was approved by HCFMUSP Institutional Review Board, and registered under CAEE 39744120.3.0000.0068. Further details about the study protocol are available elsewhere.[14,15] To accommodate for limitations in recruitment, the study included participants three to eleven months after hospital discharge. Report from this cohort study followed the principles of the STROBE statement.

ASSESSMENTS

All data was 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 includes 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 supplementary 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 ± standard deviations (S.D). Intervals at 95% confidence (C.I) for the means were estimated with Student’s t-distribution at the proper degrees-of-freedom. 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 was 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: those who did not receive oxygen support, those who did, and those who received invasive mechanical ventilation. When analyzing handgrip strength and TUG results, participants were further divided into age groups. Handgrip strength data was stratified by sex and age groups for classification. For these two variables we investigated differences among the three subgroups using two-way ANOVA tests with an additional fixed factor of age (elder participants ≥ 60 years of age; younger participants < 60 years of age) to inspect possible age interaction. Turkey’s honestly significant difference (HSD) test was used as a post-hoc test for multiple comparisons. Homoscedasticity was verified by residuals vs. 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-values < 0.05.

Finally, for pain visual analogue scale (VAS), anxiety and depression (EuroQoL-5 Dimensions-5 Levels, EQ-5D-5L), dyspnea (Medical Research Council Dyspnea Scale), fatigue (Functional Assessment of Chronic Illness Therapy – Fatigue), and muscle strength (handgrip strength measurement), participants were divided in nine groups, according to the time elapsed since hospital discharge; the groups for three and eleven months (both extremes of our range) had less than ten participants each, and were not included in the analyses. All
data analysis was performed with IBM SPSS 27.0, Python, and related libraries.[16-18] P-values were only calculated for continuous variables. Because this is a new condition, of which many aspects are yet unknown, possible predictors, confounders, or effect modifiers were not described, and subgroup and sensitivity analyses were not performed.

ROLE OF THE FUNDING SOURCE, STUDY TRANSPARENCY AND PARTICIPANTS INVOLVEMENT

This work was partially supported by donations from the public under the HC-COMVIDA crowdfunding scheme (https://viralcure.org/c/hc) and Fundação Faculdade de Medicina. L.R.P and S.K.H.A.A.C received support from the São Paulo Research Foundation (FAPESP, grants #2019/19465-0 and #2020/08317-7, respectively). Funders had no role in the study's design, collection, management, analysis, or interpretation of the data or the preparation, review, or approval of the manuscript. Authors have not been paid by a third party to write this article.

This manuscript offers a faithful and transparent report of the work carried out as originally planned. No important aspect has been omitted, nor were any discrepancies, as our methods and results intend to show.

Although study participants did not take part in the design and conduct of the work, their active participation in disseminating its findings is essential for transferring this knowledge into practice.

RESULTS

Figure 1 shows a flow diagram of study participants. As per the study protocol,[14,15] all COVID-19 patients 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), time since hospital discharge (<3 months), and lack of information on the type of oxygen support received during treatment, or any other data inconsistency.

INSERT FIGURE 1.

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 didn’t 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% C.I.: 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% C.I.: 27.92 to 32.46) compared to 6.50 ± 6.17 (95% C.I.: 5.14 to 7.86) for the group with no oxygen support, and 11.63 ± 10.16 (95% C.I.: 10.61 to 12.65) for the non-invasive support group. A large portion of participants was admitted to intensive care (n=497), with an average LoS in intensive care of 8.39 ± 12.00 days (95% C.I.: 7.56 to 9.22). Overall, the study population consisted of 421 males (52.56%) and 380 females (47.44%). The commonest comorbidities among all participants were hypertension (462/801, 57.68%) and diabetes (292/801, 36.45%). Details on other participants’ characteristics are shown in Table 1, and in the supplementary table 2.

Post-COVID Functional Status (PCFS) scale results revealed that 70.86% of participants (567/800) reported limitations in daily activities, which were severe for 5.62% (45/800) of them. The invasive mechanical ventilation group presented a slightly larger proportion of participants referring some form of limitation, reaching 78.08% (260/333). EuroQol-5D-5L results showed that 64.50% (516/800) still suffered from pain and discomfort, while 57.27% (457/798) reported anxiety and depression. Pain VAS results corroborated it by showing that 45.93% (333/725) 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%, 636/735), as with the Functional Oral Intake Scale (FOIS), in which 92.85% (727/783) of participants reported no restrictions.

Many participants (64.66%, 514/795) reported some breathlessness (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% confidence interval, the variation in oxygen saturation before and after the test was also similar, with an overall average of -0.85 ± 2.53 % (95% C.I.: -1.06% to -0.63%), where the negative value indicates a worst score after the test. Additional functional assessments are available in Table 2.

The Epworth Sleepiness Scale showed that participants, on average, have a borderline level of daytime sleepiness, markedly on the group that received no oxygen support, in line with trends observed in the Insomnia Severity Index (Table 2).
Table 1. Sociodemographic and clinical data presented as n participants (%), mean (S.D.), alongside 95% C.I. 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%)         |
| **Commonest 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)|
| **Commonest 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 (S.D.) | 95% C.I. | Range    | Mean (S.D.) | 95% C.I. | Range    | Mean (S.D.) | 95% C.I. | Range    | Mean (S.D.) | 95% C.I. | 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 |

Notes: n = number; S.D. = Standard Deviation; C.I. = Confidence Interval; ICU = Intensive Care Unit
Table 2. Functional assessments, data presented as n participants (%), mean (S.D.), alongside 95% C.I. and number of participants (n).

|                          | 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)      | 5 (6.17%, 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**   |                          |                          |                        |                    |
| 1                        | 281 (35.35%, n = 795)    | 29 (36.25%, n = 80)      | 137 (35.58%, n = 385)  | 115 (34.85%, 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) | 9 (2.37%, n = 379) | 0 (0.00%, n = 324) |
| 3 | 1 (0.13%, n = 783) | 0 (0.00%, n = 80) | 1 (0.31%, n = 324) | 0 (0.00%, n = 324) |
| 4 | 2 (0.26%, n = 783) | 1 (1.25%, n = 80) | 1 (0.31%, n = 324) | 0 (0.00%, n = 324) |

|   | Pain VAS      |   |   |   |
|---|--------------|---|---|---|
| 40-39 | 249 (34.34%, n = 725) | 25 (33.33%, n = 75) | 119 (33.33%, n = 357) | 105 (35.84%, n = 293) |
| 40-59 | 145 (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          |   |   |   |
|---|--------------|---|---|---|
| 20-18 | 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          |   |   |   |
|---|--------------|---|---|---|
| 10-7 | 355 (44.38%, n = 800) | 28 (34.57%, n = 81) | 164 (42.49%, n = 386) | 163 (48.95%, n = 333) |
| 18-9 | 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          |   |   |   |
|---|--------------|---|---|---|
| 40-7 | 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) |
| 9-15 | 94 (11.76%, n = 799) | 10 (12.35%, n = 81) | 50 (12.95%, n = 386) | 34 (10.24%, n = 332) |
| 16-28 | 23 (2.88%, n = 799) | 5 (6.17%, n = 81) | 14 (3.63%, n = 386) | 4 (1.20%, n = 332) |

|   | Basal MBS    |   |   |   |
|---|--------------|---|---|---|
| 50 | 359 (54.56%, n = 658) | 46 (68.66%, n = 67) | 177 (55.84%, n = 317) | 136 (49.64%, n = 274) |
| 0.5 | 38 (5.78%, n = 658) | 5 (7.46%, n = 67) | 16 (5.05%, n = 317) | 17 (6.20%, n = 274) |
| 1 | 58 (8.81%, n = 658) | 2 (2.99%, n = 67) | 30 (9.46%, n = 317) | 26 (9.49%, n = 274) |
| 2 | 81 (12.31%, n = 658) | 5 (7.46%, n = 67) | 38 (11.99%, n = 317) | 38 (13.87%, n = 274) |
| 3 | 55 (8.36%, n = 658) | 2 (2.99%, n = 67) | 27 (8.52%, n = 317) | 26 (9.49%, n = 274) |
| 4 | 18 (2.74%, n = 658) | 1 (1.49%, n = 67) | 8 (2.52%, n = 317) | 9 (3.28%, n = 274) |
| 5-6 | 30 (4.56%, n = 658) | 2 (2.99%, n = 67) | 15 (4.73%, n = 317) | 13 (4.74%, n = 274) |
| 7-8 | 12 (1.82%, n = 658) | 3 (4.48%, n = 67) | 3 (0.95%, n = 317) | 6 (2.19%, n = 274) |
| 9 | 3 (0.46%, n = 658) | 1 (1.49%, n = 67) | 1 (0.32%, n = 317) | 1 (0.36%, n = 274) |
|   | MRC sum score | 0 (0.00%, n = 67) | 2 (0.63%, n = 317) | 2 (0.73%, n = 274) |
|---|----------------|-------------------|--------------------|--------------------|
| 0.5 | 0 (0.00%, n = 53) | 11 (4.42%, n = 249) | 15 (6.67%, n = 225) |
| 1 | 45 (8.54%, n = 527) | 14 (5.62%, n = 249) | 27 (12.00%, n = 225) |
| 2 | 86 (16.32%, n = 527) | 40 (16.06%, n = 249) | 40 (17.78%, n = 225) |
| 3 | 102 (19.35%, n = 527) | 50 (20.08%, n = 249) | 41 (18.22%, n = 225) |
| 4 | 58 (11.01%, n = 527) | 26 (10.44%, n = 249) | 29 (12.89%, n = 225) |
| 5 | 82 (15.56%, n = 527) | 36 (14.46%, n = 249) | 36 (16.00%, n = 225) |
| 6 | 47 (8.92%, n = 527) | 20 (8.03%, n = 249) | 23 (10.22%, n = 225) |
| 7 | 9 (1.71%, n = 527) | 5 (2.01%, n = 249) | 3 (1.33%, n = 225) |
| 10 | 4 (0.76%, n = 527) | 3 (1.20%, n = 249) | 1 (0.44%, n = 225) |

| MBS variation |
|----------------|
| 0.4 | 1 (0.19%, n = 527) | 1 (1.89%, n = 53) | 0 (0.00%, n = 249) | 0 (0.00%, n = 225) |
| 0.3 | 2 (0.38%, n = 527) | 0 (0.00%, n = 53) | 2 (0.80%, n = 249) | 0 (0.00%, n = 225) |
| 0.2 | 1 (0.19%, n = 527) | 0 (0.00%, n = 53) | 1 (0.40%, n = 249) | 0 (0.00%, n = 225) |
| 0.1 | 3 (0.57%, n = 527) | 1 (1.89%, n = 53) | 1 (0.40%, n = 249) | 1 (0.44%, n = 225) |
| 0 | 1 (0.19%, n = 527) | 0 (0.00%, n = 53) | 1 (0.40%, n = 249) | 0 (0.00%, n = 225) |
| -0.5 | 6 (1.14%, n = 527) | 3 (1.20%, n = 249) | 3 (1.33%, n = 225) | 2 (0.89%, n = 225) |
| -1 | 1 (0.19%, n = 527) | 1 (1.89%, n = 53) | 1 (0.40%, n = 249) | 1 (0.44%, n = 225) |
| -1.5 | 4 (0.76%, n = 527) | 1 (1.89%, n = 53) | 1 (0.40%, n = 249) | 1 (0.44%, n = 225) |
| -2 | 7 (1.33%, n = 527) | 5 (2.01%, n = 249) | 3 (1.20%, n = 249) | 2 (0.89%, n = 225) |
| -2.5 | 117 (22.20%, n = 527) | 51 (20.48%, n = 249) | 57 (25.33%, n = 225) | 2 (0.89%, n = 225) |
| -3 | 77 (14.61%, n = 527) | 34 (13.65%, n = 249) | 35 (15.56%, n = 225) | 3 (1.33%, n = 225) |
| -3.5 | 5 (0.93%, n = 527) | 0 (0.00%, n = 53) | 1 (0.40%, n = 249) | 4 (1.78%, n = 225) |
| -4 | 26 (4.93%, n = 527) | 3 (1.53%, n = 249) | 7 (3.11%, n = 225) | 2 (0.89%, n = 225) |
| -4.5 | 1 (0.19%, n = 527) | 0 (0.00%, n = 53) | 1 (0.40%, n = 249) | 0 (0.00%, n = 225) |
| -5 | 27 (5.12%, n = 527) | 3 (1.53%, n = 249) | 13 (5.22%, n = 249) | 11 (4.89%, n = 225) |
| -5.5 | 1 (0.19%, n = 527) | 0 (0.00%, n = 53) | 0 (0.00%, n = 249) | 1 (0.44%, n = 225) |
| -6 | 7 (1.33%, n = 527) | 3 (1.20%, n = 249) | 4 (1.78%, n = 225) | 1 (0.40%, n = 225) |
| -6.5 | 1 (0.19%, n = 527) | 0 (0.00%, n = 53) | 1 (0.40%, n = 249) | 0 (0.00%, n = 225) |
| -7 | 14 (2.66%, n = 527) | 6 (2.41%, n = 249) | 6 (2.67%, n = 225) | 1 (0.44%, n = 225) |
| -7.5 | 1 (0.19%, n = 527) | 0 (0.00%, n = 53) | 1 (0.40%, n = 249) | 1 (0.44%, n = 225) |
| -8 | 5 (0.95%, n = 527) | 1 (1.89%, n = 53) | 1 (0.40%, n = 249) | 3 (1.33%, n = 225) |

| MRC sum score |
|---------------|
| 50-35 | 15 (2.05%, n = 733) | 10 (2.79%, n = 359) | 5 (1.67%, n = 299) |
| 56-47 | 130 (17.47%, n = 733) | 59 (16.43%, n = 359) | 60 (20.07%, n = 299) |
| 64-60 | 588 (80.22%, n = 733) | 290 (80.78%, n = 359) | 234 (78.26%, n = 299) |
| Right knee extension |
|----------------------|
| 0                    | 4 (0.55%, n = 732) | 3 (0.41%, n = 732) | 2 (0.56%, n = 358) | 2 (0.67%, n = 299) |
| 1                    | 3 (0.41%, n = 732) | 0 (0.00%, n = 75)  | 0 (0.00%, n = 358) | 3 (1.00%, n = 299) |
| 2                    | 4 (0.55%, n = 732) | 0 (0.00%, n = 75)  | 4 (1.12%, n = 358) | 0 (0.00%, n = 299) |
| 3                    | 38 (5.19%, n = 732) | 3 (4.00%, n = 75)  | 15 (4.19%, n = 358) | 20 (6.69%, n = 299) |
| 4                    | 243 (33.20%, n = 732) | 23 (30.67%, n = 75) | 135 (37.71%, n = 358) | 85 (28.43%, n = 299) |
| 5                    | 440 (60.11%, n = 732) | 49 (65.33%, n = 75) | 202 (56.42%, n = 358) | 189 (63.21%, n = 299) |

| Handgrip strength (all participants) |
|--------------------------------------|
| 0                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 1                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 2                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 3                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 4                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 5                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |

| Handgrip strength (male participants) |
|--------------------------------------|
| 0                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 1                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 2                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 3                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 4                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 5                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |

| Handgrip strength (female participants) |
|--------------------------------------|
| 0                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 1                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 2                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 3                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 4                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |
| 5                                    | 26.78 to 30.30 | 31.75 to 34.00 | 27.12 to 30.00 | 29.98 to 33.30 |

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| Group          | Timed Up and Go Duration (in seconds) | Handgrip Strength (All Ages) |
|---------------|--------------------------------------|-----------------------------|
| 18-30 years   | 1.70 to 24.00                        | 11.09 to 21.28 |
| 31-40 years   | 9.00 - 17.30                         | 12.83 to 16.88 |
| 41-50 years   | 11.90 to 24.00                       | 16.37 to 20.19 |
| 51-60 years   | 8.00 - 17.30                         | 11.81 to 15.94 |
| 61-70 years   | 8.00 - 24.00                         | 13.55 to 17.66 |
| 71+ years     | 8.00 - 20.00                         | 14.00 to 18.00 |

Notes: PCFS = Post-COVID-19 Functional Status; EQ-5D-5L = EuroQol-5 Dimensions-5 Levels; mMRC dyspnea scale = Modified Medical Research Council Dyspnea Scale; FPI = Functional Oral Intake Scale; VAS = Visual Analogue Scale; FIM = Functional Independence Measure; ESS = Epworth Sleepiness Scale; ISI = Insomnia Severity Index; MRC sum score = Medical Research Council Sum Score; MBS = Modified Borg Dyspnea Scale; S.D. = Standard Deviation; C.I. = Confidence Interval; FACIT-F = Functional Assessment of Chronic Illness Therapy - Fatigue; WHODAS = World Health Organization Disability Assessment Schedule.
Table 2 presents 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.

**INSERT FIGURE 2.**

The handgrip strength measurement showed many participants (52.20%, 379/726) had “poor” results when compared to normative values for the Brazilian population.[19,20] 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%, 120/297). These results can be seen on Figure 3 and Table 2, along other quantitative results. Similarly, TUG results revealed that, on average and for all age groups, participants did not reach normative results.

Two-way ANOVA tests were conducted with handgrip strength and TUG results as dependent variables. For TUG, age (elder/younger) presented a significant main effect on participants’ performance (f(1)=20.916, p<0.001), but there was no significant main effect related to the type of oxygen support received, neither significant interaction effects between these groups and age. For the handgrip strength measurement, age had, once again, a significant main effect on performance (f(1)=11.261, p<0.001). However, this time the level of oxygen support also presented a significant main effect (f(2)=26.141, p<0.001). The interaction effect between age and level of oxygen support was not significant (f(2)=0.858, p=0.424). Turkey’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.

**INSERT FIGURE 3.**

As shown in supplementary table 03, 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.
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. WHODAS 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 previous publications.[8] Having a higher number of participants admitted to intensive care may have influenced our results. Our VAS for pain results corroborated other studies showing it as a relevant PASC result.[3-5,7-9,11,12] 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 suggest 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% to 42.7%.[3,5,7,9,11] Only 26% of the population investigated by Huang et al scored one or higher on the mMRC dyspnea scale.[8] We suspect it can be attributed to the fact that in that study, six to eight 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 hospitalized and non-
hospitalized 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 two or higher and 53.3% of one 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 two 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 hospitalized patients,[21] 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 to 50 years old), our participants presented longer testing times than the worst reported results of healthy subjects,[22,23] demonstrating that this population also shows the effects of PASC. Similarly, we found abnormal results for the elderly (71+ years old),[24-26] including a systematic review spanning 34 studies from different populations.[27] We also note that less than 25% of our population was fully able to move around independently.[28] Results of 1MSTST also seem to be lower than normative data found in the literature.[29] These findings highlight the need for instrumentalized measures to capture individual rehabilitation needs.

Previous publications identified fatigue as an important PASC finding.[3-5,7,8,30] Our data does 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 day time sleepiness should be considered.

FOIS results did not show any lasting issues with oral intake three to eleven 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.[31]
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 programs. 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 specialized 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. 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. We demonstrated that even three to eleven 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 that required mechanical ventilation.

CONTRIBUTORS

LRB and MI contributed equally with conceptualization, investigation, methodology, supervision, and validation. LRB further contributed with funding acquisition and managing resources. LRB, MI, and LRP contributed with data curation and visualization. LRP conducted formal analysis. LRB, MI, LRP, SKHAAC, and VDR contributed with writing the original draft, review, and editing. VDR assisted with project administration. LRB, MI,
SKHAAC, SSTU, DM, FK, AAAO, GSN, ATS, MC, RASAC, VP, MVM, EMS, and APG all contributed with the investigation. FF provided critical review.

DECLARATION OF INTERESTS

We declare no competing interests.

DATA SHARING

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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COMPLETE DATABASE
n = 3755

DISCHARGED PATIENTS
n = 2703

SURVIVING PATIENTS
n = 2546

SURVIVING PATIENTS WHO TESTED POSITIVE FOR COVID-19
n = 1802

ELIGIBLE PATIENTS
n = 946

PATIENTS WITH FUNCTIONAL EVALUATIONS
n = 877

FINAL DATABASE
n = 801 patients

1052 hospital deaths

157 deaths after discharge

744 negative or unconfirmed cases

856 excluded from participating

62 patients missed all evaluations

7 patients missed functional evaluations

55 patients evaluated after April 31st, 2021 (not included in this study)

8 patients with inconsistencies in their records

2 patients younger than 18 years of age

2 patients with less than 3 months after hospital discharge

9 patients with no information regarding oxygen support

172x226mm (300 x 300 DPI)
### Table 1: Relevant details regarding scales and tools for clinical and functional evaluation in alphabetical order.

| Measure | Short description | Situations/Domain/Dimensions assessed | Response levels/Rating options |
|---------|------------------|-------------------------------------|-------------------------------|
| **Disability Assessment Schedule World Health Organization** | | | |
| Timed Up and Go | A 0 to 10 rated numerical score used to measure dyspnea (using the Modified Borg Dyspnea Scale) before and after the test. | | |
| | Sits and reading, watching TV, sitting, inactive in a public place (e.g., a theatre or a meeting); as a passenger in a car for an hour without a break; lying down to rest in the afternoon when circumstances permit; sitting and talking to someone; sitting quietly after a lunch without alcohol; and, in a car, while stopped for a few minutes in the traffic. | | |
| | Pain, depression or anxiety related to the infection; | | |
| | “I have no limitations in my everyday life as I can perform all usual duties/activities, although I still have persistent symptoms, pain, depression or anxiety.”; “I suffer from limitations in my everyday life as I am able to perform all usual duties/activities due to symptoms, pain, depression or anxiety.”; “I am able to perform all activities without any assistance.”; “I suffer from limitations in my everyday life as I am not able to perform all usual duties/activities due to symptoms, pain, depression or anxiety.”; “I am able to take care of myself without any assistance.”; “I suffer from severe limitations in my everyday life.” | | |
| | Mobility; self-care; usual activities; pain/discomfort; anxiety/depression. | | |
| | 1 (no problems); 2 (slight problems); 3 (moderate problems); 4 (severe problems); 5 (unable to perform these activities). | | |
| | Pain Visual Analogue Scale | | |
| | Pain | | |
| | 100 mm line with verbal descriptors “no pain” and “worst imaginable pain” at every end. It is used to ask the patient to indicate in pain intensity for the right and left side of the body. The highest of both sides was included into data analysis. | | |
| | “How much are you currently affected in your everyday life by COVID-19?” | | |
| | “I have no limitations in my everyday life and no symptoms, pain, depression or anxiety related to the infection”; “I have negligible limitations in my everyday life as I can perform all usual duties/activities, although I still have persistent symptoms, pain, depression or anxiety.”; “I suffer from limitations in my everyday life as I occasionally need to avoid or reduce usual daily activities or need to spread these over time due to symptoms, pain, depression or anxiety.”; “I am, however, able to perform all activities without any assistance.”; “I suffer from limitations in my everyday life as I am not able to perform all usual daily activities due to symptoms, pain, depression or anxiety.”; “I am, however, able to take care of myself without any assistance.”; “I suffer from severe limitations in my everyday life.” | | |
| | Mobility | | |
| | 1 (none); 2 (mild); 3 (moderate); 4 (severe); and 5 (extreme or cannot do). | | |
| | Post-COVID-19 Functional Status scale | | |
| | It measures the time in seconds taken by the participant to stand up from a chair, walk 3 meters, turn, walk back to the chair and sit without physical assistance, however with normally used walking aid. | | |
| | It captures the level of functioning in six domains of life. In each item, individuals estimate the magnitude of their difficulties during the previous 30 days using a five-point scale, from “none” to “extreme or cannot do”. | | |
| | “I am able to do my usual activities; I need to sleep during the day; I am too tired to eat; I need help doing my usual activities. I am frustrated by being too tired to do the things I want to do; I have to limit my social activity because I am tired.” | | |
| | Mobility; self-care; usual activities; pain/discomfort; anxiety/depression. | | |
| | 1 (no problems); 2 (slight problems); 3 (moderate problems); 4 (severe problems); 5 (unable to perform these activities). | | |
| | Functional Independence Measure | | |
| | It assesses the levels for performing motor and cognitive activities. It ranges from 1 to 7 points, complete dependence to complete independence. | | |
| | It captures the level of functioning in six domains of life. In each item, individuals estimate the magnitude of their difficulties during the previous 30 days using a five-point scale, from “none” to “extreme or cannot do”. | | |
| | Mobility; self-care; usual activities; pain/discomfort; anxiety/depression. | | |
| | 1 (no problems); 2 (slight problems); 3 (moderate problems); 4 (severe problems); 5 (unable to perform these activities). | | |

**Notes:** COVID-19 = Coronavirus disease 2019.
### Supplementary Table 02. All symptoms and comorbidities.

| Condition                          | All participants (n=801) | No oxygen support (n=82) | Oxygen support (n=386) | Intubation (n=333) |
|------------------------------------|--------------------------|---------------------------|------------------------|-------------------|
| Dialysis                           | 99 (12.36%, total = 801) | 4 (4.88%, total = 82)     | 19 (4.92%, total = 386)| 76 (22.82%, total = 333) |
| Hypertension                       | 462 (57.69%, total = 801) | 37 (45.12%, total = 82)   | 231 (59.84%, total = 386) | 194 (58.26%, total = 333) |
| COPD                               | 35 (4.38%, total = 800)   | 1 (1.22%, total = 82)     | 20 (5.19%, total = 385)  | 14 (4.20%, total = 335)   |
| Asthma                             | 30 (3.75%, total = 800)   | 5 (3.66%, total = 82)     | 18 (4.66%, total = 385)  | 9 (2.70%, total = 333)    |
| Renal failure, diabetes            | 29 (3.62%, total = 801)   | 4 (4.88%, total = 82)     | 18 (4.66%, total = 386)  | 7 (2.10%, total = 333)    |
| Renal failure                      | 47 (5.87%, total = 801)   | 6 (7.22%, total = 82)     | 25 (6.48%, total = 386)  | 16 (4.80%, total = 333)   |
| Liver disease                      | 26 (3.25%, total = 800)   | 7 (8.54%, total = 82)     | 9 (2.34%, total = 385)   | 4 (1.26%, total = 334)    |
| Stroke                             | 38 (4.75%, total = 800)   | 5 (6.05%, total = 82)     | 19 (4.94%, total = 385)  | 14 (4.30%, total = 333)   |
| Dementia                           | 10 (1.25%, total = 800)   | 0 (0.00%, total = 82)     | 6 (1.56%, total = 385)   | 4 (1.26%, total = 333)    |
| Rheumatic disease                  | 32 (4.00%, total = 800)   | 4 (4.88%, total = 82)     | 15 (3.90%, total = 385)  | 13 (3.90%, total = 332)   |
| Hematologic disease                | 47 (5.80%, total = 801)   | 6 (7.22%, total = 83)     | 18 (4.57%, total = 388)  | 23 (6.93%, total = 332)   |
| Diabetes                           | 292 (36.45%, total = 801) | 26 (31.71%, total = 82)   | 139 (36.01%, total = 386) | 127 (38.14%, total = 332) |
| Cancer                             | 34 (4.19%, total = 801)   | 4 (6.15%, total = 83)     | 18 (5.20%, total = 346)  | 12 (3.84%, total = 332)   |
| Obesity                            | 152 (19.02%, total = 799) | 8 (9.76%, total = 82)     | 65 (16.88%, total = 385) | 79 (23.80%, total = 332)  |
| Asthmaic proctitis                  | 98 (12.48%, total = 801) | 14 (17.95%, total = 82)   | 53 (14.10%, total = 376) | 31 (9.72%, total = 319)   |
| Rheumatoid joint disease           | 215 (27.78%, total = 774) | 15 (18.52%, total = 81)   | 110 (29.02%, total = 379) | 90 (28.66%, total = 314)  |
| Sleep apnea                        | 134 (16.23%, total = 776) | 11 (14.10%, total = 78)   | 76 (21.79%, total = 358) | 45 (15.00%, total = 308)  |
| Chest pain                         | 203 (26.06%, total = 779) | 14 (17.50%, total = 80)   | 109 (28.68%, total = 380) | 80 (25.08%, total = 319)  |
| Cough                              | 309 (39.62%, total = 780) | 28 (34.57%, total = 81)   | 129 (34.04%, total = 379) | 152 (47.50%, total = 320) |
| Falls                              | 119 (15.22%, total = 782) | 7 (8.75%, total = 80)     | 50 (13.12%, total = 381) | 62 (19.31%, total = 321)  |
| Hepatic steatosis                  | 112 (14.56%, total = 729) | 8 (10.59%, total = 77)    | 57 (16.20%, total = 350) | 47 (15.56%, total = 302)  |

Notes: COPD = Chronic Obstructive Pulmonary Disease.

### Supplementary Table 03. Participants’ results over the months since hospital discharge for selected variables.

| Variables                          | 4th            | 5th            | 6th            | 7th            | 8th            | 9th            | 10th           |
|------------------------------------|----------------|----------------|----------------|----------------|----------------|----------------|----------------|
| **Handgrip strength classification** | Good           | Average        | Poor           | Good           | Average        | Poor           | Good           |
| Fatigue                            | 12.50          | 25.00          | 62.50          | 41.67          | 25.00          | 59.00          | 40.59          |
| EQ-5D-3L anxiety and depression dimension score | 5               | 3              | 1              | 4              | 1              | 3              | 2              |
| EQ-5D-3L anxiety and depression dimension score | 4              | 3              | 2              | 1              | 3              | 2              | 1              |
| mHRC dyspnea scale                | Average        | Standard Deviation | 36.31          | 10.09          | 12.31          | 9.79           | 10.38          | 8.80           | 9.27           |
| FACIT-Fatigue                      | Average        | 38.46          | 3.95           | 9.35           | 38.23          | 39.32          | 39.32          | 39.32          | 39.32          |

Notes: VAS = Visual Analogue Scale; EQ-5D-3L = EuroQoL 5 Dimensions 3 Levels, mHRC dyspnea scale = Medical Research Council Dyspnea Scale; FACT-Fatigue = Functional Assessment of Chronic Illness Therapy – Fatigue.

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STROBE Statement—Checklist of items that should be included in reports of *cohort studies*

Based on: 09_August_Manuscript_clean

| Item No. | Recommendation |
|---------|----------------|
| 1       | (a) Indicate the study’s design with a commonly used term in the title or the abstract |
|         | (b) Provide in the abstract an informative and balanced summary of what was done and what was found |
| 2       | Explain the scientific background and rationale for the investigation being reported |
| 3       | State specific objectives, including any prespecified hypotheses |
| 4       | Present key elements of study design early in the paper |
| 5       | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| 6       | (a) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up |
|         | (b) For matched studies, give matching criteria and number of exposed and unexposed |
| 7       | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| 8*      | For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| 9       | Describe any efforts to address potential sources of bias |
| 10      | Explain how the study size was arrived at |
| 11      | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| 12      | (a) Describe all statistical methods, including those used to control for confounding |
|         | (b) Describe any methods used to examine subgroups and interactions |
|         | (c) Explain how missing data were addressed |
|         | (d) If applicable, explain how loss to follow-up was addressed |
|         | (e) Describe any sensitivity analyses |
| 13*     | (a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for |

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eligibility, confirmed eligible, included in the study, completing follow-up, and analysed

(b) Give reasons for non-participation at each stage Page 6, Figure 1, Flow chart

(c) Consider use of a flow diagram Page 6, Figure 1, Flow chart

Descriptive data 14* (a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders Page 8, Table 1 Supplementary table 02.

(b) Indicate number of participants with missing data for each variable of interest Refer to the total n in the corresponding tables.

(c) Summarise follow-up time (eg, average and total amount) Page 8, Table 1

Outcome data 15* Report numbers of outcome events or summary measures over time Page 9, Table 2 Page 6, Line 27 to Page 8, Line 28

Main results 16 (a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included Corresponding tables

(b) Report category boundaries when continuous variables were categorized Supplementary tables

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period Not applicable

Other analyses 17 Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses See paragraph Data analyses

Discussion

Key results 18 Summarise key results with reference to study objectives Page 15, Line 2 to 11

Limitations 19 Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias Page 17, Line 9 to 14

Interpretation 20 Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence Page 17, Line 19 to 24

Generalisability 21 Discuss the generalisability (external validity) of the study results Not specifically mentioned

Other information

Funding 22 Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based Page 6, Line 7 to 13

*Give information separately for exposed and unexposed groups.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.
Long-term functioning status of COVID-19 survivors: a prospective observational evaluation of a cohort of patients surviving hospitalization

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| Keywords | COVID-19, REHABILITATION MEDICINE, PUBLIC HEALTH |
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Long-term functioning status of COVID-19 survivors: a prospective observational evaluation of a cohort of patients surviving hospitalization

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ABSTRACT

Objectives: The study investigated the long-term functional status of hospitalized COVID-19 survivors to explore and document their functional situation. Design: This prospective observational study assessed 801 COVID-19 survivors at three to eleven months after hospital discharge. It analyzes participants' sociodemographic background, COVID-19 clinical manifestations, and clinical and functional evaluations. Setting: Tertiary-level university hospital in Sao Paulo, Brazil. Participants: Study participants are COVID-19 survivors admitted to hospital care for at least 24h 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, 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, 01-minute Sit to Stand Test. Results: Many participants required invasive mechanical ventilation (41.57%, 333/801). Mean age was 55.35 ± 14.58 years. With a mean of 6.56 (S.D: 1.58; 95% C.I: 6.45 to 6.67) months after hospital discharge, 70.86% (567/800) reported limited daily activities, which were severe in 5.62% (45/800). They also reported pain and discomfort (64.50%, 516/800), breathlessness (64.66%, 514/795), and anxiety and depression (57.27%, 457/798). Daytime sleepiness and insomnia evaluations showed borderline results. Most (92.85%, 727/783) participants reported unrestricted oral intake. Data indicated no generalized fatigue (mean score: 39.18, S.D: 9.77; C.I: 95% 38.50 to 39.86). Assessments showed poor handgrip strength (52.20%, 379/726) and abnormal timed up and go results (mean 13.07s, S.D 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 hospitalized COVID-19 survivors.
ARTICLE SUMMARY

Strengths and limitations of this study

1. 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.

2. The study test battery used both self-reported, clinical assessments and quantifiable measures.

3. 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.

4. 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 Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) does 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 COVID-19 patients 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 six 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] and memory[5,7] concentration[5] and sleep disorders.[5,7-9] Objective assessments including the Short Physical Performance Battery Test and the 2-Minutes 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 most effective rehabilitation needs assessments and interventions. Thus, a better understanding of functional disorders that may arise in the long-term after hospitalization 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 three to eleven months of hospital discharge, aiming at identifying their long-term functioning status and rehabilitation needs.
MATERIALS & 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 Polymerase Chain Reaction (PCR) or serology testing for SARS-CoV-2. Written informed consent was obtained from all participants included.

STUDY DESIGN

This prospective observational evaluation of a cohort of COVID-19 survivors is based on a follow-up test battery conducted three to eleven months after hospital discharge with people previously admitted to treat acute COVID-19. Participants were recruited between October 7, 2020 and April 8, 2021. Study assessments were completed between October 20, 2020 and April 16, 2021. Data was registered using the Research Electronic Data Capture (REDCap) platform. The study was approved by HCFMUSP Institutional Review Board, and registered under CAEE 39744120.3.0000.0068. Further details about the study protocol are available elsewhere.[14,15] To accommodate for limitations in recruitment, the study included participants three to eleven months after hospital discharge. Report from this cohort study followed the principles of the STROBE statement.

ASSESSMENTS

All data was 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 includes 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 Supplementary 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 ± standard deviations (S.D). Intervals at 95% confidence (C.I) for the means were estimated with Student’s t-distribution at the proper degrees-of-freedom. 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 was 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 based on 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 analyzing handgrip strength and TUG results, participants were further divided into age groups. Handgrip strength data was stratified by sex and age groups for classification. For these two variables we investigated differences among the three subgroups using factorial 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 vs. 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-values < 0.05.

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

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

All data analysis was performed with IBM SPSS 27.0, Python, and related libraries, [17-19]
except for the additional multivariate linear regression analysis which was performed with
STATA 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.

STUDY TRANSPARENCY AND PATIENT AND PUBLIC INVOLVEMENT

This manuscript offers a faithful and transparent report of the work carried out as originally
planned. No important aspect has been omitted, nor were any discrepancies, as our methods
and results intend to show.

Study participants did not take part in the design and conduct of the work. We are committed
to disseminate the results of this work to the therapists of our academic institution who will
also share the results with the patients of our institution.

RESULTS

Figure 1 shows a flow diagram of study participants. As per the study protocol,[14,15] all
COVID-19 patients 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), time since hospital discharge (<3 months), and lack of information on the type of
oxygen support received during treatment, or any other data inconsistency.

INSERT FIGURE 1.

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 didn’t 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% C.I.: 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% C.I.: 27.92 to 32.46) compared to 6.50 ± 6.17 (95% C.I.: 5.14 to 7.86) for the group with no oxygen support, and 11.63 ± 10.16 (95% C.I.: 10.61 to 12.65) for the non-invasive support group. A large portion of participants was admitted to intensive care (n=497), with an average LoS in intensive care of 8.39 ± 12.00 days (95% C.I.: 7.56 to 9.22). Overall, the study population consisted of 421 males (52.56%) and 380 females (47.44%). The commonest comorbidities among all participants were hypertension (462/801, 57.68%) and diabetes (292/801, 36.45%). Details on other participants’ characteristics are shown in Table 1, and in the Supplementary Table 2.

Post-COVID Functional Status (PCFS) scale results revealed that 70.86% of participants (567/800) reported limitations in daily activities, which were severe for 5.62% (45/800) of them. The invasive mechanical ventilation group presented a slightly larger proportion of participants referring some form of limitation, reaching 78.08% (260/333). EuroQol-5D-5L results showed that 64.50% (516/800) still suffered from pain and discomfort, while 57.27% (457/798) reported anxiety and depression. Pain VAS results corroborated it by showing that 45.93% (333/725) 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%, 636/735), as with the Functional Oral Intake Scale (FOIS), in which 92.85% (727/783) of participants reported no restrictions.

Many participants (64.66%, 514/795) reported some breathlessness (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% confidence interval, the variation in oxygen saturation before and after the test was also similar, with an overall average of -0.85 ± 2.53 % (95% C.I.: -1.06% to -0.63%), where the negative value indicates a worst score after the test. Additional functional assessments are available in Table 2 and Table 3.

The Epworth Sleepiness Scale showed that participants, on average, have a borderline level of daytime sleepiness, markedly on the group that received no oxygen support, in line with trends observed in the Insomnia Severity Index (Table 2 and Table 3).
Table 1. Sociodemographic and clinical data presented as n participants (%), mean (S.D.), alongside 95% C.I. 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%)         |
| **Commonest 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 (26.66%, total = 314) |
| Chest pain               | 203 (26.06%, total = 779) | 14 (17.50%, total = 80) | 109 (28.68%, total = 380) | 80 (25.08%, total = 319) |
| **Commonest 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 (S.D.) | 95% C.I. | Range   | Mean (S.D.) | 95% C.I. | Range   | Mean (S.D.) | 95% C.I. | Range   | Mean (S.D.) | 95% C.I. | 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 |

Notes: n = number; S.D. = Standard Deviation; C.I. = Confidence Interval; ICU = Intensive Care Unit
### Table 2. Functional assessments, categorical data presented as n participants (%).

|                | 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)      | 5 (6.17%, 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)  | 102 (47.70%, 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) | 0 (0.00%, n = 80) | 2 (0.53%, n = 379) | 0 (0.00%, n = 324) |
| 3  | 1 (0.13%, n = 783) | 0 (0.00%, n = 80) | 0 (0.00%, n = 379) | 1 (0.31%, n = 324) |
| 4  | 13 (1.66%, n = 783)| 0 (0.00%, n = 80) | 9 (2.37%, n = 379) | 4 (1.23%, n = 324) |

**Pain VAS**

| Pain VAS | 0-39 | 40-59 | 60-100 | 104-126 |
|----------|------|-------|--------|---------|
| 0-39     | 249  | 143   | 333    | 636     |
| 40-59    | 25   | 13    | 37     | 66      |
| 60-100   | 119  | 69    | 169    | 322     |
| 104-126  | 105  | 61    | 127    | 248     |

**FIM**

| FIM     | 18   | 19-60 | 61-103 | 104-126 |
|---------|------|-------|--------|---------|
| 18      | 2    | 11    | 86     | 636     |
| 19-60   | 1    | 0     | 9      | 66      |
| 61-103  | 0    | 7     | 30     | 322     |
| 104-126 | 1    | 116   | 322    | 248     |

**ESS**

| ESS     | 30-7 | 8-9  | 10-15 | 16-24 |
|---------|------|-----|-------|-------|
| 30-7    | 355  | 28  | 15     | 25    |
| 8-9     | 90   | 13  | 15     | 25    |
| 10-15   | 224  | 15  | 116    | 68    |
| 16-24   | 131  | 25  | 68     | 38    |

**HI-S**

| HI-S    | 10-7 | 18-14 | 15-21 | 22-28 |
|---------|------|-------|-------|-------|
| 10-7    | 479  | 203   | 94    | 23    |
| 18-14   | 41   | 25    | 10    | 5     |
| 15-21   | 50   | 97    | 50    | 14    |
| 22-28   | 61   | 38    | 34    | 4     |

**MRC sum score**

| MRC sum score | 0-35 | 36-47 | 48-60 |
|---------------|------|------|------|
| 0-35          | 15   | 130  | 588  |
| 36-47         | 0    | 11   | 64   |
| 48-60         | 10   | 59   | 290  |

Notes: PCFS = Post-COVID-19 Functional Status; EQ-5D-5L = EuroQol-5 Dimensions-5 Levels; mMRC dyspnea scale = Modified Medical Research Council Dyspnea Scale; FOIS = Functional Oral Intake Scale; VAS = Visual Analogue Scale; FIM = Functional Independence Measure; ESS = Epworth Sleepiness Scale; ISI = Insomnia Severity Index; MRC sum score = Medical Research Council Sum Score
### Table 3. Functional assessments, continuous data presented as mean (S.D.), alongside 95% C.I. and number of participants (n).

|                                | All participants (n=801)                          | No oxygen support (n=82)                  | Oxygen support (n=386)                  | Intubation (n=333)                  |
|--------------------------------|--------------------------------------------------|------------------------------------------|----------------------------------------|------------------------------------|
|                                | Mean (S.D.) | 95% C.I. | n | Range | Mean (S.D.) | 95% C.I. | n | Range | Mean (S.D.) | 95% C.I. | n | Range | Mean (S.D.) | 95% C.I. | 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 | 79.00 - 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 - 6.00 | -0.36 (1.95) | -0.90 to 0.18 | 53 | -7.00 - 6.00 | -1.10 (2.94) | -1.47 to -0.74 | 252 | -25.00 - 5.00 | -0.68 (2.12) | -0.96 to -0.40 | 228 | -14.00 - 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 |

Notes: S.D. = Standard Deviation; C.I. = Confidence Interval; FACIT-F = Functional Assessment of Chronic Illness Therapy - Fatigue; ISI = Insomnia Severity Index; WHODAS = World Health Organization Disability Assessment Schedule.
Table 2, Table 3 and Supplementary 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.

**INSERT FIGURE 2.**

The handgrip strength measurement showed many participants (52.20%, 379/726) had “poor” results when compared to 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%, 120/297). These results can be seen on Figure 3 and Supplementary 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 females. 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 for 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 to 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.

INSERT FIGURE 3.

As shown in Supplementary 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 dyspnea, 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 test. The full results may be found in Supplementary 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. WHODAS 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] reports a large cohort study
of hospitalized COVID-19 of whom 27% of the sample reported pain and discomfort. Despite being hospitalized, only 4% were ventilated during hospitalization. We hypothesize that the higher number of participants admitted to intensive 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 hospitalization. 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, 2021 hospitalized COVID-19 patients 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 to 0% of patients reporting pain related symptoms in a control group (p<0.01). Having a higher number of patients admitted to ICU might have influenced a higher prevalence of pain and discomfort. Besides the effects of COVID-19, patients hospitalized 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 hospitalized COVID-2019 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 suggest 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% to 42.7%.[3,5,7,9,11] Only 26% of the population investigated by Huang et al scored one or higher on the mMRC dyspnea scale.[8] We suspect it can be attributed to the fact that in that study, six to eight 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 hospitalized and non-
hospitalized 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 two or higher and 53.3% of one 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 two 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 hospitalized 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 to 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 instrumentalized measures to capture individual rehabilitation needs.

Previous publications identified fatigue as an important PASC finding.[3-5,7,8,34] Our data does 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 day time sleepiness should be considered.

FOIS results did not show any lasting issues with oral intake three to eleven 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 programs. 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 specialized 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. Fourthly, 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 our patients, when returning home from hospitalization. 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 three to eleven 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 that required mechanical ventilation.

**CONTRIBUTORS**
LRB and MI contributed equally with conceptualization, investigation, methodology, supervision, and validation. LRB further contributed with funding acquisition and managing resources. LRB, MI, and LRP contributed with data curation and visualization. LRP conducted formal analysis. LRB, MI, LRP, SKHAAC, and VDR contributed with writing the original draft, review, and editing. VDR assisted with project administration. LRB, MI, SKHAAC, SSTU, DM, FK, AAAO, GSN, ATS, MC, RASAC, VP, MVM, EMS, and APG all contributed with the investigation. FF provided critical review.

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DECLARATION OF INTERESTS

We declare no competing interests.

DATA SHARING

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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FIGURES

Figure 1. Flow diagram of study participants

Figure 2. Histogram for the FACIT-Fatigue scale

Figure 3. Handgrip strength measurement results distribution

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Supplementary Table 1. Relevant details regarding scales and tools for clinical and functional evaluation in alphabetical order.

| Short description |
|-------------------|
| **Situation/Domains/Dimensions assessed** |
| **Response levels/Rating options** |
| **Handgrip strength** was measured with a Jamar® hydraulic hand dynamometer (Sammons Preston, Bolingbrook, Illinois, USA) with patients seated at their elbows by their sides and flexed to right angles and a neutral wrist position. Three measurements were performed for both hands, and the mean score of the side with the highest score was recorded. This mean is reported as continuous data in the manuscript. For the categorical assessment of each individual patient, each measurement was classified based on the 25th and 75th percentiles per age group of the normative handgrip values reported by Vianna et al. in 2007 as a sample of 2,649 Brazilian subjects. Values equal or below the 25th percentiles are considered "poor", values between the 25th and equal or to the 75th percentiles are classified as "average", values above the 75th percentile are classified as "good". This same methodology has been previously reported by Rodrigues-Barbosa et al., 2011. The normative data reported by Vianna et al. are displayed in Supplementary Table 5. |
| **Dyspnea** |
| **Mobile**:
- **Motor**: self-care; transfer; mobility; sphincter control; communication; and cognition, including memory, social interaction and problem solving. |
| **Fatigue Measure** |
| **Oral intake** |
| **Insomnia Severity Index (ISI)** It consists of a 7-item self-report questionnaire, to evaluate the night's sleep quality and daytime sleepiness. The higher the score, the more severe the situation. It evaluates severity of problems regarding sleep onset, sleep maintenance and early morning awakening as well as sleep dissatisfaction and daytime functioning if others notice these problems, and if all of those are distress. |
| **Medical Research Council Dyspnea Scale** Five-point scale based on degrees of physical activities that cause breathlessness and it is used for the clinical measurement of dyspnea. Breathlessness is defined as the unpleasant sensation of uncomfortable, rapid or difficult breathing. The medical term is dyspnea. The Medical Research Council Dyspnea Scale used in this study is a five-point scale based on degrees of physical activities that cause breathlessness and it is used for the clinical measurement of dyspnea. |
| **Medical Research Council Sum Score** Evaluates strength in muscle groups of all four limbs. A score between 0 and 5 is assigned to each of them. Scores range from 0 to 40 and a value below 40 correlates with muscle weakness. This is considered severe if it is lower than 30. |
| **Modified Borg Dyspnea Scale** The Modified Borg Dyspnea Scale or Borg Category-Ratio 10 is a 0 to 10 rated numerical score used to measure dyspnea as reported by the patient during submaximal exercise. |
| **Pain Visual Analogue Scale** 100 mm line with verbal descriptors “no pain” and “worst imaginable pain” at every end. It is used to ask the patient to rate their pain. |

Situations/Domains/Dimensions assessed

- **Handgrip strength** was measured with a Jamar® hydraulic hand dynamometer which focuses on what the patient can do easily. A 7-point ordinal scale which ranges from 0 (no problems) to 6 (severe problems). 60
- **Sitting and reading, watching TV, sitting, inactive in a public place (e.g., a theatre or a meeting); as a passenger in a car for an hour without a break; lying down to rest in the afternoon when circumstances permit; sitting and talking to someone; sitting quietly after a lunch without alcohol, and, in a car, while stopped for a few minutes in the traffic.**
- **0 (never); 1 (slight); 2 (moderate); and 3 (high). Score ranges from 0 to 24. The classification mentioned herein is merely informative as it has been extracted from grey literature. A published scientific report of this classification has not been found by means of a literature search. 0.7 (is unlikely to be abnormally sleepy) 6-9 (The patient has an average amount of daytime sleepiness) 10-15 (There may be a suggestion of excessive sleepiness for which medical attention should be considered) 16-24 (A clear excessive sleep problem for which medical attention is required.)
- **Dyspnea** 
  - 0 (nothing at all); 1 (a little bit); 2 (something); 3 (quite a bit); and 4 (very much).
- **Pain** NA
- **60**
- **59**
- **58**
- **54**
- **53**
- **52**
- **51**
- **48**
- **46**
- **43**
- **42**
- **41**
- **37**
- **28**
- **24**
- **23**
- **20**
- **18**
- **17**
- **12**
- **8**
- **7**
- **6**
- **5**
- **3**
- **14**
- **13**
- **12**
- **11**
- **10**
- **9**
- **8**
- **7**
- **6**
- **5**
- **4**
- **3**
- **2**
- **1**
- **0**

**Response levels/Rating options**

- **Handgrip strength** measured by dynamometry is well established and generally accepted. Scores: 1 (very poor); 2 (poor); 3 (moderate); 4 (good); 5 (excellent); and 6 (best imaginable). Scores range from 0 to 10 rated numerical score used to measure dyspnea as reported by the patient during submaximal exercise. It is a rated with a 5-point Likert scale rendering a score range from zero to 28-0 (absence of insomnia) 8-14 (sub-threshold insomnia) 15-21 (moderate insomnia) 22-28 (severe insomnia) for a few minutes in the traffic.

**Pain Visual Analogue Scale** for peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

**Epworth Sleepiness Scale**

- **0.7 (is unlikely to be abnormally sleepy) 6-9 (The patient has an average amount of daytime sleepiness) 10-15 (There may be a suggestion of excessive sleepiness for which medical attention should be considered) 16-24 (A clear excessive sleep problem for which medical attention is required.)
- **Insomnia Severity Index (ISI)** It consists of a 7-item self-report questionnaire, to evaluate the night's sleep quality and daytime sleepiness. The higher the score, the more severe the situation. It evaluates severity of problems regarding sleep onset, sleep maintenance and early morning awakening as well as sleep dissatisfaction, interference with daytime functioning, if others notice these problems, and if all of these are distress.
- **Medical Research Council Dyspnea Scale** Five-point scale based on degrees of physical activities that cause breathlessness and it is used for the clinical measurement of dyspnea. Breathlessness is defined as the unpleasant sensation of uncomfortable, rapid or difficult breathing. The medical term is dyspnea. The Medical Research Council Dyspnea Scale used in this study is a five-point scale based on degrees of physical activities that cause breathlessness and it is used for the clinical measurement of dyspnea.
- **Medical Research Council Sum Score** Evaluates strength in muscle groups of all four limbs. A score between 0 and 5 is assigned to each of them. Scores range from 0 to 40 and a value below 40 correlates with muscle weakness. This is considered severe if it is lower than 30.
- **Modified Borg Dyspnea Scale** The Modified Borg Dyspnea Scale or Borg Category-Ratio 10 is a 0 to 10 rated numerical score used to measure dyspnea as reported by the patient during submaximal exercise.

**Functional Assessment of Chronic Illness Therapy – Fatigue**

- **Fatigue**
- **Mobility**
- **Fatigue Measure**
- **Pain Visual Analogue Scale**
- **Medical Research Council Sum Score**
- **Brody et al., 2008.**
| Test Name | Description | Notes |
|-----------|-------------|-------|
| Post-COVID-19 Functional Status scale | Measures the functional outcomes in everyday life after COVID-19. The five points answer options vary from “no limitations or symptoms” to “severe limitations”. | It captures the level of functioning in six domains of life. In each item, individuals estimate the magnitude of their difficulties during the previous 30 days using a five-point scale, from “none” to “extreme or cannot do.” |
| Timed Up and Go | Measures the time in seconds taken by the participant to stand up from a chair, walk 3 meters, turn, walk back to the chair and sit without physical assistance, however with normally used walking aid. | It captures the level of functioning in the domains of cognition, mobility, self-care, getting along, life activities and participation. |
| World Health Organization Disability Assessment Schedule 2.0 | Measures the time in seconds taken by the participant to stand up from a chair, walk 3 meters, turn, walk back to the chair and sit without physical assistance, however with normally used walking aid. | It captures the level of functioning in the domains of cognition, mobility, self-care, getting along, life activities and participation. |
| 01-minute Sit to Stand Test | The 01-minute Sit to Stand Test or the 60 seconds Sit to Stand Test is performed with an armless chair and consists of doing as much sit to stand movements possible in 1 minute. When completed, it registers how many repetitions performed. It also registers oxygen saturation and dyspnea level (using the Modified Borg Dyspnea Scale) before and after the test. | The test measures endurance, which is expressed in the number of repetitions performed. |

Notes: COVID-19 = Coronavirus disease 2019.
### Supplementary Table 2. All symptoms and comorbidities.

| Condition                | All participants (n=801) | No oxygen support (n=82) | Oxygen support (n=386) | Intubation (n=333) |
|--------------------------|--------------------------|--------------------------|------------------------|--------------------|
| Dialysis                 | 99 (12.36%, total = 801) | 4 (4.88%, total = 82)    | 19 (4.92%, total = 386) | 76 (22.82%, total = 333) |
| Hypertension             | 462 (57.68%, total = 801) | 37 (45.12%, total = 82)  | 231 (59.84%, total = 386) | 194 (58.26%, total = 333) |
| COPD                     | 35 (4.38%, total = 800)   | 1 (1.22%, total = 82)    | 20 (5.19%, total = 385)  | 14 (4.20%, total = 333)  |
| Asthma                   | 30 (3.75%, total = 800)   | 3 (3.66%, total = 82)    | 18 (4.66%, total = 386)  | 9 (2.70%, total = 333)   |
| Renal failure dialysis   | 29 (3.62%, total = 801)   | 4 (4.88%, total = 82)    | 19 (5.00%, total = 386)  | 10 (3.01%, total = 333)  |
| Renal failure            | 47 (5.87%, total = 801)   | 6 (7.32%, total = 82)    | 25 (6.48%, total = 386)  | 16 (4.80%, total = 333)  |
| Liver disease            | 20 (2.50%, total = 800)   | 7 (8.54%, total = 82)    | 9 (2.45%, total = 385)   | 4 (1.20%, total = 333)   |
| Stroke                   | 38 (4.75%, total = 800)   | 5 (6.10%, total = 82)    | 19 (4.94%, total = 385)  | 14 (4.20%, total = 333)  |
| Dementia                 | 10 (0.00%, total = 800)   | 0 (0.00%, total = 82)    | 6 (1.56%, total = 385)   | 4 (1.20%, total = 333)   |
| Rheumatic disease        | 33 (4.13%, total = 800)   | 4 (4.88%, total = 82)    | 15 (3.90%, total = 385)  | 11 (3.30%, total = 333)  |
| Hematologic disease      | 47 (5.87%, total = 801)   | 6 (18.18%, total = 33)   | 18 (5.57%, total = 385)  | 23 (6.93%, total = 332)  |
| Diabetes                 | 292 (36.45%, total = 801) | 26 (31.71%, total = 82)  | 139 (36.01%, total = 386) | 127 (38.14%, total = 333) |
| Cancer                   | 34 (4.59%, total = 741)   | 4 (6.35%, total = 63)    | 18 (5.20%, total = 346)  | 12 (3.61%, total = 332)  |
| Obesity                  | 152 (19.02%, total = 799) | 8 (9.76%, total = 82)    | 65 (16.88%, total = 385) | 79 (23.80%, total = 332) |
| Angina pectoris          | 98 (12.48%, total = 773)  | 14 (17.95%, total = 78)  | 53 (14.10%, total = 376) | 31 (9.72%, total = 319)  |
| Rheumatic joint disease  | 215 (27.78%, total = 774) | 15 (18.18%, total = 33)  | 110 (30.62%, total = 379) | 90 (28.66%, total = 314) |
| Sleep apnoea             | 134 (18.21%, total = 736) | 11 (14.10%, total = 78)  | 78 (21.79%, total = 358) | 45 (13.05%, total = 300) |
| Chest pain               | 203 (26.06%, total = 779) | 14 (17.50%, total = 80)  | 109 (30.68%, total = 380) | 80 (25.08%, total = 319) |
| Cough                    | 309 (39.62%, total = 780) | 28 (34.57%, total = 81)  | 129 (34.04%, total = 379) | 152 (47.50%, total = 320) |
| Falls                    | 119 (15.22%, total = 782) | 7 (8.73%, total = 80)    | 50 (13.12%, total = 381)  | 62 (19.31%, total = 321)  |
| Hepatic steatosis        | 112 (15.36%, total = 729) | 8 (10.39%, total = 77)   | 57 (16.29%, total = 350)  | 47 (15.06%, total = 302)  |

Notes: COPD = Chronic Obstructive Pulmonary Disease.
### Supplementary Table 3. Supplementary data regarding functional assessments, data presented as n participants (%), mean (S.D.), alongside 95% C.I. and number of participants (n).

|                     | All participants (n=801) | No oxygen support (n=82) | Oxygen support (n=386) | Intubation (n=333) |
|---------------------|--------------------------|--------------------------|------------------------|-------------------|
| **Basal MBS**       |                          |                          |                        |                   |
| 0                   | 339 (44.56%, n = 658)    | 46 (66.66%, n = 67)      | 177 (55.84%, n = 317)  | 136 (49.64%, n = 274) |
| 0.5                 | 38 (5.78%, n = 658)      | 5 (7.46%, n = 67)        | 16 (5.05%, n = 317)    | 17 (5.28%, n = 274) |
| 1                   | 58 (8.18%, n = 658)      | 2 (2.99%, n = 67)        | 30 (9.46%, n = 317)    | 26 (9.49%, n = 274) |
| 1.5                 | 81 (12.31%, n = 658)     | 5 (7.46%, n = 67)        | 38 (11.99%, n = 317)   | 38 (13.87%, n = 274) |
| 2                   | 55 (8.36%, n = 658)      | 2 (2.99%, n = 67)        | 27 (8.52%, n = 317)    | 26 (9.49%, n = 274) |
| 2.5                 | 18 (2.74%, n = 658)      | 1 (1.49%, n = 67)        | 8 (2.52%, n = 317)     | 9 (2.78%, n = 274) |
| 3                   | 30 (4.56%, n = 658)      | 2 (2.99%, n = 67)        | 15 (4.73%, n = 317)    | 13 (4.74%, n = 274) |
| 3.5                 | 12 (1.82%, n = 658)      | 3 (4.48%, n = 67)        | 3 (0.95%, n = 317)     | 6 (2.19%, n = 274) |
| 4                   | 3 (0.46%, n = 658)       | 1 (1.49%, n = 67)        | 1 (0.32%, n = 317)     | 1 (0.36%, n = 274) |
| 4.5                 | 4 (0.61%, n = 658)       | 0 (0.00%, n = 67)        | 2 (0.63%, n = 317)     | 2 (0.73%, n = 274) |

| **Final MBS**       |                          |                          |                        |                   |
| 0                   | 67 (12.71%, n = 527)     | 8 (15.09%, n = 53)       | 44 (17.67%, n = 249)   | 15 (6.67%, n = 225) |
| 0.5                 | 27 (5.12%, n = 527)      | 6 (11.32%, n = 53)       | 11 (4.22%, n = 249)    | 10 (4.44%, n = 225) |
| 1                   | 45 (8.84%, n = 527)      | 4 (7.55%, n = 53)        | 14 (5.62%, n = 249)    | 27 (12.00%, n = 225) |
| 1.5                 | 86 (16.32%, n = 527)     | 6 (11.32%, n = 53)       | 40 (16.06%, n = 249)   | 40 (17.78%, n = 225) |
| 2                   | 102 (19.35%, n = 527)    | 11 (20.75%, n = 53)      | 50 (20.08%, n = 249)   | 41 (18.22%, n = 225) |
| 2.5                 | 58 (11.01%, n = 527)     | 3 (5.65%, n = 53)        | 26 (10.40%, n = 249)   | 29 (12.89%, n = 225) |
| 3                   | 82 (15.56%, n = 527)     | 11 (20.75%, n = 53)      | 50 (20.08%, n = 249)   | 41 (18.22%, n = 225) |
| 3.5                 | 47 (8.92%, n = 527)      | 4 (7.55%, n = 53)        | 20 (8.03%, n = 249)    | 23 (10.22%, n = 225) |
| 4                   | 91 (17.71%, n = 527)     | 1 (1.89%, n = 53)        | 5 (2.01%, n = 249)     | 3 (1.33%, n = 225) |
| 4.5                 | 40 (7.66%, n = 527)      | 0 (0.00%, n = 53)        | 3 (1.20%, n = 249)     | 1 (0.44%, n = 225) |

| **MBS variation**   |                          |                          |                        |                   |
| -4.0                | 1 (0.19%, n = 527)       | 1 (1.89%, n = 53)        | 0 (0.00%, n = 249)     | 0 (0.00%, n = 225) |
| -3.0                | 2 (0.38%, n = 527)       | 0 (0.00%, n = 53)        | 2 (0.80%, n = 249)     | 0 (0.00%, n = 225) |
| -2.5                | 1 (0.19%, n = 527)       | 0 (0.00%, n = 53)        | 1 (0.40%, n = 249)     | 0 (0.00%, n = 225) |
| -2.0                | 3 (0.57%, n = 527)       | 1 (1.89%, n = 53)        | 1 (0.40%, n = 249)     | 1 (0.44%, n = 225) |
| -1.5                | 1 (0.19%, n = 527)       | 0 (0.00%, n = 53)        | 1 (0.40%, n = 249)     | 0 (0.00%, n = 225) |
| -1.0                | 6 (1.14%, n = 527)       | 0 (0.00%, n = 53)        | 3 (1.20%, n = 249)     | 3 (1.33%, n = 225) |
| -0.5                | 4 (0.76%, n = 527)       | 1 (1.89%, n = 53)        | 1 (0.40%, n = 249)     | 2 (0.89%, n = 225) |
| 0.0                 | 85 (16.13%, n = 527)     | 10 (18.75%, n = 53)      | 53 (21.29%, n = 249)   | 22 (9.78%, n = 225) |
| 0.5                 | 26 (5.03%, n = 527)      | 5 (9.43%, n = 53)        | 10 (4.02%, n = 249)    | 11 (4.89%, n = 225) |
| 1.0                 | 105 (19.92%, n = 527)    | 7 (13.21%, n = 53)       | 45 (18.07%, n = 249)   | 53 (23.56%, n = 225) |
| 1.5                 | 4 (0.76%, n = 527)       | 0 (0.00%, n = 53)        | 2 (0.80%, n = 249)     | 2 (0.89%, n = 225) |
| 2.0                 | 117 (22.20%, n = 527)    | 9 (16.98%, n = 53)       | 51 (20.48%, n = 249)   | 57 (25.33%, n = 225) |
| 2.5                 | 7 (1.33%, n = 527)       | 2 (3.77%, n = 53)        | 3 (1.20%, n = 249)     | 2 (0.89%, n = 225) |
| 3.0                 | 77 (14.61%, n = 527)     | 8 (15.09%, n = 53)       | 34 (13.65%, n = 249)   | 35 (15.56%, n = 225) |
| 3.5                 | 5 (0.95%, n = 527)       | 0 (0.00%, n = 53)        | 1 (0.40%, n = 249)     | 4 (1.78%, n = 225) |
| Age Group | Handgrip strength (female per age group) | Handgrip strength (male per age group) | Mean (S.D.) | 95% C.I. | n | Range | Mean (S.D.) | 95% C.I. | n | Range | Mean (S.D.) | 95% C.I. | n | Range |
|-----------|----------------------------------------|----------------------------------------|------------|---------|---|-------|------------|---------|---|-------|------------|---------|---|-------|
| 18-30 years | 31.97 (10.58) | 24.82 to 42.17 | 10 | 0.00 - 49.00 | 31.70 (0.00) | - | 1 | 30.72 - 31.70 | 28.81 (11.29) | 14.79 to 42.83 | 14 | 14.00 - 41.00 | 41.90 (9.58) | 18.10 to 65.30 | 35 | 18.70 to 60.60 |
| 31-40 years | 25.03 (10.74) | 30.75 to 39.54 | 14 | 4.00 - 68.70 | 22.35 (11.07) | 9.51 to 36.99 | 5 | 12.30 - 39.30 | 32.57 (13.96) | 26.93 to 38.20 | 26 | 4.70 - 58.67 | 46.22 (11.51) | 38.91 to 53.54 | 12 | 26.30 to 68.67 |
| 41-50 years | 30.75 (10.84) | 28.74 to 33.36 | 87 | 10.00 - 56.00 | 26.08 (9.22) | 19.09 to 34.51 | 8 | 17.30 - 42.70 | 29.00 (11.66) | 25.28 to 32.73 | 40 | 10.00 - 51.00 | 34.02 (9.68) | 30.88 to 37.16 | 39 | 17.00 to 54.00 |
| 51-60 years | 21.91 (10.72) | 26.62 to 33.17 | 84 | 6.50 - 55.70 | 24.45 (8.81) | 17.09 to 31.81 | 8 | 10.30 - 32.30 | 25.29 (8.38) | 22.29 to 28.29 | 40 | 6.70 - 41.70 | 34.23 (10.50) | 30.67 to 37.78 | 36 | 10.30 to 55.70 |
| 61-70 years | 24.74 (10.69) | 22.68 to 26.80 | 106 | 0.00 - 50.30 | 19.39 (14.62) | 5.86 to 32.91 | 7 | 1.70 - 44.00 | 21.80 (8.58) | 19.14 to 24.47 | 52 | 0.00 - 40.30 | 28.79 (10.02) | 25.85 to 31.73 | 47 | 1.30 to 50.30 |
| 71-80 years | 21.94 (9.34) | 18.76 to 23.72 | 57 | 0.00 - 45.70 | 22.88 (4.55) | 18.11 to 27.66 | 6 | 16.30 - 28.00 | 18.75 (9.76) | 15.59 to 22.10 | 35 | 0.00 - 39.70 | 18.69 (9.82) | 15.26 to 22.12 | 34 | 0.00 to 45.70 |

Notes: MHS = Modified Borg Dyspnea Scale; S.D. = Standard Deviation; C.I. = Confidence Interval
Supplementary Table 4. Participants’ results over the months since hospital discharge for selected variables.

|                             | 4th  | 5th  | 6th  | 7th  | 8th  | 9th  | 10th |
|-----------------------------|------|------|------|------|------|------|------|
| **Handgrip strength classification** |      |      |      |      |      |      |      |
| Good | 12.50% | 16.67% | 17.95% | 20.43% | 19.61% | 18.00% | 26.83% |
| Average | 25.00% | 31.25% | 30.13% | 25.81% | 35.29% | 32.00% | 19.51% |
| Poor | 62.50% | 52.08% | 51.92% | 53.76% | 45.10% | 50.00% | 53.66% |
| **Pain VAS classification** |      |      |      |      |      |      |      |
| <60 | 41.67% | 38.73% | 45.81% | 51.58% | 57.69% | 50.00% | 43.90% |
| 60-59 | 25.00% | 14.79% | 21.94% | 18.95% | 11.54% | 22.00% | 26.83% |
| >59 | 33.33% | 46.48% | 32.26% | 29.47% | 30.77% | 28.00% | 29.27% |
| **EQ-5D-5L anxiety and depression dimension score** |      |      |      |      |      |      |      |
| 4 | 16.00% | 13.25% | 15.41% | 10.00% | 23.44% | 17.39% | 21.28% |
| 3 | 28.00% | 11.92% | 16.11% | 17.00% | 9.38% | 20.29% | 8.51% |
| 2 | 4.00% | 24.50% | 25.23% | 25.00% | 18.75% | 27.54% | 27.60% |
| 1 | 44.00% | 47.02% | 41.34% | 47.00% | 43.75% | 31.88% | 42.55% |
| **mMRC dyspnea score** |      |      |      |      |      |      |      |
| 4 | 7.69% | 4.00% | 3.00% | 1.00% | 1.56% | 2.90% | 0.00% |
| 3 | 7.69% | 6.00% | 8.20% | 14.00% | 9.58% | 14.49% | 8.51% |
| 2 | 11.54% | 13.33% | 17.74% | 18.00% | 17.19% | 23.19% | 31.91% |
| 1 | 30.77% | 30.00% | 39.45% | 31.00% | 40.63% | 28.99% | 29.79% |
| 0 | 42.31% | 46.67% | 31.50% | 36.00% | 31.25% | 30.43% | 29.79% |
| **FACIT-Fatigue** |      |      |      |      |      |      |      |
| Average | 36.31 | 39.46 | 39.04 | 39.68 | 38.95 | 38.23 | 39.32 |
| Standard Deviation | 12.31 | 10.09 | 9.79 | 9.35 | 10.18 | 8.80 | 9.27 |

Notes: VAS = Visual Analogue Scale; EQ-5D-5L = EuroQoL-5 Dimensions-5 Levels; mMRC dyspnea scale = Medical Research Council Dyspnea Scale; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy – Fatigue.
## Supplementary Table 5. Values of the 25th and 75th percentiles reported in Vianna et al11 used for the classification of our individual patients in poor, average or good handgrip strength.

| Age (years) | Males | | | | Females | | | |
|-------------|-------|--|--|--|--|-------|--|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|--|---|
### Supplementary Table 6. Linear regression models

| Variables | Beta-coefficient | 95% CI LL | 95% CI UL | p-value | Adjusted R² |
|-----------|------------------|-----------|-----------|---------|-------------|
| **EPWORTH SLEEPINESS SCALE** | | | | | 0.0129 |
| Intubation (SIMPLE) | 0.0129 | -2.175 | -0.578 | 0.001 |
| Intubation (ADJUSTED) | 0.0193 | -2.179 | -0.569 | 0.001 |
| Sex | -0.399 | -1.996 | 0.307 | 0.325 |
| Age | -0.045 | -1.057 | 0.967 | 0.996 |
| Race | -0.252 | -1.288 | 0.692 | 0.289 |
| Hypertension | 0.659 | -0.241 | 1.650 | 0.151 |
| **DISPNEA** | | | | | -0.0012 |
| Intubation (SIMPLE) | 0.0062 | -0.168 | 0.135 | 0.833 |
| Intubation (ADJUSTED) | 0.0529 | -0.217 | 0.110 | 0.697 |
| Sex | -0.436 | -0.584 | -0.288 | <0.001 |
| Age | 0.0002 | -0.006 | 0.005 | 0.939 |
| Race | -0.010 | -0.160 | 0.140 | 0.894 |
| Hypertension | 0.297 | 0.130 | 0.464 | 0.001 |
| **VAS** | | | | | -0.0011 |
| Intubation (SIMPLE) | -1.259 | -6.199 | 3.722 | 0.624 |
| Intubation (ADJUSTED) | 0.0642 | -2.499 | 2.499 | 0.342 |
| Sex | -15.364 | -20.159 | -10.069 | <0.001 |
| Age | 0.242 | 0.054 | 0.429 | 0.012 |
| Race | -2.543 | -7.393 | 2.306 | 0.304 |
| Hypertension | 3.587 | -1.811 | 8.984 | 0.192 |
| **HANDGRIP** | | | | | 0.0750 |
| Intubation (SIMPLE) | 6.893 | 3.078 | 10.709 | <0.001 |
| Intubation (ADJUSTED) | 0.4598 | 3.041 | 10.868 | <0.001 |
| Sex | 15.148 | 13.762 | 16.534 | <0.001 |
| Age | -0.182 | -0.236 | -0.127 | <0.001 |
| Race | -0.972 | -2.381 | 0.437 | 0.176 |
| Hypertension | -1.950 | -3.516 | -0.384 | 0.015 |
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STROBE Statement—Checklist of items that should be included in reports of cohort studies

| Item No | Recommendation |
|---------|----------------|
| **Title and abstract** | (a) Indicate the study’s design with a commonly used term in the title or the abstract | Page 1 |
| | (b) Provide in the abstract an informative and balanced summary of what was done and what was found | Page 1 |
| **Introduction** | Explain the scientific background and rationale for the investigation being reported | Page 3, Line 2 to 28 |
| **Objectives** | State specific objectives, including any prespecified hypotheses | Page 3, Line 29 to 32 |
| **Methods** | Present key elements of study design early in the paper | Page 4, Line 8 to 18 |
| | Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection | Page 4, Line 2 to 18 |
| | Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up | Page 4, Line 3 to 11 |
| | For matched studies, give matching criteria and number of exposed and unexposed | Not applicable |
| | Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable | Page 4, Line 3 to Page 5, Line 4 |
| **Variables** | For each variable of interest, give sources of data and details of methods of assessment (measurement). | Page 4, Line 19 to Page 5, Line 4 |
| | Describe comparability of assessment methods if there is more than one group | Supplementary table 01 |
| **Bias** | Describe any efforts to address potential sources of bias | Page 16, Line 6 to 16 |
| **Study size** | Explain how the study size was arrived at | See publication study protocol |
| **Quantitative variables** | Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why | Page 5, Line 5 to Page 6, Line 13 |
| | Supplemental table 01 | |
| **Statistical methods** | Describe all statistical methods, including those used to control for confounding | Page 5, Line 5 to Page 6, Line 13 |
| | Describe any methods used to examine subgroups and interactions | Page 5, Line 14 to Page 6, Line 8 |
| | Explain how missing data were addressed | Page 5, Line 12 to 13 |
| | If applicable, explain how loss to follow-up was addressed | Not applicable |
| | Describe any sensitivity analyses | Not applicable |
| **Results** | Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for | Figure 1, Flow chart |

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eligibility, confirmed eligible, included in the study, completing follow-up, and analysed

(b) Give reasons for non-participation at each stage

(c) Consider use of a flow diagram

Descriptive data 14*

(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders

(b) Indicate number of participants with missing data for each variable of interest

(c) Summarise follow-up time (eg, average and total amount)

Outcome data 15*

Report numbers of outcome events or summary measures over time

Main results 16

(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

(b) Report category boundaries when continuous variables were categorized

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Other analyses 17

Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

Discussion

Key results 18

Summarise key results with reference to study objectives

Limitations 19

Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias

Interpretation 20

Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence

Generalisability 21

Discuss the generalisability (external validity) of the study results

Other information

Funding 22

Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

*Give information separately for exposed and unexposed groups.
Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.
Long-term functioning status of COVID-19 survivors: a prospective observational evaluation of a cohort of patients surviving hospitalization

| Journal:       | BMJ Open               |
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|---------------------------------------|-------------------------|
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Long-term functioning status of COVID-19 survivors: a prospective observational evaluation of a cohort of patients surviving hospitalization

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

ABSTRACT

Objectives: The study investigated the long-term functional status of hospitalized COVID-19 survivors to explore and document their functional situation. Design: This prospective observational study assessed 801 COVID-19 survivors at three to eleven months after hospital discharge. It analyzes participants’ sociodemographic background, COVID-19 clinical manifestations, and clinical and functional evaluations. Setting: Tertiary-level university hospital in Sao Paulo, Brazil. Participants: Study participants are COVID-19 survivors admitted to hospital care for at least 24h 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, 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, 01-minute Sit to Stand Test. Results: Many participants required invasive mechanical ventilation (41.57%, 333/801). Mean age was 55.35 ± 14.58 years. With a mean of 6.56 (S.D: 1.58; 95% C.I: 6.45 to 6.67) months after hospital discharge, 70.86% (567/800) reported limited daily activities, which were severe in 5.62% (45/800). They also reported pain and discomfort (64.50%, 516/800), breathlessness (64.66%, 514/795), and anxiety and depression (57.27%, 457/798). Daytime sleepiness and insomnia evaluations showed subthreshold results. Most (92.85%, 727/783) participants reported unrestricted oral intake. Data indicated no generalized fatigue (mean score: 39.18, S.D: 9.77; C.I: 95% 38.50 to 39.86). Assessments showed poor handgrip strength (52.20%, 379/726) and abnormal timed up and go results (mean 13.07s, S.D 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 hospitalized COVID-19 survivors.
ARTICLE SUMMARY

Strengths and limitations of this study

1. 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.

2. The study test battery used both self-reported, clinical assessments and quantifiable measures.

3. 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.

4. 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 Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) does 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 COVID-19 patients 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 six 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] and memory[5,7] concentration[5] and sleep disorders.[5,7-9] Objective assessments including the Short Physical Performance Battery Test and the 2-Minutes 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 most effective rehabilitation needs assessments and interventions. Thus, a better understanding of functional disorders that may arise in the long-term after hospitalization 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 three to eleven months of hospital discharge, aiming at identifying their long-term functioning status and rehabilitation needs.
MATERIALS & 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 Polymerase Chain Reaction (PCR) or serology testing for SARS-CoV-2.

PATIENT AND PUBLIC INVOLVEMENT

Study participants did not take part in the design and conduct of the work. Nevertheless, study results and guidance are shared with participants and patients attending post-COVID 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 three to eleven months after hospital discharge with people previously admitted to treat acute COVID-19. Participants were recruited between October 7, 2020 and April 8, 2021. Study assessments were completed between October 20, 2020 and April 16, 2021. Data was registered using the Research Electronic Data Capture (REDCap) platform. Further details about the study protocol are available elsewhere.[14,15] To accommodate for limitations in recruitment, the study included participants three to eleven months after hospital discharge. Report from this cohort study followed the principles of the STROBE statement.

ASSESSMENTS

All data was 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 includes 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 Supplementary 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 ± standard deviations (S.D). Intervals at 95% confidence (C.I) for the means were estimated with Student’s t-distribution at the proper degrees-of-freedom. 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 was 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 based on 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 analyzing handgrip strength and TUG results, participants were further divided into age groups. Handgrip strength data was stratified by sex and age groups for classification. For these two variables we investigated differences among the three subgroups using factorial 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 vs. 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-values < 0.05.
Additionally, for pain visual analogue scale (VAS), anxiety and depression (EuroQoL-5 Dimensions-5 Levels, EQ-5D-5L), dyspnea (Medical Research Council Dyspnea Scale), fatigue (Functional Assessment of Chronic Illness Therapy – Fatigue), and muscle strength (handgrip strength measurement), participants were divided in nine groups, according to the time elapsed since hospital discharge; the groups for three and eleven months (both extremes of our range) had less than ten participants each, and were not included in the analyses.

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

All data analysis was performed with IBM SPSS 27.0, Python, and related libraries, [17-19] except for the additional multivariate linear regression analysis which was performed with STATA 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 COVID-19 patients 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), time since hospital discharge (<3 months), and lack of information on the type of oxygen support received during treatment, or any other data inconsistency.

INSERT FIGURE 1.

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 didn’t 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% C.I.: 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% C.I.: 27.92 to 32.46) compared to 6.50 ± 6.17 (95% C.I.: 5.14 to 7.86) for the group with no oxygen support,
and 11.63 ± 10.16 (95% C.I.: 10.61 to 12.65) for the non-invasive support group. A large portion of participants was admitted to intensive care (n=497), with an average LoS in intensive care of 8.39 ± 12.00 days (95% C.I.: 7.56 to 9.22). Overall, the study population consisted of 421 males (52.56%) and 380 females (47.44%). The commonest comorbidities among all participants were hypertension (462/801, 57.68%) and diabetes (292/801, 36.45%). Details on other participants’ characteristics are shown in Table 1, and in the Supplementary Table 2.

Post-COVID Functional Status (PCFS) scale results revealed that 70.86% of participants (567/800) reported limitations in daily activities, which were severe for 5.62% (45/800) of them. The invasive mechanical ventilation group presented a slightly larger proportion of participants referring some form of limitation, reaching 78.08% (260/333). EuroQol-5D-5L results showed that 64.50% (516/800) still suffered from pain and discomfort, while 57.27% (457/798) reported anxiety and depression. Pain VAS results corroborated it by showing that 45.93% (333/725) 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%, 636/735), as with the Functional Oral Intake Scale (FOIS), in which 92.85% (727/783) of participants reported no restrictions.

Many participants (64.66%, 514/795) reported some breathlessness (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% confidence interval, the variation in oxygen saturation before and after the test was also similar, with an overall average of -0.85 ± 2.53 % (95% C.I.: -1.06% to -0.63%), where the negative value indicates a worst score after the test. Additional functional assessments are available in Table 2 and Table 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 (Table 2 and Table 3).
Table 1. Sociodemographic and clinical data presented as n participants (%), mean (S.D.), alongside 95% C.I. 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%)          |
| **Commonest 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) |
| **Commonest 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 (S.D.)** | **95% C.I.** | **Range** | **Mean (S.D.)** | **95% C.I.** | **Range** | **Mean (S.D.)** | **95% C.I.** | **Range** | **Mean (S.D.)** | **95% C.I.** | **Range** |
| Age (in years) | 55.35 (14.58)            | 54.34 to 56.36           | 18.80 - 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 |

Notes: n = number; S.D. = Standard Deviation; C.I. = Confidence Interval; ICU = Intensive Care Unit
Table 2. Functional assessments, categorical data presented as n participants (%).

|                      | 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)      | 5 (6.17%, 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 (23.83%, 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) |
| FOIS | 1 | 2 | 3 | 4 |
|------|---|---|---|---|
|      | 1 (0.13%, n = 783) | 2 (0.26%, n = 783) | 1 (0.13%, n = 783) | 1 (0.13%, n = 783) |
|      | 0 (0.00%, n = 80) | 1 (1.25%, n = 80) | 0 (0.00%, n = 80) | 0 (0.00%, n = 80) |
|      | 0 (0.00%, n = 80) | 0 (0.00%, n = 80) | 0 (0.00%, n = 80) | 0 (0.00%, n = 80) |
|      | 0 (0.00%, n = 80) | 0 (0.00%, n = 80) | 0 (0.00%, n = 80) | 0 (0.00%, n = 80) |
|      | 13 (1.66%, n = 783) | 6 (7.50%, n = 80) | 47 (12.21%, n = 385) | 56 (16.97%, n = 330) |
|      | 0 (0.00%, n = 379) | 1 (1.25%, n = 379) | 1 (0.26%, n = 379) | 0 (0.00%, n = 324) |
|      | 0 (0.00%, n = 324) | 0 (0.00%, n = 324) | 1 (0.31%, n = 324) | 0 (0.00%, n = 324) |

| Pain VAS | 0-39 | 40-59 | 60-100 |
|----------|------|-------|--------|
|          | 249 (34.34%, n = 725) | 143 (19.72%, n = 725) | 333 (45.93%, n = 725) |
|          | 25 (33.33%, n = 75) | 13 (17.33%, n = 75) | 37 (49.33%, n = 75) |
|          | 119 (33.33%, n = 357) | 69 (19.33%, n = 357) | 169 (47.34%, n = 357) |
|          | 105 (35.84%, n = 293) | 61 (20.82%, n = 293) | 127 (43.34%, n = 293) |

| FIM | 18 | 19-60 | 61-103 | 104-126 |
|-----|----|-------|--------|--------|
|     | 2 (0.27%, n = 735) | 11 (1.50%, n = 735) | 86 (11.70%, n = 735) | 636 (86.53%, n = 735) |
|     | 1 (1.32%, n = 76) | 0 (0.00%, n = 76) | 9 (11.84%, n = 359) | 66 (86.84%, n = 359) |
|     | 0 (0.00%, n = 300) | 7 (1.95%, n = 300) | 30 (8.36%, n = 300) | 322 (89.69%, n = 300) |
|     | 127 (43.34%, n = 300) | 4 (1.33%, n = 300) | 47 (15.67%, n = 300) | 248 (82.67%, n = 300) |

| ESS | 0-7 | 8-9 | 10-15 | 16-24 |
|-----|-----|-----|-------|------|
|     | 355 (44.38%, n = 800) | 90 (11.25%, n = 800) | 224 (28.00%, n = 800) | 131 (16.38%, n = 800) |
|     | 28 (34.57%, n = 81) | 13 (16.05%, n = 81) | 15 (18.52%, n = 81) | 25 (30.86%, n = 81) |
|     | 164 (44.49%, n = 81) | 38 (9.84%, n = 81) | 116 (30.05%, n = 81) | 68 (17.62%, n = 81) |
|     | 163 (48.95%, n = 333) | 39 (11.71%, n = 333) | 93 (27.93%, n = 333) | 38 (11.41%, n = 333) |

| ISI | 0-7 | 8-14 | 15-21 | 22-28 |
|-----|-----|------|-------|------|
|     | 479 (59.95%, n = 799) | 203 (25.41%, n = 799) | 94 (11.76%, n = 799) | 23 (2.88%, n = 799) |
|     | 41 (50.62%, n = 81) | 25 (30.86%, n = 81) | 10 (12.35%, n = 81) | 5 (6.17%, n = 81) |
|     | 225 (58.29%, n = 81) | 97 (25.13%, n = 81) | 50 (12.95%, n = 81) | 14 (3.63%, n = 81) |
|     | 213 (64.16%, n = 332) | 81 (24.40%, n = 332) | 47 (15.67%, n = 332) | 4 (1.20%, n = 332) |

| MRC sum score | 0-35 | 36-47 | 48-60 |
|---------------|------|-------|------|
|               | 15 (2.05%, n = 733) | 130 (17.74%, n = 733) | 588 (80.22%, n = 733) |
|               | 0 (0.00%, n = 75) | 11 (14.67%, n = 75) | 64 (85.33%, n = 75) |
|               | 10 (2.79%, n = 359) | 59 (16.43%, n = 359) | 290 (80.78%, n = 359) |
|               | 5 (1.67%, n = 324) | 60 (20.07%, n = 324) | 234 (78.26%, n = 324) |

Notes: PCFS = Post-COVID-19 Functional Status; EQ-5D-5L = EuroQoL-5 Dimensions-5 Levels; mMRC dyspnea scale = Modified Medical Research Council Dyspnea Scale; FOIS = Functional Oral Intake Scale; VAS = Visual Analogue Scale; FIM = Functional Independence Measure; ESS = Epworth Sleepiness Scale; ISI = Insomnia Severity Index; MRC sum score = Medical Research Council Sum Score
Table 3. Functional assessments, continuous data presented as mean (S.D.), alongside 95% C.I. and number of participants (n).

|                                | All participants (n=801) | No oxygen support (n=82) | Oxygen support (n=386) | Intubation (n=333) |
|--------------------------------|--------------------------|--------------------------|------------------------|--------------------|
| **Mean (S.D.)**                |                          |                          |                        |                    |
| Basal oxygen saturation (in %) | 96.34 (2.37)             | 96.16 to 96.52           | 97.19 (1.70)           | 96.46 (2.37)       |
| Final oxygen saturation (in %) | 95.71 (2.96)             | 95.46 to 95.96           | 96.79 (1.83)           | 96.00 (2.46)       |
| Oxygen saturation variation    | -0.85 (2.53)             | -1.06 to -0.63           | -0.36 (1.95)           | -1.10 (2.94)       |
| FACIT-F                        | 39.18 (9.77)             | 38.50 to 39.86           | 39.16 (10.51)          | 38.62 (10.06)      |
| ISI                            | 7.30 (6.11)              | 6.88 to 7.73             | 8.33 (6.77)            | 7.79 (6.43)        |
| WHODAS 2.0                     | 20.78 (9.37)             | 20.13 to 21.43           | 20.11 (9.59)           | 21.14 (9.67)       |
| Number of sit to stand repetitions | 18.96 (6.42)           | 18.42 to 19.51           | 18.57 (5.12)           | 19.08 (6.84)       |
| Handgrip strength (all participants) |                          |                          |                        |                    |
| All ages                       | 21.22 (12.70)            | 20.30 to 22.15           | 20.50 (10.79)          | 21.65 (9.22)       |
| Handgrip strength (male participants) |                          |                          |                        |                    |
| All ages                       | 27.96 (11.83)            | 26.78 to 29.15           | 27.42 (9.84)           | 26.34 (10.82)      |
| Handgrip strength (female participants) |                          |                          |                        |                    |
| All ages                       | 13.57 (8.70)             | 12.64 to 14.50           | 13.91 (6.75)           | 14.12 (7.34)       |
| Timed up and go duration (in seconds) |                          |                          |                        |                    |
| All ages                       | 13.07 (6.49)             | 12.59 to 13.55           | 12.37 (3.49)           | 12.19 (9.34)       |

Notes: S.D. = Standard Deviation; C.I. = Confidence Interval; FACIT-F = Functional Assessment of Chronic Illness Therapy - Fatigue; ISI = Insomnia Severity Index; WHODAS = World Health Organization Disability Assessment Schedule.
Table 2, Table 3 and Supplementary 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.

**INSERT FIGURE 2.**

The handgrip strength measurement showed many participants (52.20%, 379/726) had “poor” results when compared to 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%, 120/297). These results can be seen on Figure 3 and Supplementary 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 females. 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 for 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 to 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.

**INSERT FIGURE 3.**

As shown in Supplementary 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 dyspnea, 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 test. The full results may be found in Supplementary 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. WHODAS 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] reports a large cohort study
of hospitalized COVID-19 of whom 27% of the sample reported pain and discomfort. Despite being hospitalized, only 4% were ventilated during hospitalization. We hypothesize that the higher number of participants admitted to intensive 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 hospitalization. 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, 2021 hospitalized COVID-19 patients 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 to 0% of patients reporting pain related symptoms in a control group (p<0.01).

Having a higher number of patients admitted to ICU might have influenced a higher prevalence of pain and discomfort. Besides the effects of COVID-19, patients hospitalized 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 hospitalized COVID-2019 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 suggest 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% to 42.7%.[3,5,7,9,11] Only 26% of the population investigated by Huang et al scored one or higher on the mMRC dyspnea scale.[8] We suspect it can be attributed to the fact that in that study, six to eight 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 hospitalized and non-
hospitalized 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 two or higher and 53.3% of one 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 two 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 hospitalized 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 to 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 instrumentalized measures to capture individual rehabilitation needs.

Previous publications identified fatigue as an important PASC finding.[3-5,7,8,34] Our data does 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 day time sleepiness should be considered.

FOIS results did not show any lasting issues with oral intake three to eleven 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 programs. 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 specialized 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. Fourthly, 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 hospitalization. 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 three to eleven 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 that required mechanical ventilation.

CONTRIBUTORS
LRB and MI contributed equally with conceptualization, investigation, methodology, supervision, and validation. LRB further contributed with funding acquisition and managing resources. LRB, MI, and LRP contributed with data curation and visualization. LRP conducted formal analysis. LRB, MI, LRP, SKHAAC, and VDR contributed with writing the original draft, review, and editing. VDR assisted with project administration. LRB, MI, SKHAAC, SSTU, DM, FK, AAAO, GSN, ARM, FQR, ATS, MC, RASAC, VP, MVM, EMS, and APG all contributed with the investigation. FF provided critical review.

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DECLARATION OF INTERESTS

We declare no competing interests.

DATA SHARING

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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FIGURES

Figure 1. Flow diagram of study participants

Figure 2. Histogram for the FACIT-Fatigue scale

Figure 3. Handgrip strength measurement results distribution

ETHICS APPROVAL STATEMENT

The study observed the applicable ethical standards and procedures, was approved by HCFMUSP Institutional Review Board, and registered under CAEE 39744120.3.0000.0068. Written informed consent was obtained from all participants included.

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| Situations/Domain/Dimensions assessed | Response levels/Rating options |
|--------------------------------------|--------------------------------|
| Sitting and reading; watching TV; sitting, inactive in a public place (e.g., a theatre or a meeting); as a passenger in a car for an hour without a break, lying down to rest in the afternoon without circumstances permit; sitting and talking to someone; sitting quietly after a lunch without alcohol; and, in a car, white stopped for a few minutes in the traffic. | 0 (never); 1 (slightly); 2 (moderate); and 3 (high). Score ranges from 0 to 24. The classification mentioned hereunder is merely informative as it has been retrieved from the published scientific report of this classification has not been agreed by means of a literature search. 0-7 (0-9); 8-11 (0-9); 12-20 (abnormally sleepy). 8-9 (The patient has an average amount of daytime sleepiness) 10-15 (There may be a situation of excessive sleepness for which medical attention might be considered) 16-24 (A clear excessive sleepiness problem for which medical attention is required.) |
| Functional Independence Measure | A clear excessive sleepiness problem for which medical attention might be considered |
| Epworth Sleepiness Scale | Measurement of the subject’s general level of daytime sleepiness. It is based on questions referring to eight situations, based on how likely they would fall asleep. The higher the score, the more chance of falling asleep. |

**Supplementary Table 1. Relevant details regarding scales and tools for clinical and functional evaluation in alphabetical order.**

| Short description | Details |
|-------------------|---------|
| Activities; pain/discomfort; | Pain/discomfort; |
| Mobility; self-care; usual activities; pain/discomfort; anxiety/depression. | |
| 56 | 51 |
| Pain Visual Analogue Scale | It assesses quality of life in five dimensions. Each dimension has five response levels (from “no problems” to “unable” to carry out activities related to each domain). |
| Functional Independence Measure | It assesses the dependence levels for performing motor and cognitive activities. It ranges from 18 to 126 points, complete dependence to complete independence. |
| Functional Oral Intake Scale | A 7-point ordinal scale which focuses on what the patient consumes orally on a daily basis. Levels 1 through 3 relate to varying degrees of non-oral feeding. Levels 4 through 7 relate to degrees of feeding without non-oral supplementation. |
| Handgrip Strength Measurement | Handgrip strength measured by dynamometry is well established as an indicator of muscle status, particularly among older adults. The handgrip strength of older adults can be interpreted as age and sex stratified norms or T-scores from younger adults. |
| Medical Research Council Dyspnea Scale | It evaluates severity of problems regarding sleep onset, sleep disruption, early morning awakening, as well as sleep dissatisfaction, interference with daytime functioning, if others note those problems, and if all of this causes distress. |
| Medical Research Council Dyspnea Scale | It consists of a 7-item self-report questionnaire. To evaluate the nighttime and daytime components of insomnia. The higher the score, the more severe the situation. |
| Inosomnia Severity Index | It evaluates severity of problems regarding sleep onset, sleep disruption, early morning awakening, as well as sleep dissatisfaction, interference with daytime functioning, if others note those problems, and if all of this causes distress. |
| Medical Research Council Dyspnea Scale | It is a rating with a 5-point Likert scale rendering a score range from 0 to 3 (absence of insomnia) to 30 to 18 (severe insomnia). |
| Modified Borg Dyspnea Scale | The Modified Borg Dyspnea Scale is designed to ensure that performance is conducted at a level of effort similar to steady state at 50% of VO2max. |
| Pain Visual Analogue Scale | It measures the functional outcomes in everyday life after COVID-19. The five points answer options vary from “no limitations or symptoms” to “severe limitations”. |
| Post-COVID-19 Functional Status scale | How much are you currently affected in your everyday life by COVID-19? |
| Timed Up and Go | Measures the time in seconds taken by the participant to stand up from a chair, walk 3 meters, turn, walk back to the chair and sit without physical assistance, however with normally used walking aid. |
| World Health Organization Disability Assessment Schedule | It captures the level of functioning in six domains of life. In each item, individuals estimate the magnitude of their difficulties during the previous 30 days using a five-point scale, from “none” to “extreme or cannot do”. |
| World Health Organization Disability Assessment Schedule | WHO definition of disability for COVID-19 COVID-19 severity classification By patient, based on self-report: mild/moderate or non-severe (did not receive oxygen); severe oxygen for told you needed but it was not available; and critical (received invasive ventilation or mask available respiratory support) |
registers oxygen saturation and dyspnea level (using the Modified Borg Dyspnea Scale) before and after the test.

Notes: COVID-19 = Coronavirus disease 2019.
### Supplementary Table 2. All symptoms and comorbidities.

|                     | All participants (n=801) | No oxygen support (n=82) | Oxygen support (n=386) | Intubation (n=333) |
|---------------------|--------------------------|--------------------------|------------------------|-------------------|
| Dialysis            | 99 (12.36%, total = 801) | 4 (4.88%, total = 82)    | 19 (4.92%, total = 386) | 76 (22.82%), total = 333 |
| Hypertension        | 462 (57.68%, total = 801) | 37 (43.12%, total = 82)  | 231 (59.84%), total = 386 | 194 (58.26%), total = 333 |
| COPD                | 35 (4.38%, total = 800)   | 1 (1.22%), total = 82    | 20 (5.19%), total = 385  | 14 (4.20%), total = 333  |
| Asthma              | 30 (3.75%, total = 800)   | 3 (3.66%), total = 82    | 18 (4.66%), total = 385  | 9 (2.70%), total = 333  |
| Renal failure dialysis | 29 (3.62%, total = 801)  | 4 (4.88%), total = 82    | 19 (4.92%), total = 386  | 7 (2.10%), total = 333  |
| Renal failure       | 47 (5.87%, total = 800)   | 6 (7.32%), total = 82    | 25 (6.48%), total = 386  | 16 (4.80%), total = 333  |
| Liver disease       | 20 (2.50%, total = 800)   | 7 (8.54%), total = 82    | 9 (2.34%), total = 385   | 4 (1.20%), total = 333  |
| Stroke              | 38 (4.75%, total = 800)   | 5 (6.10%), total = 82    | 19 (4.94%), total = 386  | 14 (4.20%), total = 333  |
| Dementia            | 10 (1.25%, total = 800)   | 0 (0.00%), total = 82    | 6 (1.56%), total = 385   | 4 (1.20%), total = 333  |
| Rheumatic disease   | 32 (4.00%, total = 800)   | 4 (4.88%), total = 82    | 15 (3.90%), total = 385  | 11 (3.30%), total = 333  |
| Hematologic disease | 47 (5.87%, total = 801)   | 6 (7.32%), total = 82    | 18 (4.57%), total = 386  | 23 (6.93%), total = 332  |
| Diabetes            | 292 (36.45%, total = 801) | 26 (31.71%), total = 82  | 139 (36.01%), total = 386 | 127 (38.14%), total = 333 |
| Cancer              | 34 (4.38%, total = 741)   | 4 (6.35%), total = 82    | 18 (5.20%), total = 346  | 12 (3.61%), total = 332  |
| Obesity             | 152 (19.02%, total = 799) | 8 (9.76%), total = 82    | 65 (16.86%), total = 385 | 70 (23.40%), total = 332 |
| Angina pectoris      | 32 (4.00%, total = 773)   | 14 (17.65%), total = 82  | 53 (14.10%), total = 378  | 31 (9.72%), total = 319  |
| Rheumatic joint disease | 215 (27.78%, total = 774) | 15 (18.52%), total = 82  | 110 (30.02%), total = 379 | 90 (28.66%), total = 314  |
| Sleep apnea         | 134 (18.21%, total = 736) | 11 (14.10%), total = 82  | 78 (21.79%), total = 358  | 45 (15.00%), total = 300  |
| Chest pain          | 203 (26.06%, total = 779) | 14 (17.50%), total = 82  | 100 (26.88%), total = 380 | 80 (25.08%), total = 319  |
| Cough               | 309 (39.62%, total = 780) | 28 (34.57%), total = 82  | 129 (34.04%), total = 379 | 152 (47.50%), total = 320  |
| Falls               | 119 (15.22%, total = 782) | 7 (8.75%), total = 82    | 50 (13.12%), total = 381  | 62 (19.31%), total = 321  |
| Hepatic steatosis   | 112 (15.36%, total = 729) | 8 (10.39%), total = 77   | 57 (16.29%), total = 350  | 47 (15.56%), total = 302  |

Notes: COPD = Chronic Obstructive Pulmonary Disease.
Supplementary Table 3. Supplementary data regarding functional assessments, data presented as n participants (%), mean (S.D.), alongside 95% C.I. and number of participants (n).

| MBS variation | All participants (n=801) | No oxygen support (n=82) | Oxygen support (n=386) | Intubation (n=333) |
|----------------|--------------------------|-------------------------|------------------------|------------------|
| Basal MBS      |                          |                         |                        |                  |
| 0              | 339 (54.56%, n = 658)    | 46 (68.66%, n = 67)     | 177 (55.84%, n = 317) | 136 (49.64%, n = 274) |
| 0.5            | 38 (5.78%, n = 658)      | 7 (4.69%, n = 67)       | 16 (5.05%, n = 317)   | 17 (5.20%, n = 274) |
| 1              | 58 (8.81%, n = 658)      | 2 (2.99%, n = 67)       | 30 (9.46%, n = 317)   | 26 (9.49%, n = 274) |
| 2              | 81 (12.31%, n = 658)     | 5 (7.46%, n = 67)       | 38 (11.99%, n = 317)  | 38 (13.87%, n = 274) |
| 3              | 55 (8.30%, n = 658)      | 2 (2.99%, n = 67)       | 27 (8.52%, n = 317)   | 26 (9.49%, n = 274) |
| 4              | 18 (2.74%, n = 658)      | 1 (1.49%, n = 67)       | 8 (2.52%, n = 317)    | 9 (2.60%, n = 274)  |
| 5              | 30 (4.56%, n = 658)      | 2 (2.99%, n = 67)       | 15 (4.73%, n = 317)   | 13 (4.74%, n = 274) |
| 7              | 12 (1.82%, n = 658)      | 3 (4.48%, n = 67)       | 3 (0.95%, n = 317)    | 6 (2.19%, n = 274)  |
| 9              | 3 (0.40%, n = 658)       | 1 (1.49%, n = 67)       | 1 (0.32%, n = 317)    | 1 (0.36%, n = 274)  |
| 10             | 4 (0.61%, n = 658)       | 0 (0.00%, n = 67)       | 2 (0.63%, n = 317)    | 2 (0.73%, n = 274)  |
| Final MBS      |                          |                         |                        |                  |
| 1              | 67 (12.71%, n = 527)     | 8 (15.09%, n = 53)      | 44 (17.67%, n = 249)  | 15 (6.67%, n = 225) |
| 0.5            | 27 (5.12%, n = 527)      | 6 (11.22%, n = 53)      | 11 (4.42%, n = 249)   | 10 (4.44%, n = 225) |
| 1              | 45 (8.54%, n = 527)      | 4 (7.55%, n = 53)       | 14 (5.62%, n = 249)   | 27 (12.00%, n = 225) |
| 2              | 86 (16.32%, n = 527)     | 6 (11.32%, n = 53)      | 40 (16.06%, n = 249)  | 45 (17.76%, n = 225) |
| 3              | 102 (19.35%, n = 527)    | 11 (20.75%, n = 53)     | 50 (20.08%, n = 249)  | 44 (18.22%, n = 225) |
| 4              | 58 (11.01%, n = 527)     | 3 (5.66%, n = 53)       | 26 (10.44%, n = 249)  | 29 (12.89%, n = 225) |
| 5              | 82 (15.56%, n = 527)     | 10 (18.87%, n = 53)     | 36 (14.46%, n = 249)  | 36 (16.06%, n = 225) |
| 7              | 47 (8.92%, n = 527)      | 4 (7.55%, n = 53)       | 20 (8.03%, n = 249)   | 23 (10.22%, n = 225) |
| 8              | 9 (1.71%, n = 527)       | 1 (1.89%, n = 53)       | 5 (2.01%, n = 249)    | 3 (1.33%, n = 225)  |
| 9              | 4 (0.76%, n = 527)       | 0 (0.00%, n = 53)       | 3 (1.20%, n = 249)    | 1 (0.44%, n = 225)  |
| MBS variation  |                          |                         |                        |                  |
| 0.4            | 1 (0.19%, n = 527)       | 1 (1.89%, n = 53)       | 0 (0.00%, n = 249)    | 0 (0.00%, n = 225) |
| 0.3-0.4        | 2 (0.36%, n = 527)       | 0 (0.00%, n = 53)       | 2.0 (0.80%, n = 249)  | 0 (0.00%, n = 225) |
| 0.2-0.3        | 0 (0.00%, n = 53)        | 0 (0.00%, n = 53)       | 0 (0.00%, n = 249)    | 0 (0.00%, n = 225) |
| 0.1-0.2        | 1 (0.19%, n = 527)       | 1 (1.89%, n = 53)       | 1 (0.40%, n = 249)    | 1 (0.44%, n = 225) |
| 0.0-0.1        | 1 (0.19%, n = 527)       | 0 (0.00%, n = 53)       | 1 (0.40%, n = 249)    | 0 (0.00%, n = 225) |
| 0.5-1.5        | 6 (1.14%, n = 527)       | 0 (0.00%, n = 53)       | 3 (1.20%, n = 249)    | 3 (1.33%, n = 225)  |
| 0.5-1           | 4 (0.76%, n = 527)       | 1 (1.89%, n = 53)       | 1 (0.40%, n = 249)    | 2 (0.89%, n = 225)  |
| 0.0-0.5        | 85 (16.13%, n = 527)     | 10 (18.87%, n = 53)     | 53 (21.29%, n = 249)  | 22 (9.78%, n = 225) |
| 0.5             | 26 (4.93%, n = 527)      | 5 (9.43%, n = 53)       | 10 (4.02%, n = 249)   | 11 (4.99%, n = 225) |
| 1               | 105 (19.92%, n = 527)    | 7 (13.21%, n = 53)      | 45 (18.07%, n = 249)  | 53 (23.56%, n = 225) |
| 1.5             | 4 (0.76%, n = 527)       | 0 (0.00%, n = 53)       | 2 (0.80%, n = 249)    | 2 (0.89%, n = 225)  |
| 2.0             | 117 (22.20%, n = 527)    | 9 (16.98%, n = 53)      | 51 (20.48%, n = 249)  | 57 (25.35%, n = 225) |
| 2.5             | 7 (1.33%, n = 527)       | 2 (3.77%, n = 53)       | 3 (1.20%, n = 249)    | 2 (0.89%, n = 225)  |
| 3.0             | 77 (14.61%, n = 527)     | 8 (15.09%, n = 53)      | 34 (13.65%, n = 249)  | 35 (15.56%, n = 225) |
| 3.5             | 5 (0.95%, n = 527)       | 0 (0.00%, n = 53)       | 1 (0.40%, n = 249)    | 4 (1.78%, n = 225)  |
### Handgrip strength (female per age group)

| Age Group | Mean (S.D.) | 95% C.I. | N  | Range  |
|-----------|-------------|----------|----|--------|
| 19-39 yrs | 25.93 (13.28) | 21.81 to 30.06 | 151 | 0.00 - 56.00 |
| 40-59 yrs | 23.93 (11.12) | 20.14 to 27.72 | 106 | 0.00 - 35.50 |
| 60-69 yrs | 21.56 (12.08) | 18.63 to 24.47 | 166 | 0.00 - 55.70 |
| 70-79 yrs | 20.11 (11.19) | 18.46 to 21.76 | 180 | 0.00 - 50.30 |
| 80-89 yrs | 17.45 (10.27) | 15.39 to 19.54 | 106 | 0.00 - 45.70 |

### Timed up and go duration (in seconds, per age group)

| Age Group | Mean (S.D.) | 95% C.I. | N  | Range  |
|-----------|-------------|----------|----|--------|
| 19-39 yrs | 51.67 (20.27) | 43.39 to 57.84 | 106 | 1.70 - 31.70 |
| 40-59 yrs | 35.49 (11.28) | 32.47 to 38.51 | 106 | 1.70 - 40.90 |
| 60-69 yrs | 35.20 (11.47) | 32.05 to 38.34 | 93 | 0.00 - 68.67 |
| 70-79 yrs | 35.10 (10.84) | 31.97 to 38.24 | 87 | 0.00 - 56.00 |
| 80-89 yrs | 34.50 (10.72) | 31.37 to 37.63 | 84 | 0.00 - 55.70 |

### Note:
- MBS = Modified Borg Dyspnea Scale; S.D. = Standard Deviation; C.I. = Confidence Interval.
### Supplementary Table 4. Participants' results over the months since hospital discharge for selected variables.

|                  | 4th | 5th | 6th | 7th | 8th | 9th | 10th |
|------------------|-----|-----|-----|-----|-----|-----|------|
| **Handgrip strength classification** |     |     |     |     |     |     |      |
| Good             | 12.59% | 16.67% | 17.95% | 20.45% | 19.61% | 18.90% | 26.83% |
| Average          | 25.00% | 31.25% | 36.13% | 25.81% | 35.29% | 32.06% | 19.51% |
| Poor             | 62.50% | 52.00% | 51.92% | 53.76% | 45.10% | 50.00% | 53.66% |
| ≥40              | 41.67% | 38.75% | 43.41% | 51.38% | 57.69% | 50.00% | 43.95% |
| *P*              | 0.09 | 0.03 | 0.01 | 0.02 | 0.03 | 0.01 | 0.02 |
| **Pain VAS classification** |     |     |     |     |     |     |      |
| 0-30             | 33.33% | 46.48% | 32.26% | 29.47% | 30.77% | 28.00% | 29.27% |
| 31-60            | 43.75% | 41.56% | 47.00% | 43.75% | 31.88% | 42.55% |      |
| ≥60              | 24.00% | 23.41% | 20.00% | 20.29% | 8.51% |      |      |
| **EQ-5D-5L anxiety and depression dimension score** |     |     |     |     |     |     |      |
| 4                | 16.89% | 13.25% | 15.81% | 10.00% | 23.44% | 17.39% | 21.28% |
| 3                | 28.06% | 16.11% | 17.00% | 9.38% | 20.29% | 8.51% |      |
| 2                | 4.00% | 24.50% | 25.23% | 25.00% | 18.75% | 25.54% | 27.66% |
| 1                | 44.00% | 47.02% | 41.34% | 47.00% | 43.75% | 31.88% | 42.55% |
| 0                | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% | 0.00% |
| **mMRC dyspnea score** |     |     |     |     |     |     |      |
| 4                | 6.99% | 4.00% | 3.06% | 1.00% | 1.56% | 2.90% | 0.00% |
| 3                | 7.69% | 6.00% | 8.26% | 14.00% | 9.38% | 14.49% | 8.51% |
| 2                | 11.54% | 13.33% | 17.74% | 18.00% | 17.19% | 23.19% | 31.91% |
| 1                | 30.77% | 30.00% | 39.45% | 31.00% | 40.63% | 28.99% | 29.79% |
| 0                | 42.31% | 46.67% | 31.50% | 36.00% | 31.25% | 30.43% | 29.79% |
| **FACIT-Fatigue** |     |     |     |     |     |     |      |
| Average          | 36.31 | 39.86 | 39.04 | 39.68 | 38.95 | 38.23 | 39.32 |
| Standard Deviation | 12.31 | 10.09 | 9.79 | 9.35 | 10.38 | 8.80 | 9.27 |

Notes: VAS = Visual Analogue Scale; EQ-5D-5L = EuroQol-5 Dimensions-5 Levels; mMRC dyspnea scale = Medical Research Council Dyspnea Scale; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy – Fatigue.
Supplementary Table 5. Values of the 25th and 75th percentiles reported in Vianna et al.\textsuperscript{11} used for the classification of our individual patients in poor, average or good handgrip strength.

| Age (years) | Males | | | | Females | | | |
|-----|-------|-------|-------|-------|-------|-------|-------|-------|
|     | Poor (<25\textsuperscript{th} percentile) | Average (25\textsuperscript{th} to 75\textsuperscript{th} percentile) | Good (>75\textsuperscript{th} percentile) | Poor (<25\textsuperscript{th} percentile) | Average (25\textsuperscript{th} to 75\textsuperscript{th} percentile) | Good (>75\textsuperscript{th} percentile) |
| 18-25 | ≤ 36.3 | > 36.3 to ≤ 47.1 | > 47.1 | ≤ 20.6 | > 20.6 to ≤ 30.8 | > 30.8 |
| 26-30 | ≤ 38.1 | > 38.1 to ≤ 47.1 | > 47.1 | ≤ 20.4 | > 20.4 to ≤ 26.6 | > 26.6 |
| 31-35 | ≤ 38.6 | > 38.6 to ≤ 47.6 | > 47.6 | ≤ 21.0 | > 21.0 to ≤ 28.3 | > 28.3 |
| 36-40 | ≤ 35.8 | > 35.8 to ≤ 46.5 | > 46.5 | ≤ 20.1 | > 20.1 to ≤ 26.7 | > 26.7 |
| 41-45 | ≤ 36.3 | > 36.3 to ≤ 46.8 | > 46.8 | ≤ 19.4 | > 19.4 to ≤ 27.1 | > 27.1 |
| 46-50 | ≤ 34.3 | > 34.3 to ≤ 42.9 | > 42.9 | ≤ 19.8 | > 19.8 to ≤ 25.9 | > 25.9 |
| 51-55 | ≤ 32.4 | > 32.4 to ≤ 40.7 | > 40.7 | ≤ 18.2 | > 18.2 to ≤ 24.5 | > 24.5 |
| 56-60 | ≤ 31.8 | > 31.8 to ≤ 40.9 | > 40.9 | ≤ 16.7 | > 16.7 to ≤ 23.3 | > 23.3 |
| 61-65 | ≤ 28.8 | > 28.8 to ≤ 38.5 | > 38.5 | ≤ 16.4 | > 16.4 to ≤ 22.3 | > 22.3 |
| 66-70 | ≤ 27.2 | > 27.2 to ≤ 35.4 | > 35.4 | ≤ 15.4 | > 15.4 to ≤ 20.2 | > 20.2 |
| 71-75 | ≤ 24.7 | > 24.7 to ≤ 34.1 | > 34.1 | ≤ 14.1 | > 14.1 to ≤ 18.8 | > 18.8 |
| ≥76  | ≤ 21.7 | > 21.7 to ≤ 31.5 | > 31.5 | ≤ 11.4 | > 11.4 to ≤ 17.4 | > 17.4 |
**Supplementary Table 6. Linear regression models**

| Variables     | Beta-coefficient | 95% CI LL | 95% CI UL | p-value | Adjusted R² |
|---------------|------------------|-----------|-----------|---------|-------------|
| **EPWORTH SLEEPINESS SCALE** |                  |           |           |         |             |
| Intubation    | -1.377           | -2.175    | -0.578    | 0.001   | 0.0129      |
| A.DJUSTED     |                  |           |           |         |             |
| Intubation    | -1.374           | -2.179    | -0.569    | 0.001   |             |
| Sex           | -0.399           | -1.196    | 0.397     | 0.325   |             |
| Age           | -0.043           | -0.073    | -0.012    | 0.006   |             |
| Race          | -0.222           | -1.030    | 0.585     | 0.589   |             |
| Hypertension  | 0.659            | -0.241    | 1.560     | 0.151   |             |
| **DISPNEIA**  |                  |           |           |         |             |
| Intubation    | -0.0012          | -0.168    | 0.135     | 0.833   |             |
| A.DJUSTED     |                  |           |           |         |             |
| Intubation    | -0.0012          | -0.179    | 0.120     | 0.097   |             |
| Sex           | -0.436           | -0.584    | -0.288    | <0.001  |             |
| Age           | 0.0002           | -0.006    | 0.005     | 0.999   |             |
| Race          | -0.0010          | -0.160    | 0.140     | 0.894   |             |
| Hypertension  | 0.297            | 0.130     | 0.464     | 0.001   |             |
| **VAS**       |                  |           |           |         |             |
| Intubation    | -0.0011          | -0.168    | 0.135     | 0.833   |             |
| A.DJUSTED     |                  |           |           |         |             |
| Intubation    | -0.0011          | -0.179    | 0.120     | 0.097   |             |
| Sex           | -15.384          | -20.159   | -10.699   | <0.001  |             |
| Age           | 0.242            | 0.054     | 0.429     | 0.012   |             |
| Race          | -2.543           | -7.393    | 2.308     | 0.304   |             |
| Hypertension  | 3.587            | -1.811    | 8.964     | 0.192   |             |
| **HANDGRIP**  |                  |           |           |         |             |
| Intubation    | 0.0700           | 0.374     | 0.779     | <0.001  |             |
| A.DJUSTED     |                  |           |           |         |             |
| Intubation    | 0.0700           | 0.374     | 0.779     | <0.001  |             |
| Sex           | 15.148           | 13.762    | 16.534    | <0.001  |             |
| Age           | -0.182           | -0.236    | -0.127    | <0.001  |             |
| Race          | -0.972           | -2.381    | 0.437     | 0.176   |             |
| Hypertension  | -1.950           | -3.516    | -0.384    | 0.015   |             |
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### STROBE Statement—Checklist of items that should be included in reports of cohort studies

| Item No | Recommendation |
|---------|----------------|
| 1       | **Title and abstract**<br>*(a)* Indicate the study’s design with a commonly used term in the title or the abstract<br>*(b)* Provide in the abstract an informative and balanced summary of what was done and what was found |
| 2       | **Introduction**<br>**Background/rationale**<br>Explain the scientific background and rationale for the investigation being reported |
| 3       | **Objectives**<br>State specific objectives, including any prespecified hypotheses |
| 4       | **Methods**<br>**Study design**<br>Present key elements of study design early in the paper |
| 5       | **Setting**<br>Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection |
| 6       | **Participants**<br>*(a)* Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up<br>*(b)* For matched studies, give matching criteria and number of exposed and unexposed |
| 7       | **Variables**<br>Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable |
| 8       | **Data sources/measurement**<br>For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group |
| 9       | **Bias**<br>Describe any efforts to address potential sources of bias |
| 10      | **Study size**<br>Explain how the study size was arrived at |
| 11      | **Quantitative variables**<br>Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why |
| 12      | **Statistical methods**<br>*(a)* Describe all statistical methods, including those used to control for confounding<br>*(b)* Describe any methods used to examine subgroups and interactions<br>*(c)* Explain how missing data were addressed<br>*(d)* If applicable, explain how loss to follow-up was addressed<br>*(e)* Describe any sensitivity analyses |
| 13      | **Results**<br>*(a)* Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for...
eligibility, confirmed eligible, included in the study, completing follow-up, and analysed

| (b) Give reasons for non-participation at each stage | Figure 1, Flow chart |
| (c) Consider use of a flow diagram | Figure 1, Flow chart |

**Descriptive data** 14*

(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders

Table 1, Table 2 and Table 3

Supplementary Tables 2, 3, and 4.

(b) Indicate number of participants with missing data for each variable of interest

Refer to the total n in the corresponding tables.

(c) Summarise follow-up time (eg, average and total amount)

Table 1

**Outcome data** 15*

Report numbers of outcome events or summary measures over time

Table 2, Table 3

Supplementary Tables 2, 3, and 4.

Page 6, Line 21 to Page 13, Line 15

**Main results** 16

(a) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included

Corresponding tables

(b) Report category boundaries when continuous variables were categorized

Corresponding tables

Supplementary Table 1 and Supplementary Table 5

(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period

Not applicable

**Other analyses** 17

Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses

See paragraph Data analyses on page 5 and 6

**Discussion**

**Key results** 18

Summarise key results with reference to study objectives

Page 13, Line 17 to 26

**Limitations** 19

Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias

Page 16, Line 6 to 16

**Interpretation** 20

Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence

Page 13, Line 27 to Page 16 Line 26

**Generalisability** 21

Discuss the generalisability (external validity) of the study results

Not specifically mentioned

**Other information**

**Funding** 22

Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based

Page 17, Line 4 to 11

*Give information separately for exposed and unexposed groups.
**Note:** An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at http://www.strobe-statement.org.