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Saulo Gil, PhD, Gersiel Nascimento de Oliveira Júnior, MSc, Flavia Mori Sarti, PhD, Wilson Jacob Filho, MD; PhD, Igor Longobardi, MSc, José Antonio Orellana Turri, PhD, Samuel Katsuyuki Shinjo, MD; PhD, Eduardo Ferriolli, MD; PhD, Thiago Junqueira Avelino-Silva, MD; PhD, Alexandre Leopold Busse, MD; PhD, Bruno Gualano, PhD, Hamilton Roschel, PhD

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Acute muscle mass loss predicts long-term fatigue, myalgia, and health care costs in covid-19 survivors

Running title: Muscle atrophy impacts post-discharge outcomes.

Saulo Gil, PhD[1,2], Gersiel Nascimento de Oliveira Júnior MSc[1], Flavia Mori Sarti, PhD[5], Wilson Jacob Filho, MD; PhD[3], Igor Longobardi, MSc[1], José Antonio Orellana Turri, PhD[5], Samuel Katsuyuki Shinjo, MD; PhD[2], Eduardo Ferriolli, MD; PhD[4], Thiago Junqueira Avelino-Silva, MD; PhD[3], Alexandre Leopold Busse, MD; PhD[3], Bruno Gualano, PhD[1,2], Hamilton Roschel, PhD[1,2]

[1] Applied Physiology & Nutrition Research Group, School of Physical Education and Sport, Rheumatology Division, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Av. Prof. Mello Moraes, 65 - São Paulo, SP, Brazil.

[2] Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[3] Laboratorio de Investigacao Medica em Envelhecimento (LIM-66), Servico de Geriatria, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de Sao Paulo, Sao Paulo, SP, BR.

[4] Division of Internal and Geriatric Medicine, Department of Internal Medicine - Ribeirão Preto Medical School, Universidade de Sao Paulo, Ribeirao Preto, SP, BR.

[5] School of Arts, Sciences and Humanities, University of São Paulo (USP), São Paulo, Brazil, SP, BR.

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Brief summary: COVID-19-related drastic muscle loss is not restored 6 months after hospital discharge, and this related higher frequency of persistent symptoms and greater total COVID-19-related health care costs 2 and 6 months after discharge.

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Corresponding author (to whom reprint requests should be addressed):

Hamilton Roschel, PhD

Applied Physiology & Nutrition Research Group; School of Physical Education and Sport; Laboratory of Assessment and Conditioning in Rheumatology; Faculdade de Medicina FMUSP, Universidade de Sao Paulo, Sao Paulo, SP, BR.

Av. Dr. Arnaldo, 455 - Cerqueira Cesar - São Paulo, SP - Brasil

Postal code: 01246-903

Phone: + 55 11 3061.8789

e-mail: hars@usp.br

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Abstract

Objective: We examined the impact of loss of skeletal muscle mass in post-acute sequelae of SARS-CoV-2 (PASC) infection, hospital readmission rate, self-perception of health, and health care costs in a cohort of COVID-19 survivors.

Design: Prospective observational study.

Setting and Participants: Tertiary Clinical Hospital. Eighty COVID-19 survivors aged 59±14 years were prospectively assessed.

Methods: Handgrip strength and vastus lateralis muscle cross-sectional area (CSA_{VL}) were evaluated at hospital admission, discharge, and 6 months after discharge. PASC were evaluated 6 months after discharge (main outcome). Also, health care costs, hospital readmission rate, and self-perception of health were evaluated 2 and 6 months after hospital discharge. To examine whether the magnitude of muscle mass loss impacts the outcomes, we ranked patients according to relative CSA_{VL} reduction during hospital stay into either "high muscle loss" (-18±11%) or "low muscle loss" (-4±2%) group, based on median values.

Results: High muscle loss group showed greater prevalence of fatigue (76% vs. 46%, P=0.0337) and myalgia (66% vs. 36%, P=0.0388), and lower muscle mass (-8% vs. 3%, P < 0.0001) than low muscle loss group 6 months after discharge. No between-group difference was observed for hospital readmission and self-perceived health (P>0.05). High muscle loss group demonstrated greater total COVID-19-related health care costs 2 ($77283.87 vs. $3057.14, P=0.0223, respectively) and 6 months ($90001.35 vs. $12913.27, P=0.0210, respectively) after discharge vs. low muscle loss group. Muscle mass loss was shown to be a predictor of total COVID-19-related health care costs at 2

(adjusted β=$10070.81, P<0.0001) and 6 months after discharge (adjusted β=$9885.63, P<0.0001).

Conclusions and Implications: COVID-19 survivors experiencing high muscle mass loss during hospital stay fail to fully recover muscle health. In addition, greater muscle loss was associated with a higher frequency of post-acute sequelae of SARS-CoV-2 and greater total COVID-19-related health care costs 2 and 6 months after discharge. Altogether, these data suggest that the loss of muscle mass resulting from COVID-19 hospitalization may incur in an economical burden to health care systems.

Introduction

The pandemic of the coronavirus disease 2019 (COVID-19) has caused morbidity and mortality at an unprecedented global scale with millions of confirmed cases, hospitalizations, and deaths[1]. The understanding of the acute symptoms and complications related to COVID-19 has been at the center of attention amongst the scientific community; however, emergent evidence has also shown an elevated prevalence of persistent symptoms in survivors of COVID-19 months after the resolution of acute symptoms, such as fatigue, weakness, dyspnea, decline in quality of life among others[2-4], thus requiring further post-hospitalization care, which is severely impacting healthcare systems around the world.

Long-term bed rest due to prolonged hospital length of stay[5, 6], associated with a drastic increase in systemic inflammation (i.e., "cytokine storm") typical of the COVID-19[7, 8], are potent catabolic stimuli that may exacerbate the loss of muscle mass commonly observed in hospitalized patients[9]. In fact, previous data show that in critical patients, hospital stay is thought to increase muscle wasting due to considerable exacerbated inflammation, pre-existing comorbidities, multi-organ dysfunction, and prolonged bed rest [9-12]. Accordingly, among different clinical conditions, lower muscle mass is considered an important predictor of poor outcomes, such as mortality, more days on intensive care unit (ICU), general morbidity, impaired physical function, lower quality of life, surgical complications, less odds of discharge destination to rehabilitation facilities and, higher hospitalization costs [13-24].

Recently, we demonstrated that both muscle strength and mass assessed upon hospital admission are predictors of length of stay in patients with COVID-19[25], indicating the prognostic value of muscle health in this disease. However, whether the magnitude of muscle waste due to hospitalization affects post-discharge prognosis in

COVID-19 patients is still to be elucidated. Therefore, we prospectively investigated the influence of muscle mass loss during hospitalization on post-acute sequelae of SARS-CoV-2 (PASC) infection, hospital readmission rate, self-perception of health and health care costs following hospital discharge in a cohort of COVID-19 survivors.

Methods

Study design and participants

This is a prospective observational study conducted between March 2020 and August 2021 in the Clinical Hospital of the School of Medicine of the University of Sao Paulo in Brazil (HCFMUSP) the largest tertiary referral teaching hospital in Latin America. This study was approved by the local Ethics Committee (Ethics Committee Approval Number 31303720.7.0000.0068). All patients provided written informed consent before entering the study. This manuscript was reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) Statement.

The inclusion criteria were: 1) age ≥ 18 years; 2) diagnosis of COVID-19 by PCR for SARS-CoV-2 from nasopharyngeal swabs or computed tomography scan findings (bilateral multifocal ground-glass opacities ≥ 50%) compatible with the disease; 3) diagnosis of flu syndrome with hospitalization criteria on hospital admission, presenting respiratory rate ≥ 24 breaths per minute, saturation < 93% on room air or risk factors for complications, such as heart disease, diabetes mellitus, systemic arterial hypertension, neoplasms, immunosuppression, pulmonary tuberculosis, and obesity, followed by COVID-19 confirmation. Exclusion criteria were: 1) cancer in the past 5 years; 2) delirium; 3) cognitive deficit that precluded the patient from reading and signing the informed consent form; 4) prior diagnosis of muscle degenerative disease (e.g., myopathies, amyotrophic lateral sclerosis, stroke); 5) patients already admitted under invasive mechanical ventilation; 6) length of stay less than 5 days. Patients who met the inclusion criteria were considered to have moderate to severe COVID-19.

Handgrip strength and vastus lateralis muscle cross-sectional area was evaluated at the point-of-care within less than 48 hours upon hospital admission, at hospital discharge, and 6 months after discharge. Frequency of persistent symptoms (i.e., fatigue, myalgia, dyspnea, headache, chest pain, dizziness, nausea, anosmia, abdominal pain, vomiting, cough, diarrhea, runny nose, dysgeusia, earache, and fever) were evaluated 6 months after discharge. Health costs, hospital readmission rate and self-perception of health (i.e., very poor, poor, regular, good, and very good) were evaluated 2- and 6-months following hospital discharge. Demographic, clinical, and biochemical data from the patients at admission were obtained through medical records.

Handgrip strength and vastus lateralis muscle cross-sectional area assessment

Handgrip strength assessments were performed with the patient seated holding the dynamometer (TKK 5101; Takei, Tokyo, Japan) with the dominant hand and elbow positioned at a 90° angle. Three maximum attempts of 5 seconds with 1 minute interval between attempts were performed and the best result was used for analysis.

Vastus lateralis muscle cross-sectional area (CSA_{VL}) was assessed by a B-mode ultrasound with a 7.5-MHz linear-array probe (SonoAce R3, Samsung-Medison, Gangwon-do, South Korea) as previously described [26]. Cross-sectional area analyses were performed in a blinded fashion by a single investigator using ImageJ (NIH, USA). Test-retest coefficient of variation for vastus lateralis CSA_{VL} was 2.1%.

PASC *and self-perception of health*

The prevalence of PASC was assessed 6-months following hospital discharge and the self-perception of health was assessed at 2- and 6-months following discharge. Both were assessed by means of the application of a structured questionnaire applied via a phone call.

To assess the presence of fatigue, myalgia, dyspnea, headache, chest pain, dizziness, nausea, anosmia, abdominal pain, vomiting, cough, diarrhea, runny nose, dysgeusia, earache, patients were asked whether they had experienced any of these symptoms after COVID-19 infection.

Self-perception of health was assessed using a Likert scale including the following items: very poor, poor, regular, good, and very good. The patients answered the following question: "In general, how do you consider your current health status?".

Health care costs estimates

Information on health services and products required within the last 2- and 6-months after discharge were obtained using a structured questionnaire including the following items: age, sex, ethnicity, educational attainment, household income, household residents, self-assessment of health status, physician consultations, consultations with other health professionals (physiotherapist, speech therapist, nurse, physical trainer, dietitian, among others), use of health services, hospitalizations, type of treatment (clinical, surgical, psychiatric, diagnostic exams, others), type of health care facility (public or private sector), form of payment for health services (out-of-pocket, health insurance, public funding), continuous use and other medications purchased or obtained within the Brazilian Unified Health System, and monetary values paid for health services and products (consultations, hospitalizations, diagnostic exams, medications, and other health care materials). The estimation of direct health care costs of patients was based on payers' perspective.

Data referring to the number and type of health services used (physician consultations, consultations with other health professionals, and hospitalizations) were converted into costs by multiplying number of consultations or inpatient days by its monetary value, according to health specialty and type of health care facility (i.e., market prices for consultations and hospitalizations in the private sector, or public sector costs with human resources and other inputs for consultations and hospitalizations in the public sector).

Regarding medication, costs were estimated using self-declared out-of-pocket expenditures for patients who declared purchasing medication in the private sector, whereas costs with medication among patients who declared obtaining medication from the public sector were estimated using mean medication expenditures in public sector. Patients were also asked about additional out-of-pocket health expenditures necessary for diagnosis and treatment of skeletal muscle loss (exams, medical supplies, home care, among others), including type of product or service and their respective monetary value.

Monetary values of direct costs within 2- and 6- months after discharge were updated to the reference date of July 2021, to ensure comparability of data throughout time. Finally, the direct costs per patient were converted into US dollars, using the official exchange rate of the Brazilian Central Bank in the reference period.

Outcomes and stratification of patients

Our primary outcome was prevalence of PASC. Patients were ranked according to the magnitude of the relative CSA_{VL} loss following the hospitalization period, and then clustered into 50th percentiles, forming two groups: “high muscle loss” = -18 ± 11%; and “low muscle loss” = -4 ± 2%.

Statistical analyses

Data are presented as mean/median, standard deviation (SD), between-group difference and 95% confidence interval (CI), unless otherwise indicated. Normality data was assessed by Shapiro-Wilk test. Independent *t-tests* were performed to test possible between-group differences (i.e., high muscle loss vs. low muscle loss) for relative changes in handgrip strength and CSA_{VL} loss at discharge (i.e., [discharge-admission]/admission*100) and 6 months after discharge (i.e., [6-months post-discharge-admission]/admission*100). Potential between-group differences in PASC, hospital readmission rate, and self-perception of health were tested by χ^2 test.

Possible between-group differences for health care costs at 2 and 6 months after discharge were tested by independent *t-tests*. The association of relative CSA_{VL} loss with total COVID-19- related health costs was conducted using multivariable, linear regression models adjusted for age, sex, ethnicity (white, black, and yellow), body mass index (as a continuous variable), presence of type 2 diabetes mellitus and hypertension, and length of stay, or unadjusted models. Significance level was set at $P \leq 0.05$.

Results

Patients

Eighty patients who tested positive for SARS-CoV-2 during the hospitalization period were evaluated. Table 1 shows the demographic, biochemical, and clinical characteristics of the patients at hospital admission. Overall, 91.2% (73 out of 80) had a positive PCR test for SARS-CoV-2 at enrollment. The remaining patients (7 out of 80) had the diagnosis confirmed by serology assay to detect IgG against SARS-CoV-2 during hospital stay. The sample comprised patients of both sexes (51.2% male) with a mean (SD) age of 59 (±14) years, body mass index of 29.9 (±5.1) kg/m^2. The proportion of current smokers was 30.0%, and the most prevalent coexisting conditions were obesity (41.2%), hypertension (32.5%), and type 2 diabetes mellitus (31.2%).

The most commonly observed signs and symptoms at admission were dyspnea (82.0%), cough (67.5%), fever (58.8%), myalgia (28.7%), fatigue (27.5%), headache (21.2%), anosmia (20.0%), dysgeusia (18.8%), diarrhea (16.2%), chest pain (16.2%), nausea (10.0%), runny nose (10.0%), vomiting (8.8%), abdominal pain (7.5%), earache (4.3%), and dizziness (2.5%). Mean length of stay was 8 days (IQR: 5 - 12); 12.5% of the patients required intensive care; 1.2% used invasive mechanical ventilation.

Vastus lateralis muscle cross-sectional area and handgrip strength

As per design, muscle loss during hospitalization was significantly different between high and low muscle loss groups (-18% vs. -4%, P < 0.0001). Importantly, this difference was sustained during follow up (-8% vs. 3%, P < 0.0001), indicating that the high muscle loss group did not fully recover muscle mass lost during hospital stay 6 months post-discharge, whereas the low muscle loss group did (Figure 1, panel A).

Handgrip strength data followed a similar pattern, with a higher decrease in strength being observed in the high muscle loss group (-18% vs. -8%, P = 0.0195). Whilst the low muscle loss group fully recovered handgrip strength at the 6-month post-discharge assessment (9% vs. admission), the high muscle loss group still exhibited lower handgrip strength values (-7% vs. admission). However, no between-group difference was observed for this variable after 6 months of hospital discharge (P = 0.1714) (Figure 1, panel B).

PASC, hospital readmission and self-perception of health

High muscle loss group showed greater prevalence of fatigue (76% vs. 46%, P = 0.0337) and myalgia (66% vs. 36%, P = 0.0388) than low muscle loss group 6-months post-hospital discharge, with chest pain showing borderline values to statistical significance (23% vs. 3%, P = 0.0576). No between-group differences were observed for the remaining symptoms (all P > 0.05) (Figure 2, Panel A and B).

Fifteen percent of the patients in the high muscle loss group were readmitted to the hospital within 2 months after discharge vs 10% of the patients in the low muscle loss group; however, this difference did not achieve statistical significance (P = 0.1800). Both groups presented comparable hospital readmission rates 6 months after hospital discharge (9% vs. 9%, P = 0.6422) (Figure 2, Panel C).

No between-group differences were observed for any of the items of the self-perception of health questionnaire (all P > 0.05) (Figure 2, Panel D).

Health costs estimates

High muscle loss group exhibited greater costs than low muscle loss group for hospital admission and total COVID-19-related health care after 2 ($64453.20 vs. $523.54, P = 0.0419 and $77,283.87 vs. $3,057.14, P = 0.0223) and 6 months ($70,083.07 vs. $7,251.35, P = 0.0492 and $90,001.35 vs.$12,913.27, P = 0.0210) following hospital discharge.

Adjusted linear regression model revealed muscle mass loss as a significant predictor of total COVID-19-related health care costs at 2 and (adjusted β = $10,070.81, 95%IC = 5,623.17 to 14,518.44, P <0.0001) and 6 months after hospital discharge (Adjusted β = $9,885.63, 95%IC = 5,405.00 to 14,366.27, P <0.0001). Unadjusted models elicited similar findings (Table 3).

Discussion

In this study, we observed that patients showing substantial muscle mass loss during COVID-19 hospitalization were not able to fully restore muscle health 6 months following hospital discharge. These patients also exhibited greater prevalence of fatigue and myalgia. Additionally, muscle loss showed to be an independent and significant predictor of total COVID-19-related health care costs up to 6 months after hospital discharge. Altogether, these data suggest that the loss of muscle mass resulting from COVID-19 hospitalization may incur in an economical burden to health care systems.

Muscle atrophy and weakness are detrimental effects often observed after long-term hospital stay, which may persist for long periods of time affecting prognosis, morbimortality and overall quality of life of patients in several conditions [9, 27-30]. Previous studies have demonstrated a reduction of about 5-7% of quadriceps femoral cross-sectional area after 5-14 days of muscle disuse (i.e., immobilization or bed rest)[31-33]. In the current study, we observed a mean decrease of nearly two-fold (~10%) in vastus lateralis muscle cross-sectional area in about 10 days of hospitalization among patients with COVID-19, indicating a higher magnitude of muscle loss in comparison to other catabolic conditions. Of note, when patients were stratified according to the magnitude of loss in vastus lateralis muscle cross-sectional area, patients who experienced greater losses of muscle mass (i.e., ≥18%) failed to fully restore muscle mass and strength 6-months after hospital discharge. This is concerning as skeletal muscle plays a pivotal role in different physiological processes such as immune response, serves as source of amino acids to maintain protein synthesis and preserve vital tissues and organs (e.g.; brain, cardiac and hepatic tissues)[34] during stress conditions, which are of physiological relevance in maintaining a healthy cardiometabolic and immunological profile [35].

Early reports revealed that approximately 75% of COVID-19 survivors report at least 1 PASC following 6 months of in-hospital discharge[36], with fatigue, dyspnea, cough, headache, loss of taste or smell, and cognitive or mental health impairments being the most commonly observed [5, 37, 38]. Interestingly, our findings revealed a greater frequency of fatigue and myalgia in patients experiencing greater loss of muscle mass, suggesting that the magnitude of muscle mass loss may be associated with higher frequency of PASC. Although this is an interesting notion, it is important to highlight that our study design does not allow establishing causation.

In respect of self-reported perception of health, we observed an elevate frequency (i.e., > 35%) of patients reporting regular, poor, or very poor health status 2 and 6 months after hospital discharge. Despite the absence of no within- or between-group significant differences in these variables, one may argue that the slight increase (10%) in frequency of patients reporting very poor health status in the low muscle loss group may be unexpected. It is possible that self-reported perception of health may be related to other adverse effects commonly observed in COVID-19 survivors like depression, anxiety, and sleep disorders [37].

The elevated prevalence of PASC and poor health status may increase the requirement of medical assistance and thus increasing health care costs. In this context, one could speculate that patients suffering more drastic losses of muscle during hospital stay due to COVID-19 (and greater prevalence of PASC) would be in greater need of health care assistance, ultimately resulting in increased health care costs related to this disease. This notion gains traction with the current findings indicating higher total COVID-19 related health costs in the high vs. lower muscle mass loss group 2 (US$ 77283.87 *vs*. 3057.14) and 6 months (US$ 90001.35 *vs*. 12913.27) after hospital discharge. Of note, our data indicate higher expenditures for management of COVID-19 survivors than those observed in other medical conditions associated to low muscle mass during hospital stay such as major abdominal surgery (≈ US$ 40000.00)[39], thoracolumbar spine surgery (≈ US$ 53128.00)[40], and one-year postoperative (≈ US$ 40000.00)[41].

Collectively, the results of current study prompt the need for interventions able to mitigate the muscle mass loss arising from hospital stay as drastic muscle mass loss may increase the risk for long-term sequelae and health care expenditures and resource utilization after hospital discharge. In this scenario, non-pharmacological therapies such as physical exercise and nutrition emerge as inexpensive and accessible strategies to counteract muscle loss [42-45] and improve recovery from PASC [46]. Indeed, the American Heart Association has provided strong evidence of the potential of physical activity in favorably impacting the increasing burden of diseases and its associated costs [47].

This study is strengthened by the novelty of our findings highlighting that muscle health, namely the magnitude of muscle mass loss during hospitalization, is a prognostic indicator of some PASC (i.e., fatigue and myalgia) and health care costs in a prospective cohort of survivors. However, this study has some limitation, such as its observational design that hampers causative relationships; the relatively small sample size and short-term follow-up; and the patients' characteristics, which limit our inferences to hospitalized patients (most with comorbidities) who had moderate-to-severe disease; and potential recall bias occurring due to self-reported information on health care utilization and out-of-pocket expenditures. However, it is important to highlight that health care costs estimation was performed using micro-costing technique according to type of procedure, health professional specialty and type of health care facility (i.e., public, or private) to ensure that costs reflect diversity in utilization of health resources within the Brazilian health system.

Conclusions and Implications

In conclusion, COVID-19 survivors experiencing high muscle mass loss during hospital stay fail to fully recover muscle health and show greater presence of PASC, namely fatigue and myalgia, and higher costs with hospital admission and total COVID-

19-related health care 2 and 6 months after hospital discharge than those losing less muscle. These findings have two practical applications. From a clinical perspective, muscle mass loss emerges as measure of poor prognosis in hospitalized patients and, as such, should be therapeutically approached. From a public health standpoint, muscle loss following COVID-19 hospitalization was shown to be associated with greater health care costs, which can add pressure on the health care systems. Further efficacy and effectiveness studies should investigate the utility of interventions aimed at recovering muscle health in COVID-19 survivors in preventing health care costs and disease complications.

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Figures and Legends

Figure 1. Relative change of the vastus lateralis cross-sectional area (CSA_{VL}) (panel A) and handgrip strength (HGS) (panel B) at hospital discharge and 6 months after discharge (6mo), according to the magnitude of muscle loss. * Indicates between-group differences in the same timepoint.

Figure 2. Prevalence of persistent symptoms related to COVID-19 after 2 (2mo) and 6 months (6mo) of hospital discharge, according to the magnitude of muscle loss. * Indicates between-group differences for the same symptom.

Table 1. Demographics, biochemical, and clinical characteristics of patients at hospital admission.

	All patients (n=80)
Sex, n (%)	
Female	39 (48.8)
Male	41 (51.2)
Age, n (%)	
<65	49 (61.2)
>65	31 (38.8)
Ethnicity, n (%)	
White	45 (56.2)
Black	24 (30.0)
Asian	11 (13.8)
Smoking status, n (%)	
Never	60 (75.0)
Current	20 (30.0)
Comorbidities, n (%)	
Asthma	5 (6.2)
Heart failure	9 (11.2)
Obesity (BMI>30)	33 (41.2)
Type 2 diabetes	25 (31.2)
COPD	4 (5.0)
Chronic renal disease	5 (6.2)
Atrial fibrillation	4 (5.0)
Acute myocardial infarction	6 (7.5)
Systemic arterial hypertension	26 (32.5)
COVID-19 testing, n (%)	
Positive PCR for SARS-CoV-2	73 (91.2)
Positive IgG for SARS-CoV-2	7 (8.8)
Acute COVID-19 symptoms, n (%)	
Anosmia	16 (20.0)
Headache	17 (21.2)
Runny nose	8 (10.0)
Diarrhea	13 (16.2)
Dysgeusia	15 (18.8)
Dyspnea	66 (82.0)

Continuation.

	All patients (n=80)
Abdominal pain	6 (7.5)
Chest pain	13 (16.2)
Fatigue	22 (27.5)
Fever	47 (58.8)
Myalgia	23 (28.7)
Nausea	8 (10.0)
Earache	8 (4.3)
Cough	26 (67.5)
Dizziness	2 (2.5)
Vomiting	7 (8.8)
Oxygen support, n (%)	
No oxygen therapy	24 (30.0)
Oxygen therapy	51 (63.8)
Non-invasive ventilation	5 (6.2)
Biochemical parameters	
Hemoglobin, mean (SD), g/L	12.7 (2.1) [n=80]
Neutrophil, mean (SD), $x10^3/mm^3$	6.1 (4.1) [n=76]
Lymphocytes, mean (SD), $x10^3/mm^3$	1.3 (1.4) [n=74]
Platelets, mean (SD), $x10^3/mm^3$	240.0 (123.0) [n=79]
C-reactive protein, mean (SD), mg/L	77.2 (66.6) [n=74]
D-dimer, mean (SD), ng/mL	1883.0 (3168.0) [n=56]
Creatinine, mean (SD), mg/dL	1.2 (0.9) [n=75]
Urea, mean (SD), mg/dL	50.9 (36.8) [n=77]
Ground-glass opacities on CT findings (≥50%), n (%)	16 (20.0)
ICU admission, n (%)	10 (12.5)
Use of invasive mechanical ventilation, n (%)	1 (1.2)
Hospital length of stay (d), median (IQR)	8 (5 - 12)
Handgrip strength, kgF, median (IQR)	22 (16 - 30)
Vastus lateralis muscle CSA, cm^2, median (IQR)	12 (11 - 19)

Abbreviations-BMI: Body Mass Index; COPD: Chronic Obstructive Pulmonary Disease; CT: Computed Tomography; ICU: Intensive Care Unit; IQR: Interquartile Range; CSA: Cross-Sectional Area.

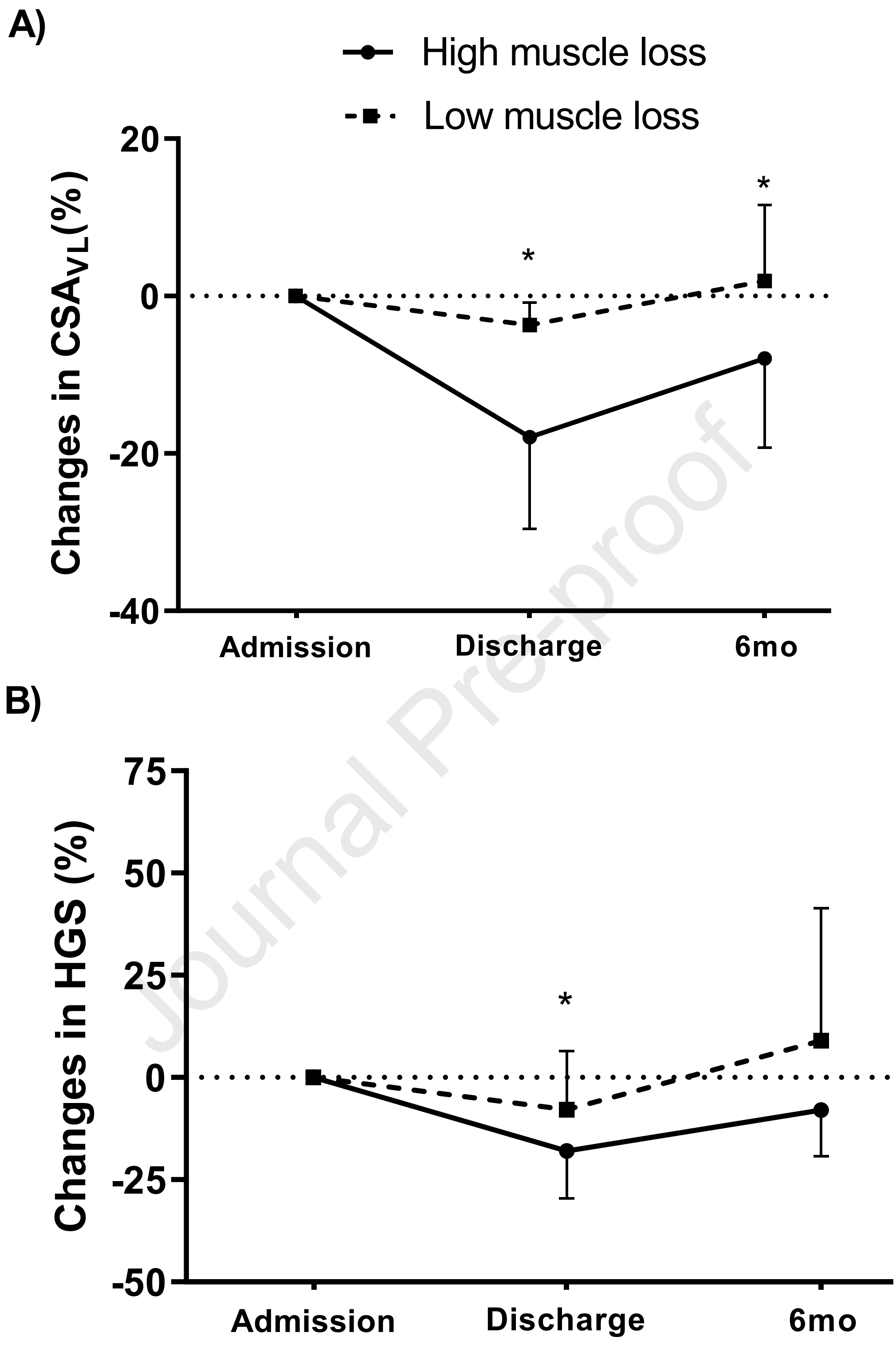
Table 2. Health care costs estimates after 2 and 6 months of hospital discharge.

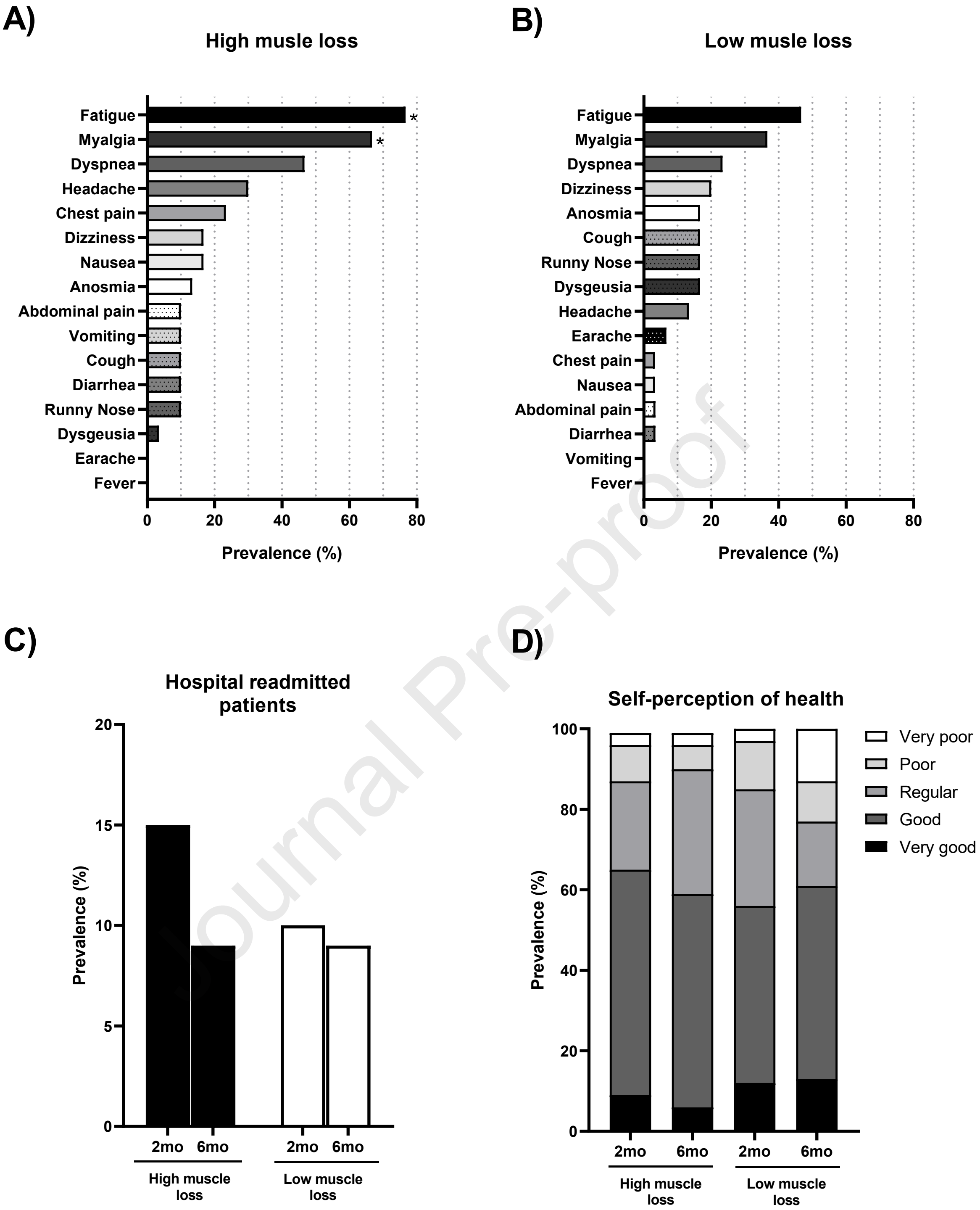
	2 months after discharge			6 months after discharge		
	High muscle loss	**Low muscle loss**	**Between-group difference (95%IC; P-value)**	**High muscle loss**	**Low muscle loss**	**Between-group difference (95%IC; P-value)**
Total COVID-19-related health costs ($)	77283.87±201245.09	3057.14±5746.25	74226.73 (10852.87 to 137600.60; **0.0223**)	90001.35±204952.34	12913.27±28854.27	77088.08 (11936.85 to 142239.32; **0.0210**)
Costs with drugs ($)	1358.74±2034.77	863.43±1023.66	495.31 (-221.68 to 1212.31; 0.1730)	4698.65±6282.79	4383.39±4967.15	315.26 (-2205.85 to 2836.38; 0.8041)
Healthcare assistance ($)	11918.27±56058.42	1739.25±4175.08	10179.01 (-7515.96 to 27873.99; 0.2556)	18944.00±62011.39	3152.22±5428.04	15791.78 (-3802.84 to 35386.39; 0.1127)
Costs with prostheses, orthotics, and exams ($)	611.43±757.79	570.03±1124.34	41.40 (-385.41 to 468.20; 0.8474)	1278.98±1514.76	1294.43±2279.02	-15.46 (-876.85 to 845.94; 0.9716)
Costs with hospital admission ($)	64453.20±195434.43	523.54±2891.95	63929.66 (2403.96 to 125455.35; **0.0419**)	70083.07±196969.27	7251.35±27594.32	62831.72 (224.14 to 125439.30; **0.0492**)

Table 3. Crude and adjusted linear regression models for the effect of muscle loss in health care costs estimates after 2 and 6 months of hospital discharge.

2 months after discharge								
	Crude β	**95%IC**	**Adjusted R^2**	**P-value**	**Adjusted[a] β**	**95%IC**	**Adjusted R^2**	**P-value**
Total COVID-19-related health costs ($)	7705.79	5282.80 to 10128.78	0.331	<0.0001	10070.81	5623.17 to 14518.44	0.822	<0.0001
6 months after discharge								
	Crude β	**95%IC**	**Adjusted R^2**	**P-value**	**Adjusted[a] β**	**95%IC**	**Adjusted R^2**	**P-value**
Total COVID-19-related health costs ($)	7944.22	5444.20 to 10444.24	0.330	<0.0001	9885.63	5405.00 to 14366.27	0.820	<0.0001

a = Adjusted for age as continuous variable, sex (male and female), ethnicity (white, black and yellow), body mass index as continuous variable, diabetes (yes or not), hypertension (yes or not), length of stay (in days) as continuous variable.


A)
High muscle loss
Low muscle loss
Changes in CSA_{VL}(%)
20
0
-20
-40
*
*
Admission
Discharge
6mo
B)
Changes in HGS (%)
75
50
25
0
-25
-50
*
Admission
Discharge
6mo


A)
High musle loss
Fatigue
Myalgia
Dyspnea
Headache
Chest pain
Dizziness
Nausea
Anosmia
Abdominal pain
Vomiting
Cough
Diarrhea
Runny Nose
Dysgeusia
Earache
Fever
*
*
0
20
40
60
80
Prevalence (%)
B)
Low musle loss
Fatigue
Myalgia
Dyspnea
Dizziness
Anosmia
Cough
Runny Nose
Dysgeusia
Headache
Earache
Chest pain
Nausea
Abdominal pain
Diarrhea
Vomiting
Fever
0
20
40
60
80
Prevalence (%)
C)
Hospital readmitted patients
Prevalence (%)
0
5
10
15
20
2mo
6mo
2mo
6mo
High muscle loss
Low muscle loss
D)
Self-perception of health
Prevalence (%)
0
20
40
60
80
100
Very poor
Poor
Regular
Good
Very good
2mo
6mo
2mo
6mo
High muscle loss
Low muscle loss