Benefits of home-based exercise training following critical SARS-CoV-2 infection: a case study

Igor Longobardi
University of Sao Paulo
Danilo Marcelo Leite do Prado
University of Sao Paulo
Karla Fabiana Goessler
University of Sao Paulo
Gersiel Nascimento de Oliveira Júnior
University of Sao Paulo
Danieli Castro Oliveira de Andrade
University of Sao Paulo
Bruno Gualano
University of Sao Paulo
Hamilton Roschel (hars@usp.br)
University of Sao Paulo https://orcid.org/0000-0002-9513-6132

Case Report

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Abstract

Purpose: We report for the first time the effect of exercise training in a survivor patient from critical COVID-19 illness.

Methods: A 67-yr-old woman who had critical COVID-19 disease underwent a 10-wk home-based exercise training aimed at recovering her overall physical condition. Before and after the intervention, we assessed cardiopulmonary parameters, skeletal muscle strength and functionality, fatigue severity and self-reported persistent symptoms.

Results: The patient was hospitalized for 71 days, being admitted in the intensive care unit (ICU) due to respiratory failure. At baseline (3 months after discharge), she presented with severe impairment in cardiorespiratory functional capacity (<50% age predicted VO_{2peak}). After the intervention, remarkable improvements in VO_{2peak} (Δ: 45.9%), oxygen uptake efficiency slope (OUES; Δ: 30.1%), HR/VO_2 slope (Δ: -43.5%), the lowest V_E/VCO_2 ratio (Δ: -7.1%), and exertional dyspnea were observed. In addition, handgrip strength (Δ: 22.7%), 30-second Sit-to-Stand (30-STS; Δ:14.3%), Timed-Up-&-Go (TUG; Δ: -15%) performance and Post-COVID Functional Status (PCFS) score (4 vs. 2) were also improved from baseline to post-intervention. Self-reported persistent symptoms were also improved and Fatigue Severity Scale (FSS) score decreased (4 vs. 2.7) from baseline to post-intervention.

Conclusions: This is the first evidence that a semi-supervised, home-based exercise training program may be safe and potentially effective in improving cardiorespiratory and physical functionality in COVID-19 survivors. Controlled studies are warranted to confirm these findings.

Introduction

As of June, 2021, there are over 180 million confirmed cases of coronavirus disease (COVID-19) worldwide.[1] It is estimated that nearly 15% of the infected patients develop severe cases,[2] usually requiring hospitalization or even intensive care unit (ICU) support, which may last for several days or weeks.[3] The combination of disease pathophysiology, treatment-related drugs' toxicity and prolonged bed rest may result in extreme deconditioning and physical disability observed at hospital discharge and months after.[4,5] Additionally, impaired cardiorespiratory functional capacity[6,7] and skeletal muscle strength and functionality[8-10] are associated with higher incidence of morbidity and all-cause mortality after hospitalization.

Therefore, despite the reasonable concerns regarding the acute phase of COVID-19 infection, attention must also be directed towards survivors’ rehabilitation. The benefits of exercise training are widely known and it has been considered as a first-line therapy in a variety of diseases and conditions.[11] In the context of the pandemic, home-based exercise training (HBET) programs have been strongly encouraged, and this modality has been shown to improve health-related parameters and fitness in several conditions.[12-14]

Nevertheless, evidence regarding the benefits of exercise training in COVID-19 survivors is still lacking. Herein, we report for the first time on the effects of HBET in a critical COVID-19 survivor.

Case Report

2.1 Participant

The patient was a 67-year-old, low-income, black, Brazilian woman. In addition to SARS-CoV-2 infection, she had essential hypertension and hypothyroidism. The patient self-reported to be sedentary and a former smoker (tobacco load: 5 pack-year for 10-yrs; 25-yrs without smoking). Her daily-use medications included hydrochlorothiazide, losartan, levothyroxine, and clonazepam, which were kept constant in the previous months and throughout the study period.

In August 2020, the patient was admitted at an emergency care unit presenting with oxygen saturation ▯70% at rest on room air and bilateral multifocal ground-glass opacities greater than 50% assessed by lung computed tomography scan. Due to the severe and refractory hypoxemic insufficiency, she was immediately transferred to the Clinical Hospital of the School of Medicine of the University of Sao Paulo, a quaternary referral hospital. Her condition rapidly progressed to an acute pulmonary respiratory failure requiring ICU admission and intubation. After 1 week, she developed renal dysfunction (without dialysis requirement) and pulmonary thromboembolism. Within the third week of hospitalization, she presented with multiple organ dysfunction and a reversed cardiorespiratory arrest. Thereafter, her condition stabilized and the patient began to improve slowly. However, after a sequence of unsuccessful extubating attempts, the clinical decision was for a tracheostomy. Decannulation occurred only 20 days later, and two weeks before her hospital discharge. In total, the patient had been hospitalized for 71 days; 49 days within the ICU, in which she remained under invasive mechanical ventilation for 47 days and received a variety of medications during hospital stay (Supplementary File 1, Table S1). Due to residual pneumopathy, she had been discharged with a prescription of home nocturnal oxygen therapy for 30 days.

2.2 Procedures

This study was approved by the Clinical Hospital of the School of Medicine of the University of Sao Paulo Ethical Committee (CAEE: 31303720.7.0000.0068) and the patient provided written informed consent.

Twelve weeks after being discharged, the patient was carefully evaluated by a physician from the research team. No contraindications for exercise were found (Supplementary File 2). Patient was not experienced with exercising before hospitalization, and she did not undergo physiotherapy or other forms of rehabilitation after hospital discharge.

2.2.1 Home-based exercise training program

The intervention included a 10-wk semi-supervised HBET program aiming to improve her physical fitness and conditioning. It comprised three weekly sessions including aerobic, strengthening and flexibility exercises. One weekly session was supervised by a trained researcher through live videoconference calls. The remaining two weekly sessions were monitored through text and/or voice messaging. The first four training sessions were directly supervised by the same researcher through live videoconference, aiming patient's familiarization to the training protocol. In addition, supplementary materials containing exercise cards and videos, and educative information about how to rate her effort were provided (Supplementary File 3). She was also advised to be aware of eventual symptoms (e.g., chest pain, dizziness, or others) and to immediately communicate the research team upon any symptoms for proper guidance.

Aerobic training sessions initially consisted of two bouts of 10-min/day of walk at “very light” to “fairly light” (9-11 Borg Scale) intensity (Supplementary File 4, Table S2). Over the following weeks, she gradually progressed towards a single 45-min bout of walking at “somewhat hard” to “hard” (14-16 Borg Scale) intensity. Additionally, she was advised to freely walk on non-training days.

Strengthening exercises comprised exercises for the major muscle groups. Exercise selection was based on baseline PCFS score, which was reassessed every two weeks as a training progression tool. A set of six strengthening exercises was designed according to each PCFS grade (Supplementary File 5, Table S3). She was carefully advised on how to use common household materials (i.e., water bottle, groceries packages, chair, bucket, and others) as exercise implements. Strengthening training sessions comprised 3-4 sets per exercise of 10-15 repetitions, and a self-suggested recovery interval between sets was adopted. Strength training intensity was also based on her perceived exertion and was initially set as “very light” to “fairly light” (9-11 Borg Scale) intensity and progressed towards a “somewhat hard” to “hard” (14-16 Borg Scale) intensity over the weeks of intervention (Supplementary File 4, Table S2). Active stretching exercises for the major muscle groups were prescribed as a cool-down.

2.2.2 Cardiopulmonary exercise test

Assessments were performed before and after 10 wks of HBET. A symptom-limited maximal cardiopulmonary exercise test (CPET) was carried out on treadmill (Centurion model 300; Micromed, Brazil) using a modified Balke protocol[15] at a controlled room temperature (21-23°C). Peak oxygen consumption (VO_{2peak}), oxygen consumption at ventilatory anaerobic threshold (VO_{2VAT}), oxygen uptake efficiency slope (OUES), heart rate-oxygen consumption relationship (HR/VO_2 slope), ventilatory equivalent (V_E), ventilatory reserve (V_E/MVV), the lowest V_E/VCO_2 ratio, and peak respiratory exchange ratio (RER_{peak}) were measured breath-by-breath through a computerized system (MetaLyzer 3B; Cortex, Germany).

2.2.3 Muscle strength and functionality assessment

Strength performance and functionality were assessed through handgrip test, 30-second Sit-to-Stand test (30-STS), and Timed-Up-&-Go test (TUG) as previously described.[16-18] Post-COVID Functional Status (PCFS) was evaluated through specific scale.[19]

2.2.4 Persistent symptoms and fatigue severity assessment

Self-reported persistent symptoms were also assessed through structured anamnesis. Fatigue severity was evaluated through a specific scale.[20]

2.2.5 Laboratory assessments

Blood samples were collected after a 12-h fast and analyzed for complete blood count, lipid profile, glucose metabolism, skeletal muscle damage, cardiac muscle damage, and systemic inflammation.

Results

3.1 Cardiopulmonary exercise test

At baseline, the patient presented with a severe impairment in cardiorespiratory functional capacity (<50% age predicted VO_{2peak}). After 10 wks of HBET, the patient showed remarkable improvements in aerobic fitness and oxygen uptake efficiency. VO_{2peak} increased from 10.61 to 15.48 $mL \cdot kg^{-1} \cdot min^{-1}$ (Δ: 45.9%), VO_{2VAT} increased from 7.83 to 9.64 $mL \cdot kg^{-1} \cdot min^{-1}$ (Δ: 23.1%), OUES increased from 1.0 to 1.3 $L \cdot min^{-1}$ (Δ: 30.1%), HR/VO_2 decreased from 92 to 52 $bpm \cdot L^{-1}$ (Δ: -43.5%), V_E increased from 32.5 to 45.9 $L \cdot min^{-1}$ (Δ: 41.2%), ventilatory reserve (V_E/MVV) increased from 41 to 63% (Δ: 53.7%), lowest V_E/VCO_2 ratio decreased from 35.4 to 32.9 $L \cdot min^{-1}$ (Δ: -7.1%), respiratory exchange ratio (RER_{peak}) increased from 1.01 to 1.07 (Δ: 5.9%), endurance time increased from 330 to 510 seconds (Δ: 56.6%), and isotime exertional dyspnea was reduced (Figures 1A-J).

3.2 Muscle strength and functionality assessments

Handgrip strength increased from 22 to 27 kg (Δ: 22.7%), 30-STS performance increased from 14 to 16 repetitions (Δ: 14.3%), and TUG performance improved from 8,25 to 7,01 seconds (Δ: -15.0%) (Figure 2A-C). Similarly, PCFS improved from 4 (severe functional impairment) to 2 (slight functional impairment).

3.3 Persistent symptoms and fatigue severity assessments

At baseline, self-reported persistent symptoms included fatigue, breathlessness, weakness, myalgia, joint pain, paresthesia, dizziness, anxiety and depression (Table 1). Only anxiety remained after the intervention. In addition, fatigue severity decreased from baseline to follow-up (pre-intervention: 4.0 vs. post-intervention: 2.7) (Figure 3).

3.4 Laboratory assessments

Hemogram was within normal limits at all times, except for the platelets that were slightly increased at hospital discharge. Lipid profile, glucose metabolism and systemic inflammation biomarkers were slightly altered at baseline; all were within normal limits after the intervention (Table 1).

3.5 Adverse events

There were no adverse events potentially associated with the intervention.

Discussion

To the best of our knowledge, this is the first report showing that exercise training may confer clinical benefits in a survivor patient from critical COVID-19 illness. Our data showed that an individualized HBET program was safe and associated with improvements in cardiorespiratory functional capacity, skeletal muscle strength and functionality, fatigue, and most of the persistent symptoms. These findings point to the potential utility of exercise as an adjuvant therapeutic tool in the recovery of post-COVID patients, which needs to be confirmed by further controlled trials.

The patient showed a severe impairment in cardiorespiratory functional capacity at baseline, which was paralleled by physical exercise intolerance and exertion dyspnea. Our results are in accordance with previous studies which demonstrated severe deconditioning at hospital discharge and months after it.[4,5] In fact, hospitalized COVID-19 patients may experience severe deconditioning due to disease pathophysiology, treatment-related drugs' toxicity, and prolonged bed rest. Such impairment could be associated with both central (i.e., cardiac and pulmonary) and peripheral factors (i.e., skeletal muscle oxidative capacity).[21-24] Unpublished data from our group also indicate substantial muscle atrophy in COVID-19 patients, which is probably accompanied by detrimental oxidative metabolism. The patient showed lower ventilatory efficiency as observed by an increase in lowest V_E/VCO_2 ratio and hyperkinetic circulatory response to exercise as noted by steeper HR/VO_2 slope. Additionally, our data demonstrated lower values for OUES suggesting an impairment in oxygen uptake efficiency during exercise.

The most striking finding of the present case study was the potential benefits associated with the HBET program in improving both cardiorespiratory functional capacity and ventilatory efficiency in the survivor of critical COVID-19 illness. Additionally, a remarkable 43.5% reduction in HR/VO_2 slope was observed in comparison to baseline, which indicates a decrease in tachycardia for a given oxygen consumption. Collectively, these findings suggest an increase in both stroke volume and/or oxygen extraction by peripheral tissues.[15,25]

Functionality is closely related to independence, performance of activities of daily living, and quality of life.[26-28] PCFS score at the baseline indicated severe functional limitations. Interestingly, all functional tests scores were within the expected range for the patient's age and sex despite the disease, suggesting that the observed physical limitations may be mostly related to cardiorespiratory deconditioning. Nevertheless, in addition to the improvements in both oxygen uptake capacity and dyspnea, the enhancement in lower-limb strength and functionality may have also contributed to a reduction in PCFS score following the intervention.

Fatigue is one of the most limiting symptoms and the most common persistent symptom reported by COVID-19 survivors,[29] which may last for several months after disease onset.[30] Importantly, fatigue and all of the other persistent symptoms, except anxiety, were resolved after the intervention.

The strengths of this study involve the longitudinal assessment of exercise as a novel adjuvant therapeutic tool in a survivor of critical COVID-19 illness, and the use of valid and comprehensive measures of physical capacity and functionality. The major limitation is inherent to the nature of the study, which provides novel insights into the potential role of exercise in post-COVID-19 but does not allow firm conclusions on safety and efficacy of the intervention in this condition, since only a single patient was examined. It cannot be rule out that the changes across time reported in this study may be resultant from the natural course of the disease and/or individual factors that have not been assessed.

Conclusions

This study provides preliminary evidence that an exercise training program may be safe and potentially effective in recovering cardiorespiratory functional capacity, functionality, fatigue, exertional dyspnea, and other persistent symptoms in COVID-19 survivors. While caution should be exercised in interpreting the present findings in light of the limitations inherent to a case study, the data reported herein are encouraging and may help pave the way for randomized controlled trials testing the safety, efficacy and feasibility of exercise interventions as an adjuvant therapeutic tool in post-COVID-19 syndrome.

Declarations

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Authors' contributions

IL participated in the design of the study, contributed to data collection, data analysis, and contributed to interpretation of results; DMLP contributed to data collection, data analysis, and interpretation of results; KFG participated in the design of the study; GNOJ contributed to data collection; DCOA, participated in the design of the study; BG and HR participated in the design of the study and contributed to interpretation of results. All authors contributed to the manuscript writing. All authors have read and approved the final version of the manuscript and agree with the order of presentation of the authors.

Competing interests

The authors declare that they have no competing interests. The results of the present study are presented clearly, honestly, and without fabrication, falsification, or inappropriate data manipulation.

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Tables

Table 1.
Patient’s physical, clinical, and laboratorial parameters.

	T1	T2	T3
Anthropometric Measurements			
BMI, kg/m^2	27.1	28.0	28.0
Height, cm	157	-	-
Weight, kg	66.0	69.0	69.1
Clinical Measurements			
Systolic Blood Pressure, mmHg	146	135	130
Diastolic Blood Pressure, mmHg	90	90	87
Mean Arterial Pressure, mmHg	109	105	101
Heart Rate, bpm	98	89	85
SpO_2, %	94	99	99
Biochemical Markers			
Erythrocytes, 10^{12}/L	3.91	4.56	4.67
Hematocrit, %	36.4	41.7	42.9
Hemoglobin concentration, g/dL	12.7	14.4	14.7
MCV, fL	94.8	92.1	91.9
MCHC, g/dL	34.9	34.3	34.3
RDW, %	13.0	14.3	12.5
White blood cell count, $\times 10^9$/L	7.09	6.09	6.29
Neutrophil count, $\times 10^9$/L	2.69	3.27	3.01
Lymphocyte count, $\times 10^9$/L	3.64	2.18	2.43
Monocyte count, $\times 10^9$/L	0.49	0.40	0.54
Platelet count, $\times 10^9$/L	466	379	375
Blood glucose, mmol/L	5.7	6.3	5.3
HbA1c, %	NA	6.2	5.9
Total cholesterol, mg/dL	NA	150	126
HDL-c, mg/dL	NA	48	44
LDL-c, mg/dL	NA	74	61
Triglycerides, mg/dL	NA	185	131
Creatine phosphokinase, U/L	NA	44	67
Troponin-T, pg/mL	NA	8	6
C-reactive protein, mg/L	1.6	5.9	1.8
Persistent symptoms			
Fatigue	-	Yes	No
Breathlessness	-	Yes	No
Weakness	-	Yes	No
Myalgia	-	Yes	No
Joint pain	-	Yes	No
Paresthesia	-	Yes	No
Dizziness	-	Yes	No
Anxiety	-	Yes	Yes
Depression	-	Yes	No

BMI: body mass index; HbA1c: glycated hemoglobin; HDL-c: high density lipoprotein cholesterol; LDL-c: low density lipoprotein cholesterol; MCHC: mean cell hemoglobin concentration; MCV: mean corpuscular volume; NA: not available; RDW: red blood cell distribution width; SpO_2: peripheral oxygen saturation; T1: at hospital discharge; T2: at baseline (pre-intervention); T3: post-intervention.

Figures

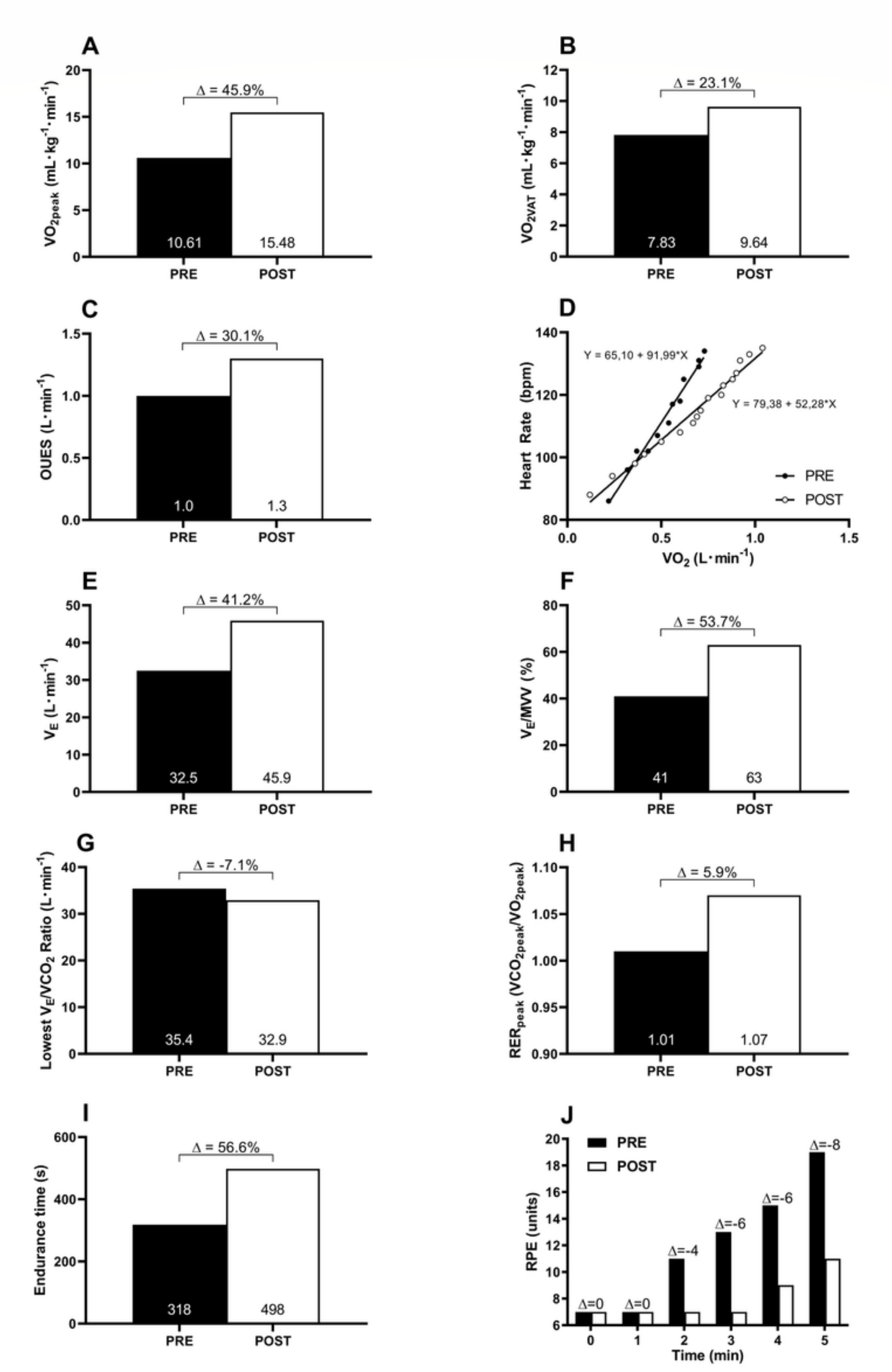

Figure 1

Cardiorespiratory functional capacity at baseline (PRE) and after 10-wk of HBET (POST). A: peak oxygen consumption (VO2peak); B: oxygen consumption at ventilatory anaerobic threshold (VO2VAT); C: oxygen uptake efficiency slope (OUES); D: heart rate-oxygen consumption relationship (HR/VO2 slope); E:

ventilatory equivalente (VE); F: ventilatory reserve (VE/MVV); G: the lowest VE/VCO2 ratio; H: peak respiratory exchange ratio (RERpeak); I: endurance time; J: isotime comparison of rate of perceived exertion (RPE) during incremental cardiopulmonary exercise test.

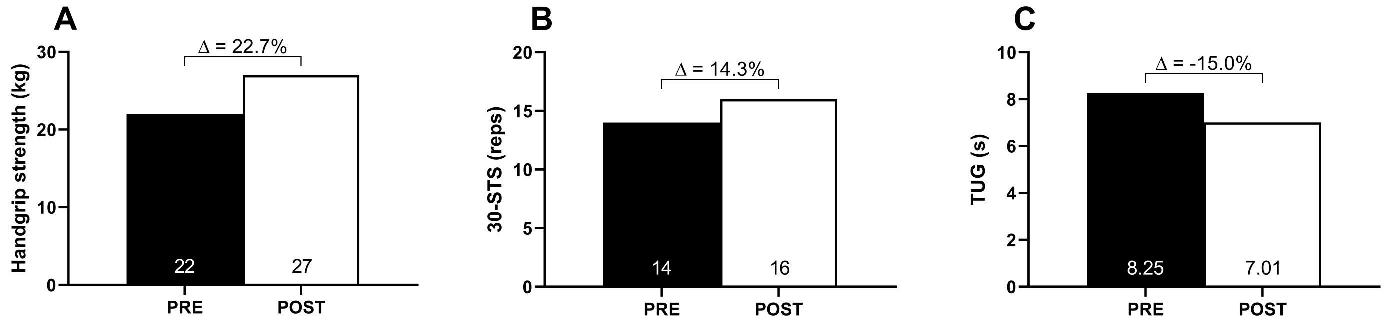

Figure 2

Muscle strength and functionality at baseline (PRE) and after 10-wk of HBET (POST). A: handgrip strength; B: 30-second sit-to-stand (30-STS); C: timed-up-and-go (TUG).

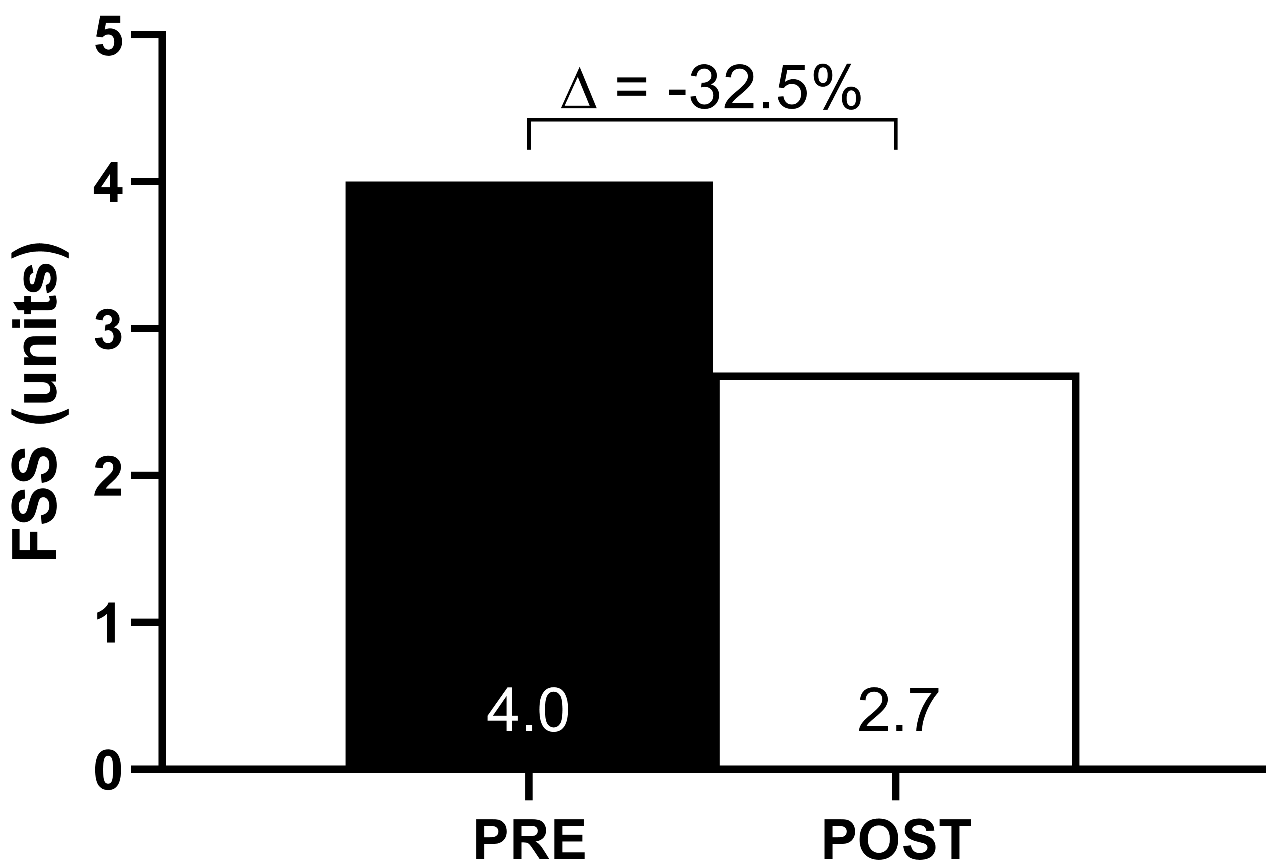

Figure 3

Fatigue severty scale (FSS) score at baseline (PRE) and after 10-wk of HBET (POST).

Supplementary Files

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