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Original

Mid-term health sequelae in Brazilian people recovered from COVID-19 according to gravity: The AEROBICOVID study

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ABSTRACT

The aims were to identify the symptoms and comorbidities predictive for severe illness and analyse the mild-term health sequelae in Brazilian recovered from COVID-19. Eighty-four participants were divided into mild (n = 16), moderate (n = 51), severe (n = 9) or critical (n = 8) gravity. A standardized assessment included: anamnesis to identify the symptoms and comorbidities; and cardiorespiratory system, body composition, haematological and immunological indicators, and physical fitness to analyze the mild-term health sequelae. Participants with higher gravity presented fever, fatigue and dyspnoea. Diabetes (p = 0.003), hypertension (p < 0.001) and metabolic syndrome (p = 0.010) were the comorbidities significantly associated for severe or critical illness. People with critical gravity reported a significant higher waist/hip ratio and level of visceral fat compared with mild and moderate severity. Severe and critical participants reported worst results in agility and balance test compared with mild (p = 0.015; p = < 0.001, respectively) and moderate (p = 0.014; p = < 0.001, respectively) gravity. Fever, fatigue and dyspnoea; and diabetes, hypertension and metabolic syndrome were the symptoms and comorbidities associated with higher gravity. Mild-term, altered values of body composition, physical functioning, enhanced glucose, reticulocytes, and lymphocytes levels were reported.

Keywords: COVID-19; Follow up; Health; Post-discharge.

Secuelas de salud a medio plazo en brasileños recuperados de COVID-19 según gravedad: estudio AEROBICOVID

RESUMEN

Los objetivos fueron identificar los síntomas y comorbilidades predictivas de enfermedad grave y analizar las secuelas de salud a corto plazo en brasileños recuperados de la COVID-19. Ochenta y cuatro participantes se dividieron en gravedad leve (n = 16), moderada (n = 51), grave (n = 9) o crítica (n = 8). Una evaluación estandarizada incluyó: anamnesis para identificar los síntomas y comorbilidades; y sistema cardiorrespiratorio, composición corporal, indicadores hematológicos e inmunológicos y condición física para analizar las secuelas de salud a medio plazo. Los participantes con mayor gravedad presentaron fiebre, fatiga y disnea. Diabetes (p = 0,003), hipertensión (p < 0,001) y síndrome metabólico (p = 0,010) fueron las comorbilidades asociadas significativamente a enfermedad grave o crítica. Las personas con gravedad crítica informaron una relación cintura/cadera y un nivel de grasa visceral significativamente mayores en comparación con las de gravedad leve y moderada. Los participantes severos y críticos reportaron peores resultados en las pruebas de agilidad y equilibrio en

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comparación con la gravedad leve (p = 0,015; p = < 0,001, respectivamente) y moderada (p = 0,014; p = < 0,001, respectivamente). Fiebre, fatiga y disnea; y diabetes, hipertensión y síndrome metabólico fueron los síntomas y comorbilidades asociados a mayor gravedad. Se informaron valores alterados a corto plazo de la composición corporal, el funcionamiento físico y niveles elevados de glucosa, reticulocitos y linfocitos.

Palabras clave: COVID-19; Seguimiento; Salud; Después del alta.

Sequelas de saúde de médio prazo em brasileiros recuperados de COVID-19 de acordo com a gravidade: O estudo AEROBICOVID

RESUMO

Os objetivos foram identificar os sintomas e comorbidades preditivos de doença grave e analisar as sequelas leves de saúde em brasileiros recuperados da COVID-19. Oitenta e quatro participantes foram divididos em gravidade leve (n = 16), moderada (n = 51), grave (n = 9) ou crítica (n = 8). A avaliação padronizada incluiu: anamnese para identificação dos sintomas e comorbidades; e sistema cardiorrespiratório, composição corporal, indicadores hematológicos e imunológicos e aptidão física para analisar as sequelas de saúde de médio prazo. Os participantes com maior gravidade apresentaram febre, fadiga e dispneia. Diabetes (p = 0,003), hipertensão (p < 0,001) e síndrome metabólica (p = 0,010) foram as comorbidades significativamente associadas para doença grave ou crítica. Pessoas com gravidade crítica relataram uma relação cintura/quadril e nível de gordura visceral significativamente mais elevados em comparação com gravidade leve e moderada. Participantes graves e críticos relataram piores resultados nos testes de agilidade e equilíbrio em comparação com gravidade leve (p = 0,015; p = < 0,001, respectivamente) e moderada (p = 0,014; p = < 0,001, respectivamente). Febre, fadiga e dispneia; e diabetes, hipertensão e síndrome metabólica foram os sintomas e comorbidades associados à maior gravidade. Foram relatados valores alterados de leve duração da composição corporal, funcionamento físico, aumento dos níveis de glicose, reticulócitos e linfócitos.

Palavras-chave: COVID-19; Seguir; Saúde; Pós-alta.

Introduction

In December 2019, a series of pneumonia cases of unknown cause emerged in China, whose deep sequencing analysis indicated a novel coronavirus, later named by the World Health Organization (WHO) as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) to cause Coronavirus disease 2019 (COVID-19), a public health emergency of international concern ([1]). Globally, there have been over 500 million confirmed cases, including more than 6 million reported deaths due to COVID-19 ([2]). Brazil is one of the most affected countries (the second country with the most deaths and the third with the most cases worldwide ([3]), with a current projection scenario of over 800,000 total COVID-19 deaths in 2022 ([4]).

A growing body of literature was available on common symptoms and treatments of the acute phase of the disease, such as fever, dry cough, dyspnoea, gastrointestinal and musculoskeletal symptoms([5]). However, the new strain of coronavirus is spreading far more quickly and has higher contagiousness ([6]). Thus, defining the risk factors for severe COVID-19 infections is essential ([7]) to pay more attention to the susceptible population ([8]). Besides, people with comorbidities, such as cardiovascular disease and hypertension, may be more susceptible to severe disease ([9]). A report of the WHO in China indicated that the people at highest risk for severe COVID-19 and death might be patients with underlying conditions such as hypertension, diabetes, cardiovascular disease, chronic respiratory disease, and cancer ([10]). Therefore, early identification of individuals could help the public health system - protect vulnerable people and prevent the spread of infection. In this sense, previous studies which identifying the symptoms and comorbidities related to COVID-19 severity indicated that cough and fever ([11],[12]) were the most common symptoms, but dyspnoea may discriminate between mild or severe illness([9]).

Another relevant issue refers to the ongoing symptoms or long-term health sequelae after overcoming the disease ([13]). The vast majority of recovered people from COVID-19 are not systematically assessed for their recovery and need specific rehabilitation programs ([14]). After viral infection, several damages could occur in multiple body systems([15]). COVID-19 survivors could show a high burden of cardiac, renal, gastrointestinal, nervous, endocrine, and musculoskeletal complications, a multisystem illness ([16]). Although the exact mild and long-term health consequences are not yet largely determined, it is hypothesized that a significant number of patients will suffer from decreased physical capacity, loss of muscle mass, fatigue, and, ultimately, a poor health status ([17]). In line with these arguments, a reduced physical capacity was observed post-COVID-19 compared with healthy adults ([17],[18]). In addition to reduced functional capacity, previous studies reported that, at follow-up periods of 1 and 3 months post-COVID-19, both hospitalised and non-hospitalised patients had acquired weakness and acute sarcopenia ([19],[20]), associated with poor functional capacity and long-term disability ([21]).

Despite the need for rehabilitation care for recovered COVID-19 patients, it needs to be specific delivered by specialists and managed according to the needs of the individuals participating in each program ([14]). Following this important argument, this study represents an initial systematic assessment of recovered Brazilian patients of COVID-19 with different gravity before completing a rehabilitation program based on exercise. Thus, the study aims are: firstly, to identify the symptoms and comorbidities predictive for severe illness in Brazilian people with COVID-19; and secondly, to analyse the mild-term health sequelae in Brazilian people recovered from COVID-19 according to gravity.

Material and Methods

Design

The prospective observational study took place in a local community of Ribeirao Preto, in the Sao Paulo state of Brazil. The data presented in this study is the baseline evaluation from AEROBICOVID project that proposed physical training and hypoxia exposure intervention. Participants were enrolled in the following inclusion criteria: 1) age between 30 and 69 years old; 2) convalescent

from COVID-19 (positive diagnosis); 3) mild to severe symptoms; 4) approximately 30 days since recovery from clinical signs or medical discharge (if they had been hospitalised). In addition, the following exclusion criteria were established: 1) to have an exposure to high-altitude places > 1,500 m in the previous three months; 2) presenting significant physical limitations to be assessed or to join the intervention; 3) presenting acute or chronic clinical illnesses without medical supervision; having anaemia; using immunosuppressive drugs; to be pregnant; hormone replacement; smokers or excessive use of alcohol or drugs.

Participants

Eighty-four participants were included and divided into four groups, based on National Institutes of Health (NIH) of United States of America criteria for COVID-19 severity ([22,23]): mild (n = 16), who have any symptoms of COVID-19, such as fever, cough, etc., but do not have shortness of breath or dyspnoea; moderate (n = 51), who have any symptoms of COVID-19 and have shortness of breath or dyspnoea; severe (n = 9), who have any symptoms of COVID-19 and need hospitalisation, but not intensive care; or critical (n = 8), who have any symptoms of COVID-19 and need hospitalisation and intensive care. The present study was approved by the research ethic committees of the School of Physical Education and Sport of Ribeirao Preto – University of Sao Paulo (USP) and the Faculty of Pharmaceutical Sciences of Ribeirao Preto – USP (CAAE: 33783620.6.0000.5659, and CAAE: 33783620.6.3001.5403, respectively). Activities started after signing the free and informed consent term presented by the study coordinator. All care was taken for the safety of the participants and the work team. Data were added to a confidential dataset, and an alphanumeric code was assigned to each participant.

Procedure

A standardized health assessment included questionnaires, physical measurements, collected blood samples, and multidisciplinary consultations. These data are related to the participants' baseline evaluation of the AEROBICOVID project, a more extensive project with other evaluations after an intervention of hypoxic training. The experimental protocol has been published elsewhere ([24]). A register of anamnesis was used to identify the symptoms and comorbidities predictive. Furthermore, the cardiorespiratory system, body composition, haematological and immunological indicators, and physical fitness were assessed to analyze the mild-term health sequelae.

Anamnesis: sociodemographic data, general and specific health status (COVID-19 symptoms) related to lifestyle and information on comorbidity were collected through questionnaires. The definition of metabolic syndrome used for this study is according to the International Diabetes Federation (IDF): central obesity (waist circumference ≥ 90 cm for men or ≥ 80 cm for women) plus two of the following factors: triglyceride levels ≥ 150 mg/dl or specific treatment for this lipid abnormality; HDL cholesterol < 40 mg/dl in men, < 50 mg/dl in women or specific treatment for this lipid abnormality; systolic blood pressure (SBP) ≥ 130 mmHg, diastolic blood pressure (DBP) ≥ 85 mmHg or treatment for arterial hypertension; and fasting plasma glucose ≥ 100 mg/dl or diagnosis of type 2 diabetes mellitus ([25]).

Anthropometric and body composition assessment: height and body mass were assessed following standard procedures. The body mass index (BMI) was calculated based on height and body weight. A constant tension tape with an accuracy of 0.1 cm was used to determine the waist and hip circumferences. The waist-to-hip ratio was calculated by dividing the waist circumference by the hip circumference (both in cm). Body composition variables such as visceral fat (g), muscle mass (%) and fat mass (%) were obtained using dual-energy X-ray absorptiometry (iDXA - GE Lunar – DPX-NT).

Physical fitness: lower limb strength was evaluated through sit and stand-up test ([26]). The agility and dynamic balance were also evaluated ([27]).

Haematological indicators: glucose, total cholesterol, LDL-c, HDL-c, and triglycerides were analyzed from blood samples, collected by specialized professionals, after fasting for 12 hours and storage of pre-analysis samples at -80ºC. The analyses were performed using the serum at the Clinical Analysis Laboratory of the Faculty of Pharmaceutical Sciences of Ribeirao Preto of the University of Sao Paulo (Brazil), utilising an enzymatic analysis kit (Wiener Lab, Rosario, Argentina) on an automatic device (CT 600i; Wiener Lab, Rosario, Argentina). Additionally, a complete blood cell count of red blood cells, white blood cells, lymphocytes, neutrophils, platelets and lactate dehydrogenase were measured using the protocol described above.

Immunological indicators: standardized methods were used to measure cytokines IL-6, IL-8, IL-10 and TNF-α by ELISA kits (R&D Systems, Billings, EUA). Reactions were performed on 96-well ELISA plates (Ultra-High Binding EIA Plates; Corning, Corning, NY, USA). The absorbance was read on a microplate reader (μQuant; BioTek Instruments Inc., Winooski, VT, USA) at a wavelength of 450nm. The cytokine concentration in each sample was estimated by interpolation of a standard curve by a four-parameter curve-fitting program. Sensitivities were >12.5pg/mL.

Statistical Analysis

Descriptive statistics were calculated for sociodemographic characteristics, symptoms and comorbidities, and physical function and health variables. Cut-off of the evaluated indicators were reported ([28–32]). Using Fisher's exact test, data analysis was performed to verify the statistical association between categorical variables symptoms and comorbidities with the COVID-19 gravity. Comparison of continuous variables between groups was analyzed using analysis of variance adjusted for potential confounding variables identified in descriptive analysis, such as body mass index, age and sex ([33]), all criteria and assumptions were checked. The plots were run from R (version 4.0) using the ggplot2 package. The significance level was 5%, and the program used was SAS version 9.2, using the PROC GLM, PROC MEANS and PROC TABLE (SAS/STAT® User's Guide. Version 9.0, 2002).

Results

Baseline characteristics for groups are presented in Table 1 (Supl.). Significant differences were observed for physical activity level, with a lower level for critical severity (p = 0.019) compared with moderate.

Symptoms and comorbidities

Association between COVID-19 gravity and common symptoms are presented in Figures 1 and 2. Fisher's exact test showed an association between fever (p = 0.007), cough (p = 0.003), loss of smell (p = 0.024), sore throat (p = 0.016), headache (p = 0.023), body pain (p = 0.003), fatigue (p = 0.002) and dyspnoea (p < 0.001). Predominately, participants with higher gravity presented fever (87.5% critical and 77.8% severe), fatigue (100% severe and critical) and dyspnoea (100% moderate, severe and critical).

Association between COVID-19 severity and comorbidities are presented in Figure 2. Diabetes (p = 0.003), hypertension (p < 0.001) and metabolic syndrome (p = 0.010) were the comorbidities

Table S1. Characterization of the participants (n = 84).

	Mild (n = 16)	Moderate (n = 51)	Severe (n = 9)	Critical (n = 8)	p- values
Age	46.6 (12.1)	47.8 (9.8)	50.3 (7.1)	54.3 (5.2)	NS
Total physical activity /week (min)	509.7 (406.8)	410.9 (418.3)	475.6 (506.6)	142.5 (200.1)[b]	0.019
Race[a]					0.484
White	12 (75.0)	30 (58.8)	6 (66.7)	5 (62.5)	
Parda	0 (0.0)	5 (9.8)	2 (22.2)	0 (0.0)	
Black	4 (25.0)	16 (31.2)	1 (11.11)	3 (37.5)	
Sex[a]					0.479
Female	11 (68.7)	34 (66.7)	4 (44.4)	4 (50.0)	
Male	5 (31.2)	17 (33.3)	5 (55.6)	4 (50.0)	
Medication					0.110
Hypertension	1 (11.1)	6 (19.4)	2 (28.6)	1 (12.5)	
Diabetes	2 (22.5)	2 (6.5)	0 (0)	0 (0)	
Depression	1 (11.1)	5 (16.1)	0 (0)	1 (12.5)	
Hypertension and diabetes	0 (0)	4 (13)	3 (42.9)	5 (62.5)	
Others	5 (55.6)	13 (41.9)	2 (28.6)	1 (12.5)	

Values are mean (standard deviation) and p values of analysis of variance (ANOVA).**a** Values are expressed as N (%) and p values of Fisher's exact test.**b** Significant differences versus mild.

significantly associated for severe or critical symptoms compared with mild severity. Asthma was not significantly associated with COVID-19 gravity.

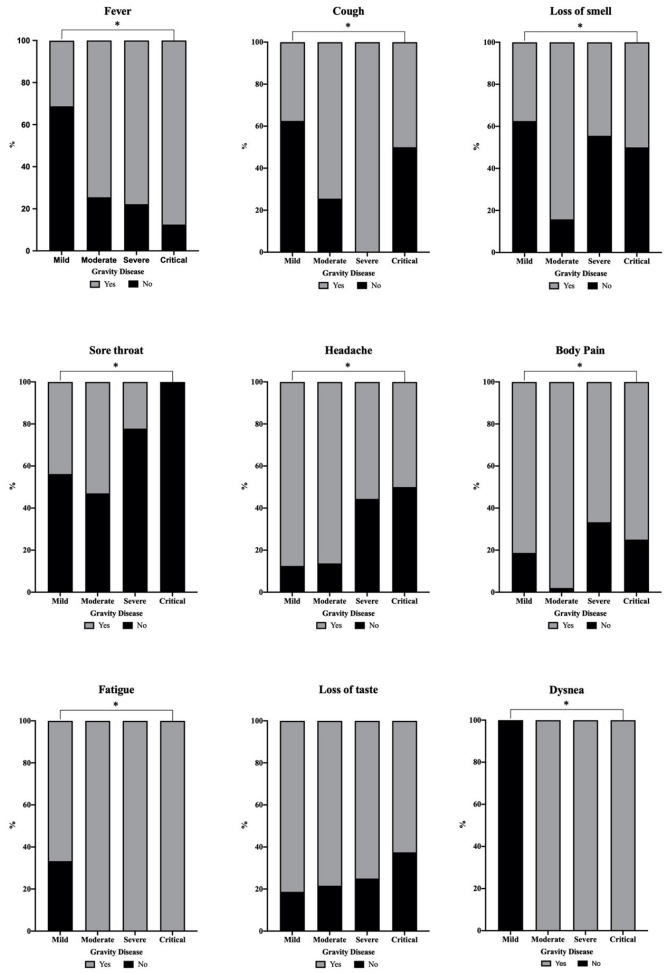

Figure 1. Association between COVID-19 gravity and common symptoms

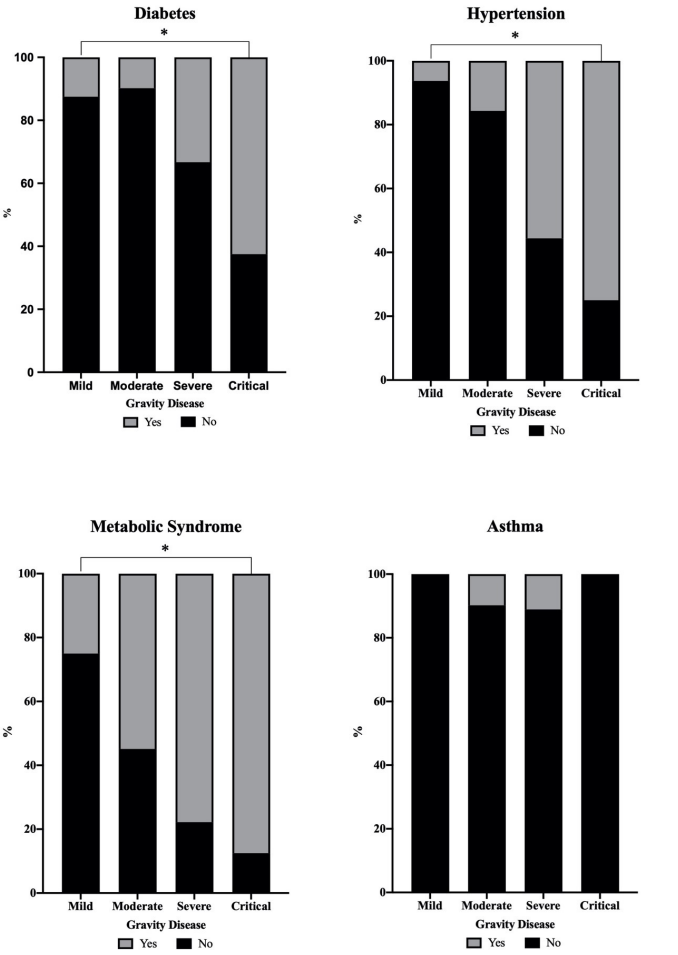

Figure 2. Association between COVID-19 gravity and different diseases

Mild-term health sequelae

Table 2 (Supl.) provides outcomes on Body Composition, Physical Functioning and Cardiorespiratory status one month after

Table 2. Body Composition, Physical Functioning and Cardiorespiratory status one month after recovery from COVID-19 in Brazilian participants.

	Mild (n = 16)	Moderate (n = 51)	Severe (n = 9)	Critical (n = 8)	Cut-off
BODY COMPOSITION					
W/H ratio	0.85 (0.12)	0.89 (0.07)	0.93 (0.08)	**0.99 (0.08)**[a,b]	0.85- 0.90
Visceral fat (g)	968.8 (797.7)	1233.8 (786.7)	**1855.7 (636.7)**[a,b]	1889.6 (507.0)	1086
Body mass index	27.9 (4.7)	29.9 (4.8)	29.1 (4.2)	34.5 (6.0)[a]	30
Fat mass (%)	39 (6)	40 (8)	40 (8)	42 (10)	21.9
PHYSICAL FUNCTIONING					
Sit and stand up (reps)	13.5 (27)	12.8 (4.0)	12.1 (4.2)	9.9 (1.1)	12 - 16
Agility and balance (sec)	25.2 (4.0)	26.7 (5.3)	**30.6 (8.7)**[a,b]	**36.7 (8.3)**[a,b]	12.7
CARDIORESPIRATORY					
Glucose (mg/dL)	96.3 (18.1)	98.7 (31.2)	115.1 (48.9)	**128.3 (38.3)**[a,b]	70-110
Total Cholesterol (mg/dL)	197.6 (43.1)	198.0 (33.2)	192.7 (43.2)	194.4 (45.5)	200
Triglycerides (mg/dL)	99.1 (56.0)	132.8 (89.1)	123.4 (38.3)	189.1 (38.7)	150
LDL – c (mg/dL)	124.4 (38.7)	126.3 (31.7)	124.0 (37.5)	115.5 (39.5)	129
HDL – c (mg/dL)	52.9 (11.1)	46.4 (12.5)	44.3 (11.2)	41.1 (12.7)	60

Values are mean (standard deviation). LDL – c: low-density lipoprotein cholesterol; HDL – c: high-density lipoprotein cholesterol; W/H ratio: waist-to-hip ratio. 1-way analysis of variance adjusted for confounding variables body mass index, age, and sex.**a** p < 0.05 versus mild**b** p < 0.05 versus moderate. Significant are shown in bold.

recovery from COVID-19. Although all the groups showed an increased fat mass percentage above cut-off for healthy adults, people with critical symptoms reported a significant higher waist/hip ratio compared with mild (p = 0.017) and moderate severity (p = 0.049). Moderate and especially severe and critical people, showed a level of visceral fat highly above of cut-off for Brazilian adults. All of groups presented worst performance in agility and balance compared with cut off, showing severe and critical people more time compared with mild (p = 0.015; p = < 0.001, respectively) and moderate (p = 0.014; p = < 0.001, respectively) gravity. According to haematological indicators, critical gravity reported a significant higher level of glucose compared with mild (p = 0.037) and moderate COVID-19 (p = 0.046). In addition, mild, moderate, severe and critical people showed anomalous values of HDL-cholesterol compared with cut-off for healthy adults.

Figure 3 shows haematological status one month after recovery from COVID-19. The critical group presented a higher level of reticulocytes in comparison with mild (p = 0.037) and moderate COVID-19 (p = 0.034), and over the 84 uL (recommended cut-off). Also, the critical group presented a higher level of lymphocytes in comparison with mild (p = 0.043) and moderate (p = 0.015). Both groups were within normal values (< 4000 cm^3).

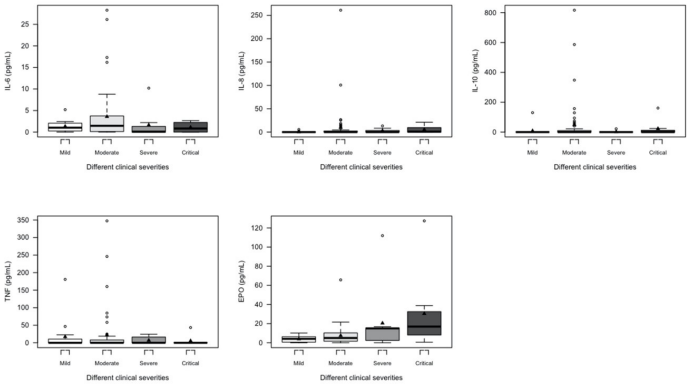

Figure 3. Haematological status one month after recovery from COVID19

The biochemical status is shown in Figure 4. Glucose levels were higher in the critical group compared to the moderate (p=0.046) and mild (p=0.037) groups. GOT concentration showed a difference between critical and moderate groups (p=0.042). Moreover, GPT concentration is lower in the critical group compared with severe (p=0.007) and moderate (p= 0.047) groups and higher when mild and severe groups are compared (p = 0.009).

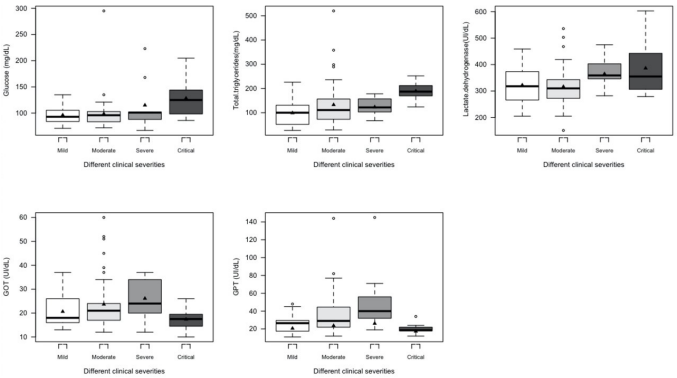

Figure 4. Biochemical Status one month after recovery from COVID-19

The level of inflammatory indicators and EPO values are shown in figure 5. No significant differences were found in the inflammatory cytokines. The severe and critical groups reported above the cut-off level of erythropoietin (>18.5 uL) and significantly different compared to mild (p = 0.031; p = 0.004, respectively) and moderate gravity (p = 0.043; p = 0.004; respectively).

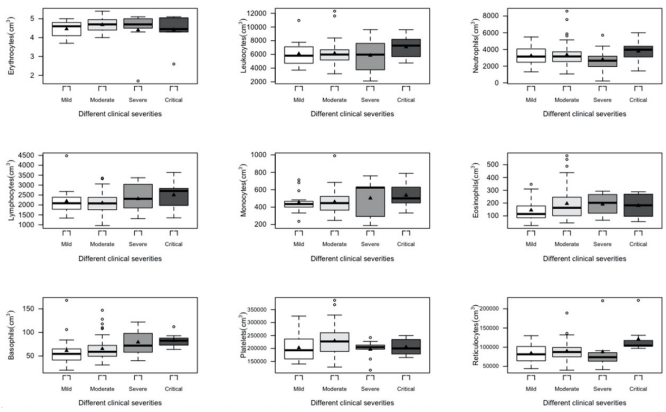

Figure 5. Level of inflammatory indicators and EPO values

Discussion

The present study identified the symptoms and comorbidities predictive for severe COVID-19, and the mild-term health sequelae in Brazilian participants recovering from COVID-19 according to severity. On this way, the most prevalent symptoms were fever and fatigue. Besides, diabetes, hypertension and metabolic syndrome were the comorbidities significantly associated with moderate, severe or critical gravity compared with mild severity. Furthermore, participants with severe and critical gravity showed altered values of body composition and physical functioning; enhanced glucose and haematological level.

Symptoms and comorbidities

Consistent with previous studies, AEROBICOVID participants presented fever, fatigue and dyspnoea as common symptoms of severe COVID-19 ([9,12]). The prevalence of dyspnoea was found to be relatively high in the most severe patients ([9]), a common characteristic of patients with moderate, severe and critical COVID-19. In fact, to have shortness of breath has been proposed by NIH of the United States of America as criteria to consider a higher gravity of disease ([22,23]). In survival analyses, comorbidities have been associated with COVID-19 gravity ([34]). According to previous studies, metabolic diseases such as diabetes, hypertension, or metabolic syndrome were the most common comorbidities associated with a higher gravity of the disease ([35]). On this way, patients with these comorbidities may represent a high-risk population for COVID-19. This population should be prioritized and taken into account by the public health system ([34]), as they are more susceptible to severe infection.

Mild-term health sequelae

Critical and severe infection have been linked to an overstated inflammatory process denominated “cytokine storm” ([36]) a coordinated innate immune response that acts on the first line of defence against COVID-19 ([37]). A great deal of evidence suggests that an acute inflammatory response is likely associated with COVID-19 severity and clinical outcomes ([38–40]). Increased cytokine levels have been found in COVID-19 participants during the acute infection phase ([16,41]), and are associated with a greater gravity of the disease ([42]). Among the long list of cytokines, IL-6 and TNF-α have been recognized to play a key role in the inflammation process induced by SARS-CoV-2 ([18]). Surprisingly, in the present study, critical participants showed a lower level of some biomarkers in the blood (as cytokines, GOT or GPT) even above the cut-off for healthy people. In this sense, the current anti-inflammatory drugs administered to fight against the virus could play a critical role in the progression of COVID-19 after the disease ([43]).

Besides leading risk factor, previous reports observed hyperglycemia at the time of presentation and following months after COVID-19 infection in participants without a prior diagnosis of diabetes ([44–46]). In the present study, glucose levels were maintained higher in the most severe participants compared with mild and moderate participants. Although this study did not examine physiology, previous studies that assessed the pathophysiological mechanism of hyperglycemia in acute and severe COVID-19 suggested that the severe systemic inflammation during the acute phase of infection, may damage the pancreatic beta cells ([47]) and produce adipose dysfunction ([48]), causing insulin resistance and insulin secretion dysregulated ([49]), even post-COVID-19.

Thus, as ACE2 insulin receptors are expressed in the liver, adipose tissue and skeletal muscle, different damages could occur in the body systems post-COVID-19 after overcoming the disease ([15]). Functional decline and reduced physical capacity were evident as agility-balance results compared with cut-off values in healthy adults (< 12 seconds) were found. Besides the above-mentioned mechanisms, the reduced work participation and regular daily routines ([50]), as declines in physical activity levels were reported in previous studies with patients recovered from acute respiratory distress syndrome ([51]), could be another important factor. In line with this argument, muscle weakness has been observed among individuals infected with SARS-CoV-2 ([19,20]) and is associated with poor functional capacity and long-term disability ([21]). Furthermore, in acute respiratory distress syndrome survivors, an expansion in the fat compartment ([51,52]), is often characterized by a greater rate of fat mass vs. lean mass ([53]). In the present study, patients who had experienced severe or critical SARS-CoV-2 infection showed an increased located fat in the trunk and visceral fat mass ([54]). Especially, in hospitalised patients (severe and critical), sedentary behaviours (as a consequence of larger recovery in hospital, quarantine and isolation period) may be a source of inactivity, causing a disproportioning accumulation in fat mass ([15]), that might further worsen body composition, functional status and cardiometabolic risk.

Altered haematological status has been shown even two months after the acute phase of infection ([55]). Considering that the red blood cells life average is estimated at 120 days ([56]) changes in blood cells could be detected even several months after SARS-CoV-2 infection ([57]). In addition, in terms of immunological analysis in recovery participants (follow-up of 4 weeks after discharge), anormal values of leukocytes, lymphocytes, erythrocytes and C-reactive protein have been found in participants with severe COVID-19 compared with non-severe ([43]). Among them, lymphocytes have been assigned a key role in regulating immune response to the virus that causes COVID-19 ([43]), and lymphopenia has been strongly associated with the issue gravity ([41]). Although all the groups presented normal values compared with the cut-off of lymphocytes, 4 weeks after discharge, high lymphocyte levels were observed in critical participants. These results are in line with previous findings where lymphocytes returned to normal values in convalescent patients ([58]).

Limitations should be considered when interpreting these findings. Firstly, the study was designed retrospectively, and baseline prior to infection were not available in the participants to unequivocally explain changes in plasma outcomes. Secondly, the sample size is limited, especially for severe and critical participants, and studies with larger sample sizes are strongly recommended. Therefore, the current literature includes the assessment of patients in specific regions or countries (more than 50% from China) different to Brazil, one of the most affected regions by the COVID-19 pandemic, which limits the generalizability of the findings. Despite limitations, to our knowledge, this is one of the first studies to describe mild-

term health follow-up in Brazilian COVID-19 patients with different severity levels. Its strengths provide a measure of different clinical outcomes which could be used in all the fields of public health to improve the general health of COVID-19 survivors. Commonly, convalescent patients have been tested for specific antibodies or factors that could influence these antibodies. Still, as other clinical outcomes could be affected after discharge, the present study provides valuable insights into issues regarding post- COVID-19 sequelae.

Future study perspectives include analyzing the long-term sequelae in a larger sample and determining the effectivity of multidisciplinary therapies aimed at improving the parameters described above.

In conclusion, the most prevalent symptoms were fever, fatigue and dyspnoea, being diabetes, hypertension and metabolic syndrome, the comorbidities associated with higher gravity. In addition, the current descriptive study showed mild-term, altered values of body composition, physical functioning, enhanced glucose, reticulocytes and lymphocytes levels. Future studies are warranted to describe natural trajectories of COVID-19 recovery on clinical status and, thus, develop new therapies to decrease mild-term COVID-19 sequelae.

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Ethic Committees. The present study was approved by the research ethic committees of the School of Physical Education and Sport of Ribeirao Preto – University of Sao Paulo (USP) and the Faculty of Pharmaceutical Sciences of Ribeirao Preto – USP (CAAE: 33783620.6.0000.5659, and CAAE: 33783620.6.3001.5403, respectively)**Disclosure Statement** The authors declare they have no conflict of interest.**Authorship Statement** Alba Camacho-Cardenosa: designed research/study, analyzed data, wrote the first draft.Javier Brazo-Sayavera: designed research/study, analyzed data, reviewed the first draft.Marta Camacho-Cardenosa: designed research/study, analyzed data, reviewed the first draft.Gabriel Peinado Costa: performed research/study, collected data, reviewed the first draft.Ester Wiggers: performed research/study, collected data, reviewed the first draft.Elisangela Aparecida da Silva Lizzi: performed research/study, analyzed data, reviewed the first draft.Pedro Vieira da Silva-Neto: performed research/study, collected data, reviewed the first draft.João Pedro Rodrigues Campos Renon: contributed important reagents, collected data, reviewed the first draft.Carlos Arterio Sorgi: contributed important reagents, collected data, analyzed data, reviewed the first draft.Átila Alexandre Trapé: designed research/study, collected data, analyzed data, reviewed the first draft.**Acknowledgments** The present study received funding from the 'USP Vida' Project (code – 3518/2020) and the Integrated Research Projects in Strategic Areas (PIPAE 2021.1.10424.1.9) from the Dean of Research-USP.

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