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Cardiopulmonary Exercise Testing in Patients with Post-COVID-19 Syndrome

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ABSTRACT

Background and aim: Several reports have shown the persistence of long term symptoms after the initial COVID-19 infection (post-COVID-19 syndrome). The objective of this study was to analyze the characteristics of cardiopulmonary exercise testing (CPET) performed in patients with a history of COVID-19, comparing subjects according to the presence of post-COVID-19 syndrome.
Methods: A cross-sectional study was performed. Consecutive patients >18 years with history of SARS-CoV-2 infection confirmed by polymerase chain reaction test and a CPET performed between 45 and 120 days after the viral episode were included. The association between variables related to CPET and post-COVID-19 syndrome was assessed using univariate and multivariate analysis.
Results: A total of 200 patients (mean age 48.8 ± 14.3 years, 51% men) were included. Patients with post-COVID-19 syndrome showed significantly lower main peak VO_2 (25.8 ± 8.1 mL/min/kg vs. 28.8 ± 9.6 mL/min/kg, $p = 0.017$) as compared to asymptomatic subjects. Moreover, patients with post-COVID-19 syndrome developed symptoms more frequently during CPET (52.7% vs. 13.7%, $p < 0.001$) and were less likely to reach the anaerobic threshold (50.9% vs. 72.7%, $p = 0.002$) when compared to asymptomatic subjects. These findings were not modified when adjusting for confounders.
Conclusion: Our data suggest that post-COVID-19 syndrome was associated with less peak VO_2, a lower probability of achieving the anaerobic threshold and a higher probability of presenting symptoms during the CPET. Future studies are needed to determine if these abnormalities during CPET would have prognostic value.

Prueba cardiopulmonar del ejercicio en pacientes con síndrome post-COVID-19

Palabras clave:
COVID-19
Síndrome post-COVID-19
Prueba de esfuerzo cardiopulmonar
VO_2 pico
Umbral anaeróbico

RESUMEN

Antecedentes y objetivo: Varios informes han demostrado la persistencia de síntomas a largo plazo luego de la infección inicial por COVID-19 (síndrome post-COVID-19). El objetivo de este estudio fue analizar las características de la prueba de esfuerzo cardiopulmonar (PECP) realizada en pacientes con antecedentes de infección por COVID-19, comparando sujetos según la presencia de síndrome post-COVID-19.
Métodos: se realizó un estudio transversal. Se incluyeron pacientes consecutivos >18 años con antecedentes de infección por SARS-CoV-2 confirmada por la prueba de reacción en cadena de la polimerasa y una PECP realizada entre 45 y 120 días luego del episodio viral. Se evaluó la asociación entre variables relacionadas con la PECP y síndrome post-COVID-19 mediante análisis univariante y multivariado.

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Resultados: Se incluyeron 200 pacientes (edad media 48,8 ± 14,3 años, 51% hombres). Los pacientes con síndrome post-COVID-19 mostraron un VO_2 pico significativamente menor (25,8 ± 8,1 mL/min/kg frente a 28,8 ± 9,6 mL/min/kg, $p = 0{,}017$) en comparación con los sujetos asintomáticos. Además, los pacientes con síndrome post-COVID-19 desarrollaron síntomas con mayor frecuencia durante la PECP (52,7% vs. 13,7%, $p < 0{,}001$) y tenían menos probabilidades de alcanzar el umbral anaeróbico (50,9% vs. 72,7%, $p = 0{,}002$) en comparación con sujetos asintomáticos. Estos hallazgos no se modificaron al ajustar por factores de confusión.

Conclusión: Nuestros datos sugieren que el síndrome post-COVID-19 se asoció con un menor VO_2 pico, una menor probabilidad de alcanzar el umbral anaeróbico y una mayor probabilidad de presentar síntomas durante la PECP. Se necesitan estudios futuros para determinar si estas anomalías durante la PECP tendrían valor pronóstico.

Introduction

In late 2019, a novel coronavirus SARS-CoV-2 (COVID-19) appeared in Wuhan, China. Subsequently, the year 2020 witnessed an outbreak of pandemic coronavirus disease.

Effects of the inflammatory response vary according to the impacted organ system, ranging from acute respiratory distress syndrome and pleuritis in the lung, to myocarditis and pericarditis in the heart and encephalitis and meningitis in the brain.[1] Complications can also result from visceral thrombosis.[2]

Beyond acute complications, the medical community has also focused its research on the long term sequelae that may derive from COVID-19. A chronic post-viral syndrome characterized by chronic fatigue, variable nonspecific myalgia, depression, and sleep disturbances has previously been reported following SARS coronavirus infection, which emerged from South East Asia in early 2000.[3] Likewise, several reports demonstrate the persistence of symptoms in subjects recovering from hospital admission with COVID-19, even those admitted with mild disease.[4,5]

Cardiopulmonary exercise testing (CPET) is well recognized as the gold standard aerobic exercise testing assessment.[6] It can discriminate cardiovascular, ventilatory, and musculoskeletal limitations during exercise by monitoring disturbances in key variable responses such as oxygen, carbon dioxide, minute ventilation, and heart rate.[7] In this context, CPET emerges as one of the most effective noninvasive methods for comprehensive evaluation in post-COVID-19 subjects.

Previously, one study showed that half of non-severe COVID-19 survivors exhibit functional capacity limitation mainly explained by muscular impairment, although cardiopulmonary causes are possible.[8] However, this study did not compare the characteristics of the CPET in patients who had post-COVID-19 syndrome versus those who did not. In addition, another pilot study demonstrated that more than one-fourth of subjects recovering from hospitalized COVID-19 have exercise ventilatory inefficiency.[9]

The objective of this study was to analyze the characteristics of CPET performed in a population with a history of COVID-19, comparing the subjects who presented post-COVID-19 syndrome with those who did not.

Material and methods

A cross-sectional study was performed from a secondary database (electronic medical records). A consecutive sample was obtained from a private health system constituted by two university hospitals and a network of 21 associated peripheral centers distributed in Buenos Aires City, Argentina.

Inclusion criteria: (a) patients ≥18 years old who have had infection by SARS-CoV-2 confirmed by polymerase chain reaction test; (b) patients with a CPET performed between 45 and 120 days after the viral infection diagnosis. This period was set according to an institutional standard, following the recommendations of the Infectious Diseases Committee, the Pneumonology Department and the Cardiology Department.

The clinical records of the patients included were revised, obtaining information about their history, cardiovascular risk factors and medication received. A cardiovascular history was considered when the patient had a history of coronary disease, cerebrovascular disease, or peripheral vascular disease.

Post-COVID-19 syndrome was defined as dyspnea or fatigue persisting for at least 45 days after symptom onset. This cut-off point was chosen arbitrarily, following the institutional norm for carrying out exercise tests after an episode of COVID-19. Although there is no universally accepted time horizon to define post-COVID-19 syndrome, this cut-off point is within the range of values usually reported.[10–12] It was defined as dyspnea at a level greater than 1 on the mMRC scale and fatigue at more than 4 points on a visual analog scale.[13–14]

Symptom-limited treadmill exercise testing (H/P Cosmos®, Mercury Med, Germany) with continuous breath-by-breath respiratory gas exchange analysis was performed (Quark CPET by Cosmed, OMNIA software 1.6.7). A Bruce protocol or modified Bruce protocol were followed for treadmill testing. The medical operator of the CPET chose the protocol according to his clinical criteria. Electrocardiograms were continuously monitored, and dynamic changes were considered when an ST segment depression >1 mm was observed. The appearance of arrhythmias was reported. Exercise duration was expressed in minutes.

Measurements included heart rate (HR), blood pressure, arterial blood oxygen saturation (SaO_2), oxygen consumption (VO_2), carbon dioxide production (VCO_2) and minute ventilation (VE). Quality of exercise effort was assessed by respiratory exchange ratio [RER (VCO_2/VO_2)]. RER > 1.1 was considered maximum effort.

Expiratory flow measurements were performed by a mass flow sensor, calibrated with a gas mixture of known concentration before each test.

Peak VO_2 was defined as the average VO_2 during the last minute of exercise and is expressed as mL/kg body weight per min. It was also reported as a percentage of predicted value (according to pre-specified tables that consider sex, age, and body surface area). Functional capacity was defined as normal when the predicted peak VO_2 was greater than or equal to 85%. Likewise, the deterioration of functional capacity was classified as mild, moderate, or severe when the predicted VO_2 peak was between 65% and 85%, between 50 and 65% and less than 50%, respectively. In turn, deterioration of functional capacity according to its etiology was classified as cardiovascular, respiratory, peripheral (deconditioning) or mixed (cardiovascular or/and, respiratory or/and peripheral).

VO_2 at the anaerobic threshold (AT) was identified as the oxygen uptake before the systematic increase in the ventilatory equivalent for oxygen (VE/VO_2), without a concomitant increase in the ventilatory equivalent for carbon dioxide (VE/VCO_2), with the ventilation-slope method. The ventilatory response to exercise was defined as VE/VCO_2 at peak exercise. The oxygen pulse was calculated through the VO_2/HR ratio and the oxygen uptake efficiency slope (OUES) was defined as the gradient of the linear relationship of $\log_{10}$ VE to VO_2.

Breathing reserve represents the ratio between VE during exercise and maximum voluntary ventilation (MVV) at rest, both variables in L/min (a value greater than 15 was considered normal). Equations to predict MVV were used (forced expiratory volume in the first second – FEV1 × 40), although it can be measured directly on pre-test spirometry.

Statistical analysis: Continuous data between two groups were analyzed using a Student's *t* test if the variables were normally distributed or with a Wilcoxon–Mann–Whitney test otherwise. Categorical data analysis was performed using a chi-squared test. Continuous variables are summarized as mean ± standard deviation (SD) or median (25–75 interquartile range) according to their distribution, while categorical variables are given as percentages.

The association between CPET related variables and the presence of post-COVID-19 syndrome was determined using univariate and multivariate analysis (adjusting for variables that showed statistically significant differences in bivariate analysis). Linear or logistic regression models were used to evaluate the association of continuous or categorical dependent variables to a given set of independent variables. The strength of the association was expressed as an odds ratio (OR) or the difference of means between groups and its respective 95% confidence interval (95% CI).

A sample of 134 subjects was estimated to provide 90% power (beta error of 0.1) and an alpha error of 0.05 to detect an absolute difference ≥10% between the means of peak VO_2 values. Assuming that the information could be incomplete in some of the subjects selected, we requested the sample to be 20% larger.

A value of $p < 0.05$ was considered statistically significant. STATA 13.0 software packages were used for statistical analysis.

Ethics considerations: The study was conducted in compliance with the recommendations for medical research contained in the Declaration of Helsinki, Good Clinical Practice standards, and the applicable ethical regulations. The protocol was reviewed and approved by the Ethical Board of the Institution.

Results

A total of 200 patients (mean age 48.8 ± 14.3 years, 51% men) were included in the study. The average time and SD between the COVID-19 diagnosis and the CPET were 80 ± 21 days. Average body mass index was 26.4 ± 6.4 kg/m^2 and mean total cholesterol level was 183.9 ± 38.8 mg/dl. Importantly, the prevalence of type 2 diabetes mellitus in the population was 5.5% and 28.1% of patients were hypertensive. Globally, 56% of the population exhibited post-COVID-19 syndrome. Regarding the initial COVID-19 severity, 19.5% required hospitalization (66.7% required oxygen therapy and 3% required intensive care). Baseline characteristics of the study population are described in Table 1.

Subjects with post-COVID-19 syndrome had a significantly lower prevalence of male gender (41.1% vs. 63.6%, $p = 0.002$), cardiovascular history (2.7% vs. 15.9%, $p = 0.001$), use of beta-blockers (2.8% vs. 22.7%, $p < 0.01$) and use of aspirin (4.5% vs. 17.1%, $p = 0.003$) as compared to group without post-COVID-19 syndrome. No other statistically significant differences between groups were observed. Table 2 presents the characteristics of the groups with and without post-COVID-19 syndrome.

Regarding CPET, the main peak VO_2 was 27.2 ± 8.9 mL/min/kg (main predicted VO_2 91.2 ± 19.4%) and 60.5% achieved the AT (the average value at which the AT was detected was 63.4% ± 6.2 of peak VO_2). The main slope VE/VCO_2 was 32.8 ± 5.7. Further, 89.5% and 44.5% of the population showed normal oxygen pulse and OUES values, respectively.

Table 1
Characteristics of the population.

Continuous variables, mean (SD)	Total population $n = 200$
Age, years	48.8 (14.3)
Body mass index, kg/m^2	26.4 (6.4)
Total cholesterol, mg/dl	183.9 (38.8)
LDL-C, mg/dl	107.9 (35.9)
HDL-C, mg/dl	51.6 (14.8)
Triglycerides, mg/dl	133.3 (125.8)
Blood glucose, mg/dl	99.9 (17.0)
Categorical variables, %	
Male gender	58.0
Type 2 diabetes	5.5
Hypertension	28.1
Current smoking	6.0
Dyslipidemia	24.1
Cardiovascular history	8.5
Chronic kidney disease	0
Chronic obstructive pulmonary disease	1.5
Treatment	
ACE inhibitors/angiotensin antagonists	23.1
Beta-adrenergic blockers	15.1
Statins	21.0
Aspirin	10.0
Calcium channel blockers	9.0

Patients with post-COVID-19 syndrome showed significantly lower main peak VO_2 (25.8 ± 8.1 mL/min/kg vs. 28.8 ± 9.6 mL/min/kg, $p = 0.017$) as compared to asymptomatic subjects. Moreover, patients with post-COVID-19 syndrome showed symptoms more frequently during the CPET (52.7% vs. 13.7%, $p < 0.001$) and reached the AT in a smaller proportion of times (50.9% vs. 72.7%, $p = 0.002$) as compared to subjects without post-COVID-19 syndrome. Table 3 shows the characteristics of CPET according to the presence or not of post-COVID-19 syndrome.

In the multivariate analysis, patients with post-COVID-19 syndrome, compared to asymptomatic patients, had 3.2 mL/min/kg less peak VO_2 (95% CI −0.9 to −5.5), regardless of gender, cardiovascular history and use of beta-blockers or aspirin.

Additionally, after adjusting for the same variables, patients with post-COVID-19 syndrome had a smaller chance of achieving the AT (OR: 0.38; 95% CI 0.20–0.72) and had a greater chance of presented symptoms during the CPET (OR: 7.0, 95% CI 3.5–16.2), when compared with asymptomatic patients. The multivariate analysis is shown in Table 4.

Discussion

This study is the first to compare CPET findings in subjects depending on the presence of post-COVID-19 syndrome. The main findings of our study were that post-COVID-19 syndrome was associated with less peak VO_2, a lower probability of reaching the AT and a higher probability of presenting symptoms during the CPET.

The so-called "post-COVID-19 syndrome" includes persistent symptoms that could be related to residual inflammation (convalescent phase), organ damage, non-specific effects from the hospitalization or prolonged ventilation, social isolation, or impact on pre-existing health conditions.[15] In this study, post COVID-19 syndrome was defined as dyspnea or fatigue persisting for at least 45 days after symptom onset.

Several studies have reported the prevalence of persistent symptoms after COVID-19, which may range from 40 to 90% after hospital discharge. An Italian study followed up 143 individuals 7 weeks post-hospitalization and found that 53% reported fatigue,

Table 2
Characteristics of the population according to the presence or not of post-COVID-19 syndrome.

Continuous variables, mean (SD)	Without post-COVID-19 syndrome N = 88	With post-COVID-19 syndrome N = 112	p
Age, years	50.0 (15.4)	47.9 (13.4)	0.296
Body mass index, kg/m²	26.6 (5.8)	26.3 (6.8)	0.694
Total cholesterol, mg/dl	182.9 (43.2)	184.9 (34.7)	0.744
LDL-C, mg/dl	107.2 (39.6)	108.9 (31.0)	0.780
HDL-C, mg/dl	51.2 (14.5)	52.1 (15.2)	0.709
Triglycerides, mg/dl	137.5 (160.2)	128.4 (66.1)	0.664
Blood glucose, mg/dL	99.0 (14.9)	100.9 (18.8)	0.476
Time between the COVID-19 diagnosis and the CPET, days	81.9 (21.8)	78.8 (20.5)	0.448
Categorical variables, %			
Male gender	63.6	41.1	0.002
Cardiovascular history	15.9	2.7	0.001
Hypertension	30.7	26.1	0.478
Dyslipidemia	29.1	20.2	0.150
Type 2 diabetes	4.6	6.3	0.613
Current smoking	3.4	8.0	0.171
Chronic obstructive pulmonary disease	0.0	2.6	0.176
Treatment			
ACE inhibitors angiotensin antagonists	23.9	22.5	0.824
Beta-adrenergic blockers	22.7	9.8	0.01
Statins	27.3	16.1	0.054
Aspirin	17.1	4.5	0.003
Calcium channel blockers	11.4	7.1	0.301
Required hospitalization	19.3	19.6	0.954
Required oxygen therapy	64.7	68.2	0.819
Required admission to intensive care	17.7	13.6	0.731

Table 3
Characteristics of cardiopulmonary exercise testing.

Continuous variables, mean (SD)	Total N = 200	Without post-COVID-19 syndrome N = 88	With post-COVID-19 syndrome N = 112	p
Peak VO_2, mL/min/kg	27.2 (8.9)	28.8 (9.6)	25.8 (8.1)	0.017
Exercise time, minutes	9.0 (2.9)	9.8 (2.6)	8.4 (3.0)	0.007
Predicted VO_2, %	91.2 (19.4)	92.9 (18.7)	89.7 (19.9)	0.257
Slope VE/VCO_2	32.8 (5.7)	32.5 (5.5)	33.1 (5.9)	0.521
Maximum RR	32.7 (7.2)	33.5 (5.9)	32.0 (8.1)	0.131
RR difference (maximum-basal)	15.1 (7.3)	16.3 (6.6)	14.1 (7.7)	0.037
Oxygen saturation at maximum effort, %	97.5 (2.0)	97.7 (1.9)	97.4 (2.1)	0.453
Categorical variables, %				
RER > 1.1	59.5	68.2	52.7	0.03
Dynamic changes of the ST segment	7.5	9.1	6.3	0.333
Normal oxygen pulse	89.5	89.8	89.3	0.911
Normal OUES	44.5	45.5	43.8	0.810
Achieved anaerobic threshold	60.5	72.7	50.9	0.002
Appeal to the respiratory reserve	0	0	0	
Preserved functional capacity	65.5	65.9	65.2	0.914
Decreased functional capacity				
Cardiovascular pattern	61.2	58.6	63.2	0.706
Respiratory pattern	13.4	0	23.7	0.004
Peripheric pattern	67.2	89.7	50.0	0.001
Mixed pattern	41.8	48.3	36.8	0.347
Normal course of BP	86.0	87.5	84.8	0.588
Exaggerated behavior of BP	6.5	3.4	8.9	0.116
Symptoms in the test	35.5	13.7	52.7	<0.001
Dyspnea	92.9	75.0	96.6	0.008
Dizziness	9.9	8.3	10.2	0.846
Chest pain	9.9	0	11.9	0.257
Arrhythmias	21.5	19.3	23.2	0.506
Normal course of heart rate	95.5	93.2	97.3	0.161

BP: blood pressure, OUES: oxygen uptake efficiency slope, RER: respiratory exchange ratio; RR: respiratory rate, SD: standard deviation, VO_2: peak oxygen consumption; VE: minute ventilation.

43% breathlessness, and 27% joint pain.[16] Halpin et al. reported that new illness-related fatigue was the most reported symptom: 72% of participants who required intensive care and 60.3% of non-intensive care subjects.[17] Likewise, breathlessness occurred in 65.6% of patients admitted to intensive care units and 42.6% in those who were in hospital wards. Research by Tenforde et al. indicated that COVID-19 can result in prolonged illness even among persons with milder outpatient illness, including young adults.[18] This is particularly relevant, since most patients evaluated in our study were mild to moderate COVID-19 episodes.

Table 4
Multivariable analysis.

	Peak VO_2 coefficient (95% CI)	p
Lineal regression model		
Post-COVID-19 syndrome	−3.2 (−0.9 to −5.5)	0.007
Male gender	5.8 (3.5 to 8.1)	<0.01
Beta-adrenergic blockers	−6.6 (−2.5 to −10.7)	0.002
Aspirin	−0.6 (−6.1 to 4.9)	0.821
Cardiovascular history	−4.7 (−10.3 to 0.8)	0.095
	OR (95% CI) Achieved anaerobic threshold	p
Logistic regression model		
Post-COVID-19 syndrome	0.38 (0.20 to 0.72)	0.003
Male gender	1.5 (0.83 to 2.84)	0.172
Beta-adrenergic blockers	0.63 (0.21 to 1.88)	0.412
Aspirin	1.73 (0.37 to 8.14)	0.485
Cardiovascular history	0.47 (0.83 to 2.83)	0.327
	Symptoms in the test	
Post-COVID-19 syndrome	7.0 (3.5 to 16.2)	<0.001
Male gender	0.59 (0.30 to 1.16)	0.125
Beta-adrenergic blockers	1.66 (0.48 to 5.69)	0.422
Aspirin	0.95 (0.17 to 5.32)	0.958
Cardiovascular history	1.69 (0.30 to 9.30)	0.544

VO_2: peak oxygen consumption; CI: confidence interval.

This medical dilemma is not exclusive to COVID-19 infection. A meta-analysis of 28 follow-up studies found that one-quarter of hospitalized survivors of severe acute respiratory syndrome (SARS, 2002) and Middle East respiratory syndrome (MERS, 2012) had reduced lung function and exercise capacity at 6 months postdischarge.[19]

The peak VO_2 represents the combined capacity of the pulmonary, cardiovascular and muscle systems to uptake, transport and utilize O_2, respectively.[20] Therefore, the decrease in peak VO_2 observed in patients with post-COVID-19 syndrome compared to asymptomatic subjects in our study could be explained by multiple factors. Previously, Clavario et al. reported that half of non-severe COVID-19 survivors show functional capacity limitation mainly explained by muscular impairment.[8] In our study, approximately one third of the patients with post-COVID-19 syndrome had a decrease in functional capacity. There were no differences between patients with COVID-19 syndrome and asymptomatic patients. However, the respiratory pattern was more frequently reported in the post-COVID-19 syndrome group.

The AT is a simple marker of exercise fitness and intensity. A widely referenced definition of the anaerobic threshold is “that intensity of exercise above which anaerobic mechanisms supplement aerobic mechanisms”.[21] The AT, as measured by CPET, is frequently used to determine the prognosis of cardiovascular and respiratory diseases.[22] In our study, approximately half of the subjects achieved the AT, a significantly lower proportion when compared with asymptomatic patients.

Finally, this study showed that patients with post-COVID-19 syndrome were seven times more likely to present symptoms during the CPET compared to patients without the post-COVID-19 syndrome. Dyspnea was present in almost all the patients evaluated. Cortés-Telles et al. examined the physiological mechanisms of persistent dyspnea in non-critical COVID-19 survivors.[23] This report suggests that patients with persistent dyspnea show greater impairments in resting and exertional pulmonary gas exchange and have greater evidence of a restrictive pattern on spirometry. Furthermore, the increased restrictive pattern may have influenced the higher rates of dyspnea and leg fatigue observed during the 6-minute walk test. The authors speculate that COVID-19 patients with persistent dyspnea are more likely to have greater constraints on tidal volume expansion, exertional hypoxemia; adoption of a more rapid and shallow breathing pattern; and higher levels of respiratory neural drive during CPET. Given that the persistence of dyspnea has been reported even in subjects who did not have severe cases of COVID, some authors suggest that dyspnea could be related not only to a possible ventilatory alteration but also to a component of muscular weakness or alteration of perception of central origin.[24]

This study presented several limitations. First, as in any cross-sectional study, the possibility of bias (mainly selection bias) potentially influencing the results cannot be ruled out. Indeed, the higher proportion of subjects with previous cardiovascular disease in the group of patients without post-COVID-19 syndrome, would reflect that the referrals come to a greater extent from the cardiology service, while in the group with post-COVID-19 syndrome, the main sources of referral may have been the clinical or pulmonology departments. However, the multivariate analysis showed that the differences found in our study persisted even when adjusting for these potential confounders. In addition, we could conjecture that said bias could strengthen our findings, since more comorbid non-post-COVID-19 subjects should have underperformed in the CPET. Second, the inclusion of patients in our study was carried out consecutively. However, the number of patients with post-COVID-19 syndrome was slightly higher than asymptomatic patients. We believe this phenomenon occurred due to two circumstances: (1) In the period in which the study was carried out, a multidisciplinary unit for the evaluation of post-COVID-19 patients was created in our institution, which derived a large proportion of symptomatic subjects; (2) A lower flow of asymptomatic patients who were usually referred by clinicians and cardiologists, for fear of conducting this type of study in the context of the pandemic. Third, information on lung function estimated by spirometry could not be reliably obtained retrospectively; therefore, this data could not be included in the analysis. Fourth, prevalence of post-COVID-19 syndrome could not be derived from our sample due to the recruitment method. Finally, in our study, post-COVID-19 syndrome was arbitrarily defined. However, there is no universal consensus on the definition of this condition. Our definition was based on previous publications where the definition considered patients with distant symptoms, between 3 weeks and 3 months after the viral infection. In addition, our criteria did not include non exercise related symptoms, as post COVID-19 syndrome can include a myriad of manifestations. This is due both to sampling having been defined by CPET testing and the low probability of an association of non-exercise related symptoms and CPET results. Despite its limitations, this study represents a valuable contribution, as it examined physical fitness in a group of patients with post-COVID-19 syndrome.

Conclusion

Our data suggest that post-COVID-19 syndrome was associated with less peak VO_2, a lower probability of achieving the AT and a higher probability of presenting symptoms during the CPET. Future studies are needed to determine if the aforementioned abnormalities during CPET would have prognostic value and may be modified by therapeutic interventions such as rehabilitation programs.

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Conflicts of interest

None declared.

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