Post-COVID-19 syndrome: prospective evaluation of clinical and functional outcomes

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Introduction: Coronavirus disease 2019 (COVID-19) is a highly pathogenic coronavirus characterized by by systemic inflammatory response with endothelial damage and a dysregulated coagulation system. Despite most patients survive the acute setting of COVID-19, their long-term clinical sequelae are highly unclear. We have sought to identify the impact of post-COVID-19 syndrome on mid-term follow-up and gain some additional insights about the potential explanation for persistence of dyspnea.

Methods: This is a 3-month prospective cohort study of previously hospitalised COVID-19 patients recruited from a single Spanish center, a small outpatient group without prior hospitalisation was also evaluated. Patients underwent serial testing with cardio-pulmonary exercise test (CPET), transthoracic echocardiogram, pulmonary lung test, six-minute walking test, serum biomarker analysis and quality of life questionaries. They were classify according to the presence of persistent dyspnea. Primary study outcome was predicted peak oxygen consumption (V02) according to CPET and predicted carbon monoxide diffusion capacity.

Results: Our study included 41 (58.6%) patients with dyspnea and 29 (41.4%) asymptomatic. Symptomatic patients had a higher proportion of females (73.2% vs. 51.7%), but comparable age and prevalence of cardiovascular risk factors. We did not observe differences among the assessed variables in transthoracic echocardiogram and pulmonary function test. Patients who referred dyspnea had smaller predicted peak O_2 consumption (77.8 [64–92.5] vs. 99 [88–105]: p<0.001), total distance in the 6-minute walking test (535 [467–600] vs. 611 [550–650] meters; p=0.001), and quality of life (KCCQ-23 60.1±18.6 vs. 82.8±11.3; p<0.001). Additionally, abnormalities in CPET were suggestive of a ventilation/perfusion misthmach or hyperventilatory syndrome characterized by impaired ventilatory efficiency with a greater VE/VCO2 slope (32 [28.1–37.4] vs. 29.4 [26.9–31.4]; p=0.022) and low PETCO2 (34 [32–39] vs. 38 [36–40]; p=0.025).

Interpretation: In this study >50% of COVID-19 survivors present a symptomatic functional impairment irrespective of age or prior hospitalization. Compared to asymptomatic patients, among those who referred dyspnea our findings suggest potential ventilatory inefficiency.

	All population N= 70	Dyspnea n = 41 (60)	Asymptomatic n= 29 (40)	p-value
Resting echocardiographic findings				
LVEF (%)	64 [59-68]	65 [59-68]	63 [60-69]	0.962
LVEDVi (ml/m²)	75 [66-100]	41.2 [36.2-50.6]	45.3 [40.5-54.2]	0.123
LVESVi (ml/m²)	16.2 [12.3-20.1]	14.1 [12.4-21]	16.7 [14-21]	0.194
Average E/e´ ratio	6.5 [4.9-7.9]	6.6 [4.9-8.9]	6.2 [5-7.3]	0.284
TAPSE (mm)	23 [20-26]	23 [20-27]	23 [22-25]	0.472
S' (cm/sec)	13 [12-15]	13 [12-14.5]	13 [12-15]	0.392
RVSP (mmHg)	19 [15-24]	22 [18-26]	18 [12-19]	**0.020**
Global longitudinal strain (%)	20 [22-19]	20 [22-19]	20 [22-19]	0.806
Cardio-pulmonary exercise test				
Breathing reserve (%)	41 [32-51]	46 [30-54]	40 [36-46]	0.319
RER	1.11 [1.05-1.21]	1.08 [1.05-1.16]	1.13 [1.05-1.28]	0.172
Peak V_{O_2} (ml/min/kg)	19.4 [17.2-24.8]	17.8 [15.8-21.2]	22.8 [18.8-27.7]	**<0.001**
% of predicted pV_{O_2}	88 [76-100]	77.8 [64-92.5]	99 [88-105]	**<0.001**
V_{O_2} at AT_1 (ml/min/kg)	15.4 [12-19.2]	13.6 [9.2-17]	18.3 [15.2-19.5]	**0.003**
% of predicted V_{O_2}/HR	101 [83-110]	98 [73-110]	106 [96-110]	0.054
VE/V_{CO_2} slope	30.3 [27.5-34.9]	32 [28.1-37.4]	29.4 [26.9-31.4]	**0.022**
VE/V_{CO_2} at AT_1	34.7 [32.3-39.5]	37.2 [31.5-42.3]	33.7 [32.5-36.4]	0.194
$PETCO_2$ (mmHg) at AT_1	38 [33.5-39.5]	34.5 [32-39]	38 [36-40]	**0.025**
Resting HR (beats/min)	79 [71-85]	78 [70-80]	80 [74-86]	0.357
% of predicted HR	90.3 [83.9-97.4]	87 [79.3-94.5]	95 [88-100]	**0.003**
Resting O_2 saturation (%)	97 [96-98]	97 [96-98]	97 [96-98]	0.620
Peak O_2 saturation (%)	97 [96-98]	97 [96-98]	97 [96-98]	0.388
Pulmonary lung function				
DLCO % of predicted	88.8 [80-97]	86 [74.5-95.3]	90 [83.5-100]	0.098
KCO % of predicted	95.3 [88.7-109]	94.6 [86.5-107]	96 [89-110.5]	0.493
FEV1/FVC (%)	100 [91.6-105]	98.5 [86.5-106]	102 [97-104]	0.466
6-MWT distance (meters)	558 [500-615]	535 [467-600]	611 [550-650]	**0.001**

Tabla de resultados