Cardiac Autonomic Function and Pulmonary Function in Hypertensive Individuals Post Mild COVID-19: A Cross-Sectional Study

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Abstract

The long-term impact of COVID-19 on cardiac autonomic function and pulmonary function in patients with systemic arterial hypertension (SAH) was evaluated in a cross-sectional study with 52 individuals. Participants were allocated into two groups based on their COVID-19 history. All volunteers underwent heart rate variability analysis using 24-hour Holter electrocardiographic monitoring, lung function was assessed by spirometry, and functional capacity (FC) was assessed by cardiopulmonary exercise testing. Worsening of lung function was revealed in SAH patients recovered from COVID-19, indicated by lower forced expiratory volume in one second (FEV_1). However, no significant differences were found in cardiac autonomic control. A negative and moderate association was observed between $VO_{2máx}$ and the 0V% index. These results indicated that as functional capacity increases, sympathetic modulation during wakefulness decreases. This observation was consistently corroborated by adaptations of the cardiovascular system in favor of better FC. The findings suggest that mild COVID-19 in SAH patients may not cause significant changes in HRV in the long term. However, there is a worsening of lung function that persists over the long term.

1. Introduction

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the agent responsible for coronavirus disease 2019 (COVID-19), led to a global pandemic declared by the World Health Organization in 2020. COVID-19 is characterized by its high transmissibility and substantial morbidity and mortality [1-3]. Beyond the acute phase, many survivors experience prolonged symptoms, including fatigue, dyspnea, chest pain, arrhythmias, tachycardia, and autonomic dysfunction, for more than three months [4].

Cardiovascular diseases (CVDs) and related risk factors, particularly systemic arterial hypertension (SAH), are strongly associated with worse COVID-19 outcomes [3,5,6]. Evidence also suggests that SARS-CoV-2 can cause persistent autonomic dysfunction even in non-hospitalized patients [7,8], although the long-term impact of the infection on autonomic control in individuals with SAH remains unclear [9–11].

In addition to dysautonomia, several studies have reported lasting reductions in lung function and functional capacity (FC) following COVID-19, especially among previously hospitalized individuals [12,13]. These alterations appear to result from inflammatory injury to the respiratory system, leading to decreased forced vital capacity (FVC), total lung capacity (TLC), and diffusing capacity [14]. Furthermore, up to 85% of recovered patients exhibit impaired exercise response during cardiopulmonary exercise testing (CPET) [15,16].

This combination of autonomic, cardiovascular, and respiratory disturbances underscores the importance of assessing pulmonary and functional sequelae and promoting cardiorespiratory rehabilitation [17]. Therefore, this study aimed to investigate the long-term effects of mild COVID-19 on cardiac autonomic function and pulmonary function in adults with SAH.

2. Methods

2.1 Study design and sample selection

This is a cross-sectional observational study, approved by the Research Ethics Committee of the University of Pernambuco (UPE), (CAAE - 66973322.0.0000.5191).

Fifty-two individuals with SAH were evaluated, of both sexes, aged between 40 and 75 years, who had or had not been infected with the SARS-CoV-2 virus. The sample selection was carried out based on publicity on radio, television and digital media.

2.2 Eligibility criteria

Participants with systemic arterial hypertension (SAH) for at least one year, on stable antihypertensive therapy for the previous three months, aged 40–75 years, were included. Group 1 (G1-) comprised individuals without a confirmed history of COVID-19, while Group 2 (G2+) included those with laboratory-confirmed mild infection 6–18 months prior, who did not require hospitalization. All participants underwent evaluations of cardiac autonomic control, pulmonary function, and maximal functional capacity.

2.3 Experimental protocol

Participants underwent assessments of cardiac autonomic function, pulmonary function and maximum functional capacity in the afternoon from 2 to 6 pm.

Heart rate variability (HRV) was assessed through a 24-hour electrocardiogram (CARDIOS, São Paulo, Brazil) recorded at 800 samples per second with 12-bit resolution. RR interval series were automatically processed and manually reviewed to remove ectopic beats and artifacts, ensuring that corrections did not exceed 5% of total samples. Recordings contained at least 18 hours of sinus rhythm and were segmented into wake and sleep periods. [18].

Heart rate variability (HRV) was analyzed using nonlinear routines developed by Prof. Dr. Alberto Porta (Università degli Studi di Milano, Italy). Symbolic analysis was performed by grouping sequences of three symbols into four pattern families: no variation (0V), one variation (1V), two similar variations (2LV), and two different variations (2UV). The relative frequencies of these patterns (0V%, 1V%, 2LV%, 2UV%) were calculated, representing markers of sympathetic (0V%), mixed (1V%), and vagal (2LV% and 2UV%) modulation [19].

Pulmonary function was assessed to identify and quantify ventilatory disorders through the analysis of airflow, lung volumes, and capacities, following the standards established by the American Thoracic Society/European Respiratory Society (ATS/ERS) [20]. The evaluation was performed using a spirometer (Quark CPET, Cosmed, Italy). Measured variables included forced expiratory volume in 1 second (FEV_1) and the FEV_1/FVC ratio (Tiffeneau index).

Cardiopulmonary exercise testing (CPET) was performed on an electronically braked cycle ergometer (Quinton Corival 400, USA) following ERS [21]. The protocol consisted of one minute of seated rest followed by a two-minute warm-up at a minimal workload (~4 W). A ramp protocol was then applied, with continuous increments of 15 W per minute, targeting a total exercise duration of 8–12 minutes. Participants maintained a pedaling cadence of 60–65 rpm. Systolic and diastolic blood pressure, together with perceived exertion for dyspnea and limb fatigue, were recorded every two minutes during exercise. The main outcome variable was VO_2max (maximum oxygen consumption).

2.4 Statistical analysis

Statistical analyses were performed using SPSS 22.0. Normality was assessed with the Kolmogorov–Smirnov test. Data are presented as median [IQR]. Intergroup comparisons used Mann–Whitney tests. Spearman's coefficients were interpreted as negligible (0–0.25), low (0.26–0.49), moderate (0.50–0.69), high (0.70–0.89), or very high (0.90–1.00). Significance was set at $p < 0.05$. Subanalyses accounted for potential confounders such as age and medication use.

3. Results

The sample comprised 52 participants (55.6±9.1 years), predominantly female (78.8%). Participants were allocated to G1 (n=25; 19 women, 6 men) and G2 (n=27; 22 women, 5 men). The mean body mass index (BMI) was 32.61±6.16 kg/m² in G1 and 32.03±5.62 kg/m² in G2. No significant differences were observed in baseline between groups.

Table 1 presents the comparison of spirometric indices between groups. The G1- group showed higher FEV_1 (L) and FEV_1 (% predicted) values than the G2+ group ($p < 0.05$). Likewise, the Tiffeneau index (FEV_1/FVC, % predicted) was significantly higher in G1-, indicating better pulmonary function among participants without a history of COVID-19. Regarding cardiac autonomic function, no significant differences were observed in HRV indices between groups.

Figure 1 illustrates the relationship between VO_2max and the 0V% HRV index during wakefulness, a marker of sympathetic modulation. A negative correlation was observed in both groups, weak in G1- and moderate in G2+, indicating that higher aerobic capacity is associated with lower sympathetic predominance during the waking period. No significant correlations were found for other variables.

Table 1. Comparison of spirometric indices e VO_2max between individuals with systemic arterial hypertension who had no confirmed history of SARS-CoV-2 infection (G1-) and those with a confirmed history (G2+).

Index	G1- (n=25)	G2+ (n= 27)	*p*
FEV_1 (L)	2.5(2.2-3.0)	2.3(1.9-2.6)	0.02*
FEV_1 (%pred)	95(89-102)	86(76-99)	0.00*
FEV_1/FVC (%)	84.6(80.8-87.7)	81.8(77.5-83.9)	0.00*
VO_2max[1]	16.4(13.3-20.0)	15.7(14.0-17.7)	0.70

Data expressed as median (1st - 3rd interquartile). FEV_1: forced expired volume in the first second in L and % of predicted; FVC: forced vital capacity; FEV_1/FVC: Tiffeneau Index; [1]VO_2max (maximum oxygen consumption) expressed in $mL.Kg^{-1}.min^{-1}$ *$p<0.05$.

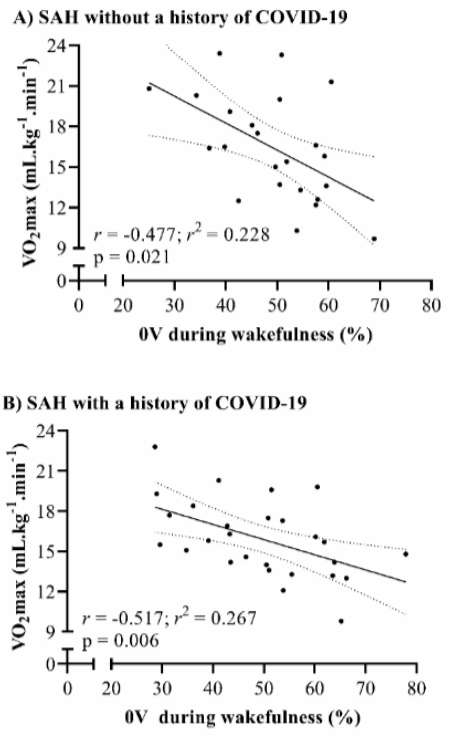

Figure 1. Correlation between VO_{2max} and HRV indices. Caption: The figure shows a scatterplot illustrating a negative correlation between VO_{2max} and 0V% index of HRV across groups, with values representing significant data for both groups.

4. Discussion

This study investigated the long-term impact of mild COVID-19 on cardiac autonomic function and pulmonary function in adults with systemic arterial hypertension (SAH). The main finding was that hypertensive individuals with a history of COVID-19 exhibited reduced pulmonary function compared to those without prior infection. Even 6–18 months after recovery, participants showed spirometric signs suggestive of restrictive impairment, evidenced by lower FEV_1 and FEV_1/FVC values.

Previous reports have identified the lungs as primary targets of SARS-CoV-2, with structural and functional damage persisting beyond six months [22,23], although most data derive from hospitalized patients. The present results extend these observations to non-hospitalized hypertensive individuals.

Conversely, no significant long-term changes in cardiac autonomic modulation were detected. Despite earlier studies reporting post-COVID autonomic dysfunction [23,24], such effects may depend on disease severity and individual vulnerability. Given that SAH is already associated with sympathovagal imbalance and impaired vagal anti-inflammatory responses [3,26], the absence of additional autonomic alterations in our cohort likely reflects the mild clinical presentation, suggesting that any dysfunction was transient or subclinical [26,27].

Although HRV provides a reliable index of autonomic control, it is influenced by multiple neural and physiological inputs, including respiratory, baroreceptor, and chemoreceptor activity. Future research should adopt multivariate analyses integrating RR intervals, respiration, and beat-to-beat blood pressure to clarify the causal dynamics between COVID-19 and autonomic regulation [28–30].

Regarding functional capacity, no significant group differences were found. Both groups achieved VO_{2max} values >85% of predicted, while the overall aerobic capacity reserve was classified as low. This reduced performance likely reflects pre-existing conditions—such as hypertension, obesity, or sedentary behavior—rather than residual effects of infection. The absence of pre-infection fitness data, common across studies, limits causal interpretation.

A negative correlation between VO_{2max} and 0V% during wakefulness was observed in both groups, weak in G1 and moderate in G2, indicating that greater aerobic fitness is associated with lower sympathetic predominance. This relationship aligns with known cardiovascular adaptations that accompany improved functional capacity.

5. Conclusion

Based on our findings, no significant alterations in autonomic nervous system (ANS) activity were detected in hypertensive individuals who had recovered from mild COVID-19. Nevertheless, a reduction in pulmonary function, predominantly characterized by a restrictive pattern, was observed, which may have contributed to the diminished cardiopulmonary exercise testing (CPET) performance. These findings underscore the importance of comprehensive post-infection evaluations in hypertensive patients to better understand potential residual functional impairments.

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