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 (FEV1) FEV1/FVC, with 30% presenting restrictive disorder. However, no significant differences were found in cardiac autonomic control. A negative and moderate association was observed between VO2peak and the 0V% index, these results indicate that as functional capacity increases, sympathetic modulation during wakefulness decreases. This observation is 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, with the presence mainly of restrictive disorder in 30% of cases.

1. Introduction

The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for coronavirus disease 2019 (COVID-19), caused a global pandemic declared by the World Health Organization (WHO) in 2020. COVID-19 is marked by its remarkable transmission capacity and high level of morbidity and mortality [1-3]. After the acute phase of SARS-CoV-2 infection, survivors often experience persistent symptoms like fatigue, dyspnea, chest pain, arrhythmias, tachycardia, autonomic dysfunction, anxiety, and depression for over 3 months [4].

It is known that individuals with Cardiovascular Diseases (CVDs) and their risk factors, such as Systemic Arterial Hypertension (SAH), have a strong association with the severity and mortality by COVID-19 [3,5,6].

Studies already indicate that COVID-19 can cause sequelae in the autonomic nervous system (ANS) that are not limited to critically ill patients [7,8]. However, there are still no studies investigating the long-term effects of COVID-19 on the ANS of patients with SAH [9–11].

In addition to dysautonomia, studies indicate that individuals who have been hospitalized due to COVID-19 face a significant decrease in lung function and functional capacity (FC), which can persist for months after recovery [12,13]. This impairment appears to be intrinsically linked to specific injuries caused by viral inflammation, especially in the respiratory system, with a consequent reduction in lung function analyzed by indices such as forced vital capacity (FVC), total lung capacity (TLC) and diffusion capacity [14].

Additionally, deficits in FC have been associated with direct damage to the ANS and respiratory system. Previous studies show that 85% of those recovered from COVID-19 have an impaired exercise response during cardiopulmonary exercise testing (CPET) [15,16]. This intricate network of changes in the ANS, cardiovascular and respiratory systems highlights the need for cardiorespiratory rehabilitation, which demonstrates the fundamental importance of evaluating pulmonary and functional sequelae [17]. Therefore, the main objective of this study was to evaluate the long-term impact of COVID-19 on cardiac and pulmonary autonomic function in patients with AH. We hypothesize that individuals with SAH after COVID-19 infection, even those who experienced mild symptoms, not requiring hospitalization, may present greater impairment in cardiovascular autonomic balance and lung function, in addition, that these impairments may be associated with a worse FC

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 AH 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 diagnosed with SAH for at least one year, using continuous and unchanged antihypertensive medication for at least 3 months, aged between 40 and 75 years of both sexes, were included. For (G1), individuals with AH who did not have a confirmed history of COVID-19 infection, and for (G2), individuals previously infected by SARS CoV-2 and with diagnostic confirmation, there are at least 6 and at most 18 months, who had mild symptoms of COVID-19, without the need for hospital admission, whether in a ward or ICU. All volunteers underwent assessments of long-term autonomic control, lung function and maximum 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. The iRR time series was transferred to a personal computer, where it underwent automated preliminary processing followed by manual review by a trained team to remove ectopic beats and artifacts, ensuring that data cleaning did not exceed 5% of the iRR samples. All recordings included at least 18 hours of sinus rhythm and were segmented into sleep and wake periods [18]. HRV was analyzed using specific non-linear routines developed by Prof. Dr. Alberto Porta (Università degli Studi di Milano, Italy) to access the symbolic analysis, was performed by grouping the 3-symbol patterns into four types of clusters: (a) patterns without variation (0V); (b) patterns with a variation (1V: 2 consecutive symbols are the same and one symbol is different); (c) patterns with two similar variations (2LV); (d) 2 different variations (2UV: 3 symbols that form a peak or a valley). The occurrence rate of each pattern is defined as 0V%, 1V%, 2LV%, and 2UV%. Where 0V% can be considered as a marker of sympathetic modulation, 1V% as a marker of mixed modulation, 2LV% and 2UV% as markers of vagal modulation

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) [19]. The evaluation was performed using a spirometer (Quark CPET, Cosmed, Italy).

Cardiopulmonary exercise testing (CPET) was conducted to assess functional capacity (FC), in accordance with the guidelines of the European Respiratory Society (ERS) [20]. The test was performed on a horizontal cycle ergometer (Quinton Corival 400, USA), with continuous monitoring of ergospirometric parameters via a gas analyzer (Quark CPET, Cosmed, Italy).

The protocol included 1 minute of rest with the participant seated on the bike, followed by a 2-minute warm-up at minimal load (~4 W). Thereafter, a ramp protocol was initiated, with progressive increments of 15 Watts per minute, aiming for a total exercise duration of 8 to 12 minutes. Participants were instructed to maintain a pedaling cadence of 60–65 revolutions per minute (rpm). Every 2 minutes after the workload began, systolic and diastolic blood pressure (SBP/DBP), as well as perceived exertion for dyspnea and limb fatigue, were assessed using the Modified Borg Scale.

2.4 Statistical analysis

Statistical analysis was conducted using IBM® SPSS® Statistics version 22.0. Data normality was tested with the Kolmogorov–Smirnov test. Parametric data were expressed as mean ± standard deviation, and non-parametric data as median and interquartile range. Intragroup comparisons (sleep vs. wakefulness) used the Wilcoxon Signed-Rank test, and intergroup comparisons used the Mann-Whitney U test. Categorical variables were analyzed with the Chi-square test.

Spearman's test assessed correlations between HRV, functional capacity, and spirometry, with coefficients classified as negligible (0–0.25), low (0.26–0.49), moderate (0.50–0.69), high (0.70–0.89), and very high (0.90–1.00), according to Munro (2001). Subanalyses considered potential confounders such as age and medication use. Statistical significance was set at $p < 0.05$, with p-values between 0.05 and 0.08 considered trends.

3. Results

The sample consisted of 52 individuals with an average age of (55.62 ± 9.09), with a higher prevalence of females (78.8%), divided into G1- (n=25; 19 women/6 men) and G2+ (n=27; 22 women/5 men). Of these, two participants from G1- were excluded during the CPET phase, but continued to evaluate the results of cardiac and pulmonary autonomic function. No statistically significant difference was characteristics of the studied population.

In **Table 1**, the results of the comparison of

Table 1. Comparison of spirometric indices between groups (n = 52)

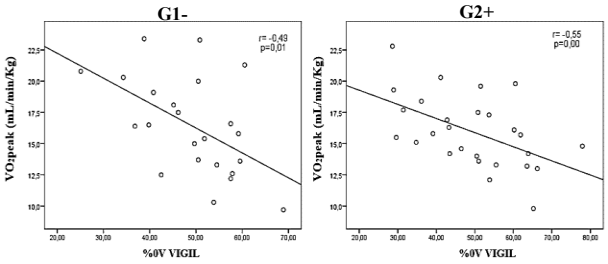
Index	G1 - (n=25)	G2 + (n= 27)	*p*
FEV1, measured (L)	2,5 (2,2 – 3,0)	2,3 (1,9 – 2,6)	0,02*
% of predicted, FEV1	95 (89 – 102)	86 (76 - 99)	0,00*
FEV1/FVC, measured (%)	84,6 (80,8 – 87,7)	81,8 (77,5 – 83,9)	0.00*

Data expressed as median (1st - 3rd interquartile). FVC: forced vital capacity; FEV1: forced expired volume in the first second; FEV1/FVC: Tiffeneau Index. * **p<0.05.**

spirometry indices between the groups are presented. The measured FEV1 variable, as well as the % achieved from the predicted value, were higher in G1-, in individuals who did not have a COVID-19 infection, with a statistically significant difference (P<0.05). Furthermore, the Tiffeneau index (FEV1/FVC) and its % of predicted were also higher in G1- when compared to G2+, which demonstrates better lung function in individuals who did not have a history of COVID-19 infection.

The **Fig. 1** shows the relationship between VO2peak and the 0V% index of HRV measured during the waking period, which represents sympathetic modulation. There was a negative correlation in both groups, however this correlation was low in G1- and moderate in G2+. Demonstrating that the higher the VO2peak, the lower the sympathetic predominance during the waking period. The other variables did not show a signifcant correlation in both groups.

Figure 1 - Correlation between VO_2peak and HRV index



4. Discussion

This study aimed to assess the long-term impact of COVID-19 on cardiac autonomic function and pulmonary function in individuals with systemic arterial hypertension (SAH) and mild acute symptoms. The main finding was that hypertensive individuals with a history of COVID-19 showed worse pulmonary function compared to those without prior infection. Notably, even 6 to 18 months after infection, these individuals exhibited predominantly restrictive ventilatory changes, evidenced by reduced FVC.

Previous studies have shown that the lungs are the main target of SARS-CoV-2 due to its ability to directly invade pulmonary tissue, with functional impairments persisting beyond six months [21,22]. However, most of this evidence is limited to hospitalized patients.

We hypothesized that, due to the direct respiratory damage caused by SARS-CoV-2, even individuals with mild COVID-19 could present long-term pulmonary impairment. Our findings support this, as the G2+ group showed reduced lung function, evidenced by lower FEV1 and Tiffeneau index values compared to controls.

In contrast, no long-term alterations in cardiac autonomic function were observed. Analysis of 24-hour HRV revealed no significant differences, suggesting preserved autonomic modulation. Although previous studies have reported cardiovascular sequelae and autonomic dysfunction post-COVID-19 [23,24], these outcomes may depend on disease severity and host vulnerability.

Conditions like SAH are associated with sympathovagal imbalance and may influence COVID-19 severity through impaired vagal-mediated anti-inflammatory responses [3,25]. However, the absence of significant autonomic changes in our cohort may reflect the mild clinical presentation during infection. As hypertensive individuals already present autonomic imbalance, additional COVID-19-related dysfunction may have been subtle or transient, with no lasting effects beyond the short- or medium-term [25, 26].

Although we used validated indices to evaluate changes in cardiac autonomic control, it is known that the ANS is influenced by several afferent and efferent neural physiological mechanisms, which come from the respiratory systems, baroreceptors, chemoreceptors, mechanoreceptors, among others. Therefore, future studies should include multivariate analysis approaches, considering not only the iRR, but also biological signals, such as respiratory and beat-to-beat blood pressure oscillations, as well as analyzes that consider the causality of biological signals to better understand the impact of disease on the ANS [27–29].

Regarding functional capacity assessed by CPET, no significant differences were observed between groups. Although both groups achieved a VO_2peak >85% of the predicted value, the aerobic capacity reserve (ACR) was classified as weak or very weak across the sample. This suggests that the reduced performance may be more related to pre-existing conditions—such as hypertension, obesity, and sedentary behavior—than to the effects of COVID-19 itself. It is important to note the absence of pre-infection cardiorespiratory fitness (CRF) data in most studies, including ours, which limits the ability to determine whether low CRF levels are a consequence of SARS-CoV-2 infection or preexisting factors.

Despite the lack of significant differences in functional capacity between the groups, we found a significant negative correlation was observed between VO_2peak and the 0V% index during the waking period,

reflecting sympathetic modulation. This correlation was low in G1- and moderate in G2+, indicating that higher functional capacity is associated with reduced sympathetic modulation during wakefulness. This finding aligns with the cardiovascular adaptations that facilitate improved functional capacity.

5. Conclusion

Based on our findings, we conclude that there is no significant alteration in the autonomic nervous system (ANS) or heart rate (HR) in hypertensive patients who have recovered from COVID-19. However, a deterioration in lung function was observed, primarily characterized by restrictive disorders, which may negatively affect CPET performance. These results highlight the importance of a comprehensive post-infection evaluation in hypertensive patients. We recommend further studies to assess ANS dysfunction as a potential post-infection sequela in different patient populations.

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