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Journal of Medical Case Reports and Case Series ISSN: 2692-9880

Research Article Volume 4 Issue 07

Hospitalized Patients With Covid-19 Have Changes In The Cardiac Autonomic Control? A Cohort Study

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Received date: 11 November 2022; **Accepted date:** 05 March 2023; **Published date:** 09 May 2023

Citation: Oliveira MR, Domingos BC, da Luz Goulart C, Dionir Back G, Borghi-Silva A (2023) Hospitalized Patients With Covid-19 Have Changes In The Cardiac Autonomic Control? A Cohort Study. J Med Case Rep Case Series 4(07): https://doi.org/10.38207/JMCRCS/2023/MAY04070443

Abstract

Objectives: To evaluate cardiac autonomic control through heart rate variability (HRV) in hospitalized patients with COVID-19 and compare, considering the severity.

Methods: This is an observational and cohort study. All patients with suspected and diagnosed COVID-19 were invited to participate as soon as they arrived at the hospital. The HRV was recorded at rest in the supine position for 10 minutes using a cardio frequency (Polar S810i, Kempele, Oulu, Finland). Patients were followed until death or discharge.

Results: 120 patients were evaluated, of which 60 were in the Non-COVID-19 group and 60 patients in the COVID-19 group. The COVID-19 group was divided according to severity (30 patients were classified as mild-to-moderate and 30 as severe-to-critical). The COVID-19 group remained hospitalized longer ($p<0.01$), had a higher mortality rate ($p<0.01$), more excellent sympathetic modulation (LF, nu) ($p < 0.01$), sympathovagal balance (LF/HF) ($p=0.01$) and lower parasympathetic modulation (HF, nu) ($p < 0.01$) compared to the Non-COVID-19 group. In COVID subgroups, the severe/critical COVID-19 group had higher sympathetic activity (LF, nu) ($p=0.01$) and lower parasympathetic activity (HF, nu) ($p=0.01$) compared to patients in the mild/moderate COVID-19.

Conclusion: Patients hospitalized with COVID-19 for up to 48 hours had sympathovagal imbalance found through HF (nu), LF (nu), and HF/LF. In addition, the more severe patients had more significant impairment of cardiac autonomic control and consequently had lower total HRV and more excellent sympathetic modulation.

Highlights

1. This is the first study that evaluated early HRV in hospitalized patients with COVID-19.
2. Patients with COVID-19 had marked cardiac autonomic dysfunction.
3. The more severe patients had more significant impairment of cardiac autonomic control.

Keywords: COVID-19, sympathetic activity, severity, and parasympathetic activity.

Introduction

Patients with COVID-19 must be evaluated in the early stages of the disease, even during hospitalization, given the worldwide repercussion of SARS-CoV-2 **[1]**. From simple and direct instruments that show predictive rates of cardiac complications; we can delve deeper into the cardiovascular conditions of these patients, suggesting an appropriate treatment and reducing the risk of mortality in this population. Among these markers, the heart rate variability (HRV) captures the intervals between consecutive heartbeats (R-R intervals)

and is influenced by the Autonomic Nervous System (ANS) on the sinus node **[2–4]**.

Kaliyaperumal et al. found that COVID-19 is associated with autonomic dysfunction, the mechanism and prognostic implications of which need to be evaluated in more detail. The HRV measurement, a simple, non-invasive, and low-cost tool, is helpful in clinical practice as a possible diagnostic marker and rapid prognosis and needs to be evaluated in future research **[5]**. Pan et al. suggest in their study that COVID-19 patients with autonomic dysfunction are more likely to have increased disease severity **[6]**. The underlying mechanism of these findings for the prognosis of COVID-19 is unclear. However, this knowledge of HRV as a predictor of severity and outcome is essential for monitoring disease progression and evaluating treatment effects. Recruitment of additional studies may shed more light on the predictive ability of HRV. Therefore, HRV indices can be combined with other clinical predictors to monitor disease conditions and estimate prognosis **[6]**.

The assessment of cardiac autonomic control can be obtained at the bedside, making it a relevant, validated, and reliable instrument in clinical practice and which may be necessary for understanding the pathophysiology of COVID-19. Based on the early assessment of HRV, this study may show prognostic indices and help to understand these patients' cardiovascular health conditions. Therefore, we aimed to evaluate cardiac autonomic control through HRV in patients with a positive diagnosis of COVID-19 and to contrast the cardiac autonomic responses with hospitalized patients with a negative diagnosis of COVID-19. In addition, we compared cardiac autonomic control in different severities of COVID-19.

Methods

Design and Ethical approval

This is an observational, cohort, and prospective study performed in São Carlos - SP hospitals. This study adhered to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) **[12]**. The local ethics committees (protocol number: 33265220.9.0000.5504) of the Federal University of Sao Carlos (UFSCAR) approved the study.

Population

All patients with suspected and diagnosed COVID-19 admitted to the University Hospital (HU) of the Federal University of São Carlos and Santa Casa de Misericórdia Hospital of São Carlos-SP, Brazil, were invited to participate as soon as they arrived at the respective emergencies, admitted to the ward or ICU, preferably in the first 24 to 48 hours of hospitalization. The patients included in this study were over 18 years of age and were of both sexes, hospitalized (i.e., ward or intensive care unit - ICU) from July (2020) to December (2021). Measurements included in this study occurred between 24-48 hours after hospitalization. Patients with a positive diagnosis of COVID-19 by real-time reverse-transcriptase polymerase chain reaction (RT-PCR) from the nasopharyngeal swab **[14]** were included in the COVID-19 group. The COVID-19 group was divided into patients with mild to moderate severity and severe to critical patients, as suggested by the WHO**[15]** and in the study by Riou et al. **[16]**. Patients with a negative diagnosis for COVID-19 RT-PCR but with hospitalized with similar signs and respiratory symptoms (e.g., cough, fever, runny nose, pain in the body and throat) comprised the Non-COVID-19 group **[14]**.

Exclusion criteria were: 1) Patients or family members who did not accept to participate in the study and did not sign the Free and Informed Consent Form; 2) Patients under palliative care because the hospitals do not accept assessment in these patients; 3) Readmission cases, because they may have chronic effects of COVID-19 infection; 4) Patients using non-invasive ventilation (NIV) during the time of evaluation because this ventilatory support generates changes in vascular function and autonomic nervous system **[17]** 5) Patients in the prone position during the assessment, as our assessment methods cannot be applied in this position, but in the supine position; 6) Patients with cardiac arrhythmias, pacemakers and with the presence of atrioventricular block are not eligible to perform HRV assessed from medical records and bedside electrocardiogram (ECG) when present **[3,4]**.

Patients were screened and recruited by research team members who visited the hospital daily. A brief evaluation of the patient's medical record was conducted to confirm the potential for eligibility. In the first face-to-face meeting, the patients or responsible family members received a description of the study and informed consent for them to read, have any questions answered, and sign the Informed Consent if they agreed to participate. Patients who consented were then familiarized with the procedures, and data collection was initiated. By World Health Organization recommendations, research team members were adequately equipped with personal protective equipment (PPE), including a waterproof apron, goggles, latex gloves, mask n95, disposable mask, disposable cap, and face shield (WHO) **[18]**.

Assessments

The assessment procedure of the current study has been published previously **[19]**. All assessments were carried out at the same time of the day (afternoon), avoiding different physiological responses due to the influence of the circadian cycle. The evaluations occurred at the bedside as soon as possible following hospital admission, always within the first 24-48 hours of access. It is also noteworthy that all assessments were carried out with a minimum time of 1 hour after patient feeding or any intervention by the staff, avoiding any confounding factor in the HRV indices. The following evaluations were carried out:

Clinical and epidemiological evaluation

Clinical data, including age, sex, weight, height, race, comorbidities, medication use, vital signs, and oxygen supplementation, were collected from the medical records to characterize the sample.

Follow-up

After the evaluations, the research team followed patients' outcomes through medical record review, verifying hospitalization days, hospital discharge development, and deaths.

Record of R-R intervals (iRR) for analysis of Heart Rate Variability (HRV) indices

The patients were rested in the supine position for approximately 10 minutes. No nursing or medical procedures were performed during collection to reduce potential collection problems, and patients were instructed not to speak or move during the assessment. A calm and peaceful environment was ensured, with a controlled temperature of 22-24°C and relative humidity between 50-60%. Subsequently, heart rate (HR) in beats per minute (bpm) and iRR were recorded at rest in the supine position for 10 minutes using a cardio frequency (Polar S810i, Kempele, Oulu, Finland) fixed on the chest with simultaneous transmission using the telemetry system to a watch that will store the data. After that, the data were transferred to a computer through an interface (Polar Advantage, Kempele, Oulu, Finland) for analysis. Electrocardiogram was monitored by a heart monitor in the MC5 derivation for all patients during data collection.

The exams were reviewed for quality and saved individually by a blind researcher about the evaluations to verify the quality and the removal of noise. The iRR was processed to calculate the indices of the frequency, time, and non-linear domains of HRV using the KUBIOS HRV program (Kuopio, Finland), with the area of 256 consecutive beats being delineated. The most stable stretch within the chosen period of the 10 minutes collected and, when necessary, application of filters obtained by the software **[3,4,20,21]**. In the present study, artifacts were removed by 2 methods, 1 digitally using the equipment's software and the other manually, characterized by visual inspection of RR intervals and exclusion of irregular intervals. In this work, only series with more than 95 % pure sinus beats were included in the study **[22]**.

HRV was analyzed by linear (time and frequency domain) and non-linear mathematical and statistical models **[2]**. In the time domain, the mean HR; SDNN (standard deviation of all normal iR-R, in ms), estimated total HRV index; and rMSSD (square root of the mean of the square of the differences between the successive iR-R, in ms), representative of the parasympathetic modulation, percentage of intervals differing more than 50 ms different from the previous break (PNN50 %) and Triangular Index. In the frequency domain, the components of low frequency (LF), in normalized units (nu) and absolute (ms^2), representing sympathetic modulation, high frequency (HF), in normalized units (nu) and complete (ms^2), representative of parasympathetic activity and LF/HF ratio, representative of the sympathovagal balance **[21]**. Non-linear indices that represent parasympathetic modulation and overall HRV variability included instant beat-to-beat variability (SD1) and continuous beat-to-beat variability (SD2), respectively; in addition to the complexity indices: Shannon entropy, approximate entropy (ApEn), sample entropy (SampEn), DFAα1: short-term scale exponent in an i-RR time series and DFAα2: long-term scale exponent in an i-RR time series **[21]**.

Statistical analysis

The results are presented as mean and standard deviation (SD) for continuous variables and percentages for categorical variables. The Kolmogorov-Smirnov test was used to verify data distribution. Student's t-test, ANOVA one-way test, and chi-square test were used to compare COVID-19 and non-COVID-19 groups and subgroups, depending on the severity of COVID-19. A linear and logistic regression model was used to detect the influence of age, sex, BMI, and comorbidities on HRV indices. All tests were performed using GraphPad Prism 8.0 (GraphPad Software, California, USA) with statistical significance set at $p \leq 0.05$.

Results

According to the flowchart, represented by Figure 1, 200 patients were initially recruited, and 80 were excluded. Therefore, 120 patients were evaluated in this study.

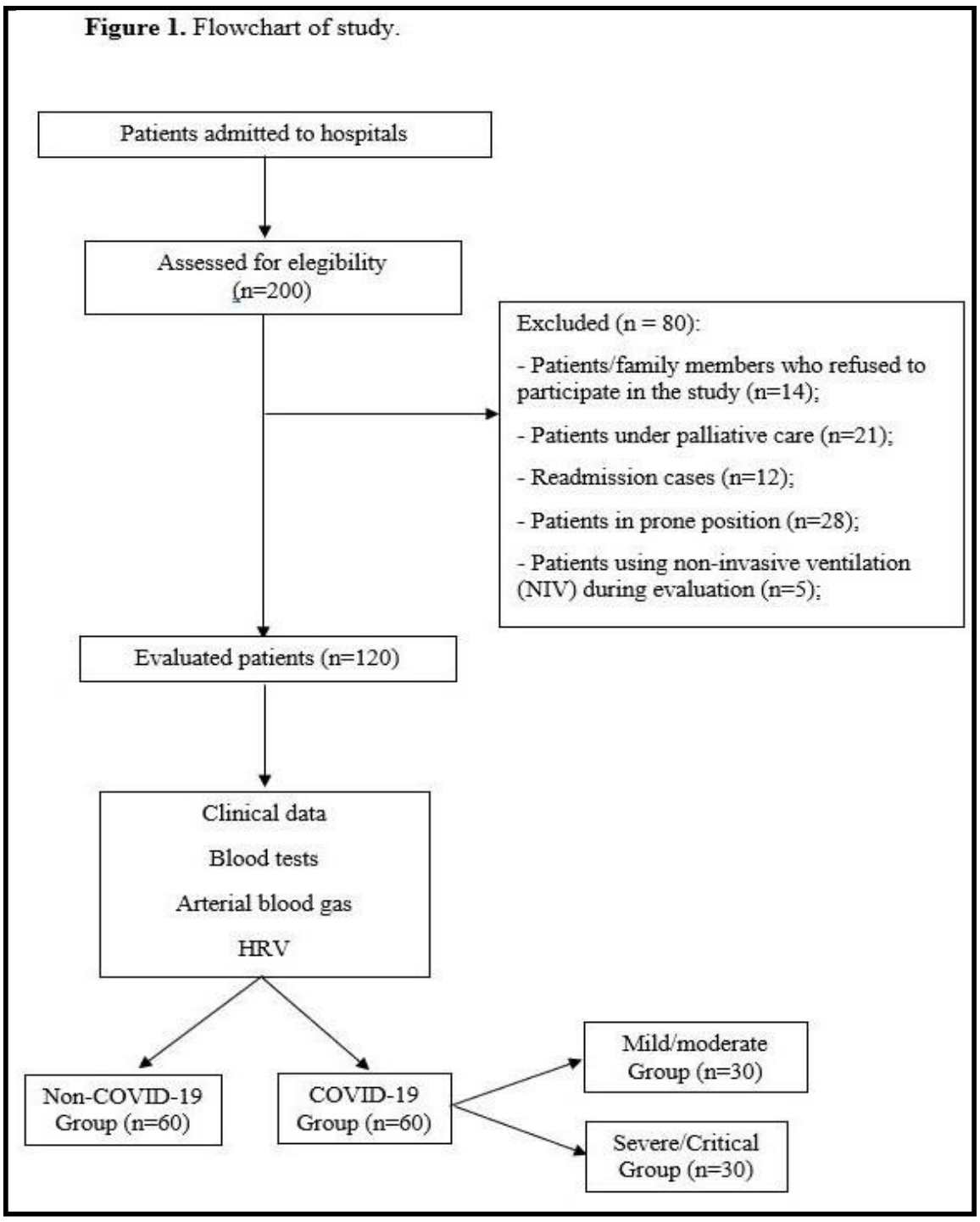

Figure 1. Flowchart of study

Clinical data, comorbidities, number of deaths, hospitalization days, medications, blood count, and blood gas analysis of patients in the COVID-19 and non-COVID-19 groups are described in **Table 1**. The COVID-19 group remained hospitalized longer ($p < 0.01$) and had a higher mortality rate ($p < 0.01$) compared to the Non-COVID-19 group. In the COVID-19 group, in which there are 60 patients, there were 12 deaths, representing a mortality rate of 20 %.

Table 1. Clinical data, comorbidity, number of deaths, hospitalization days, medications, blood count in patients of Non-COVID-19 group and COVID-19 group.

Variables	***Non-COVID-19 (n=60)***	***COVID-19 (n=60)***	***P value***
Age (years)	63±17	57±17	0.06
Sex, n (%)			0.17
Male	32 (53)	38 (63)	
Female	28 (47)	22 (37)	
Weight, (kg)	74±28	87±24	< 0.01
Height (m)	1.67±0.09	1.69±0.07	0.14
Body mass index (BMI) (kg/m²)	26±8.4	30±7.5	0.01
Race, n (%)			0.93
White	40 (66)	35 (66)	
Brown	17 (28)	16 (30)	
Black	3 (5)	2 (4)	
Comorbidity, n (%)			
Hipertension	36 (60)	21 (35)	< 0.01
COPD	18 (30)	7 (12)	0.01

Diabetes	15 (25)	10 (17)	0.18
Hospitalization days	5.7±5.2	13±12	< 0.01
Evaluation location, *n (%)*			< 0.01
Nursery	57 (95)	30 (50)	
ICU	1 (2)	30 (50)	
Emergency	2 (3)	0 (0)	
Death, n (%)	0 (0)	12 (20)	< 0.01
Oxygen supplementation, n (%)	29 (49)	17 (29)	0.01
Mechanical ventilation, n (%)	0 (0)	30 (50)	< 0.01
Medications during hospitalization, n (%)			
Corticosteroids	1 (2)	19 (32)	0.00
Inhibits plaletet aggreagation	2 (3)	26 (43)	0.00
Antibiotics	38 (63)	22 (37)	<0.01
Diuretics	0 (0)	1 (2)	0.50
Antivirals	1 (2)	6 (10)	0.05
Abbreviations: COPD: Chronic Obstructive Pulmonary Disease; BMI: Body Mass Index; ICU: Intensive Care Unit; Student t test and Chi Square Test.			

When comparing HRV indices between the COVID-19 and Non-COVID-19 groups, we found that in the time domain, patients in the COVID-19 group had lower values in their mean HR ($p < 0.01$). While in the frequency domain, patients with COVID-19 showed more excellent sympathetic modulation, represented by LF (nu) ($p < 0.01$) and sympathovagal balance, represented by LF/HF ($p=0.01$) and lower parasympathetic modulation, described by HF (nu) ($p < 0.01$) compared to patients in the Non-COVID-19 group **(Table 2 and Figure 2)**.

Table 2. Comparison of HRV data between Non-COVID-19 and COVID-19 groups.

Variables	***Non-COVID-19 (n=60)***	***COVID-19 (n=60)***	***P value***
Linear indexes			
Time Domain			
Mean HR (bpm)	91±18	80±18	<0.01
Triangular index (RRtri - ms)	5.8±4.2	4.6±3.3	0.09
RMSSD (ms)	18±15	14±16	0.13
SDNN (ms)	25±22	19±18	0.12
pNN50 (%)	5.4±9.3	3.3±9.0	0.20
Frequency domain			
LF/HF	2.4±2.3	3.8±2.0	0.01
LF (ms^2)	201±419	220±457	0.82
HF (ms^2)	159±296	82±226	0.11
Non-linear indices			
SD1	13±10	9.1±9.3	0.03
SD2	33±30	29±33	0.47
SD1/SD2	0.4±0.2	0.3±0.2	0.06
ApEn	0.96±0.14	0.9±0.2	0.37
SampEn	1.6±1.9	1.3±0.5	0.31
DFA α1	0.98±0.36	1.15±0.33	0.01
DFA α2	0.97±0.35	1.10±0.24	<0.01
Abbreviations: LF: low frequency; HF: high frequency; LF/HF, ratio between LF and HF; Student t test.			

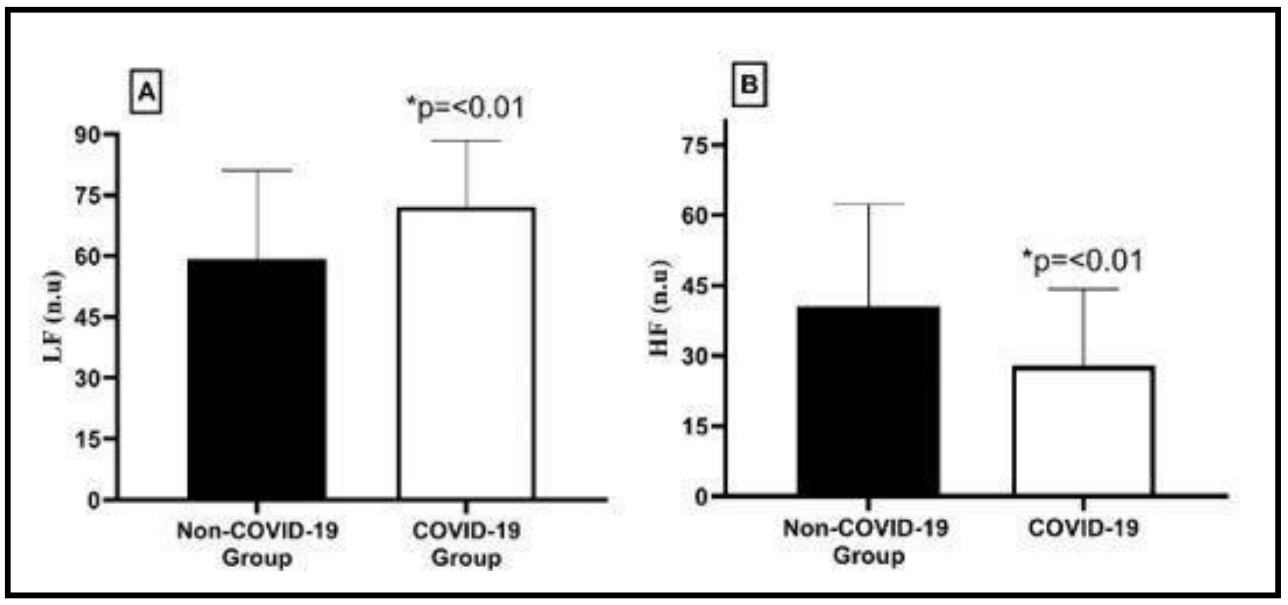

Figure 2. Comparison of LF (n.u) (A) and HF (n.u) (B) indices between Non-COVID-19 and COVID-19 groups.

Table 3 presents clinical data, comorbidities, number of deaths, days of hospitalization, medication use, blood count results, and symptoms of patients with COVID-19, which were classified according to severity. The severe/critical COVID-19 group had the highest number of ICU admissions ($p < 0.01$), remained hospitalized longer ($p < 0.01$), required mechanical ventilation ($p < 0.01$), and used more medications during hospitalization.

Table 3. Clinic, comorbidity, medication and blood count in mild/moderate COVID-19 and severe/critical COVID-19 patients.

Variables	***COVID-19 mild/moderate (n=30)***	***COVID-19 severe/critical (n=30)***	***P value***
Age (years)	64±15	49±15	<0.01
Sex, n (%)			<0.01
Male	14 (37)	24 (63)	
Female	16 (73)	6 (27)	
Weight, (kg)	79±14	94±30	0.01
Height (m)	1.68±0.07	1.70±0.06	0.38
Body mass index (BMI) (kg/m²)	27±4.4	33±9.8	0.03
Race, n (%)			0.41
White	18 (53)	16 (47)	
Brown	10 (59)	7 (42)	
Black	2 (100)	0 (0)	
Comorbidity, n (%)			
Hipertension	17 (81)	4 (19)	0.00
COPD	5 (71)	2 (29)	0.21
Diabetes	7 (70)	3 (30)	0.14
Hospitalization days, (dias)	9±8	18±13	<0.01
Evaluation location, n (%)			0.00
Nursery	30 (100)	0 (0)	
ICU	0 (0)	30 (100)	
Emergency	0 (0)	0 (0)	
Oxygen supplementation, n (%)	17 (57)	0 (0)	<0.01
Mechanical ventilation, n (%)	0 (0)	30 (100)	<0.01
Death, n (%)	4 (33)	8 (66)	0.15
Medications during hospitalization, n (%)			
Corticosteroids	3 (16)	16 (84)	0.00
Inhibits platelet agregation	6 (23)	20 (77)	0.00
Antibiotic	18 (82)	4 (18)	0.00

Abbreviations: COPD: Chronic Obstructive Pulmonary Disease; BMI: Body Mass Index; ICU: Intensive Care Unit. Student t test and Chi Square Test.

Regarding HRV indices in COVID subgroups, according to severity, in the time domain, patients in the mild/moderate COVID-19 group had higher RMSSD values ($p<0.01$) than patients in the severe/critical COVID-19. In the frequency domain, patients with severe/acute COVID-19 had higher sympathetic activity, represented by LF (nu) ($p=0.01$), and sympathovagal balance, represented by LF/HF ($p=0.02$). Lower parasympathetic activity, characterized by HF (nu) ($p=0.01$) compared to patients with mild/moderate COVID-19 **(Table 4 and Figure 3)**.

Table 4. Comparison of HRV data between mild/moderate COVID-19 and severe/critical COVID-19 patients.

Variables	***COVID-19 mild/moderate (n=30)***	***COVID-19 severe/critical (n=30)***	***P value***
Linear indeces			
Time Domain			
Mean HR (bpm)	79±13	81±23	0.65
Triangular index (RRtri - ms)	5.0±3.7	4.5±3.1	0.57
RMSSD (ms)	17±15	8.4±9.2	<0.01
SDNN (ms)	23±21	14±13	0.07
pNN50 (%)	5.3±11	1.2±4.9	0.08
Frequency domain			
LF/HF	2.8±2.1	4.4±3.2	0.02
LF (ms^2)	128±172	131±292	0.96
HF (ms^2)	76±106	35±83	0.10
Non-linear indices			
SD1	12±10	5.9±6.5	<0.01
SD2	39±42	20±18	0.02
SD1/SD2	0.40±0.32	0.31±0.12	0.10
ApEn	0.93±0.21	0.92±0.18	0.72
SampEn	1.34±0.60	1.32±0.47	0.91
DFA α1	1.13±0.35	1.17±0.32	0.63
DFA α2	1.04±0.23	1.15±0.24	0.09

Abbreviations: LF: low frequency; HF: high frequency; LF/HF, ratio between LF and HF; Student t test.

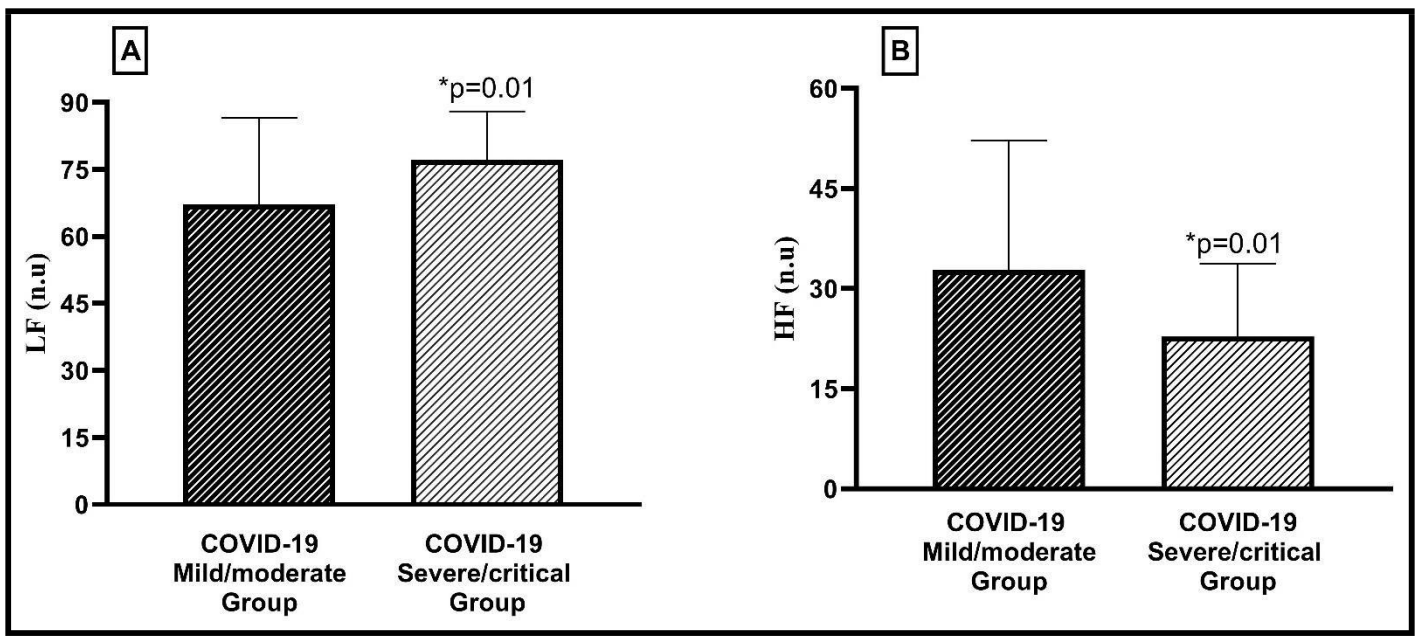

Figure 3. Comparison of LF (n.u) (A) and HF (n.u) (B) indices between mild/moderate and severe/critical COVID-19 groups.

In addition, we performed linear and logistic regression to eliminate confounders and found that there was no influence of age (B coefficient: -0.44; Standard error 0.31; CI95 %: -1.08 to 0.18; p-value: 0.16), sex (B coefficient: -1.71; Standard error 4.40; CI95 %: -10.55 to 7.11; p-value: 0.69), BMI.

(B coefficient: -0.08; Standard error 0.09; CI95%: -0.34 to 0.18; p-value: 0.54), and comorbidities (Hypertension: B coefficient: -5.66; Standard error 4.90; CI95 %: -15.49 to 4.16; p-value: 0.25; Diabetes: B coefficient: -9.25; Standard error 5.72; CI95 %: -20.73 to 2.21; p-value: 0.11; Chronic obstructive pulmonary disease (COPD): B coefficient: -4.97; Standard error 7.00; CI95 %: -19.00 to 9.06; p-value: 0.48) on the LF (nu) index of HRV .analyzed using simple linear and logistic regressions.

Discussion

To our knowledge, this is the first study that evaluated early HRV in hospitalized patients with suspected (Non-COVID-19 group), confirmed COVID-19 (COVID-19 group), and divided patients according to the severity of COVID-19. We found that patients with COVID-19 had marked cardiac autonomic dysfunction, demonstrated by the sympathetic imbalance found through LF (nu), HF (nu), and LF/HF compared to patients without COVID-19; the greater the severity, the greater the dysfunction. In addition, patients with COVID-19 stayed in the hospital for longer days and had a higher mortality rate. Additionally, when performing regressions based on comorbidities, age, sex, and BMI, we confirmed that cardiac autonomic control indices change due to acute SARS-CoV-2 infection.

Aragon-Benedi et al. **[23]** conducted a single observational and pilot study with 14 patients with COVID-19 admitted to the ICU, 7 survivors, and 7 non-survivors. HF (nu) and SDNN were analyzed using an analgesia nociception index monitor. They concluded that the different components of the HRV spectral analysis allow us to infer the state of ANS and the immune system of critically ill patients. Still, emphasize that future studies using non-invasive techniques of neuromodulation of ANS are necessary and can favor the balance between the sympathetic/parasympathetic components, which can be used as a therapeutic strategy in critically ill patients with COVID-19 **[23]**.

Porzionato et al. **[26]** observed that COVID-19 could increase sympathetic activity through changes in blood gases, from intermittent hypoxia, hyperpnea, ACE2 imbalance, immune responses, inflammatory factors, and emotional stress. However, ANS still needs to be elucidated in the pathophysiology of COVID-19 **[26]**. Jin et al. **[27]** highlights that the alteration in the cardiac autonomic control can occur due to 4 factors: 1-the chemosensory entry of the carotid body in the brain stem contributes to the hyperactivation of the sympathetic nervous system due to the hypoxia induced by the respiratory distress syndrome; 2- SARS-CoV-2 can induce neuroinflammation in central sympathetic sites [solitary tract nucleus (NTS), hypothalamic paraventricular nucleus (PVN) and rostral ventrolateral medulla (RVLM)]; 3- The inflammatory cytokines released during the systemic inflammatory response can invade the blood-brain barrier; and 4- extreme anxiety leads to a more significant release of endogenous catecholamines **[27]**. In addition, Li et al. **[28]** claims that COVID-19 can also activate the sympathetic system by increasing the production and release of Ang II **[28]**. These facts corroborate our findings, where we found more excellent sympathetic modulation, but further studies are still needed to explain better the mechanisms of COVID-19 in ANS.

In this way, we affirm that our data emphasize the authors' information in which it is necessary to evaluate the cardiac autonomic control of recently hospitalized patients still in the acute phase of the disease so that we can understand the systemic manifestations that occur in these patients and achieve, in a preventive way, distinguish more severe cases to start with the necessary therapies before more serious images arise.

Regarding mortality, we found that severe/critical patients had eight deaths out of 12, representing 66 % of patients, while in the mild/moderate group, it was 34 %. Although there was no significant difference, there is clinical relevance since there were twice as many deaths in the most severe patients, requiring us to recognize these patients at the beginning of hospitalization from predictive assessments, such as HRV **[9]**. By identifying these patients, a more specific treatment can be performed and prevent the severity and even mortality. As found in the systematic review with the meta-analysis by Lim et al. **[32]**, the death rate of patients with COVID-19 on invasive mechanical ventilation ranged from 47.9 % to 84.4 %, depending on age progression. In a study that analyzes morbidity and mortality patterns in the 10 main countries in the world, Brazil was the second country with the most cases and deaths due to COVID-1933.

Limitation of study

The study has some limitations that must be considered. First, the lack of baseline HRV results before COVID-19 infection makes comparison with developments during the COVID-19 condition difficult, as these patients have comorbidities and are overweight/obese. Second, regarding blood count, arterial blood gases, and vital signs, we can observe that some variables did not show differences or did not show the expected values according to some epidemiological studies **[1,34]**. This may be because our sample is smaller in these studies.

In the present study, we considered it essential to exclude potential confounder factors that could interfere with HRV analysis, such as VNI and neuromuscular blockers usage, that could reduce our findings' reliability. Finally, the results of the present study are limited to hospitalized patients with acute respiratory infection, with assessments taking place within the first 48 hours.

Implications for future practice and research

Using a heart rate monitor, which is an accessible, validated, and non-invasive method, it is possible for patients to start rehabilitation programs with the assessment of autonomic control and for exercises to be directed to improve sympathovagal balance. The results reinforce the utility of some strategies targeted at reducing sympathetic activation may be effective in enhancing the parasympathetic modulation and provide a rationale for the improvement of sympathovagal balance with selected interventions (medications, mobilizations, respiratory exercises) used by health professionals during a hospital stay to reduce the days of hospitalization and assisting in the post-discharge hospital. This is essential for the individual's homeostasis and impacts the reduction of heart disease and mortality rates.

Conclusion

We conclude that patients hospitalized with COVID-19 for up to 48 hours had sympathovagal imbalance found through HF (n.u), LF (n.u), and HF/LF compared to patients without COVID-19. Finally, our data suggest that these patients are more likely to have alterations in cardiac autonomic control and, consequently, risk of cardiovascular disease and higher death rates than the group hospitalized for other respiratory causes. In addition, the more severe patients had more significant impairment of cardiac autonomic control than the mild to moderate group and consequently had lower total HRV and more excellent sympathetic modulation.

Conflict of interest: The authors reported no potential conflict of interest.

Funding

This study is supported by a research grant from Fundação de Amparo à Pesquisa do Estado de São Paulo, São Paulo, Brazil (FAPESP) Process N° 2015/26/501-1 and N◦ 2018/03233-0, by the Coordenação de Aperfeiçoamento de Pessoal de Nível Superior- Brasil (CAPES - 001) Process N° 88887.507811/2020-00 and by Conselho Nacional de Desenvolvimento Científicoe Tecnológico (CNPq): 141803/2019-3.

Author's contribution

MRO, BCD, and GDB participated in all data collection and analysis. CLS and MRO performed the statistical analysis and data interpretation. MRO and ABS completed the manuscript writing. ABS conducted the submission of the manuscript.

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