Hemodynamic Behaviour During Tilt Test in Patients with Long COVID

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Abstract

The Tilt Test is an exam used to assess the cardiovascular autonomic response to postural changes. This study investigated the hemodynamic behavior of patients with Long COVID during the Tilt Test, focusing on changes in systolic (SBP) and diastolic (DBP) blood pressure, in addition to heart rate (HR). The sample consisted of 56 participants, divided into a control group and a study group with a history of COVID-19 infection. The test protocol consisted of 15 min in the supine position, 15 min in the inclined position and 20 min in the recumbent position. The results showed that patients in the study group had lower blood pressure variability and lower autonomic response compared to the control group, especially in the orthostatic phase of the exam. The mean difference in SBP-DBP in the second phase was 35.5 ± 14.0 mmHg in the study group vs 35.7 ± 8.53 mmHg in the control group, showing lower hemodynamic adaptation in patients with Long COVID. Such findings may be related to changes in the sensitivity of baroreceptors or reduced venous return. It is concluded that the Tilt Test can be a useful tool to identify autonomic dysfunctions in patients with Long COVID, contributing to the early diagnosis and appropriate clinical management of these individuals.

1. Introduction

In 2020, the world faced a pandemic that resulted in more than 250 million people infected by the COVID-19 virus. The scientific community has focused primarily on the development of strategies that reduce hospitalizations and deaths in the early stages of the disease, with emphasis on the administration of vaccines[1].

With the control of these acute complications, researchers around the world began to investigate the possible long-term side effects caused by this viral infection, which came to be called Long COVID[2].

Postural Orthostatic Tachycardia Syndrome (POTS) is a condition that affects the autonomic nervous system (ANS), and can cause tachycardia, fainting, fatigue, among other symptoms that significantly impact quality of life[3]. Recent research suggests that individuals who have had COVID-19 have autonomic dysfunction, which can trigger POTS[4], [5].

The Tilt Test is considered the standard exam for ANS assessment. It is divided into three phases: i) horizontal position, ii) inclined, and iii) decubitus. During stretcher elevation, a physiological response of increased heart rate and changes in blood pressure due to the action of gravity is expected. However, in patients in the control group with no history of COVID-19, the heart rate tends to remain stable throughout the test[6].

Blood pressure is influenced by several factors, such as wakefulness, temperature, emotions, and body position. The latter is especially relevant because it directly involves autonomic regulation[7]. In patients with cardiovascular autonomic dysfunction, such as those affected by Long COVID, changes in blood pressure levels may occur, evidencing an imbalance in circulatory homeostasis.

Thus, the objective of this study is to identify abnormal hemodynamic responses, related to changes in blood flow and blood pressure, which deviate from the expected pattern, as a clinical manifestation of Long COVID.

2. Objectives

To describe changes in blood pressure levels in patients with Long COVID by applying techniques in the processing of signals in the time domain, in order to assist in early diagnosis and contribute to the improvement of the quality of life of these patients.

3. Material and Methods

The data collection was scheduled at the Polyclinic Hospital / University of Mogi das Cruzes (UMC), Dom Antônio Cândido de Alvarenga Street, 170 -Centro, Mogi das Cruzes, SP, Brazil. The sample consisted of 56

participants of both sexes (27F and, 29M), 37 from the study group (SG) and 19 from the control group (CG). The sample is balanced, as shown in Table 1.

Initially, the patient goes through the inclusion and exclusion criteria, having to be between 18 and 75 years old, not have COVID-19 or be pregnant, not use medications that alter autonomous responses.

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The patient entering the office, the first step is the explanation and collection of signatures for the ICF (Informed Consent Form) and the Term of Authorization for the Use of Image and Voice. Soon after, the patient undergoes data collection, including personal information, date and brand of vaccines taken, preexisting diseases, medicines for continuous use, date of positive COVID tests, hospitalization history, etc. Patients are also measured and weighed to calculate BMI.

Table 1. Clinical Profile

	SG	CG
Male	15	14
Age Female (Years	39.8 ± 16	35 ± 17.9
Age Male (Years)	39.1 ± 13.3	32.1 ± 14.8
Weight Female (Kg)	73 ± 18.2	68.2 ± 14.1
Male Weight (Kg)	83.8 ± 12	81.9 ± 16.5
Height Female (cm)	162 ± 5.7	165 ± 8.2
Male Height (cm)	174 ± 6.7	175 ± 6.8
BMI Female (Kg/m2)	27.8 ± 6.4	25 ± 3.6
BMI Male (Kg/m2)	27.7 ± 3.1	26.7 ± 3.1

The exam begins with the patient lying down for 15 minutes, then the stretcher is reclined, remaining in this position for another 15 minutes and, finally, it is placed horizontally again for 20 minutes. As an example, Figure 1 presents results.

Figure 1. Patient prepared

The volunteer is laid on the reclining stretcher, the electrodes are placed on the patient's chest, which will have the information sent to the Tilt Test, and the pressure is measured every one minute by an automatic pressure device (Figure 2).

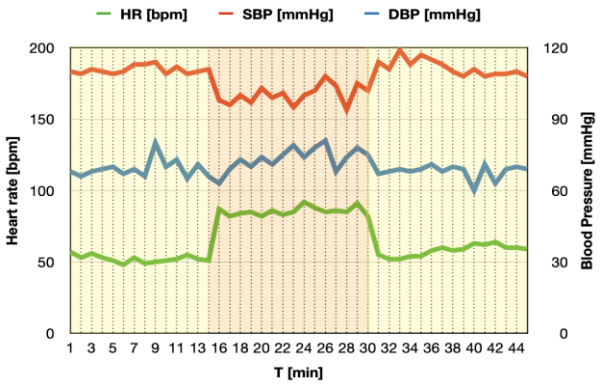

Figure 2. Normal results during Tilt Test

Power Bl is used to locate all collection and anamnesis information in a unified system, as well as to help visualize data and statistical calculations[8]. After that, we used PhyBios to process the data divided into phases.

4. Results

Table 1 presents the clinical characteristics of the sample. The study group had a higher proportion of women (81.48%) compared to the control group (18.52%), a difference considered statistically significant (p = 0.042). Mean ages were slightly higher in the study group, for both women and men.

Regarding hemodynamic parameters, the behavior of blood pressure during the three phases of the Tilt Test was evaluated by means of the difference between systolic and diastolic blood pressure (SBP-DBP). The mean PAS-DBP values throughout the phases showed a trend towards a reduction in the orthostatic phase (phase 2) in both groups, followed by an increase in the final phase of rest (phase 3), as evidenced in Table 2.

Table 2. Hemodynamic parameters

	SG	CG
Mean PAS-PAD [mmHg]	41.4 ± 12.4	43.8 ± 10.1
SD PAS-PAD [mmHg]	6.76 ± 2.2	7.49 ± 2.7
RMSSD [mmHg2]	6.7 ± 1.87	6.9 ± 2.23
Triangular Index	2.12 ± 0.578	2.16 ± 0.561
Pas-pad Phase 1[mmHg]	44.2 ± 12.4	46.9 ± 12.1
SD PAS-PAD Phase 1[mmHg)	3.76 ± 1.78	3.56 ± 1.26
RMSSD Phase 1[mmHg2]	5.11 ± 2.64	4.76 ± 1.86
Triangular Index Phase 1	1.49 ± 0.522	1.46 ± 0.380
PAS-PAS Phase 2[mmHg]	35.5 ± 14	35.7 ± 8.53
SD PAS-PAD Phase 2[mmHg]	5.68 ± 2.64	6.12 ± 2.88

RMSSD Phase 2[mmHg2]	7.57 ± 3.13	8.02 ± 3.47
Triangular Index Phase 2	1.85 ± 0.742	2.09 ± 0.711
PAS-PAD Phase 3[mmHg]	43.6 ± 12.4	47.5 ± 10.6
SD PAS-PAD Phase 3[mmHg]	4.19 ± 1.58	4.05 ± 1.78
RMSSD Phase 3[mmHg2]	5.53 ± 2.06	5.70 ± 2.72
Triangular Index Phase 3	1.67 ± 0.460	1.64 ± 0.393

In the control group, SBP-DBP values were consistently higher in all phases, especially in phase 3, where the mean difference reached 47.5 ± 10.6 mmHg, compared to 43.6 ± 12.4 mmHg in the study group. In the orthostatic phase, the values were similar between the groups (35.5 ± 14.0 mmHg in the OS vs 35.7 ± 8.53 mmHg in the CG), indicating a physiological response similar to the inclination, but with lower pressure variability in the study group, which may suggest less autonomic flexibility.

In addition to the difference between SBP and DBP, variability indices such as standard deviation (SD PAS-PAD), RMESSD (ROOT MEAN SQUARE OF SUCCESSIVE DIFFERENCES) and Triangular Index were calculated. In all phases, the patients in the study group had lower values of these indices, denoting less hemodynamic oscillation.

Figure 3 graphically illustrates this behavior, showing lower reactivity of the autonomic nervous system in patients with Long COVID. This pattern may be associated with baroreflex dysfunction, as proposed by Urroz Lopez et al. (2022) and Acanfora et al. (2022).

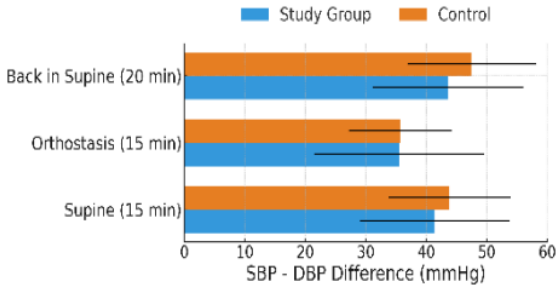

Figure 3. Blood pressure by phase compared by group

From a clinical point of view, it was also observed that the study group had a higher prevalence of comorbidities such as hypertension (81.8% of cases), diabetes, hypothyroidism, and obesity — factors that, although controlled by inclusion/exclusion criteria, can impact autonomic regulation and amplify postviral effects.

Figure 3 shows the comparison of the hemodynamic response to the Tilt Test between participants in the control and study groups. It is observed that the individuals in the control group (GLSV29fev24) generally demonstrate greater stability of blood pressure values, with physiological variations expected during the orthostatic phase.

In the participants of the study group, less adaptive changes are observed. It presents maintenance of blood pressure levels throughout all phases, with a slight increase in SBP at the end of collection. In general, the data indicate that participants in the control group tend to have better hemodynamic regulation in the face of postural change, while those in the study group show signs of possible autonomic dysfunction.

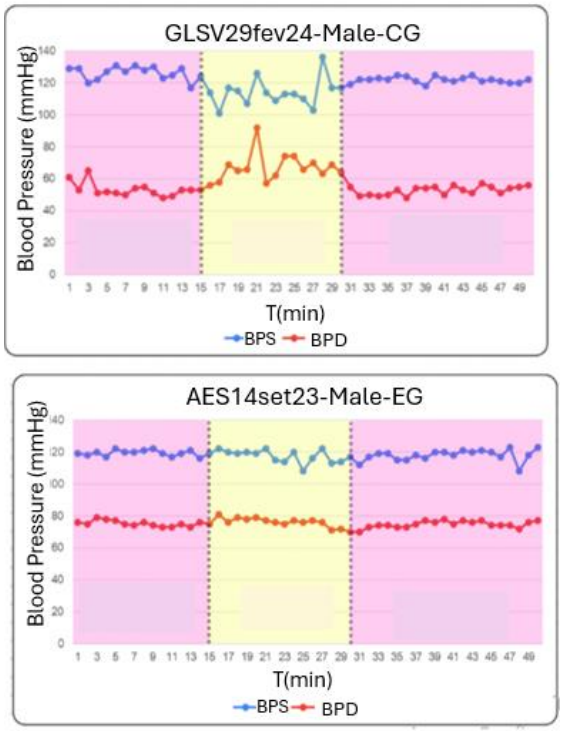

Figure 4. SBP and DBP by group and sex

5. Discussion

The results obtained in this study indicate that patients with a history of COVID-19 infection (study group) showed subtle but consistent changes in hemodynamic regulation during the Tilt Test. Although the absolute values of SBP-DBP were similar between the groups, the lower pressure variability in the study group — evidenced by lower values of SD, RMSSD and Triangular Index — points to a possible impairment of the autonomic response.

This lower oscillation may be related to a deficit in sympathetic activation or baroreflex dysfunction, since the baroreceptor reflex is responsible for quickly adjusting blood pressure in the face of postural changes. Under normal conditions, tilting generates blood redistribution and activates this reflex, promoting compensatory tachycardia and peripheral vasoconstriction. However, in patients with Long COVID, this mechanism may be attenuated, as discussed by Urroz Lopez et al. [9] and Fedorowski et al. [11].

In the orthostatic phase (phase 2), the mean SBP-DBP values decreased in both groups, reflecting physiological adaptation to postural stress. However, the study group

exhibited a more cushioned response in the final phase (phase 3), suggesting impairment in the reestablishment of circulatory homeostasis. This pattern may be associated with Postural Orthostatic Tachycardia Syndrome (POTS), a condition more frequently described in post-COVID-19 patients [4], [5].

The study group also had a higher prevalence of hypertension, diabetes, obesity, and hypothyroidism — conditions known to be associated with reduced baroreflex sensitivity [7], [10]. This reinforces the need to consider comorbidities in the context of hemodynamic assessment and in the differentiation between sequelae of viral infection and preexisting risk factors.

Although no statistically significant differences were found between the groups in the measures analyzed, the trend towards lower hemodynamic variability in the study group may have important clinical implications, especially in symptomatic patients. The introduction of complementary temporal analysis tools — such as the RMSSD — and the use of smartwatches integrated into the FLEEM System® platform show promise for screening and remote monitoring of autonomic dysfunctions on a large scale [8].

The comparative analysis of Figure 4 suggests that individuals in the control group have a more stable response to postural change. However, in the study group, the slight reduction in SBP during orthostasis may indicate a subtle autonomic dysfunction, a characteristic observed in some post-COVID-19 patients.

Additional studies with a larger sample, analysis by sex, and application of multiple logistic regression are recommended to deepen the understanding of post-COVID dysautonomia and its clinical manifestations. The integration of Tilt Test into remote monitoring strategies may represent an innovative approach to early diagnosis and management of POTS and other autonomic dysfunctions in vulnerable populations.

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References

[1] L. Jin, Z. Li, X. Zhang, J. Li, e F. Zhu, “CoronaVac: A review of efficacy, safety, and immunogenicity of the inactivated vaccine against SARS-CoV-2”, *Human Vaccines & Immunotherapeutics*, v. 18, n. 6, p. 2096970, nov. 2022, doi: 10.1080/21645515.2022.2096970.

[2] S. Lopez-Leon *et al.*, "More than 50 Long-term effects of COVID-19: a systematic review and meta-analysis", 29 January 2021, *Infectious Diseases (except HIV/AIDS)*. doi: 10.1101/2021.01.27.21250617.

[3] S. Vernino *et al.*, "Postural orthostatic tachycardia syndrome (POTS): State of the science and clinical care from a 2019 National Institutes of Health Expert Consensus Meeting - Part 1", *Autonomic Neuroscience*, v. 235, p. 102828, nov. 2021, doi: 10.1016/j.autneu.2021.102828.

[4] Y. Amekran, N. Damoun, e A. J. El Hangouche, “Postural orthostatic tachycardia syndrome and post-acute COVID-19”, *GCSP*, v. 2022, n. 1–2, jun. 2022, doi: 10.21542/gcsp.2022.13.

[5] D. Acanfora *et al.*, "Impaired Vagal Activity in Long-COVID-19 Patients", *Viruses*, v. 14, n. 5, p. 1035, May 2022, doi: 10.3390/v14051035.

[6] L. C. M. Vanderlei, C. M. Pastre, R. A. Hoshi, T. D. D. Carvalho, and M. F. D. Godoy, "Basic notions of heart rate variability and its clinical applicability", *Rev Bras Cir Cardiovasc*, v. 24, n. 2, p. 205–217, jun. 2009, doi: 10.1590/S0102-76382009000200018.

[7] L. M. Ferreira, S. S. D. Silva, L. D. C. Sousa, R. G. L. Costa, R. D. S. Maranhão, and A. A. D. Souza, "Post-exercise blood pressure response and its associated factors", *Educ. fís. Cienc.*, v. 24, n. 2, p. e221, apr. 2022, doi: 10.24215/23142561e221.

[8] A. L. G. D. Santos *et al.*, "Data-Driven Health: Using Power BI for Physiological Data Analysis in Clinical Research," 2025, doi: 10.17605/OSF. IO/8D642.

[9] M. Urroz Lopez, J. R. Mitchell, R. S. Sheldon, and J. V. Tyberg, "Effector mechanisms in the baroreceptor control of blood pressure", *Advances in Physiology Education*, v. 46, n. 2, p. 282–285, jun. 2022, doi: 10.1152/advan.00160.2021.

[10] "Baroreceptor Modulation of the Cardiovascular System, Pain, Consciousness, and Cognition", in *Comprehensive Physiology*, 1st ed., Wiley, 2021, p. 1373–1423. doi: 10.1002/cphy.c190038.

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