Systemic impact of the post-Coronavirus disease syndrome in Brazil

Impacto sistêmico da síndrome da doença pós-Coronavírus no Brasil

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ABSTRACT
Background: Symptom persistence following severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has been recognized as the post-coronavirus disease (post-COVID-19) syndrome. We aimed to assess the long-term sequelae of COVID-19 in a local Brazilian population, and to identify risk factors for the onset and severity of this syndrome.Methods: This cross-sectional study was conducted in a tertiary-care hospital. Participants who had recovered from COVID-19 underwent a clinical evaluation and completed a questionnaire on post-COVID-19 symptoms that they had experienced.Results: In a sample of 141 patients, the most prominent post-COVID-19 symptoms were associated with the cardiovascular, respiratory, and neurological systems. Participants aged over 40 years had a significantly higher mean number of symptoms than those aged 40 years or younger (14.6 vs. 11.1). Patients with more severe disease in the acute phase, had significantly more symptoms than those with mild or moderate disease. Most post-COVID-19 symptoms were associated with diabetes mellitus (21.8) and renal failure (21.8), but without a significant difference in the number of associated symptoms according to the presence of preexisting comorbidities.Conclusions: Post-COVID-19 syndrome was more common and comprised more symptoms in participants aged over 40 years and in participants with severe disease during the acute phase. Future studies should assess the duration of post-COVID-19 syndrome symptoms and evaluate the impact of COVID-19 vaccination on post-COVID-19 syndrome.

Keywords: Brazil, COVID-19, post-COVID-19 syndrome, SARS-CoV-2, sequelae of COVID-19.

RESUMO
Antecedentes: A persistência dos sintomas após a infecção por coronavírus 2 da síndrome respiratória aguda grave (SARS-CoV-2) foi reconhecida como a síndrome da doença pós-coronavírus (pós-COVID-19). Nosso objetivo foi avaliar as sequelas de longo prazo da COVID-19 em uma população local brasileira e identificar fatores de risco para o aparecimento e gravidade dessa síndrome.Métodos: Este estudo transversal foi realizado em um hospital terciário. Os participantes que se recuperaram do COVID-19 foram submetidos a uma avaliação clínica e preencheram um questionário sobre os sintomas pós-COVID-19 que experimentaram.Resultados: Em uma amostra de 141 pacientes, os sintomas pós-COVID-19 mais proeminentes foram associados aos sistemas cardiovascular, respiratório e neurológico. Os participantes com mais de 40 anos apresentaram um número médio de sintomas significativamente maior do que aqueles com 40 anos ou menos (14,6 vs. 11,1). Pacientes com doença mais grave na fase aguda apresentaram significativamente mais sintomas do que aqueles com doença leve ou moderada. A maioria dos sintomas pós-COVID-19 esteve associada a diabetes mellitus (21,8) e insuficiência renal (21,8), mas sem diferença significativa no número de sintomas associados de acordo com a presença de comorbidades preexistentes.Conclusões: A síndrome pós-COVID-19 foi mais comum e compreendeu mais sintomas em participantes

com mais de 40 anos e em participantes com doença grave durante a fase aguda. Estudos futuros devem avaliar a duração dos sintomas da síndrome pós-COVID-19 e avaliar o impacto da vacinação contra a COVID-19 na síndrome pós-COVID-19.

Palavras-chave: Brasil, COVID-19, síndrome pós-COVID-19, SARS-CoV-2, sequelas do COVID-19.

1 INTRODUCTION

Complications associated with the coronavirus disease (COVID-19) occur during or shortly after the infection. However, some complications may persist,[1-5] including persistent muscle fatigue or weakness, respiratory system disorders, sleep disorders, smell disorders, skin and phrenic changes, neurological disorders, and cardiovascular complications.[1-6] The World Health Organization recently defined post-COVID-19 syndrome as a condition that usually manifests within 3 months after acute severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, with symptoms lasting for at least 2 months that cannot be explained by alternative diagnoses.[7] Isolated or combined symptoms, usually impacting daily life, may arise in the initial recovery phase, persist in the acute phase, and reappear with varying intensities after periods of remission.[7] Observational studies of other post-viral syndromes, such as SARS,[8] indicate similar pathophysiological mechanisms for post-COVID-19 syndrome.

In Wuhan, approximately 76% of participants had at least one sequela of the disease during the 6-month follow-up, and main long-term complications included persistent fatigue and muscle weakness, sleep disorders, alopecia, smell disorders, palpitations, joint pain, decreased appetite, taste disorders, vertigo, vomiting, diarrhea, chest pain, pharyngeal pain, swallowing difficulties, skin rash, myalgia, and headache.[2] Other studies have detected important long-term pulmonary effects, including pulmonary fibrosis and hypoperfusion, in a significant number of patients.[6] More than 30% of hospitalized COVID-19 patients presented with acute kidney injury,[9] leading to chronic kidney disease and other systemic sequelae. Myocardial injuries caused by SARS-CoV-2 induce atrial or ventricular fibrosis leading to COVID-19-associated arrhythmia.[10]

Although the global impact of COVID-19 sequelae has been widely studied, research in the Brazilian population is limited. This study aimed to assess the long-term sequelae of COVID-19 in a local Brazilian population and to identify risk factors

for the onset and worsening of post-COVID-19 syndrome.

2 METHODS

This cross-sectional observational study was conducted between June and October 2021 in Goiânia, Brazil, using clinical evaluation and a questionnaire, for reporting clinical manifestations of the infection, among COVID-19 patients who had recovered and was approved by the Research Ethics Committee of the Pontifical Catholic University of Goiás (number: 47544021.9.0000.0037). The study population included adult patients (age >18 years) previously infected by SARS-CoV-2. All participants provided written informed consent.

Epidemiological data, such as age, sex, and time since infection onset, of the patients were recorded. Data were collected on the acute phase of infection, including disease severity, pulmonary involvement, clinical management, and comorbidities prior to infection. The presence or absence of post-COVID-19 alterations was recorded using the questionnaire.

Symptomatic patients without evidence of major viral pneumonia or hypoxemia were classified as mild cases; those with clinical signs of pneumonia, but no complications, including SpO_2 ≥90% on room air, were classified as moderate cases; and those with clinical signs of pneumonia accompanied by tachypnea or hypoxemia, acute respiratory distress syndrome, sepsis, thromboembolic events, or systemic inflammatory response syndrome were classified as severe cases. Pulmonary involvement was evaluated using chest-computed tomography (CT) during acute-phase disease. SARS-CoV-2 infection was confirmed either by reverse-transcription polymerase chain reaction, serology, or typical alterations observed on chest CT.

The post-COVID-19 alterations evaluated in this study were related to cardiovascular disorders (arrhythmia, myocarditis, new systemic arterial hypertension, increased resting heart rate, and palpitations), respiratory disorders (cough, chest pain, sleep apnea, post-activity apnea, dyspnea, and sputum), neurological disorders (headache, memory loss, attention disorders, nausea and vomiting, sleep disorders, dizziness, ageusia, and psychiatric disorders (anxiety, depression, obsessive-compulsive disorder, mood disorders, dysphoria, paranoia, mental health changes, and psychiatric illness), integumentary disorders (hair loss, skin signs), or were general/nonspecific symptoms (fatigue, arthralgia, generalized pain, fever, sweat, gastrointestinal disorders, weight loss, chills, hearing loss or tinnitus, red eyes, edema, sore throat, renal failure, and diabetes

mellitus).

For statistical analysis, the data were entered into a spreadsheet using Microsoft Excel (Microsoft, Redmond, WA, USA). Continuous variables were initially analyzed using descriptive statistics: frequencies (absolute and relative percentage) were calculated for categorical variables, and mean and standard deviation were calculated for continuous variables. Subsequently, inferential statistics were used. The D'Agostino–Pearson normality test was used to define the type of distribution. For variables with a normal distribution, the Student's *t*-test was used to compare the means of two variables whereas analysis of variance was used to compare three or more variables. For variables with non-normal distribution, the Mann–Whitney *U* test was used to compare the medians of two variables. The analyses were performed using BioEstatsoftware 5.3 (Federal University of Pará, Belém, Pará, PA, Brazil) and a significance level of 5% ($P<0.05$) was used for all tests.

3 RESULTS

A total of 141 patients participated in the study. Table 1 summarizes the post-COVID-19 symptoms based on the patient's characteristics and the disease severity. Of the 141 study participants, 85 (60.3%) were female. There was no significant difference in the mean number of associated post-COVID-19 symptoms between females and males (13.7 and 11.9, respectively; $P=0.1288$).

The mean age of the participants was 43.8 (range: 18–89) years. A cutoff value of 40 years was established based on the average age and difference in young, middle-aged, and older adults. Of the participants, 46.8% were aged 40 years or younger and 53.2% were older than 40 years; the mean number of post-COVID-19 symptoms was significantly higher in patients who were older than 40 years (11.1 and 14.6, respectively; $P=0.0025$).

Furthermore, 85.8% and 14.2% of participants had COVID-19 <6 and >6 months, respectively, before the questionnaire was completed (mean: 3.6 months; range: 8 days to 13 months). There was no significant difference in the number of post-COVID-19 symptoms between participants who had COVID-19 within the previous 6 months and those who had COVID-19 more than 6 months previously (12.6 and 15.1. respectively; $P = 0.1441$).

More than half of the participants (52.5%) had mild disease, and 23.4% and 24.1% had moderate and severe disease, respectively. The mean number of post-

COVID-19 symptoms in was significantly lower in participants with mild disease than in those with severe disease (10.1 and 17.9. respectively, $P<0.001$).

In the acute phase of the disease, 73 participants had been treated at home, 16 had been admitted to a ward the provided O_2 via a nasal catheter, 16 had been admitted to a ward that provided maximum ventilation, 20 had been treated in the intensive care unit (ICU) with maximum ventilation, and 16 were had been provided with mechanical ventilation. There was a significant difference in the mean number of post-COVID-19 symptoms between patients treated at home and those treated in the ICU (10.1 and 17.7, respectively).

There was a significant difference in the mean number of post-COVID-19 symptoms between participants who had no pulmonary involvement and those who had an impairment of 76%–95% (9.9 and 20.1, respectively, $P < 0.001$).

Most of the post-COVID-19 symptoms presented were related to the cardiovascular, respiratory, and neurological systems, in addition to some general symptoms, such as fatigue and arthralgia (Table 2). The most common integumentary and psychiatric alterations were hair loss (f = 48.2%) and anxiety (f = 70.9%), respectively. The most prevalent alterations were post-activity polypnea, fatigue, palpitations, increased resting heart rate, chest pain, and sleep disorders, which were present in more than half of the participants.

Participants with diabetes mellitus (21.8) and renal failure (21.8) experienced the greatest number of symptoms. Additionally, participant with psychiatric alterations experience an average of more than 20 associated symptoms (psychiatric disease, 21.2; paranoia, 20.8; obsessive-compulsive disorder, 20.8; and dysphoria, 20.1). Among the cardiovascular, respiratory, and neurological alterations, the highest mean number of symptoms were associated with myocarditis (21.0), sleep apnea (18.9), and dizziness (17.6).

All alterations, except for anosmia, when present were associated with a significantly higher number of symptoms than when they were absent. Thus, the association of symptoms with post-COVID-19 syndrome is evident.

The relationships between previous comorbidities and post-COVID-19 symptoms are shown in Table 3. More than half of the participants (53.2%) did not have any pre-existing comorbidities. Of the comorbidities recorded, the most prevalent was systemic arterial hypertension, seen in 19.9% of the participants. However, the comorbidities that presented with the highest and lowest mean number

of associated symptoms were obesity (17.4) and coronary artery disease (9.5), respectively. No significant difference was seen in the mean number of post-COVID-19 symptoms between participants with and without previous comorbidities. There was no significant difference in the mean number of post-COVID-19 symptoms associated with various comorbidities (P = 0.1240).

4 DISCUSSION

The impact of SARS-CoV-2, on different populations globally, depends on several genetic, environmental, geographical, and population-related factors.[11] The result of this study enabled us to draw a profile of how the long-term consequences of the infection manifest in the Brazilian population.

Although not significantly different, the mean number of post-COVID-19 symptoms in females was slightly higher than that in males. While the severity of COVID-19 and the associated mortality rate was higher in males,[12,13] the incidence of the post-COVID-19 symptoms was not. However, the inflammatory response is deregulated and more pronounced in males,[13] which, in theory, could be related to the higher incidence and severity of persistent symptoms after COVID-19.

Age is directly associated with the severity of post-COVID-19 symptoms,[14] and an age of >55 years is a predictor of severe COVID-19 in the acute phase.[15] Similarly, we found that participants aged over 40 years had a significantly higher number of post-COVID-19 symptoms than those aged 40 years or younger, which could be due to the association between greater severity of symptoms in the acute phase and a higher number of chronic symptoms.

The number of chronic symptoms also varied according to the severity of the disease and pulmonary involvement. Participants admitted to the ICU and treated with mechanical ventilation had a significantly higher mean number of symptoms than those admitted to the ward or treated at home. Similarly, participants with moderate and severe disease who had significantly more post-COVID-19 symptoms than those with a mild disease. This is assumed to be partly related to the structural and functional damage caused to the main organ systems (cardiopulmonary, neurological, and renal), such as pulmonary fibrosis, thromboembolic events, inflammation of the central nervous system, myocardial inflammation, arrhythmias, and acute kidney injury.[6,9,14]

A relationship has been found between severe disease in the acute phase and a greater severity of long-term symptoms.[14] Imaging studies on post-COVID-19 changes

have detected persistent inflammation in the lungs, myocardium, kidneys, liver, pancreas, and spleen in patients with severe COVID-19.[2,16] Severe COVID-19 results in higher levels of pro-inflammatory cytokines during the acute phase, which persist at high levels in the circulation during the chronic phase of the infection, resulting in more chronic symptoms.[17] The acute inflammatory response in COVID-19 is responsible for tissue damage that contributes to the disease complications.[18]

Additionally, it is important to highlight the "post-intensive treatment syndrome," which is reportedly an important component in the emergence of persistent post-COVID-19 sequelae.[19] The long immobilization periods, use of large amounts of sedatives and neuromuscular blockers, respiratory shock, and viral toxicity, are believed to contribute to several symptoms of physical limitation, such as fatigue and persistent muscle pain. They also contribute to psychiatric symptoms, such as anxiety, depression, and post-traumatic stress disorder, along with neurological symptoms such as memory loss, attention deficiency, and delirium, which may be irreversible in the most severe cases.[19]

Although patients with more severe COVID-19 tend to experience a greater number of post-COVID-19 symptoms, we found that participants with mild disease also experienced some post-COVID-19 symptoms. Therefore, lower severity of the disease in the acute phase does not reduce the risk of a chronic post-COVID syndrome.[20] Similarly, while comorbidities influence the course of the disease in its acute phase, they do not appear to influence the post-COVID-19 symptoms.[20]In this study, there was no significant difference in the number of post-COVID-19 symptoms in participants with and without comorbidities.

There was significant association between the time since infection and the severity of post-COVID-19 symptoms, suggesting that most symptoms persist for more than 12 weeks. It is not known how long it takes before the symptoms begin to regress.[19] Moreover, as the disease is still a recent phenomenon, it is too early to know how long these chronic symptoms will persist and whether they are permanent or transient sequelae.

As in previous studies, the main post-COVID-19 symptoms reported in this study involved the cardiovascular, respiratory, neurological, and muscular systems.[2-6.20] Long-term studies in patients who survived severe acute respiratory syndrome revealed that psychiatric morbidities and clinically significant chronic fatigue could persist for up to 4 years after the acute respiratory phase.[7] Psychiatric disorders are believed to be caused by the trauma from the severity of the respiratory condition and the social, economic, and cultural impacts of the long recovery process, while persistent fatigue is probably due to

the high serum levels of cortisol and pro-inflammatory cytokines that persist after the disease.[7,16] Additionally, post-febrile chronic fatigue syndrome, generalized myalgia, muscle weakness, and sleep disorders have also been reported in these patients.[21] Given that the course of SARS-CoV-2 infection follows a similar pattern to SARS-CoV-1 infection,[22] it is inferred that the high incidence of psychiatric disorders and chronic fatigue in the long term is caused by the same mechanisms already studied in SARS, and can, therefore, also last for long periods. Chronic fatigue in individuals with post-COVID-19 syndrome has been reported to persist for more than 100 days in some individuals, configuring the main alteration of the syndrome.[23]

Studies on the angiotensin-converter enzyme 2, the SARS-CoV receptor, in transgenic rats have shown that the virus, by colonizing the upper airways, also colonizes the olfactory bulb and thus enters the central nervous system, causing chronic neuronal inflammation, which may be responsible for SARS-COV-1- and SARS-CoV-2-associated neurological disorders.[24,25] Furthermore, based on post-mortem studies on SARS-CoV-1 colonizing the central nervous system, it is assumed that SARS-CoV-2 colonizes the cerebrovascular endothelium and the cerebral parenchyma, reaching neurons and glial cells, especially in the medial temporal lobe, resulting in apoptosis and necrosis. Additionally, the tissue damage caused by the systemic inflammatory response[25] also contributes to permanent damage to the central nervous system. Therefore, the neurological symptoms in SARS and COVID-19 may last for indeterminate periods or could even be irreversible, partly explaining, the absence of a significant relationship between the time elapsed after infection and the severity of post-COVID symptoms.

Consistent with previous studies,[23,26] we found that the most common neurological symptoms included sleep disorders, memory loss, attention disorder, headache, dizziness, general pain, ageusia, anosmia, hearing loss or tinnitus, and nausea and vomiting.

The most significant psychiatric disorders were anxiety, attention disorder, mood disorders, and depression. Post-COVID-19 neuropsychiatric disorders are partially due to neuronal damage caused by the virus, resulting in primary encephalopathy with consequent psychiatric repercussions.[22] Additionally, a respiratory syndrome caused by SARS-CoV-2 can lead to the release of corticotropic hormones, hypothalamic stimulation, and production of glucocorticoids that interfere with brain metabolism,[22] affecting consciousness and reasoning. Finally, psychiatric disorders during and after COVID-19 may also have a sociocultural component. Due to social isolation, the

psychological trauma caused by the disease and fear in the face of the pandemic can cause depression, anxiety, and post-traumatic stress syndrome, which in turn can trigger systemic symptoms, such as dyspnea, fatigue, and palpitations.[22,27,28]

As reported in a previous study,[23] more than half of the participants in our study presented with sleep disorders. Sleep disorders can result from direct neurological damage caused by the virus when crossing the blood-brain barrier, leading to changes in the circadian cycle due to the systemic inflammatory response and psychiatric disorders caused by the pandemic.[29]

Cardiovascular alterations, such as palpitations, increased resting heart rate, chest pain, myocarditis, and arrhythmias are mainly due to the persistent inflammatory state of the myocardium after COVID-19.[6,30] The main cardiovascular alterations in this study are consistent with those reported previously,[20] including palpitations, ventricular arrhythmias, and sinus or supraventricular tachyarrhythmias.[20]

Pulmonary involvement, demonstrated by high rates of post-activity polypnea and dyspnea, is largely due to the reduced diffusion capacity resulting from viral involvement and pulmonary scar fibrosis.[31] However, cardiovascular sequelae also play an important role in the genesis of respiratory sequelae, as they can lead to pulmonary hypertension from a reduction of the left ventricular function.[31] As reported in a previous study,[24] this study found an association between cardiovascular and pulmonary symptoms.

The most common symptom associated with the integumentary system was hair loss, most likely due to post-viral syndrome.[32] Most post-COVID-19 cases of hair loss are reported to be due to telogen effluvium,[32] wherein an increase in interleukin-6 inhibits the proliferation of matrix cells of the hair follicle.[33] In addition to causing excess fluoride in the telogen, COVID-19 may exacerbate cases of fluoride that preceded infection. Moreover, stress caused by the pandemic and the infection itself is a risk factor for hair loss.[31]

4.1 LIMITATIONS

This study has some limitations. It did not monitor patients long enough to record the disappearance of symptoms, so the duration of symptoms of post-COVID-19 syndrome was not estimated. In addition, the symptoms were reported by the patients, without clinical evidence of signs. Finally, no information was recorded about the vaccination status of participants, so that the impact of the COVID-19 vaccine on the post-COVID-19 syndrome was not assessed.

5 CONCLUSIONS

Based on the definition of post-COVID-19 syndrome, several independent associations between symptoms may occur, revealing the conditions that underpin the symptoms.[7] This study demonstrates a strong association of symptoms, based on the significant difference in the number of symptoms according to the presence of specific alterations. The study results reinforce the importance of the systemic interactions that lead to the accumulation of alterations in post-COVID-19 syndrome.

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ANEXOS

Table 1. Post-COVID-19 symptoms according to epidemiological characteristics and evolution of infection.

Variable (N=141)	*n*	*f(%)*	Number of Symptoms		*p-value*
			Mean	SD	
Gender					
Female	85	60,3	**13,7**	6,3	
Male	56	39,7	**11,9**	7,7	0,1288
Age					
Up to 40 years old	66	46,8	**11,1**	6,8	
More than 40 years old	75	53,2	**14,6**	6,7	**0,0025**
Mean (SD)	43,8	14,8			
Min - Max	18	89			
Time after COVID-19					
Up to 6 months	121	85,8	**12,6**	7,0	
More than 6 months	20	14,2	**15,1**	6,5	0,1441
Mean (SD)	3,6	2,6			
Min - Max	0,27	13			
COVID-19 degree					
Mild	74	52,5	**10,1**	5,8	
Moderate	33	23,4	**14,2**	6,0	
Severe	34	24,1	**17,9**	6,9	**<0.0001**
Treatment					
Home	73	51,8	**10,1**	5,9	
ICU/Maximum Ventilation	20	14,2	**17,7**	6,6	
ICU/Orotracheal Intubation	16	11,3	**18,6**	7,1	
Hospitalization/Oxygen cannula	16	11,3	**12,7**	5,8	
Hospitalization/Maximum Ventilation	16	11,3	**15,4**	5,9	**<0.0001**
Pulmonary Impairment					
None	26	18,4	**9,9**	6,5	
Up to 25%	48	34,0	**10,7**	5,8	
26% to 50%	26	18,4	**12,5**	6,2	
51% to 75%	27	19,1	**16,6**	6,3	
76% to 95%	14	9,9	**20,1**	6,2	**<0.0001**
Mean (SD)	34,4%	29,0%			
Min - Max	0%	95%			

Table 2. Post-COVID-19 changes and associated symptoms

Symptom (N=141)	*n*	*f(%)*	Number of Symptoms		*p-value*
			Average	DP	
Fatigue					
Present	89	63.1	**15.4**	6.3	
Absent	52	36.9	**8.8**	5.9	**<0.0001**
Headache					
Present	56	39.7	**16.7**	6.1	
Absent	85	60.3	**10.5**	6.3	**<0.0001**
Attention Disorder					
Present	66	46.8	**16.3**	6.1	
Absent	75	53.2	**10.0**	6.3	**<0.0001**
Hair Loss					
Present	68	48.2	**15.6**	6.7	
Absent	73	51.8	**10.5**	6.2	**<0.0001**
Dyspnea					
Present	53	37.6	**17.7**	5.9	
Absent	88	62.4	**10.1**	5.9	**<0.0001**
Ageusia					
Present	38	27.0	**17.1**	6.8	
Absent	103	73.0	**11.4**	6.3	**<0.0001**
Anosmia					
Present	38	27.0	**14.5**	7.1	
Absent	103	73.0	**12.4**	6.8	0.1131
Post-Activity Polypnea					
Present	101	71.6	**14.4**	6.6	
Absent	40	28.4	**9.3**	6.3	**<0.0001**
Arthralgia					
Absent	90	63.8	**11.1**	6.5	**<0.0001**
Cough					
Present	41	29.1	**18.0**	6.5	
Absent	100	70.9	**10.9**	6.0	**<0.0001**
Sweat					
Present	40	28.4	**16.6**	6.3	
Absent	101	71.6	**11.5**	6.7	**<0.0001**
Nausea/Vomiting					
Present	31	22.0	**16.7**	5.2	
Absent	110	78.0	**11.9**	7.0	**0.0002***
Memory Loss					
Present	69	48.9	**15.6**	6.2	
Absent	72	51.1	**10.4**	6.7	**<0.0001**
Obsessive Compulsive Disorder					
Present	12	8.5	**20.8**	6.5	
Absent	129	91.5	**12.2**	6.5	**<0.0001**
Anxiety					
Present	100	70.9	**14,6**	6.3	

Absent	41	29.1	**9.0**	6.9	**<0.0001**
Gastrointestinal Tract Disorders					
Present	44	31.2	**15.6**	5.3	
Absent	97	68.8	**11.7**	7.2	**0.0007***
Weight Loss					
Present	40	28.4	**16.2**	7.8	
Absent	101	71.6	**11.7**	6.1	**0.0004**
Cutaneous Signs					
Present	24	17.0	**16.8**	6.6	
Absent	117	83.0	**12.2**	6.8	**0.0023**
Palpitations					
Present	84	59.6	**15.9**	6.0	
Absent	57	40.4	**8.6**	5.8	**<0.0001**
General Pain					
Present	44	31.2	**17.9**	5.3	
Absent	97	68.8	**10.7**	6.4	**<0.0001**
Fever					
Present	9	6.4	**21.1**	4,8	
Absent	132	93.6	**12.4**	6.7	**0.0002**
Sleep Disorders					
Present	73	51.8	**16.2**	6.2	
Absent	68	48.2	**9.5**	6.0	**<0.0001**
Sleep Apnea					
Present	21	14,9	**18.9**	5.1	
Absent	120	85.1	**11.9**	6.7	**<0.0001**
Chills					
Present	34	24,1	**17.5**	6.5	
Absent	107	75.9	**11.5**	6.4	**<0.0001**
Psychiatric Disease					
Present	16	11.3	**21.2**	4,1	
Absent	125	88.7	**11.9**	6.5	**<0.0001***
Red Eyes					
Present	33	23.4	**17.0**	6.4	
Absent	108	76.6	**11.7**	6.6	**0.0001**
Hearing Loss or Tinnitus					
Present	36	25.5	**16.9**	6.0	
Absent	105	74,5	**11.6**	6.7	**<0.0001**
Mental Health Change					
Present	19	13.5	**18.5**	6.2	
Absent	122	86.5	**12.1**	6.7	**0.0001**
Diabetes Mellitus					
Present	12	8.5	**21.8**	4,3	
Absent	129	91.5	**12.1**	6.5	**<0.0001***
Sputum					
Present	38	27.0	**16.8**	6.3	
Absent	103	73.0	**11.5**	6.6	**<0.0001**

Edema					
Present	30	21.3	**19.0**	5.7	
Absent	111	78.7	**11.3**	6.3	**<0.0001**
Dizziness					
Present	53	37.6	**17.6**	5.9	
Absent	88	62.4	**10.2**	5.9	**<0.0001**
Sore Throat					
Present	21	14.9	**18.0**	5.8	
Absent	120	85.1	**12.1**	6.7	**0.0002**
Mood Disorder					
Present	50	35.5	**16.6**	7.4	
Absent	91	64.5	**11.0**	5.8	**<0.0001***
Dysphoria					
Present	14	9.9	**20.1**	8.0	
Absent	127	90.1	**12.2**	6.3	**<0.0001**
Myocarditis					
Present	9	6.4	**21.0**	6.6	
Absent	132	93.6	**12.4**	6.6	**0.0002**
Renal Failure					
Present	13	9.2	**21.8**	6.5	
Absent	128	90.8	**12.0**	6.3	**<0.0001**
Arrhythmia					
Present	31	22.0	**19.5**	6.2	
Absent	110	78.0	**11.1**	5.9	**<0.0001**
Paranoia					
Present	10	7.1	**20.8**	5.0	
Absent	131	92.9	**12.4**	6.7	**0.0002**
Depression					
Present	39	27.7	**18.1**	6.6	
Absent	102	72.3	**11.0**	6.0	**<0.0001**
Chest Pain					
Present	75	53.2	**15.8**	5.7	
Absent	66	46.8	**9.7**	6.7	**<0.0001**
New Systemic Arterial Hypertension					
Present	26	18.4	**18.3**	7.2	
Absent	115	81.6	**11.7**	6.3	**<0.0001**
Increased Resting Heart Rate					
Present	75	53.2	**15.4**	5.5	
Absent	66	46.8	**10.1**	7.3	**<0.0001***

Table 3. Relationship of post-COVID alterations with pre-existing comorbidities

Variable (N=141)	*n*	*f(%)*	Number of Symptoms		*p-value*
			Mean	SD	
Comorbidities					
None	75	53,2	**12,0**	6,3	
Systemic Arterial Hypertension	28	19,9	**14,9**	7,3	
Obesity	11	7,8	**17,4**	6,5	
Chagas Disease	9	6,4	**12,1**	6,4	
Dyslipidemia	8	5,7	**12,4**	8,7	
Diabetes melittus	7	5,0	**10,1**	6,5	
Coronary Artery Disease	6	4,3	**9,5**	6,1	
COPD	3	2,1	**15,3**	12,2	0,1240
Asthma	1	0,7			

COVID-19, coronavirus disease; SD, standard deviation; COPD, chronic obstructive pulmonary disease