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Cardiac Markers in Apparently Non-COVID-19 Individuals and Post-COVID-19 Individuals with and without Metabolic Syndrome, Trujillo-Peru 2023

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Purpose: To compare the levels of cardiac troponin I (cTnI) and N-terminal pro-brain natriuretic peptide (NT-proBNP) in apparently non-COVID-19 (COVID-19-) and post-COVID-19 (COVID-19+) persons with metabolic syndrome (MetS+) and without metabolic syndrome (MetS-).

Methods: The descriptive correlational study was carried out in 275 inhabitants of the city of Trujillo in 2023. Cardiac markers were determined by time-resolved immunofluorescence.

Results: It was determined that 58.2% of the participants presented COVID-19 and 46.5% presented a diagnosis of MetS according to the harmonized ATP III criteria. Levels of cTnI greater than 0.05 ng/mL were found in low percentages in the COVID-19-/MetS-, COVID-19-/MetS+, and COVID-19+/MetS- groups at 0.7% each, and in the COVID-19+/SM+ group, it was 0.4%. NT-proBNP concentrations higher than 125 pg/mL were found in 2.9% of participants, of which 1.1% were in the COVID-19+/MetS+ group, a slightly higher proportion compared to the other groups.

Conclusion: The proportion of individuals with normal or elevated cTnI and NT-ProBNP levels does not differ significantly in both healthy individuals, with MetS only, and those with mild Post COVID-19 with or without MetS; however, longitudinal studies are required to detect possible myocardial events in either group for adequate treatment, especially in those with COVID-19+/MetS+.

Keywords: COVID-19, metabolic syndrome, troponin, natriuretic peptides

Introduction

In Peru, so far in the period 2020–2023, the number of accumulated deaths from COVID-19 is 220 617, of which 11,070 correspond to the Department of La Libertad, with a case fatality rate of 6.02%; however, cases and deaths for 2023 have decreased considerably compared to previous years.[1,2]

SARS-CoV-2 caused terrible morbidity and mortality worldwide due to severe damage to multiple organs. Although many people survived the acute phase of COVID-19, there is also evidence that the residual effects of the virus can affect a person's quality of life and even work performance or absenteeism.[3] After recovery from the acute phase of COVID-19, dyspnea and fatigue may continue, possibly linked to the persistence of an inflammatory state, the presence of tissue abnormalities in the lungs, heart and kidneys due to the severity of the disease or due to the presence of two or more comorbidities.[4]

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an RNA-type virus, which has the ability to bind to the angiotensin-converting enzyme receptor 2 (ACE-2) present in the membrane of cells of the heart, lung, kidney and vascular endothelium via the S protein, which allows a transmembrane type II serine protease to cleave it into S1 and S2

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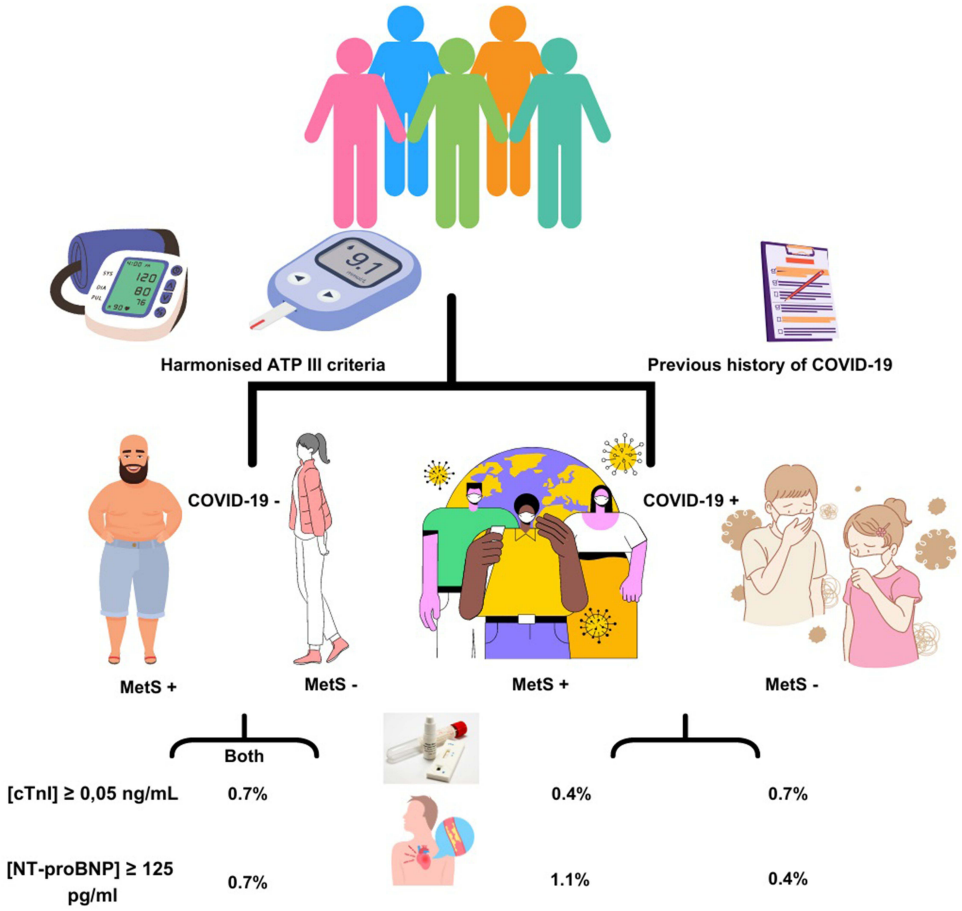
Graphical Abstract



subunits, where the latter cleaves it into the S1 and S2 subunits, the latter of which establishes the fusion of the virus with the membrane and subsequent endocytosis. The entry of the virus into endothelial cells generates an inflammatory process that eventually leads to thrombotic complications.[5]

Angiotensin 1 and 2 are peptide substrates for the activity of ACE-2, which transforms them respectively into angiotensin 1–9 and angiotensin 1–7, both peptides with cardioprotective function, and which due to the binding of SARS-CoV-2 to ACE-2 predispose to cardiac and vascular damage.[6]

Cardiac troponins (cTn) are myofibril proteins in cardiac myocytes that regulate actin-myosin binding in the presence of calcium. The release of these proteins into the bloodstream as a consequence of myocardial tissue injury allows it to be considered as a useful serological marker in patients with suspected myocardial tissue damage.[7]

A study in athletes with mild COVID-19 found elevated cardiac troponin I (cTnI) levels two weeks after illness, suggesting that a mild SARS-CoV-2 virus infection may cause persistent myocardial injury.[8]

Natriuretic peptides (NP) are involved in hydrosaline maintenance and thus in blood pressure regulation through their natriuretic, diuretic and vasodilatory effects.[9] One example is the brain natriuretic peptide or B-type natriuretic peptide (BNP), whose precursor is NT-proBNP, which is a biomarker in the diagnosis and monitoring of heart failure (HF), ischaemic heart disease and myocardial injury, although it may also be useful for prognosis in non-cardiac conditions such as obstructive pulmonary disease.[10]

It has been found that patients who recovered from COVID-19 after three weeks to two months with symptoms such as palpitations and effort fatigue had higher levels of NT-proBNP than those who were asymptomatic.[11]

But also in 6-month follow-up, cardiovascular sequelae have been found, such as decreased left ventricular ejection force demonstrated by echocardiographic analysis, and in which NT-proBNP levels were elevated when compared with control groups.[12]

In a previous study in 2019, the prevalence of metabolic syndrome in a sample of Trujillo citizens was 48.6%;[13] this fact already indicates a high-risk condition, especially in the case of respiratory infections such as COVID-19, and is corroborated by the higher number of people infected by SARS-CoV-2 when they had 1 or more risk factors for metabolic syndrome or comorbidities such as hypertension, obesity and diabetes mellitus.[14]

It has been observed that the presence of 2 or more comorbidities is risk factors for the persistence of COVID-19 symptoms during follow-up, altering pulmonary functions 3 months after hospital discharge, although others such as cardiac function are also involved.

People with MetS have an increased risk of cardiovascular disease; however, the association between asymptomatic myocardial damage and MetS has not been sufficiently investigated. If this is added in a patient who has suffered from COVID-19, the cardiac conditions of those recovered are not really known.

For this reason, the aim of the present investigation was to compare the levels of two cardiac markers, cTnI and NT-proBNP, in apparently non-COVID-19 persons with and without MetS and post-COVID-19 persons with and without MetS.

Materials and Methods

Type and Design of Research

This study was cross-sectional and compared four groups: group 1: apparently non-COVID-19 persons without MetS; group 2: apparently non-COVID-19 persons with MetS; group 3: post-COVID-19 persons without MetS and group 4: post-COVID-19 patients with MetS, taking into account the values of cTnI and NT-proBNP.

Population, Sample and Sampling

The population consisted of all citizens of the province of Trujillo, approximately 106,030 people.[15]

Initially, there was a sample of 300 participants, but 9% of them were lost during the research, so 275 citizens were considered, representing a 5.9% estimation error and a 95% confidence level. The non-probabilistic convenience sampling technique was used, since we worked with the people who could be reached in the different districts of Trujillo.[16]

As a strategy for recruiting participants, we considered administrative staff and workers from three important institutions in the city, two secondary schools and a private university, with whom we coordinated through their directors to carry out the analysis to identify MetS in the same place where the intervention took place. We also considered administrative staff, workers and patients from public sector hospitals invited by the intern students of the Professional School of Nutrition of the Universidad César Vallejo, to whom the analyses were performed in the Research Laboratory of the Professional School of Medicine and the Nutritional Evaluation Laboratory of the Professional School of Nutrition of the Universidad César Vallejo. Participants were instructed to be fasting for 10 h prior to laboratory testing.

All persons over 18 years of age, healthy or with comorbidities (diabetes, hypertension, dyslipidemia) were included, with an initial number of 300 participants. Those with hypothyroidism, cerebrovascular accident (CVA), Alzheimer, pregnant women, people with any condition that did not allow their nutritional evaluation, and those who practice long-distance running were excluded. Also excluded were those taking medications such as corticosteroids, olanzapine, antiplatelet agents and levothyroxine. There was exclusion in the data analysis of those individuals with incomplete information in the questionnaires or missing data for the identification of the MetS. Finally, 275 participants remained for data analysis and are summarized in Figure 1. Also considered for exclusion were those with a positive COVID-19 diagnosis or with less than one month of diagnosis and those with chronic renal failure and chronic congestive heart failure; however, there were no cases for this last group of exclusion criteria.

The data collection technique was non-experimental field observation, using as an instrument a registration form where the participant's general data such as age, sex, marital status, and level of education were included; the data to determine the MetS: abdominal circumference, systolic and diastolic blood pressure, glycemia, triglyceride concentration

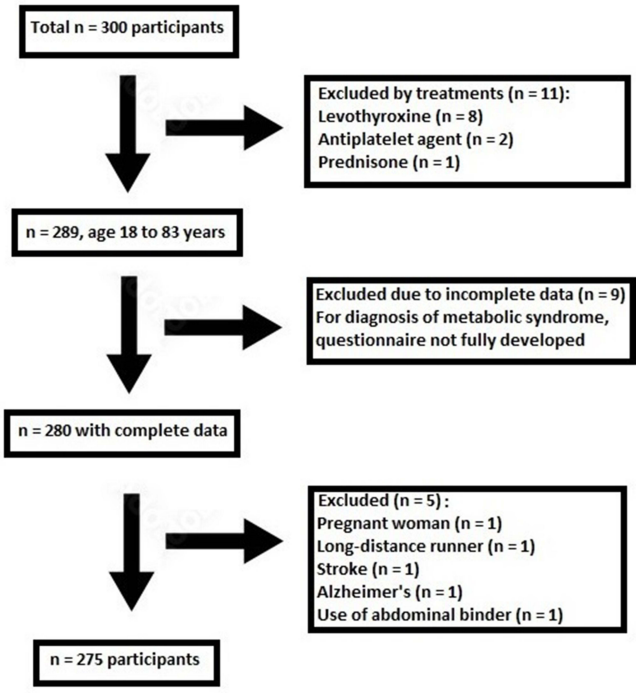


Figure 1 Flow diagram of subject inclusion and exclusion.

and HDL concentration and consideration of the harmonized ATP III criteria, and finally, the corresponding data for cardiac markers such as cTnI and NT-proBNP. Each participant was also asked if presented COVID-19, how long ago had it, and if was in an intensive care unit. Those who reported presenting any symptoms were given a screening test. The blood samples for the analysis of the participants were taken in the months of September to December 2023.

Identification of MetS

Whole blood was obtained from the patients by venipuncture using the Vacutainer blood collection system, in a 5mL vacuum tube with coagulum activator, following the recommendations of the laboratory sampling manual of the Brazilian Society of Clinical Analysis.[17] Once the samples were obtained, 35 uL of blood was collected in a capillary tube, which was placed vertically in the central hole of the reagent strip previously inserted into the cholesterol monitoring equipment (Mission®, Acon laboratories, San Diego, USA). The results of the lipid profile, total cholesterol, LDL, HDL and triglycerides were recorded in the data collection form. Normal values for Total Cholesterol <200 mg/dL; triglycerides is <150 mg/dL; LDL <100 mg/dL; HDL in men and women, acceptable values are considered ≥40 mg/dL and ≥50 mg/dL, respectively.[18]

In the case of glycemia, blood from the same tube used for cholesterol was used, placing it on the test strip previously inserted into a glucometer (Accu-Chek® Performa Nano, Roche, USA). Fasting glucose values of less than 100 mg/dL were considered normal.[19]

Blood pressure was measured after a rest period of at least five minutes. A digital upper arm blood pressure monitor (Riester® Ri-Champion N, Jungingen, Germany) was used. Two measurements were considered in those patients whose systolic/diastolic pressure was equal to or greater than 130/85 mmHg, to confirm the result. In reference to nutritional status, abdominal perimeter was evaluated with a metallic tape measure; Lufkin, Model W606PM, Queretaro, Mexico.[13] For the diagnosis of MetS in the participants, the harmonized ATPIII criteria were used, the main condition being abdominal obesity with waist circumference ≥ 94 cm in men and ≥ 88 cm in women and two risk factors: elevated fasting glycemia (≥100mg/dL), hypertriglyceridemia (≥150 mg/dL) with or without treatment for dyslipidemia, or finally presenting elevated blood pressure (SBP ≥ 130 mmHg and/or DBP ≥ 85 mmHg) or with specific treatment to the same.[20]

Diagnosis of COVID-19 in Apparently Healthy People

The rapid test kit for SARS-CoV-2 antigen from Labnovation Technologies® was used, which consists of a dropper, nasal and oropharyngeal swab, buffer solution and test cassette. Before taking the sample, the analyst put on his respective personal protective equipment, filled the dropper with 23 drops of buffer solution, introduced the swab to the patient through the nostrils to the nasopharyngeal area, rotating the swab on its axis up to 5 times, in order to obtain superficial cells of the respiratory epithelium that present the virus, for the buccopharyngeal sample, the patient was instructed to open his mouth to expose the tonsils, the swab was introduced to perform a smear as up and down movements for 3 times, once the samples were obtained, the swabs were embedded in the buffer solution present in the dropper with circular motion and pressing against the bottom, and using a dropper 3 drops of the sample and buffer mixture was placed in the test cassette, waited 15 minutes to obtain the results. For the interpretation of the results, the cassette presents two bands: control (C) and test (T), in a negative test only a colored line appeared in band C, while in a positive test, a colored line appeared in both band C and T, the test where no color was presented in line C invalidated the test.[21]

Evaluation of Cardiac Markers

The levels of cTnI and NT proBNP were evaluated by the advanced time-resolved fluorescence immunoassay (TRFIA) method, through the LS-1100 dry immunofluorescence analyzer (Lansionbio®, Nanjing, China), at the Research Laboratory of the Faculty of Health Sciences of the César Vallejo University.

The sample obtained for the evolution of lipid profile and glucose was allowed to clot, then centrifuged at 3000 rpm for 10 minutes to obtain the patients' serum. For NT-proBNP, 100 µL was placed on the test strip, which diffused by capillary action until reaching the immobilized antibody, generating the antigen-antibody reaction within 15 minutes at room temperature. For cTnI, 100 µL of serum was placed in a tube with sample diluent present in the test kit, and gently mixed until completely dissolved, and then placed on the test strip for 10 minutes at room temperature. The QR code of the test to be analyzed was placed in front of the equipment's scanner camera to save it. The test strip was inserted into the test opening of the equipment, and the results were printed.[22]

Elevated NT-proBNP was defined as greater than 125 pg/mL according to the limit used for adults under 75 years of age.[23]

Elevated troponin was defined as greater than 0.5 ng/mL according to the threshold of 99th percentile levels in population studies.[24]

Statistic Analysis

The data from the biochemical evaluations recorded on a data collection form were entered into a Microsoft Excel spreadsheet and then exported to the SPSS version 26 statistical program, where statistical calculations such as measures of central tendency, dispersion and frequency tables were performed. To test the hypothesis of whether there are significant differences between the study variables, the Cramer's V statistical test was used for qualitative variables and the Mann–Whitney *U*-test for quantitative variables.[25]

Ethical Considerations

This research was approved by the Research Ethics Committee of the School of Nutrition with opinion PI-CEI-NUTRICIÓN-2023-007. The ethical principles of the Declaration of Helsinki of beneficence, non-maleficence, autonomy and justice were considered. People were asked to voluntarily provide their consent to participate in this study. For this purpose, each participant received information on the objectives, basic protocols of the analyses to be performed, and knowledge of the investigator's institutional affiliations to ensure that they understood the information and could decide to accept or withdraw from participation in the research.

Results

Table 1 shows that the values of perimeter, glycaemia and average triglyceride concentration, as well as the prevalence of SBP/DBP ≥130/85 mmHg are significantly higher in men; however, in women, there is a significantly higher average concentration of cholesterol, HDL and LDL than in men. Regarding risk factors for MetS, men have more risk factors,

Table 1 Characteristics of the Patients Analyzed

Features	Female (n=164)	Male (n=111)	Sig.
Age (years)	47.76 ± 11.85	47.83±11.27	0.991
Perimeter (cm)	87.67±10.30	98.11±1.38	0.000
Glycemia (mg/dL)	105.26±31.07	107.22±43.06	0.035
Cholesterol (mg/dL)	212.15±51.41	185.62±37.35	0.000
HDL-c (mg/dL)	46.28±14.06	33.04±9.97	0.000
Triglycerides (mg/dL)	146.65±88.76	165±104.84	0.122
LDL-c (mg/dL)	146.39±111.41	133.34±93.93	0.004
SBP (mmHg)	111.97±17.58	118.47±14.77	0.000
DBP (mmHg)	73.27±10.85	76.53±9.91	0.012
SBP/DBP <130/85 mmHg (%)	128 (46.5%)	72(26.2%)	0.016
SBP/DBP ≥130/85 mmHg (%)	36(13.1%)	39(14.2%)	
Number of Risk Factors for metabolic syndrome			
None	16(5.8%)	4(1.5%)	
1 risk factor	42(15.3%)	16(5.8%)	0.00
2 risk factors	49(17.8%)	20(7.3%)	
3 or more risk factors	57(20.7%)	71(25.8%)	
Diagnosis of COVID-19			
Yes	94(34.2%)	66(24%)	0.72
No	70(25.5%)	45(16.4%)	

Notes: Mann–Whitney *U*-test was used for quantitative variables and Cramer's V for qualitative variables.

and overall MetS is present in 46.5% of the participants. As for the diagnosis of COVID-19, the majority of those diagnosed were women, and in the total number of participants, it represents 58.2%.

Table 2 shows that the majority of people have cTnI concentrations of less than 0.05 ng/mL, and of these, a higher percentage (30.5%) have not been diagnosed with COVID-19 or MetS. As for patients with cTnI greater than 0.05, only 7 patients were identified, who are located with diagnoses COVID-19-/SM-, COVID-19-/MetS+, COVID-19+/MetS- and COVID-19+/MetS+, with similar percentages.

The Cramer's V statistical test found no significant relationship between the presence or absence of COVID-19 in patients with or without MetS and Troponin values ($p > 0.05$).

Table 3 shows that most patients had NT-proBNP less than 50 pg/mL and did not have COVID-19 or MetS (26.2%). Likewise, in the group of patients with NT-proBNP from 50 to 124 was greater in those with COVID-19, being slightly higher in those with MetS- than those with MetS+, and finally, only 8 patients (2.9%) were identified with NT-proBNP at

Table 2 Comparison of Cardiac Troponin I Values in Apparently Non-COVID-19 and Post-COVID-19 Individuals with and without Metabolic Syndrome

Diagnosis		cTnI (ng/mL)						
		<0.05	%	Greater than 0.05	%	Total	%	Sig.
COVID-19 (-)	MetS (-)	84	30.5	2	0.7	86	31.3	0.97
	MetS (+)	72	26.2	2	0.7	74	26.9	
COVID-19 (+)	MetS (-)	59	21.5	2	0.7	61	22.2	
	MetS (+)	53	19.3	1	0.4	54	19.6	
Total		268	97.5	7	2.5	275	100.0	

Notes: Cramer's V statistical test was used.

Table 3 Comparison of N-Terminal Pro-Brain Natriuretic Peptide (NT-proBNP) Values in Apparently Non-COVID-19 and Post-COVID-19 Individuals with and without Metabolic Syndrome

Diagnosis		NT proBNP (pg/mL)								
		<50	%	50–124	%	125 to more	%	Total	%	Sig.
COVID- 19 (-)	MetS (-)	72	26.2	12	4.4	2	0.7	86	31.3	
	MetS (+)	61	22.2	11	4.0	2	0.7	74	26.9	
COVID- 19 (+)	MetS (-)	44	16.0	16	5.8	1	0.4	61	22.2	0.18
	MetS (+)	36	13.1	15	5.5	3	1.1	54	19.6	
Total		213	77.5	54	19.6	8	2.9	275	100.0	

Notes: Cramer's V statistical test was used.

125 pg/mL or more, of which 5 present MetS (1.8%), and in them the COVID-19+/SM+ group is the majority; however, in all these comparative observations it was not statistically significant.

The Cramer's V statistical test did not identify a significant relationship between the presence of COVID-19 with and without MetS in the patients analyzed with NT-proBNP values ($p > 0.05$).

Discussion

The prevalence of MetS, presenting 3 to more risk factors through the harmonized ATPIII criteria in the participants, is higher than another study developed by Tejada et al[26] in users of a level I Hospital in the city of Trujillo, screened between 2014 and 2017 in which it reached 38.97%, which means a significant increase of this pathology of high cardiovascular risk at present.

Most remarkably, the glycemia values in both men and women exceed the 100 mg/dL threshold established by the criteria so that in the medium-term future they may lead to insulin resistance. Moreover, the existing imbalance of HDL-c concentration <40 m/dL and 50 mg/dL in men and women, respectively, provides the necessary conditions for increased cardiovascular risk, and also the pre-existing inflammatory condition and detrimental against COVID-19 infection.

No difference in cTnI level observed in Table 2 in all comparative groups has also been observed in the study by Keefe et al[23] when comparing SARS-CoV-2 RT- PCR negative and SARS-CoV-2 RT-PCR positive patients, being in both groups constituted by people aged 18 to 49 years asymptomatic or with mild symptomatology treated on an outpatient basis, as well as in both groups presented similar proportion of comorbidities.

Likewise, cTnI levels have been observed in COVID-19 patients with myocardial damage with values of 1.27 ± 2.1, compared to those of patients without myocardial damage 0.02 ± 0.02, $p < 0.05$; an aspect not observed in the present investigation because the participants presented mild COVID-19 symptomatology.[27]

In addition to the respiratory symptoms present in COVID-19, a significant proportion of hospitalized patients with myocardial injury have been observed, in which cTnI emerges as a relatively inexpensive and rapid test to stratify the risk of this condition, with prognostic value and independently associated with increased mortality. However, it is necessary to consider an adequate etiology in patients with COVID-19 with evidence of myocardial injury, to establish its correct management.[28]

When the elevated values of these markers are static, it is attributed to chronic cardiac damage, but in patients in whom the change in concentrations is dynamic, the diagnosis of acute coronary syndrome (ACS) is assumed. Therefore, this is another limitation of the study in which it was not possible to discern in those patients in whom elevated cTnI levels were found, whether this corresponded to a chronic situation or to dynamic changes.[29]

It is known that cardiac troponins are released into the circulation up to four hours after the onset of infarction symptoms, due to their localization in the contractile mechanism, maintaining the concentration of elevated cTnI for up to seven days.[30] However, despite this, it is considered that of the 7 participants with elevated cTnI values, this is due to their chronic situation established in patients with MetS and/or in those infected by SARS-CoV-2 in which probably left some sequelae at the cardiac level already in the post COVID stage. Likewise, the coexistence of people with some

congenital or physical activity-related problem, which in the latter case was not investigated before performing the analyses.

The similarity observed in the frequencies of patients with and without COVID-19 and with and without MetS, with values below 0.05 ng/mL, is probably due to the fact that in COVID-positive patients, the disease is mild and systemic inflammation has not been caused, since cTnI values increase according to the clinical involvement of the patient, generally increasing as a result of myocardial injury caused by the virus due to secondary and systemic consequences of the effects it produces in the human organism, which is why it is considered a predictor of complications that mostly end in the death of those infected.[31,32] In the case of people with MetS with low cTnI values, it has more to do with the chronology of the disease, for example, in a recently established MetS the cTnI level will not be elevated, but later with time, due to cardiac risk factors, this level is established if it is not treated properly.

On the other hand, people with MetS have a higher probability of suffering severe forms of COVID-19, in which the mortality rates of this class of patients are very high. This condition starts from the existence of an inflammatory process in patients with COVID-19, which is exacerbated by the comorbidities of MetS; it is justified by the role played by adipocytes, macrophages, endothelial cells and fibroblasts, which are responsible for the production of interleukin-6, tumor necrosis factor-alpha (TNF-α), among other cytokines and plasminogen activator inhibitor-1 (PAI-1), which silently cause irreparable damage to human tissues and organs.[33]

The proportion of individuals with NT-proBNP values <125 pg/mL in the group that did not present COVID-19 (56.8%) versus those who presented the disease (40.4%) differed slightly whether or not they presented MetS. However, we can say that this behavior is observed in the study of Gul et al[11] who in a more quantitative way found that the group with COVID-19 presented a median and interquartile range 43 (10–505) pg/mL slightly higher and significantly compared to a group without COVID-19 with a median and interquartile range 37.7 (4.2–135) pg/mL ($p < 0.05$). The present study was unable to detect concentrations below 50 pg/mL, thus our comparative between established groups was more three-level oriented for NT-proBNP.

In recent years, new metabolic functions of natriuretic peptides such as NT-proBNP have been identified, including lipid oxidation at hepatic and muscular level, as well as mitochondrial respiration, and therefore a favorable effect against lipoproteins, triglycerides, insulin resistance and BMI,[34,35] related to MetS. It seems that NT-proBNP values up to <100 pg/mL constitute a protective physiological function due to the effects mentioned above and their involvement in reducing LDL to values close to 115 mg/dL.[34] However, it is important to emphasize that substantially elevated NT-proBNP levels, potentially due to the presence of subclinical cardiovascular disease, can no longer influence blood lipids, nor insulin resistance, where the peptide has a greater preponderance to heart remodeling.[28] Probably, this phenomenon could be happening chronically in the participants evaluated in which there is a decrease of such physiological function of NT-proBNP beyond 100 pg/mL and in accordance with the averages of LDL concentration of 146.39 ± 111.41 pg/mL in women and 133.34 ± 93.93 pg/mL in men.

As is known, SARS-CoV-2 causes inflammation and myocardial damage through the human angiotensin II-converting enzyme receptor. Therefore, it is presumed that it could cause myocardial injury and myocarditis in patients with COVID-19. In addition, it is speculated that the cytokine storm caused by the coronavirus produces an overreaction of the immune system in many organs, including the heart. However, NT-proBNP is considered an optimal biomarker for heart failure.[31] This marker is sensitive to the hemodynamic stress of the heart and may be related to left ventricular systolic or diastolic dysfunction, as well as ischemic or inflammatory reactions, and may also be associated with right heart overload due to pulmonary consequences of diseases such as pulmonary embolism, pulmonary hypertension, hypoxic vasoconstriction or acute respiratory distress syndrome.[36]

Although the proportion of people who presented NT-proBNP values above 125 pg/mL with COVID-19+/SM+ is slightly higher than the other groups, this is not significant, it is mainly due to the small number of cases found and even more so in a community setting, where COVID-19 infection was mild in 58.2% of the participants. This situation could be observed differently with more severe COVID-19 symptomatology and MetS in a hospital setting where the proportion of patients with NT-proBNP >125 pg/mL would be higher versus those COVID-19+/SM-, COVID-19-/SM- individuals.

Thus, Deng et al[31] observed that in non-severe COVID-19 patients the NT-proBNP concentration reached a median of 101.9 pg/mL and that in patients with severe symptomatology it reached a value of 1142 pg/mL for the case of myocardial injury, approximately 9 times more than the acceptable limit value.

Likewise, also in a community setting, the presence of elevated NT-proBNP values >125 pg/mL can also occur in apparently healthy subjects with COVID-19 and without MetS due to the presence of a possibly congenital cardiac pathology, or probably due to physical activity in which the values of this marker can be elevated, although in a short time in those with intense and short exercise or also if constant activity is performed, as in the case of runners, even if they are not elite, aspects that were not identified in the investigation.[37]

One of the limitations of the study is the semi-quantitative evaluation of the equipment used, since the lower measurement threshold was 0.05 ng/mL for cTnI. Machado and Olmos[30] state that the threshold in men is approximately twice as high as in women and the most accepted reference values are 0.034 ng/mL in male patients and 0.016 ng/mL in female patients. This aspect could not be observed; however, in the present study, the threshold of 0.05 ng/mL was considered.

Likewise, the availability of more test strips and the participant's time was another aspect that made it difficult to corroborate in a second measurement the increased values of troponin concentration in the lapse of one hour and to be able to evaluate the existence of such variation. However, as mentioned above this was solved by contacting the participants who showed values over the normal limit, recognizing a chronic situation due to the knowledge of the use of medications for comorbidities and which were inquired at the time of applying the harmonized ATP III criteria and recommending a preventive check-up of cardiac function.

Because the instrument used had a minimum threshold of 50 pg/mL, a more quantitative comparison of Nt-proBNP values between the comparative groups in the present study could not be established. Therefore, the cross-sectional study design made it impossible to determine the actual effects of MetS on cardiac markers in both COVID-19 and non-COVID-19 individuals.

A strength of the research is the identification of probable suspicion of cardiac injury not only in persons who have been infected with COVID-19 but also in conjunction with those persons with MetS and those apparently healthy due to their physical and/or congenital activities that should be previously investigated, which indicates the importance of considering these cardiac markers in a preventive manner.

Conclusion

It is concluded that the proportion of both normal and elevated levels of cTnI and NT-proBNP in individuals without COVID-19, with or without MetS, does not differ as much from those who presented with COVID-19, with or without MetS, during the pandemic. Longitudinal studies are needed to confirm the usefulness of cardiac markers in the detection of cardiac disease, which would contribute to adequate treatment in the face of pre-existing congenital situations, comorbidity present, and possible sequelae left by SARS-CoV-2 in those who presented COVID-19, especially in those who already have chronic MetS, in whom there is a slight tendency to present possible cardiovascular events due to heart failure or injury in non-hospitalized human groups.

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Disclosure

The authors declare that they have no conflict of interest in this research.

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