# **ORIGINAL ARTICLE**

# Correlation of Diagnostic Components of Metabolic Syndrome with Electrocardiographic and Echocardiographic Alterations in Patients with Obesity

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#### **Abstract**

**Introduction:** Metabolic syndrome (MS) and obesity are risk factors for cardiovascular diseases (CVD). However, the development of cardiovascular pathologies in obese individuals without MS is being investigated.

**Objective:** To investigate whether there are similar electrocardiographic (ECG) and echocardiographic changes in individuals with obesity with and without MS.

**Methodology:** A retrospective, descriptive cross-sectional study was carried out with obese patients at a university hospital in Belém, Pará, Brazil. Anthropometric, laboratory, ECG and echocardiographic data were evaluated in both populations. The chi-square test was used to describe the relationship between variables among groups; hypothesis tests with p < 0.05 were considered statistically significant values.

**Results:** The study evaluated 100 individuals with obesity, 60 of whom had MS. The average age was 54 years, and the female sex was prevalent. Systolic blood pressure, HDL, and waist circumference were altered in both groups. Systemic arterial hypertension and low HDL demonstrated 4.27 times and 3.32 times greater likelihood of presenting changes in the ECG and echocardiogram for both groups. On the ECG, diffuse changes in ventricular repolarization were observed in both groups. On echocardiography, left ventricular diastolic dysfunction and left ventricular hypertrophy were present in both populations studied.

Conclusion: Obese individuals without MS present a similar risk, requiring adequate attention to their cardiac health.

Keywords: Metabolic Syndrome; Obesity; Risk Factors; Cardiovascular Diseases.

#### Introduction

Behavioral changes over the past decades, especially in terms of eating habits, directly contribute to the rise in individuals with obesity. In the year 2022, there were approximately 6.7 million obese individuals in the Brazilian population, making it the most prevalent endocrine disorder in the country. Thus, excess body fat is associated with the development of metabolic disorders, other endocrine disorders, and metabolic syndrome (MS), which has a significant impact on cardiovascular health.

As per the definition by the National Cholesterol Education Program's Adult Treatment Panel III (NCEP-

ATP III), MS can be diagnosed based on criteria,¹ where an individual must have at least 3 of the following components: elevated waist circumference (> 88 cm for women and > 102 cm for men), elevated serum triglycerides (≥ 150 mg/dL), reduced serum HDL cholesterol levels (< 40 mg/dL for men and < 50 mg/dL for women), high blood pressure (≥ 130/85 mmHg), and elevated fasting glucose (≥ 110 mg/dL). All these variables are associated with an increased risk of various heart conditions.²,³ Currently, 6 disorders are recognized as components of MS: abdominal obesity, atherogenic dyslipidemia, high blood pressure, insulin resistance, pro-inflammatory state, and pro-thrombotic state.⁴

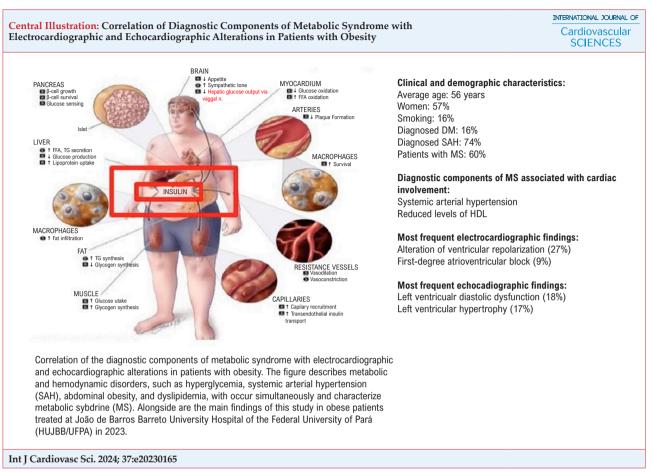
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DM: diabetes mellitus; HDL: high-density lipoprotein; MS: metabolic syndrome; SAH: systemic arterial hypertension.

In this context, obesity, another factor related to the development of cardiovascular diseases (CVD), is a chronic disease characterized by abnormal or excessive fat accumulation in the body. Additionally, it increases the risk of diabetes mellitus, musculoskeletal disorders, and certain neoplasms.<sup>2</sup> The diagnosis of obesity is defined by dividing weight in kilograms by the square of height in meters (kg/m²), with a body mass index (BMI) greater than or equal to 30 kg/m².<sup>5,6</sup> Thus, it has become a highly prevalent factor for the development of cardiac alterations. While studies demonstrate that the components of MS individually increase the risk of CVD development, a condition known as metabolically healthy obesity (MHO) has been suggested. This is characterized as a subgroup of obese individuals without cardiometabolic alterations.<sup>7,8</sup>

Moreover, MHO has been associated with the emergence of cardiovascular pathologies; obstructive sleep apnea; renal, biliary, and orthopedic diseases; the onset of neoplasms; and the prevalence of metabolic disorders, all stemming from the detrimental effects of excess adipose

tissue in the body. Studies have been conducted to clarify the cardiovascular repercussions of obesity without MS; however, the results are not as conclusive as the influence of MHO on cardiovascular health. To address the concept and identification of obesity without MS, studies have been conducted to investigate the impact of excess adipose tissue on cardiovascular health. However, the results are controversial and provide little clarity regarding the benign nature of obesity for cardiac function and structure. In this context, the present study aimed to describe whether there is a difference in the occurrence of electrocardiographic (ECG) and echocardiographic alterations in obese individuals with and without MS. The Central Figure presents the most relevant aspects and results of this study.

#### Methods

The present study is part of a larger project titled "Cardiovascular Risk and Cardiac Involvement in Patients with Obesity and Metabolic Syndrome in a

University Hospital in the Amazon Region." The study was approved by the Research Ethics Committee of the Federal University of Pará (CEP/UFPA) in Brazil under reference number CAAE 69722423.3.0000.0018. A descriptive retrospective cross-sectional study was conducted with obese patients under follow-up at the Cardiology Outpatient Clinic of João Barros Barreto University Hospital (HUJBB) in the city of Belém, Pará, Brazil. Individuals aged 18 years and older with a diagnosis of obesity, with or without MS, who had updated laboratory, ECG, and echocardiographic exams were included in the study.

Out of the 180 patients selected for the study, only 100 were eligible. Patients under the age of 18 or over 75, overweight individuals without a diagnosis of MS, and those lacking laboratory, ECG, and echocardiographic exams were excluded. The sample was selected for convenience. Data were collected regarding patients' demographics (sex and age), laboratory tests (fasting glucose, total cholesterol, HDL, LDL, and triglycerides), blood pressure measurement, anthropometry (weight, height, BMI, and waist circumference), and up-to-date ECG and echocardiographic exams. All information was obtained from the patient records selected for the study, and the informed consent form was used to obtain permission for using clinical data from outpatient evaluations and medical records for research purposes.

The diagnosis of obesity was adopted according to the fourth edition of the Brazilian Association for the Study of Obesity and Metabolic Syndrome, considering an adult as obese when their BMI was greater than or equal to 30 kg/m<sup>2</sup>.<sup>2</sup> For the diagnosis of MS, the NCEP-ATP III criteria were adopted, as they align better with the clinical routine of Brazilian health institutions. These criteria involve identifying 5 variables: abdominal obesity via waist circumference, triglycerides, HDL cholesterol, systolic blood pressure, and fasting glucose.<sup>2</sup>

The ECG and echocardiogram were conducted at the institution where the study was developed as part of the cardiological evaluation protocol. They were meticulously assessed by the cardiologist who was part of the research team, ensuring increased confidence in the results of this study regarding the identification of ECG and echocardiographic alterations. ECG findings, combined with clinical data, were used for further cardiovascular investigation. ECG exams were assessed for rhythm, frequency, electrical axis, P-wave and QRS complex duration and amplitude, PR interval duration, and ventricular repolarization

analysis. Echocardiograms were assessed for cardiac chamber dimensions, wall thickness, heart valves, valve flows, systolic function, diastolic function, and pericardium. The assessment references for the ECG and echocardiogram in this study are based on the Guidelines for the interpretation of resting ECG by the Brazilian Society of Cardiology and the American Society of Echocardiography, respectively.

### Statistical analysis

For the analysis of cardiovascular risk and cardiac involvement in patients with MS, data were tabulated in Microsoft Office Excel 2016 spreadsheets. These were used to construct tables and graphs, aiding in data visualization and interpretation. Categorical variables were described in terms of their absolute frequency and relative frequency. After data tabulation, the statistical program BioEstat 5.4 was used to formulate statistical tests, showing frequencies of cardiovascular risk and cardiac complications in patients with MS. Continuous variables were described as mean ± standard deviation. The comparison of these variables between groups was done using Student's t-test for independent samples. The chi-square test was used to compare the frequency of ECG and echocardiographic alterations between groups with and without MS, as well as each variable of the NCEP-ATP III criteria. For variables that showed significant differences (p < 0.05), calculating the odds ratio with a 95% confidence interval is suggested. The Shapiro-Wilk test was conducted to assess the normality of the data. The significance level considered for tests was 5%. For improved statistical analysis, the variable "occurrence of cardiac alterations in imaging exams" was classified as "no" or "yes" (0 or 1).

#### Results

The study was conducted through the analysis of medical records of 100 obese adults seen at the Cardiology Outpatient Clinic of HUJBB in the city of Belém, Pará, Brazil. Among these individuals, 60 had MS, and 40 did not. The mean age of the study population was 54 years, with a prevalence of females. There was no difference in the proportion of males and females in both groups (obese with MS and obese without MS). Regarding the degree of obesity, assessed by BMI and waist circumference, the two groups were statistically similar. Except for waist circumference and systolic blood pressure, individuals with MS showed

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unfavorable values for the variables assessing MS when compared to the group without MS (p < 0.05). In the group of obese individuals without MS, there were no individuals with abnormal values of triglycerides and fasting glucose. In the MS group, abnormal values were found for all components of MS. Table 1 provides a more detailed overview of the patient profiles, categorized into different groups.

Additionally, the relationship of diagnostic variables as established by the NCEP-ATP III with ECG and echocardiographic findings was assessed. Table 2 presents the distribution of these variables in the sample of studied patients, segmented according to the presence or absence of MS, and compares them with ECG alterations.

Table 3 presents the comparison with alterations in echocardiography. The variables include systemic arterial hypertension, elevated triglyceride levels (above 150 mg/dL), low HDL (below 40 mg/dL), hyperglycemia (above 126 mg/dL), and abdominal obesity (waist circumference above 102 cm). Regarding the ECG, the observations from the chi-square test found statistically significant values in both the groups without and with MS, which may be associated with certain health conditions, such as low HDL (in the MS group), hyperglycemia, and systemic arterial hypertension. In both groups, systemic arterial hypertension and low HDL showed 4.27 times and 3.32 times greater association with the presence of alterations in echocardiography. The other variables did not emerge as risk factors or protective factors for cardiac function and structure.

The ECG analysis revealed a variety of findings in both groups. Notably, nearly half of the patients in each group, specifically 57.5% in the group without MS and 58.3% in the group with MS, showed no alterations on the ECG. The most frequent ECG alterations were diffuse ventricular repolarization alteration and left ventricular overload. This pattern was observed both in individuals with MS and those without the condition. It is essential to highlight that both groups demonstrated susceptibility to such alterations in similar proportions. A more detailed description of other ECG findings in the two groups is presented in Table 4.

Regarding the echocardiography exams, it was observed that 13 patients (32.5%) in the group without MS and 23 patients (38.3%) in the group with the condition showed no abnormalities. A more detailed graphical representation of the other echocardiographic findings is presented in Table 5. It is worth noting that left ventricular diastolic dysfunction and left ventricular hypertrophy were significantly present in both groups.

Variables	Obese with MS
Age	56 + 7 91

Table 1 – Distribution of patients with and without MS

Variables	Obese with MS	Obese without MS	P value
Age	$56 \pm 7.91$	52 ± 4.76	<0.05
Men	14 (35%)	29 (48.3%)	0.42
Women	26 (65%)	31 (51.7%)	0.42
Waist Circumference (cm)	$101.69 \pm 7.78$	$101.27 \pm 7.72$	0.99
BMI	$29.65 \pm 4.26$	$31.38 \pm 1.42$	0.68
HDL cholesterol (mg/dl)	42.97 ± 21.25	$43.55 \pm 5.23$	<0.05
Triglycerides (mg/dl)	196.75 ± 87.43	131.46 ± 1.48	<0.001
Blood sugar (mg/dl)	$136.80 \pm 54.60$	115.27 ± 7.72	<0.001
Systolic BP (mmHg)	144.23 ± 23.81	141.50 ± 17.61	<0.001
Diastolic BP (mmHg)	81.90 ± 10.61	$81.37 \pm 8.47$	<0.001
	3: 14 (23.3%)	1: 14 (35%)	
MS components number	4: 19 (31.66%)	2: 26 (65%)	
	5: 27 (45%)		

Data presented as mean  $\pm$  standard deviation or number (%). BMI: body mass index; BP: blood pressure; HDL: high-density lipoprotein; MS: metabolic syndrome.

Table 2 – Frequency of ECG alterations for the groups with and without MS					
		ECG alteration		OR	n 1
Variable		With MS	Without MS	(95%)	- P value
SAH	Yes: 72	28	16	2.84	0.02
	No: 28	3	5		
Elevated TG	Yes: 56	23	11	2.28	0.14
Elevated 1G	No: 34	6	10		
Low HDL	Yes: 51	20	0	2.90	0.03
LOW HDL	No: 49	11	21		
High blood sugar	Yes: 28	19	15	3.41	0.01
	No: 32	12	16		
High WC	Yes: 61	18	15	1.47	0.44
	No: 39	13	6		

Data presented as the number of individuals. HDL: high-density lipoprotein; MS: metabolic syndrome; OR: odds ratio; SAH: systemic arterial hypertension; TG: triglycerides; WC: waist circumference; ECG: electrocardiographic.

Table 3 – Frequency of echocardiographic alterations for the groups with and without MS

Variable		ECG alteration		OR	n 1
		With MS	Without MS	(95% CI)	P value
SAH	Yes: 68	31	14	2.79	0.03
	No: 32	6	15		
High TG	Yes: 66	24	14	0.52	0.27
	No: 34	13	13		
Low HDL	Yes: 36	22	0	2.94	0.01
	No: 64	27	15		
High blood sugar	Yes: 28	20	0	2.16	0.14
	No: 62	17	27		0.14
High WC	Yes: 52	21	16	1.42	0.51
	No: 48	16	11		0.51

Data presented as the number of individuals. HDL: high-density lipoprotein; MS: metabolic syndrome; OR: odds ratio; SAH: systemic arterial hypertension; TG: triglycerides; WC: waist circumference; ECG: electrocardiographic.

# Discussion

MS is characterized as a complex disorder whose development depends on an intricate interaction between genetic and environmental factors (inadequate diet, smoking, alcohol consumption, sedentary lifestyle, and anthropometric changes), combined with concomitant cardiovascular risk factors such as hypertension, hyperglycemia, central obesity, and

insulin resistance.<sup>1,2</sup> Moreover, these alterations also represent potential risk factors for CVD and target organ damage, significantly associated with higher mortality rates.<sup>3</sup> Obesity has been described as an inflammatory pathology capable of generating risk factors for CVD.<sup>1,3</sup> Thus, the obesity presented by all the study patients is a significant risk factor for the occurrence of cardiac alterations and is associated with ECG and echocardiographic changes.

48%

No alterations

Table 4 – Frequency of ECG alterations for the groups with and without MS		
Category	Frequency (%) Obese without MS	Frequency (%)* Obese with MS
Diffuse ventricular repolarization alteration	27%	31%
Long QT	13%	15%
First-degree atrioventricular block	10%	9%
Left ventricular overload	5%	7%
Left bundle branch block	4%	5%
Right bundle branch block	4%	4%
Ventricular premature beats	3%	3%
Atrial fibrillation	3%	2%

<sup>\*</sup> A patient may have more than one alteration on the ECG. ECG: electrocardiogram; MS: metabolic syndrome.

Table 5 – Frequency of echocardiographic alterations for the group with and without MS				
Category	Frequency (%) Obese without MS	Frequency (%)* Obese with MS		
Left ventricular diastolic dysfunction	19%	18%		
Left ventricular hypertrophy	15%	17%		
Left ventricular systolic dysfunction	15%	16%		
Mitral regurgitation	13%	11%		
Aortic regurgitation	9%	8%		
Tricuspid regurgitation	8%	8%		
Left atrial hypertrophy	6%	5%		
Aortic calcification	4%	3%		
Mitral reflux	4%	3%		
Abnormal left ventricular contractility	2%	2%		
Mitral reflux	2%	2%		
No alterations	49%	46%		

<sup>\*</sup> A patient may have more than one alteration on the echocardiogram. MS: metabolic syndrome.

However, there is a condition known as MHO, characterized by BMI  $\geq$  30 kg/m² that meets all the criteria: serum triglycerides  $\leq$  150 mg/dL, serum HDL cholesterol > 40 mg/dL (in men) or > 50 mg/dL (in women), systolic blood pressure  $\leq$  130 mmHg, diastolic blood pressure  $\leq$  85 mmHg, no antihypertensive treatment as an alternative indicator, fasting glucose  $\leq$  99 mg/dL, and no medication

with hypoglycemic agents.<sup>5-7</sup> Thus, it is a condition defined as the absence of any metabolic disorder and/or CVD, including type 2 diabetes, dyslipidemia, hypertension, and atherosclerotic CVD, in a person with obesity.

Data from large epidemiological studies and metaanalyses demonstrate that individuals with MHO are

at a higher risk of CVD, cerebrovascular disease, heart failure, cardiovascular events, type 2 diabetes, and all-cause mortality compared to metabolically healthy individuals with normal BMI.<sup>7,8</sup> A retrospective cohort study conducted by Kramer et al. with adults aged 18 to 65 found that, out of 18,070 individuals analyzed, 1,805 (10%) had MHO (mean age of  $38 \pm 11$  years), while 3,047 had normal weight and were metabolically healthy (mean age of 35 ± 11 years). After a mean follow-up of 15 years, 80% of MHO patients versus 68% of metabolically healthy individuals with normal weight developed at least one cardiovascular and/or metabolic risk factor. There was a consistent increase in the rate of developing components of MS in individuals with MHO compared to metabolically healthy normal-weight individuals, with glucose dysregulation developing more rapidly and women showing a greater tendency to develop MS compared to men.6,10,11

A homogeneous sample, in terms of the degree of obesity among subjects, was crucial in this study to eliminate confounding factors, considering that the groups with and without MS did not statistically differ in BMI and waist circumference values. In relation to the others variables related to MS, the unfavorable mean of the variables, with the exception of WC and systolic BP, presents by the group with MS compared to the group without SM, confirms the difference in the metabolic profile in both groups, demonstrating the suitability of the sample for answer the study question. In our sample, the MS group had a higher mean age than the group without MS, with an average age of 56.4 years for the MS group and 52.21 without MS. Age is a risk factor for CVD, being associated with changes in cardiac structure and function, even in healthy individuals. However, in this study, age showed no association with ECG and echocardiographic alterations.

Regarding anthropometric parameters, both BMI and waist circumference were elevated for both groups. In this context, both obesity and increased waist circumference play an important role in the development of MS and CVD due to their association with other risk factors, such as insulin resistance, hyperglycemia, increased blood pressure levels, and dyslipidemia. Additionally, the distribution of body fat, especially in the abdominal region, is related to metabolic changes and is a significant cardiovascular risk factor.<sup>6,9</sup>

Regarding blood pressure levels, systolic blood pressure was elevated for both groups, while diastolic blood pressure remained within the normal range in both study populations. In this context, hypertension is another diagnostic criterion for MS that is closely related to the risk of developing cardiovascular pathologies, particularly elevated systolic blood pressure. This relationship persists even in individuals with mild hypertension,<sup>6,10</sup> as observed in the population of the present study.

Regarding biochemical tests, the mean fasting glucose was elevated in both groups. Thus, the chronic hyperglycemic condition contributes to vascular and atherosclerotic disorders. This leads to the impairment of large blood vessels that supply target organs such as the heart, brain, and kidneys. Furthermore, hyperglycemia increases the risk of CVD. As for the mean values of total cholesterol and triglycerides, they were elevated only in the group with MS. The average level of HDL was reduced in both groups. Therefore, dyslipidemia is a factor responsible for vascular dysfunctions, especially in target organs, and premature cardiovascular mortality. 10-12

In this context, the hemodynamic adaptations and intense metabolism of adipose tissue, especially in obese individuals with MS, require increased oxygen consumption, with a consequent increase in cardiac output, at the expense of an increase in circulating volume. This results in a decrease in systemic vascular resistance, but leads to chronic elevation of preload, favoring cardiac injuries, described as ventricular chamber hypertrophy and systolic and diastolic dysfunctions. Thus, pressure and extracellular volume overload and preload, typical of obesity, reduce left ventricular contractile reserve, predisposing to the development of heart failure.

The action of MS components on the cardiac muscle is still controversial, but findings suggest that angiotensin II can promote cardiomyocyte hypertrophy and that PAI-1 modulates myocardial fibrosis.<sup>17</sup> Additionally, HDL is capable of inhibiting the expression of cytokineinduced adhesion molecules in endothelial cell culture and modulating endothelial function, probably by stimulating endothelial production of nitric oxide. Thus, low serum HDL levels may be related to myocardial fibrosis due to reduced cardiac protective factors. 18,19 In the present study, when the association of the factors that compose the MS diagnosis was evaluated with the prevalence of cardiac impairment, hypertension and low HDL were observed to be factors related to the presence of described ECG and/or echocardiographic abnormalities in both study groups.

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Thus, it is evident that obesity exhibited by all individuals in the sample is an important risk factor for the occurrence of cardiac alterations and is associated with a wide variety of ECG abnormalities. In this context, diffuse ventricular repolarization (Figure 1) alteration was the most frequent in both groups, and an increase in the QT interval was observed, especially in obese individuals without MS. Studies by Clemente et al. and Haverkamp et al. also found a significantly longer QT interval in obese individuals compared to non-obese individuals.<sup>20,21</sup> The QT interval is the most commonly used ECG parameter in repolarization assessment, and its prolongation is associated with a higher risk of arrhythmogenesis.<sup>22</sup> Obesity, along with hypertension and low HDL, is associated with greater regional repolarization heterogeneity due to differences in action potential duration, favoring malignant ventricular arrhythmias and resulting in sudden death.<sup>23</sup>

Chronic elevation of blood pressure increases cardiac afterload, causing the myocardium to increase contractile force to maintain cardiac output for coronary and systemic circulation. These adaptations culminate in left ventricular hypertrophy, which was more frequent in echocardiography in the present study, in both the non-MS and MS groups (Figure 2). These findings were also found in similar studies of populations with MS. Left ventricular hypertrophy makes the cardiac muscle more susceptible to ischemia, and evidence suggests that the secretion of hormones and endothelial stimulation factors in response to volume and pressure overload act

on cardiac remodeling, especially in the left ventricle. <sup>28-30</sup> The impairment of ventricular distensibility in diastole, present in left ventricular hypertrophy, results in left ventricular diastolic dysfunction, as observed in 15% of patients in this study. Patients with left ventricular diastolic dysfunction are more susceptible to developing heart failure. <sup>31,32</sup>

Studies by Masugata et al. and Fontes-Carvalho et al. found that individuals with MS presented worse diastolic function parameters and significantly increased risk of left ventricular diastolic dysfunction. 33,34 Similarly, individuals with obesity undergoing elective coronary angiography were correlated with left ventricular diastolic dysfunction. 45,36 Various pathophysiological mechanisms may be involved in the association of obesity and MS with systolic dysfunction. 33,36,37

In this context, the concomitant association with cardiac alterations in both groups is observed, justifying the prevalence of alterations in both echocardiographic and ECG frequencies when the two groups were compared. These findings are consistent with current studies in which obese individuals, even without MS, present up to two MS components and are thus exposed to the deleterious effects of such metabolic disorders on the cardiovascular system. The methodological limitations of this study may be considered in the development of subsequent work. The absence of a control group composed of normal-weight individuals precluded establishing a causal relationship between MS and cardiac alterations.

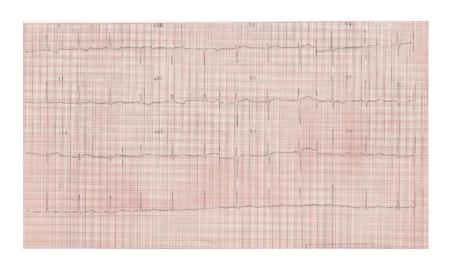


Figure 1 - Electrocardiogram demonstrating changes in ventricular repolarization in the anterior wall. Belém, Pará, Brazil, 2022.



Figure 2 – Echocardiogram showing marked increase in myocardial thickness. Belém, Pará, Brazil, 2022.

# Conclusion

Based on the assessment of the association between the NCEP ATP-III diagnostic criteria for MS and the presence of cardiac alterations in the ECG and echocardiogram in obese patients with MS and MHO, this study suggests that the presence of systemic arterial hypertension and low HDL levels are associated with an increased risk of developing cardiac function and structural disorders for both groups. Thus, this study highlights the complex interaction between obesity, MS, and cardiovascular health, emphasizing the importance of health care, especially in individuals with MHO.

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# **Author Contributions**

Conception and design of the research: Luz AS, Ribeiro CHMA, Oliveira Júnior RM; acquisition of data, analysis

and interpretation of the data, statistical analysis: Luz AS; otaining financing: Ribeiro CHMA, Oliveira Júnior RM, Luz AS; writing of the manuscript: critical revision of the manuscript for intellectual content: Costa JG, Ribeiro CHMA, Oliveira Júnior RM; manuscript translation: Costa JG.

## **Potential Conflict of Interest**

No potential conflict of interest relevant to this article was reported.

#### **Sources of Funding**

There were no external funding sources for this study.

#### **Study Association**

This study is not associated with any thesis or dissertation work.

#### **Ethics Approval and Consent to Participate**

This study was approved by the Ethics Committee on Animal Experiments of the Universidade Federal de Pará (UFPA) under the protocol number 69722423.30000.0018.

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