THE EFFECT OF THE METABOLIC SYNDROME ON THE INCIDENCE AND DEGREE OF LEFT VENTRICULAR MYOCARDIAL HYPERTROPHY IN HYPERTENSIVE PATIENTS

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Summary : **INTRODUCTION.** Metabolic syndrome (MetS) is characterized by the simultaneous presence of obesity, hypertension, dyslipidemia and hyperglycemia in an individual, which leads to an increased risk of cardiovascular disease (CVD). Left ventricular hypertrophy (LVH) is thickening of the heart muscle wall - hypertrophy of cardiomyocytes in concentric and/or elongation of cardiomyocytes and hyperplasia of connective tissue in eccentric hypertrophy with the participation of hemodynamic and non-hemodynamic factors (genetics, stress, other external factors). MetS, which essentially includesinsulin resistance, hyperinsulinemia, and hyperglycemia, alters myocardial metabolism and promotes myocardial inflammation, fibrosis, hypertrophy, and left ventricular remodeling. **OBJECTIVE:** To determine the impact of MetS, that is, obesity to the incidence and degree of severity of LVH in hypertensive patients with metabolic syndrome in comparison with the control group - hypertensive patients without metabolic syndrome.
PATIENTS AND METHODS: Consecutive patients of the Office of Internal Medicine "Dr. Bastać" were examined, a total of 55 patients with hypertension, who were divided into two groups: the first group with MetS, 22 people, average age 56±8.5 years with BMI>30kg /m ^{2} and waist circumference more than 80 cm for women and >94 cm for men, the second control group without MetS-33 people, average age 52±14 years, with BMI<30kg/m ^{2}. Echocardiography was done for all subjects on a Power Vision 6000 Toshiba echo camera with standard echocardiographic measurements in the M, B and Doppler technique, and the mass of the left ventricular myocardium was determined for them using the Devereux formula.
RESULTS: The prevalence of LVH in group 1 with metabolic syndrome (MetS) was 64%, while in the control group without (MetS) it was 36%. There was a statistically significantly higher number of patients with LVH in hypertension with MetS compared to hypertensive patients of the control group without MetS (X2, p=0.027). In the group of hypertensive patients with MetS, the degree of severity of myocardial hypertrophy, that is, the myocardial mass , was statistically significantly higher compared to the control group (respectively 302±84g versus 224±89g, p=0.0002). Arterial pressure values were higher for both systolic and diastolic blood pressure 168/106 mmHg in hypertensive patients with MetS, but did not reach statistical significance in relation to blood pressure values in hypertensive patients without MetS (156/95 mmHg, p=0.16).
CONCLUSION. Patients with metabolic syndrome and hypertension have a statistically significantly higher prevalence of left ventricular myocardial hypertrophy and a highly statistically significant degree of left ventricular hypertrophy compared to the control group of hypertensive individuals without MetS.
Given that mean values of arterial pressure do not differ between groups, it can be concluded that non-hemodynamic factors for the development of LVH have an important role in the induction of a more severe degree of LVH in hypertensive patients with metabolic syndrome.
Key words: left ventricular hypertrophy, metabolic syndrome, arterial hypertension, obesity, hyperglycemia, diabetes mellitus

INTRODUCTION

Metabolic syndrome (MetS) is a cluster of several disorders and includes abdominal obesity, dyslipidemia of HDL and LDL cholesterol, elevated triglycerides, elevated blood pressure, glucose intolerance or type 2 diabetes [1]. The term cardiometabolic syndrome has been used increasingly. According to the NCEP-ATPIII -2001 classification and harmonized definition [1] metabolic syndrome exists if three of the five risk factors are positive:

1. Abdominal obesity-waist circumference in men ≥ 94 cm (previously >102 cm), and in women ≥80 cm (previously >88 cm)
2. triglycerides higher than 1.9 mmol / L (> 1.7 mmol/L)
3. HDL cholesterol lower than 1.1 mmol / L (1 , 2 ; 1,4)
4. glycemia higher than 5.6 mmol / L
5. blood pressure >130/85 mmHg or higher

MetS is characterized by the simultaneous presence of obesity, hypertension, dyslipidemia, and hyperglycemia in an individual, which leads to an increased risk of cardiovascular disease (CVD). It affects nearly 35% of the US adult population, and its prevalence increases with age. Elevated blood pressure is an almost regular component of the metabolic syndrome; however, optimal antihypertensive therapy has not yet been defined [2].

Abdominal obesity, glucose intolerance, hypertension and diabetes synergistically interact and lead to left ventricular remodeling. These facts may explain the significantly increased risk of heart failure with preserved ejection fraction and cardiovascular disease when these factors are grouped together [3].

Left ventricular hypertrophy (LVH) is thickening of the wall of the heart muscle - hypertrophy of cardiomyocytes and hyperplasia of connective tissue, the consequence of which is a decrease in the volume of the ventricles in concentric hypertrophy, which is typical for hypertension with the participation of non-hemodynamic factors (genetics, stress, other external factors) as well. [4]. The consequences of concentric hypertrophy are: left ventricular diastolic dysfunction with preserved left ventricular ejection fraction, reduction of longitudinal systolic function, electrical instability (arrhythmias) and subendocardial microvascular ischemia (Figure 1). Eccentric and dilatational hypertrophy (elongation of cardiomyocytes via sarcomere replication) increases chamber volume and is typical for athletes but also occurs in obesity and volume overload. A more severe degree of myocardial hypertrophy (Figure 2) increases overall cardiovascular risk and mortality (congestive heart failure, sudden cardiac death). LVH is an independent prognostic factor and lethal marker of hypertension

Figure 1. taken from https://remixeducation.in/case-of-ischemic-heart-disease-hid/

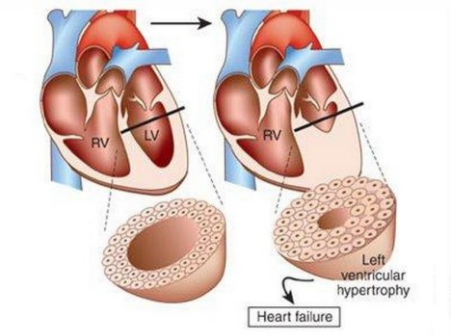
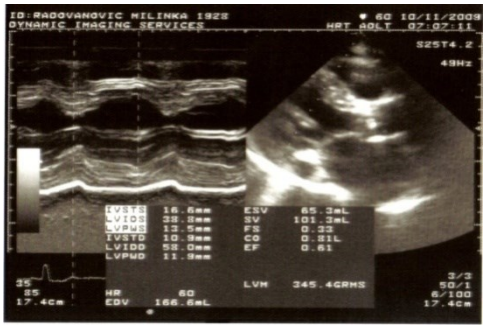


Figure.2. Echocardiographic image of a patient with extreme LVH of 345 g



Metabolic syndrome, which essentially includes insulin resistance, hyperinsulinemia, and hyperglycemia, alters myocardial metabolism and promotes myocardial inflammation, fibrosis, and left ventricular remodeling [5-8]. The ejection fraction of the left ventricle is most often preserved in metabolic syndrome and diabetes because the altered metabolic milieu leads to remodeling of the heart cavities, left ventricular hypertrophy and diastolic dysfunction, but also to subtle impairment of systolic function, which is detected through longitudinal global strain echocardiography [5-9]. For these reasons, the development of left ventricular hypertrophy doubles the risk for heart failure with preserved ejection fraction.

OBJECTIVE:

Determination of the impact of obesity to the incidence and degree of severity of myocardial hypertrophy in hypertensive patients with metabolic syndrome in comparison with the control group - hypertensive patients without metabolic syndrome .

PATIENTS AND METHODS

Consecutive patients of the Office of internal medicine "Dr. Bastać" were examined, a total of 55 patients with hypertension, who were divided into two groups :

- with metabolic syndrome N=22 (40%) patients , 10 male and 12 female, average age 56 ± 8.5 years with BMI>30kg/m ^{2} and waist circumference higher than 80 cm for females and > 94cm for men
- control group without metabolic syndrome 33 (60%) 11 male and 22 female, average age 52 ± 14 years, with BMI<30 kg / m ^{2}

Body mass index (BMI in kg/m^2) in the control group is 24.9±3 kg/m^2 , and in the examined group 32.5±2.5 kg/m^2 , a highly statistically significant difference is evident in body weight (p<0.001)

The number of cardiovascular risk factors that make up metabolic syndrome in the individual .

distribution was in the study group with metabolic syndrome - study group (N = 22 pts)

- 5 factors - 5 patients (22%)
- 4 factors - 8 patients (36%)
- 3 factors - 9 patients (42%)

It was not possible to observe other factors, e.g. parameters of systemic inflammation (hsCRP, interleukins, etc.) and measurement of insulin resistance (HOMA index, insulinemia during the OGTT test, etc.).

All patients had standard biochemical results, including serum concentrations of lipid fractions and blood glucose.

Echocardiography was done for all subjects on a Power Vision 6000 Toshiba echo camera with standard echocardiographic measurements in the M, B and Doppler technique, and the mass of the left ventricular myocardium was determined for them using the Devereux formula [10]:

$$\mathbf{LVM(g)= ((EDD+IVSd+PWd)^3 - EDD^3) \times 1.05 - 13.4}$$

Also, myocardial mass is indexed to the body surface and myocardial mass index-LVMI (g/m^2) is obtained.

The echocardiographic criterion for normal myocardial mass is up to 224g for men and 162g for women, on average less than 193g for both sexes. Normal myocardial mass index is less than 95 g/m^2 for women, less than 115 g/m^2 for men, on average less than 105 g/m^2.

Statistical processing was done through descriptive processing, for attributive characteristics using chi-squared test, and for numerical ones the Student's T test, both by means of the Mikrostat program.

RESULTS

Individual distribution - prevalence of left ventricular hypertrophy (LVH) in groups (for women LVMI >95 g/m^2 and for men LVMI >115 g/m$^{2)}$ is shown in Chart 1

CHART 1a. Prevalence of LVH in the group with metabolic syndrome and hypertension

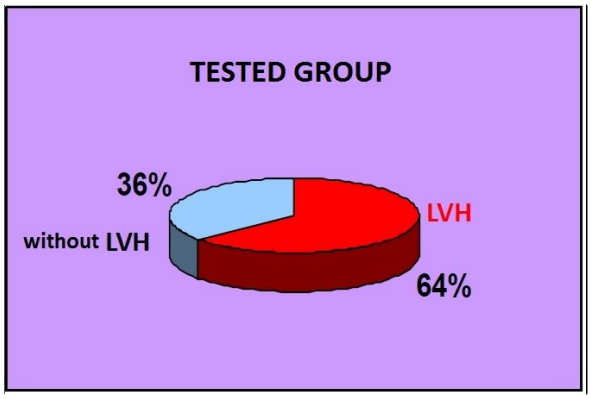
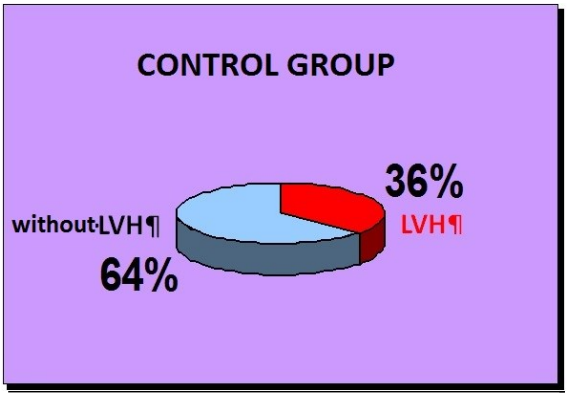


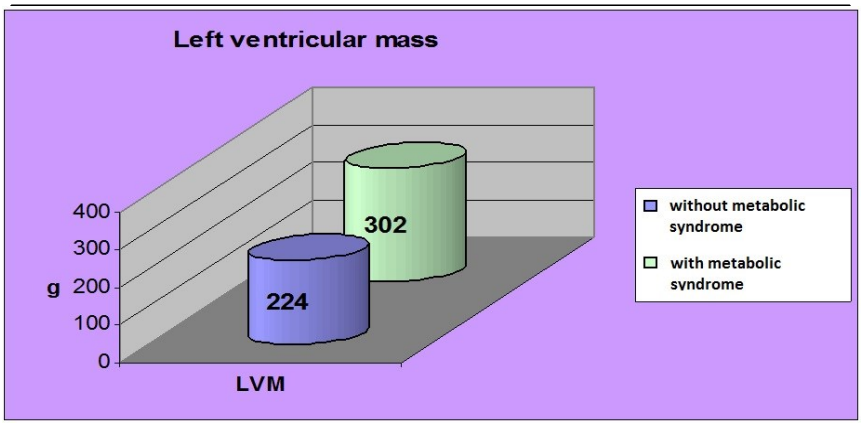
CHART 1b. Prevalence of LVH in the group with hypertension without metabolic syndrome



In the examined group 64% had LVH (Chart 1a), while in the control group 36 % had it (Chart 1b). There is a statistically significantly higher number of patients with LVH in hypertension with metabolic syndrome compared to hypertensive patients of the control group without metabolic syndrome (X^2 , p = 0.027)

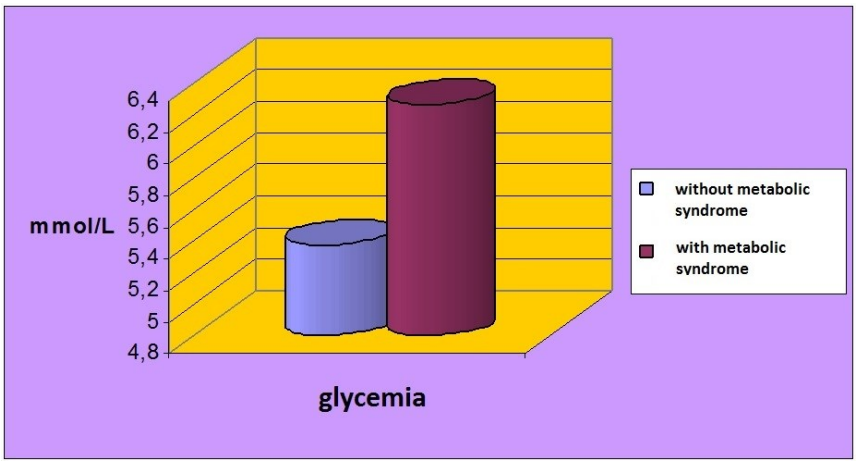
In the group of hypertensive patients with metabolic syndrome, the degree of severity of myocardial hypertrophy ie. myocardial mass is statistically significantly higher compared to the control group (respectively 302±84g versus 224±89g , p=0.0002) (Graph 2.)

Graph. 2. The degree of severity of hypertrophy - left ventricular myocardial mass in grams (g) in relation to the presence of metabolic syndrome



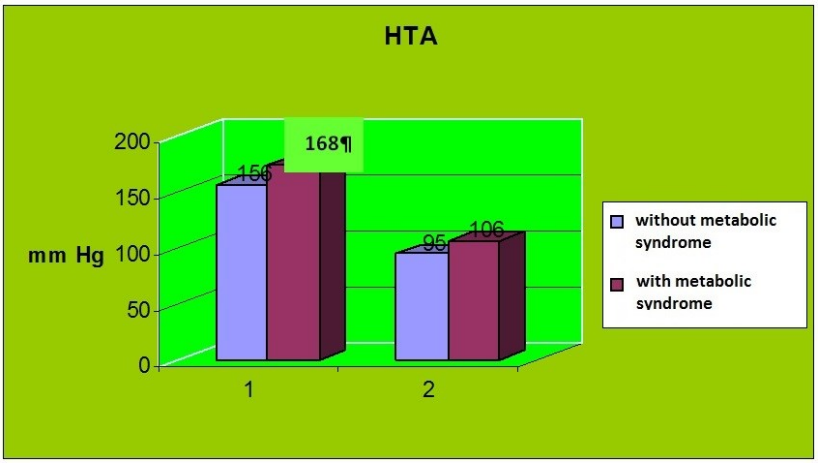
Glycemia values are slightly elevated in hypertensive patients with metabolic syndrome, on average 6.1 mmol/L, and in hypertensive patients without metabolic syndrome, they are normal at 5.5 mmol / L. (p<0.05) (Graph 3.)

Graph.3. Glycemia values in hypertensive patients with and without metabolic syndrome



Arterial pressure values were higher for both systolic and diastolic blood pressure 168/106 mmHg in hypertensive patients with metabolic syndrome, but did not reach statistical significance in relation to blood pressure values in hypertensive patients without metabolic syndrome (156/95 mmHg, p=0.16) (Chart 4).

Graph 4. Arterial pressure values in hypertensive patients with and without metabolic syndrome



DISCUSSION

The prevalence of left ventricular hypertrophy (LVH) in the examined group with metabolic syndrome (MetS) was quite high (64%), almost twice as high as the prevalence of the control group with isolated hypertension (36%). In the Second Strong heart study, De Simone et al. out of 1648 patients, they found 406 (25%) patients with LVH [11], which is a much lower number. We explain this difference by the fact that it is difficult to compare the given data, due to different patient selection factors, as well as genetic predisposition for hypertrophy. It is evident that the prevalence of hypertrophy is higher in our group because there were more severe patients with more metabolic syndrome factors. In patients without MetS with hypertension, our result of the prevalence of myocardial hypertrophy is 36%, while in the 2nd Strong Heart there were only 13% of subjects with LVH, which can be explained by the fact that they were without hypertension and that it was physiological hypertrophy or incipient hypertrophic cardiomyopathy [12]

Von Jensen et al. [3] in a population cohort study of 5741 participants of the Framingham study published in 2020, state that the prevalence of LVH is increased in subjects with associated hypertension, obesity and diabetes. Also, MetS and diabetes affect the reduction of left ventricular ejection fraction

(LVEF), which is not the case when there is hypertension with MetS without diabetes.

In our group of hypertensive patients with MetS, the degree of severity of myocardial hypertrophy, i.e. myocardial mass is statistically significantly higher compared to the control group (respectively 302±84g versus 224±89g, p=0.0002). On average, the contribution of the metabolic syndrome gives a higher myocardial mass by 26% than in hypertension without the metabolic syndrome, while this increase in the Von Jensen study of 36% is comparable because it was done on a very large sample [3]. In both, differences are highly statistically significant for the impact of metabolic syndrome on the increase in myocardial mass.

Arterial pressure values were higher for both systolic and diastolic blood pressure 168/106 mmHg in hypertensive patients with MetS, but did not reach statistical significance in relation to blood pressure values in hypertensive patients without MetS (156/95 mmHg, p=0.16). Given that the mean values of arterial pressure do not differ between groups, it is concluded that non-hemodynamic factors for the development of myocardial hypertrophy: abdominal obesity, hyperglycemia, insulin resistance and dyslipidemia associated with hypertension synergistically affect cardiac remodeling in terms of a more severe degree of left myocardial hypertrophy chambers. Similar conclusions are drawn on a large sample by von Jensen et al. [3]. These findings may explain the significantly increased risk of heart failure and cardiovascular disease when these factors are grouped together and play an important role in the induction of a more severe degree of myocardial hypertrophy in hypertensive patients with metabolic syndrome.

Metabolic syndrome (MetS) is associated with an increased prevalence of electrocardiographically and echocardiographically determined (LVH) and is a powerful predictor of cardiovascular outcome [11]. LVH is a strong predictor of composite fatal and nonfatal cardiovascular events over 8 years of follow-up, either in the presence or in the absence of the metabolic syndrome, and accounts for a significant portion of the high CV risk associated with MetS [11].

In the study by von Jeinsen B. et al. [3], 5741 participants of the Framingham study were examined who underwent echocardiographic measurements of left ventricular mass (LVM), ejection fraction (LVEF) and global longitudinal strain (GLS) through multivariable regression analysis. Statistically significant differences were obtained between BMI category, hypertension and diabetes with LVH, LVEF and GLS ($p < 0.01$). Obesity, hypertension and diabetes status were individually and jointly associated with greater severity of left ventricular hypertrophy (LVM) and worse GLS ($p<0.01$ for all). Obesity, hypertension and diabetes synergistically affect cardiac remodeling. These findings may explain the significantly increased risk of heart failure and cardiovascular disease when these factors are grouped together in the metabolic syndrome [3].

Determining the etiology of left ventricular hypertrophy (LVH) can be a challenge due to the similarity of various manifestations in clinical presentation and morphological characteristics [12,13]. Patients with LVH remain asymptomatic for several years, but disease progression will lead to the development of systolic or diastolic dysfunction and end-stage heart failure. Distinguishing individuals with treatable causes of LVH is important for the prevention of cardiovascular events and mortality. An athlete's heart with physiological LVH does not require treatment [13] The most common causes of hypertrophy, usually concentric type, include etiologies due to pressure overload, such as systemic hypertension, less common aortic valve stenosis and very rarely infiltrative heart diseases such as amyloidosis, Fabry disease and sarcoidosis. Volume overload is common in aortic and mitral insufficiency and extreme obesity [12,13].

Concentric myocardial hypertrophy occurs as a compensatory mechanism for pressure overload in hypertension [14-16]. Myocyte hypertrophy is associated with interstitial fibrosis, changes in cardiomyocyte metabolism, myocyte apoptosis, and microvascular dysfunction. These myocardial changes in hypertension are manifested as pathological remodeling of the left atrium and left ventricle accompanied by diastolic dysfunction, LVH and subtle myocardial systolic dysfunction, while LVEF is initially preserved [14-17]. Thus, obesity, diabetes mellitus and arterial hypertension cause LVH, but it is still not entirely clear how their joint presence can affect cardiac structure, function and ventricular geometry [17-35].

Finally, the results of epidemiological studies in the last 30 years have shown that visceral adipose tissue, precisely measured by CT or MRI, is an independent marker of the risk of cardiovascular and metabolic morbidity and

mortality [36]. Emerging evidence also suggests that ectopic fat deposition, including hepatic and epicardial fat, may contribute to increased atherosclerosis and cardiometabolic risk.

CONCLUSION

Patients with metabolic syndrome and hypertension have a statistically significantly higher prevalence of myocardial hypertrophy compared to the control group of hypertensive individuals without metabolic syndrome. The degree of myocardial hypertrophy of the left ventricle is statistically significantly higher compared to hypertensive patients without metabolic syndrome .

Given that mean values of arterial pressure do not differ between groups, it is concluded that non-hemodynamic factors for the development of myocardial hypertrophy play an important role in the induction of a more severe degree of myocardial hypertrophy in hypertensive patients with metabolic syndrome. Abdominal obesity, hyperglycemia and insulin resistance associated with hypertension synergistically affect heart remodeling in terms of a more severe degree of left ventricular hypertrophy than in hypertension without metabolic syndrome. These results may partly explain the significantly increased risk of heart failure and cardiovascular disease when the metabolic syndrome, including obesity, prediabetes or diabetes, dyslipidemia and hypertension factors are grouped together.

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