Myocardial hypertrophy in hypertensive patients with and without metabolic syndrome

Hipertrofija miokarda kod bolesnika sa arterijskom hipertenzijom sa metaboličkim sindromom i bez njega

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Abstract

Background/Aim. Beside arterial hypertension as the most important factor of a myocardial hypertension development, very important risk factors are obesity, hypercholesterolemia, insulin resistance, etc. The aim of the study was to examine the influence of metabolic syndrome (MetS) on left ventricular hypertrophy in patients with arterial hypertension.

Methods. We checked medical records for 138 patients with arterial hypertension, and compared them with the control group of 44 normotensive subjects. The patients with arterial hypertension were divided into two groups considering the presence of MetS: with MetS (59 patients), and without MetS (79 patients). We defined MetS as presence of three (or more) within five criteria: central obesity (> 102 cm male, > 88 cm female), raised triglycerides (> 1.7 mmol/L, or drug treatment for elevated triglycerides), reduced high density lipoprotein (HDL) cholesterol (< 1.03 mmol/L male, < 1.3 mmol/L female), raised blood pressure (> 130 mmHg systolic, > 90 mmHg diastolic), raised fasting glucose (> 6.11 mmol/L, or drug treatment for elevated glucose level). In each group routine laboratory, echocardiography and 24-hour ambulatory blood pressure monitoring were performed.

Results. We found statistically significant higher left ventricular mass in both subgroups hypertensive patients in comparison with the control group (p < 0.05). We did not find statistically significant difference (227.31±63.44 vs 219±59.5, p > 0.05) in left ventricular mass between these two groups of patients. In the patients with arterial hypertension and MetS we found hypertrophy more frequently than in the subgroup without MetS (43/57 vs 34/69, p < 0.001).

Conclusion. Our results suggest that associated cardiometabolic risks increase the prevalence of myocardial hypertrophy, but do not influence left ventricular mass.

Key words: metabolic syndrome X; hypertrophy, left ventricular; hypertension; risk factors; risk assessment.
Introduction

Myocardial hypertrophy is a chronic left ventricular (LV) adaptation caused by increased burden of pressure or volume. These two hemodynamic factors are crucial for molecular changes that take part in cascade reactions, which are necessary for compensatory effects. Increasing wall stress and stretching are the stimuli for transcriptional messenger ribonucleic acid (mRNA) and increasing protein level in the cardiomyocytes.

Numerous factors participate in myocardial LV hypertrophy appearance and development. Arterial hypertension has the main role, but obesity, insulin resistance, hypercholesterolemia, a salt-rich diet, terminal renal failure, anemia, etc. also play an important role.

Some of these metabolic disorders are most important in the pathogenesis of metabolic syndrome (MetS). This disease changed its name few times in the past – insulin resistance syndrome, X-syndrome, deadly quartet and dysmetabolic syndrome are all the old terms used for MetS. About ten years ago, World Health Organization (WHO) defined MetS and put emphasis on its clinical importance and possible consequences. Today we use two formal definitions of this disease. According to The National Cholesterol Educational Program Third Adult Treatment Panel (NCEP-ATP III) MetS is defined as the presence of three or more of five abnormalities: glucose metabolism disorder, arterial hypertension, hypertriglyceridemia, low high density lipoprotein (HDL) cholesterol level and central obesity. Other definition, created by the International Diabetes Federation (IDF), is based on the presence of central obesity, together with two (out of remaining four) criteria.

Negative influence of the presence of MetS in cardiovascular patients was proven. Screening of subclinical organ damage could be very useful for cardiovascular risk evaluation – including LV hypertrophy.

The aim of the study was to examine the influence of the MetS on LV hypertrophy development in patients with arterial hypertension, without any clinical manifestation of cardiovascular disease.

Methods

This study included 182 patients, divided into two groups. The first group consisted of 138 patients (72 females and 66 males) with arterial hypertension. The other group contained 44 patients (24 females and 20 males) with normal blood pressure values, a maximum of one (other) criteria for MetS and no evidence of any cardiovascular diseases. They were used as controls.

Our criteria for including patients in the group I were: the presence of hypertension for no more than three years with ambulatory measured values (3 times in 7 days) higher than 130/90 mmHg, or normotensive under antihypertensive therapy. We included patients without any clinical or laboratory signs of heart failure, coronary disease, stroke, valvular diseases, any cause of (possible) secondary hypertension or other chronic diseases such as cirrhosis, renal failure or endocrine diseases.

Glucose and triglycerides levels were statistically significant in the group of patients with hypertension as a part of MetS compared with patients who had isolated hypertension \((p < 0.05)\). The level of HDL cholesterol was slightly lower in the group of hypertensive patients with MetS compared with the patients with isolated hypertension and the control group, but without statistical significance \((p > 0.05)\). The body mass index and waist circumference were statistically significantly higher in the group of patients with MetS compared with both the patients with both hypertension and the control group \((p < 0.05)\).

The average end-diastolic and end-systolic diameters of the LV were in the range of physiological values in both groups, without any significant discord compared to the control group, IVSTD was significantly higher in all patients with hypertension, regardless of whether it was part of the MetS or not. PWDT was higher in both subgroups compared to control group, but without significant variation between the subgroups with/without MetS.

The values of the EF and FS parameters were in the range of the physiological values in all the groups, without any significant discord.

### Table 1

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Control group (\bar{x} \pm SD)</th>
<th>Patients with MetS (\bar{x} \pm SD)</th>
<th>Patients without MetS (\bar{x} \pm SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>47±4</td>
<td>51 ± 4</td>
<td>53 ± 5</td>
</tr>
<tr>
<td>Body mass index</td>
<td>23.8±3.8</td>
<td>30.8 ± 3.7</td>
<td>26.1 ± 3.4 (^4)</td>
</tr>
<tr>
<td>Waist circumference, male (cm)</td>
<td>82±7</td>
<td>109±8(^*)</td>
<td>97±9(^*), (^5)</td>
</tr>
<tr>
<td>Waist circumference, female (cm)</td>
<td>79±8</td>
<td>98±8(^*)</td>
<td>88±7(^*), (^5)</td>
</tr>
<tr>
<td>Glucose level (mmol/l)</td>
<td>4.84±0.7</td>
<td>5.37±0.8(^*)</td>
<td>4.92±0.7(^1)</td>
</tr>
<tr>
<td>HDL, male (mmol/l)</td>
<td>1.68±0.4</td>
<td>1.09±0.2</td>
<td>1.59±0.3</td>
</tr>
<tr>
<td>HDL, female (mmol/l)</td>
<td>1.71±0.3</td>
<td>1.32±0.3</td>
<td>1.45±0.4</td>
</tr>
<tr>
<td>Triglycerides (mmol/l)</td>
<td>0.98±0.7</td>
<td>2.2±0.7(^*)</td>
<td>1.87±0.7(^*), (^1)</td>
</tr>
<tr>
<td>Heart rate (n/min)</td>
<td>71±6</td>
<td>86±9.2</td>
<td>80±8.6</td>
</tr>
<tr>
<td>SAP (mmHg)</td>
<td>118±7.81</td>
<td>152±10.42(^*)</td>
<td>150±9.89(^*)</td>
</tr>
<tr>
<td>DAP (mmHg)</td>
<td>76±5.7</td>
<td>102±6.4</td>
<td>99±5.2</td>
</tr>
<tr>
<td>24h SAP (mmHg)</td>
<td>115±7.80</td>
<td>146±10.52(^*)</td>
<td>142±11.20(^*)</td>
</tr>
<tr>
<td>24h DAP (mmHg)</td>
<td>75±5.2</td>
<td>98±6.4(^*)</td>
<td>96±5.4(^*)</td>
</tr>
<tr>
<td>24h heart rate (n/min)</td>
<td>72±7</td>
<td>86±8.7</td>
<td>80±8.6</td>
</tr>
</tbody>
</table>

\(^*\) \(p < 0.05\) vs the control group; \(^1\) \(p < 0.05\) vs patients with MetS

HDL – high density lipoprotein cholesterol
SAP – systolic arterial pressure
DAP – diastolic arterial pressure

Systolic and diastolic isolated pressure values and heart rate measured in ambulance, and also the values from 24-hour ambulatory monitoring, are presented in Table 1. It is obvious that blood pressure values were higher in both groups of patients, compared with the control group. There was no significant difference in these values between the two groups of patients \((p > 0.05)\).

Table 2 shows echocardiography parameters in the groups of patients observed.

### Table 2

<table>
<thead>
<tr>
<th>ECHO parameters</th>
<th>Control group (\bar{x} \pm SD)</th>
<th>Patients with MetS (\bar{x} \pm SD)</th>
<th>Patients without MetS (\bar{x} \pm SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVIDD (cm)</td>
<td>4.54 ± 0.4</td>
<td>4.79 ± 0.3</td>
<td>4.78 ± 0.2</td>
</tr>
<tr>
<td>LVISD (cm)</td>
<td>2.9 ± 0.2</td>
<td>3.2 ± 0.2</td>
<td>2.9 ± 0.2</td>
</tr>
<tr>
<td>Interventricular septum (cm)</td>
<td>0.8 ± 0.04</td>
<td>1.13 ± 0.06</td>
<td>1.08 ± 0.04(^*)</td>
</tr>
<tr>
<td>Posterior wall (cm)</td>
<td>0.8 ± 0.02</td>
<td>1.07 ± 0.04(^*)</td>
<td>1.07 ± 0.04(^*)</td>
</tr>
<tr>
<td>Ejection fraction (%)</td>
<td>65.04</td>
<td>63.72</td>
<td>64.45</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td>33.74</td>
<td>34.02</td>
<td>33.59</td>
</tr>
<tr>
<td>Left ventricular mass (g)</td>
<td>129.81 ± 22.24</td>
<td>227.31 ± 63.44(^*)</td>
<td>219.02 ± 59.5(^*)</td>
</tr>
<tr>
<td>RWT</td>
<td>0.35 ± 0.02</td>
<td>0.44 ± 0.03(^*)</td>
<td>0.44 ± 0.03(^*)</td>
</tr>
</tbody>
</table>

\(^*\) \(p < 0.05\) vs the control group; LVIDD – left ventricular internal dimension in diastole; LVISD – left ventricular internal systolic diameter; RWT – relative ventricular wall thickness

The values of the RWT were statistically significantly higher in the patients with hypertension (regardless of the subgroup) compared to the control group.

The average LV mass values were significantly higher in patients with raised blood pressure compared to the control group – regardless of the presence of MetS \((p > 0.05)\).

The LVmass/BSA showed a significant frequency of hypertrophy in the patients with MetS \((43/57\ vs\ 34/69\ vs\ patients\ with\ isolated\ hypertension\ \(p < 0.001\)).
Discussion

In the patients with hypertension, with or without MetS, PWDT and IVSTD, RWT and LV mass were all significantly higher as compared to normotensive people. At the same time, there was no significant difference of these parameters between two subgroups of hypertensive patients (with or without MetS). That unmistakably demonstrated the central role of hypertension in the (patho)genesis of these structural changes. Human hypertension has an important attribute: pressure burden or volume burden causes various adaptations of the heart LV. According to epidemiologic information – the prevalence of concentric heart remodelling and concentric myocardial hypertrophy – the conclusion is that a pressure burden is the main abnormality in arterial hypertension, with volume burden as an associated component. The cellular adaptation basis in a pressure burden is based on the sarcomeres and extracellular changes, which are more pronounced in this process than in the case of volume burden. In case of an additional volume burden present (with a dominant pressure burden) it is common to see collagen accumulation – though this process does not appear to be important in causing concentric remodelling and concentric myocardial hypertrophy 6.

An important difference between our subgroups of hypertensive patients is the significant occurrence of myocardial hypertrophy in the patients with MetS. The absence of (significant) differences between blood pressure values in the subgroups of patients rules out the influence of the blood pressure level on the frequency of myocardial hypertrophy. A number of studies have suggested that hypertrophy is more frequent in hypertensive patients with MetS as compared to the patients with hypertension without MetS7-12.

In the PAMELA study 13, normotensive patients with MetS were examined and an increased prevalence of elevated values for LVmass index and myocardial hypertrophy was found 3. One of the conclusions was that changes in the heart structure connected were not only with hypertension – metabolic and neural components of this syndrome were important, too. The role of sympathetic stimulation (their influence on cardiomuscular hypertrophy and connective tissue proliferation) was emphasised. It is likely that other metabolic factors will be considered as responsible for a higher frequency of myocardial hypertrophy.

Different levels of carbohydrate metabolism disturbance – glucose metabolism disorder, diabetes mellitus type II and insulin resistance are the cause of LVmass increase 14. In vitro (animal and human model) effects of insulin are salt retention and sympathetic stimulation, as well as peripheral vascular resistance. The first two mechanisms could be seen as responsible for increasing the LVmass index. Concentric hypertrophy in patients with insulin resistance could be explained by vasoconstriction and pressure burden.

An important negative effect of obesity on the cardiovascular system is hypertrophy of the left side of the heart. Volume burden is a characteristic of this, so it was thought that the manifestation should be eccentric hypertrophy of the LV. However, echocardiography studies showed different structural changes. Avelar et al. 15 suggested that both patterns of hypertrophy could be found in overweight people – but concentric hypertrophy was more frequent. Indirectly, they came to the conclusion that sympathetic stimulation together with hypertension are responsible for this finding. They also found that obstructive sleep apnoea leads to hypertrophy development in obesity - because there is intermittent hypoxia during the obstruction of the airways and increased sympathetic tone with a consequential increase in heart frequency and blood pressure.

It is a premise that increasing levels of triglycerides in blood could be a reason for structural and functional changes in the LV, by increasing the influx of fatty acids in the myocytes. Investigation of this hypothesis showed that there were no significant changes in structure, but signs of diastolic dysfunction were found in this metabolic disorder 16.

Here we mentioned data on the influence of the single risk factors (in MetS) on the development of myocardial hypertrophy as a subclinical form of heart damage. The global influence of the MetS has been shown through linear association between the number of risk factors and the prevalence of target organ damage and cardiovascular complications 17. Grandi et al. 12 showed the dominant effect of the 24-hour average values of systolic pressure and body mass index on the development of LV hypertrophy in patients with MetS without diabetes. Palmieri and Bella 18 considered that the results of Grandi’s investigation emphasised insulin resistance as an important additional factor in hypertrophy in patients without diabetes.

Conclusion

The results of this investigation suggest that arterial hypertension has a leading role in the development of myocardial hypertrophy, both in patients with and without MetS. Other components of MetS are important in increasing the occurrence of LV hypertrophy. Myocardial hypertrophy is an intermediary marker of heart damage and an important predictor of heart failure, coronary disease and stroke. Because of that, therapy for hypertension and also other components (obesity and insulin resistance above all) is obligatory.

REFERENCES


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