Metabolic syndrome and left ventricular function: Is the number of criteria actually important?

Authors' Contribution:
A Study Design
B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
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Summary

Background: Metabolic syndrome (MS) is a clustering of cardiovascular risk factors responsible for the development of target organ damage. The aim of this study was to determine the effect of the increasing number of MS risk factors on left ventricular function assessed by noninvasive methods.

Material/Methods: The study included 204 subjects with MS and 76 controls with no MS risk factors. MS was defined by the presence of 3 or more of ATP-NCEP III criteria. MS subjects were grouped according to the number of criteria they fulfilled: 3 criteria (n=91), 4 criteria (n=65) and 5 criteria (n=48). All subjects underwent laboratory blood tests, complete 2-dimensional, pulse and tissue Doppler echocardiography. Echocardiography was used to assess systolic (LVEF, s_{septal}), diastolic function, by pulse-wave Doppler (E/A ratio) and tissue Doppler imaging (E/e'$_{average}$), and global left ventricular function (Tei index). Appropriate time intervals for the estimation of the Tei index were obtained by tissue Doppler.

Results: Transmitral E/A ratio decreased significantly and progressively from the 3 criteria to the 5 criteria group (0.82±0.25 *vs.* 0.79±0.24 *vs.* 0.67±0.14, p<0.001). The transmitral E/E'$_{average}$ ratio was significantly and gradually increased from the 3 criteria to the 5 criteria group (7.76±1.81 *vs.* 9.44±2.35 *vs.* 10.82±2.56, p<0.001). The left ventricle Tei index progressively increased from the 3 criteria to the 5 criteria group (0.43±0.11 *vs.* 0.48±0.10 *vs.* 0.54±0.12, p<0.001).

Conclusions: The increasing number of MS criteria is associated with cardiac diastolic dysfunction.

key words: metabolic syndrome • left ventricle • diastolic function • global function

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BACKGROUND

Metabolic syndrome (MS) is a group of risk factors which includes high blood pressure, hyperglycemia, abdominal obesity and dyslipidemia, and increases morbidity and mortality, both overall and from cardiovascular diseases [1,2]. One of the consequences of the negative effects of the metabolic syndrome is a change in the structure and function of the left ventricle [2,3]. It is well-known how certain risk factors like hypertension, diabetes or obesity affect the structural and functional changes of the left ventricle [4,5]. A small number of studies have focused on examining the impact of the metabolic syndrome [6]. However, there have been extremely few studies of the influence of the increasing number of metabolic syndrome risk factors on the structure and function of the left ventricle (diastolic, systolic and global) [7]. Furthermore, Azevedo et al did not assess left ventricular global function, they did not use precise tissue Doppler indexes for the estimation of left ventricular diastolic function, and they did not identify MS criteria independently associated with the parameters of structure and function of the left ventricle [7].

The aim of this study was to determine whether the increased number of metabolic syndrome (MS) risk factors caused deterioration of the structure and function of the left ventricle in subjects with metabolic syndrome.

MATERIAL AND METHODS

This cross-sectional study included 280 consecutive subjects with some cardiovascular risk factors who were sent from the primary care clinic to the echo laboratory at the Clinic for Cardiology, the Clinical Centre of Serbia, from 1 January 2006 to 31 December 2008. The study group was divided into 2 groups: the first group involved 204 subjects (108 women and 96 men) with MS, while the control group included 76 subjects (41 women and 35 men) with no MS risk factors. Patients with clinical or laboratory signs of heart failure, coronary artery disease, previous cerebrovascular insult, valvular heart disease, secondary hypertension or other chronic diseases such as cirrhosis of the liver, kidney failure, or endocrinological diseases (except diabetes mellitus type 2) were excluded from the study. MS was defined by the presence of 3 or more of the American National Cholesterol Education Program's Adult Treatment Panel III (NCEP-ATP-III) criteria from 2001 [8]: abdominal obesity (waist circumference $\geqslant$102 cm in men and $\geqslant$88 cm in women), increased fasting triglycerides ($\geqslant$1.7mmol/l), decreased HDL cholesterol (<1.0mmol/l in men and <1.3mmol/l in women), high blood pressure ($\geqslant$130/85 mmHg or antihypertensive therapy), and increased level of fasting glucose ($\geqslant$6.1mmol/l).

Considering the number of risk factors and in order to examine the impact of the increasing number of factors on the structural and functional changes of the left ventricle, the MS group was divided into 3 subgroups; subjects with 3, 4 and 5 risk factors.

The anthropometric measurements (height, weight, waist circumference) were taken from all subjects included in the study in order to calculate body surface (BSA) and body mass index (BMI). Regarding laboratory analyses, we used the level of fasting glucose, hemoglobin A1C, total cholesterol, low and high-density lipoprotein cholesterol (HDL, LDL), triglycerides and uric acid.

Arterial blood pressure values were obtained by measuring the average value of 2 consecutive measurements in the sitting position with 5 minutes between measurements in the morning hours, obtained by conventional sphygmomanometer.

The diagnosis of diabetes was based on the criteria of the World Health Organization published in 2006 [9], and arterial hypertension was diagnosed according to recommendations of the European Association for Hypertension in 2007 [10]. The protocol was approved by the Research Ethics Committee of the Faculty of Medicine, University of Belgrade.

Echocardiography

Echocardiographic examination was performed on the Acuson Sequoia 256 ultrasound system by using a 2-to-4 MHz transducer. The values of all echocardiographic parameters were obtained as the average value of 5 consecutive cardiac cycles. The left ventricle end-systolic (LVESD) and end-diastolic diameters (LVEDD), the left ventricle free wall (PWT), septum thickness (IVS) and the left atrium (LA) diameter were determined according to the recommendations of the American Society of Echocardiography [11]. End-systolic and end-diastolic volumes and parameters of systolic function (ejection fraction – EF, and fractional shortening – FS) were estimated by using the Teicholz formula. Relative wall thickness (RWT) was calculated as $(2 \times PWT)/LVEDD$.

The left ventricular mass (LVmass) was calculated by using the Penn formula: LV mass=$1.04 \times [(LVEDD+PWTD+IVS)^3 - (LVEDD)^3] - 13.6$ g [12]. The left ventricular mass index (LVmass/$Ht^{2.7}$) was calculated as the ratio of the left ventricular mass and height$^{2.7}$. The left ventricular hypertrophy was defined as LVmass/$Ht^{2.7} \geqslant 51$ g/$m^{2.7}$ for men and $\geqslant$49.5g/$m^{2.7}$ for women [13].

The analysis of transmitral inflow velocities was obtained by pulsed-wave Doppler in the apical 4-chamber view with the sample volume placed at the mitral valve leaflet tips [14]. Measurements included transmitral early diastolic (E-wave) and atrial (A-wave) velocities which were used to calculate E/A ratio and E-wave deceleration time (DT).

Tissue Doppler imaging was used to obtain the left ventricle myocardial velocities in the apical 4-chamber view with a 2-mm sample volume placed at the septal and lateral segments of mitral annulus during early diastole (e'_{septal} and $e'_{lateral}$) and systole (s_{septal} and $s_{lateral}$) [14]. The E/e'_{septal} and $E/e'_{lateral}$ ratios were determined using previously estimated values of E and e'_{septal} and $e'_{lateral}$ flow velocities during early diastole obtained by pulsed Doppler and tissue Doppler. $E/e'_{average}$ was determined in the same way ($e'_{average}$ was calculated as average of e'_{septal} i $e'_{lateral}$).

The presence of the left ventricular diastolic dysfunction was based on the recommendations of the European and the American Society of Echocardiography using E/A ratio, deceleration time (DT), isovolumic relaxation time (IVRT), $e'_{lateral}$, e'_{septal}, and $E/e'_{average}$ ratio [15]. Systolic function was

Table 1. Clinical characteristics of the study population.

	Controls (n=76)	3 factors (n=91)	4 factors (n=65)	5 factors (n=48)
Age (years)	52±7	53±9	52±7	53±8
Gender (female/male)	41/35	49/42	31/34	28/20
BMI (kg/m^2)	24.8±3.9	25.8±3.5	25.5±3.7	26.2±3.1
Systolic BP (mmHg)	129±9*	143±10	145±10	144±9
Diastolic BP (mmHg)	83±7*	91±7[c]	93±7	94±8[c]
Fasting glucose (mmol/L)	4.59±0.44*	5.60±0.84[d]	5.83±0.75	6.10±0.70[d]
HbA1c (%)	4.23±0.37*	5.12±0.70	5.26±0.78	5.40±0.81
Uric acid (umol/L)	271±46*	405±87	386±73	420±95
Triglycerides (g/L)	1.50±0.26*	1.88±0.32	1.94±0.44	2.03±0.51
HDL (g/L)	1.43±0.29*	1.28±0.31[a,d]	1.10±0.25[a,f]	0.94±0.21[d,f]
LDL (g/L)	2.84±0.32*	3.16±0.29	3.21±0.27	3.27±0.35
Total cholesterol (g/L)	4.50±0.58*	5.14±0.58	5.08±0.70	5.27±0.6
Waist circumference (cm): Women Men	85±8* 96±13*	97±8 105±10	98±9 107±11	100±9 109±10
Hypertension (%)	/	64 (70)[d]	47 (72)[f]	45 (94)[d,f]
Diabetes (%)	/	7 (8)[a,c]	13 (20)[a]	10 (21)[c]

3 *vs.* 4 MS criteria (a<0.05, b<0.01); 3 *vs.* 5 MS criteria (c<0.05, d<0.01); 4 *vs.* 5 MS criteria (e<0.05, f< 0.01). * p<0.001 for all comparisons (0 *vs.* 3, 0 *vs.* 4 and 0 *vs.* 5 MS criteria).

assessed by ejection fraction, shortening fraction, as well as the parameters obtained by using tissue Doppler (s$_{septal}$ and s$_{lateral}$).

The parameters necessary for calculation of Tei index were obtained by tissue Doppler in the apical 4-chamber view. A 2-mm sample volume was placed in the lateral corner of the mitral annulus. The isovolumetric contraction time (IVCT) and isovolumetric relaxation time (IVRT) were measured from the end of the mitral annular velocity pattern to the onset of the S-wave and from the end of the S-wave to the onset of the mitral annular velocity pattern, respectively. The ejection time (ET) was defined as the duration of the left ventricle outflow Doppler velocity profile. Tei index was calculated according to the formula: Tei index =(IVCT+IVRT)/ET [16].

Statistical analysis

Continuous variables were presented as mean ± standard deviation (SD) and the analysis of equal variance (ANOVA) was used to detect differences between groups as they showed normal distribution. Differences in proportions were compared by using the χ² test. The odds ratios and 95% confidence interval (CI) were calculated by using univariate logistic regression. We calculated p value for the trend of LV hypertrophy and LV diastolic dysfunction prevalence. Stepwise multiple variable regression analysis determined which MS criteria were independently associated with

parameters of left ventricular structure and function (RWT, E/A ratio, DT, E/e'$_{septal}$, and E/e'$_{lateral}$). To determine the difference between groups we used Bonferroni post-hoc analysis. P-values <0.05 were considered statistically significant.

RESULTS

There was no statistically important difference in mean age between the subjects with MS and controls (53±8 *vs.* 52±7 years, p>0.05). Among subjects with MS, 91 of them (44.6%) had 3 risk factors, 65 of them (32%) had 4 factors, and the remaining 48 patients (23.4%) had all 5 risk factors.

Among the patients with metabolic syndrome, the most common risk factors were high blood pressure (76%) and abdominal obesity (75%), followed by elevated levels of triglycerides (56%), glucose (55%) and HDL (52%) which were almost equally presented. If the subgroups with 3 and 4 risk factors are considered separately, distribution of risk factors is different. In this case, in the subgroup with 3 criteria the most common factor was abdominal obesity (85%), elevated blood pressure was in second place (75%), elevated glucose level was third (42%), low HDL with 41% was fourth, and higher level of triglycerides had the lowest prevalence (30%). In the subgroup with 4 MS components, elevated blood pressure was in first place (78%), elevated triglycerides in second place (60%), abdominal obesity was in third place (43%), elevated glucose level was right behind (40%), and low HDL had the lowest frequency (32%). Hypertension

Table 2. Echocardiographic parameters of left ventricular structure and function.

	Controls (n=76)	3 factors (n=91)	4 factors (n=65)	5 factors (n=48)
Left ventricular structure				
LVEDD (cm)	4.63±0.43	4.65±0.47	4.67±0.49	4.71±0.50
LVESD (cm)	2.92±0.44	2.91±0.37	2.94±0.41	2.97±0.47
LA (cm)	3.4±0.4*	3.7±0.5[b,d]	4.0±0.6[b]	4.1±0.5[d]
IVS (cm)	0.84±0.13*	0.89±0.14[b,d]	0.98±0.15[b,f]	1.06±0.15[d,f]
RWT	0.36±0.06**	0.38±0.07[b,d]	0.42±0.09[b,f]	0.45±0.08[d,f]
LVM/Ht2.7 (g/m2.7)	38.8±7.3*	42.2±7.9[b,d]	45.5±9.5[b]	47.2±8.9[d]
Left ventricular systolic function				
EF (%)	68±7	69±9	68±7	67±8
FS (%)	40±7	41±8	40±7	39±8
s_{septal} (m/s)	0.081±0.021	0.079±0.018	0.076±0.017	0.074±0.018
$s_{lateral}$ (m/s)	0.084±0.022	0.082±0.019	0.080±0.017	0.078±0.019
Left ventricular diastolic function				
E (m/s)	0.82±0.17	0.81±0.18	0.80±0.19	0.81±0.17
A (m/s)	0.60±0.15*	1.01±0.18[d]	1.05±0.21[f]	1.23±0.19[d,f]
E/A	1.34±0.24*	0.82±0.25[d]	0.79±0.24[f]	0.67±0.14[d,f]
DT (ms)	192±33*	216±33[b,d]	230±40[b,e]	246±45[d,e]
e'_{septal} (m/s)	0.11±0.02*	0.10±0.02[b,d]	0.08±0.01[b,f]	0.07±0.01[d,f]
$e'_{lateral}$ (m/s)	0.13±0.02*	0.11±0.02[b,d]	0.09±0.01[b,f]	0.08±0.01[d,f]
E/e'_{septal}	7.32±1.9*	8.21±1.73[b,d]	9.61±2.26[b,f]	11.80±2.71[d,f]
$E/e'_{lateral}$	6.56±1.7*	7.52±1.86[b,d]	8.64±2.05[b,f]	10.10±2.12[d,f]
$E/e'_{average}$	6.87±1.82*	7.76±1.81[a,d]	9.44±2.35[a,f]	10.82±2.56[d,f]
Global left ventricular function				
IVRT (ms)	79±16*	89±13[a,d]	95±19[a,f]	108±24[d,f]
IVCT (ms)	32±4*	49±4[b,d]	53±6[b,f]	58±9[d,f]
ET (ms)	326±28*	313±22[d]	308±20	302±16[d]
Tei index	0.35±0.04*	0.43±0.11[b,d]	0.48±0.10[b,f]	0.54±0.12[d,f]

3 *vs.* 4 MS criteria (a<0.05, b<0.01); 3 *vs.* 5 MS criteria (c<0.05, d<0.01); 4 *vs.* 5 MS criteria (e<0.05, f<0.01). * p<0.001 for all comparisons (0 *vs.* 3, 0 *vs.* 4 and 0 *vs.* 5 MS criteria); ** p<0.05 for comparison 0 *vs.* 3 MS criteria and p<0.01 for comparisons 0 *vs.* 4 and 0 *vs.* 5 MS criteria.

was the most prevalent in the subgroup with all 5 factors, while it was equally distributed in subgroups with 3 and 4 factors. On the other hand, diabetes was equally present in subgroups which had 4 and 5 criteria, and was significantly less in the subgroup with 3 risk factors (Table 1).

All clinical parameters of the study group are shown in Table 1. Values of all the parameters of MS were significantly higher in all MS subgroups compared to controls (Table 1). No statistically significant difference was shown in almost all parameters of the metabolic syndrome, except

for HDL level, which decreases with the increasing number of factors.

There were no differences in the LV diameters, EF and FS between the observed subgroups, nor when compared to the controls (Table 2). The LA diameter in subjects with 3 MS risk factors was significantly smaller compared to subjects with 4 or 5 factors. The RWT exhibited stepwise increases from the group with 3 factors to the group with all 5 risk factors, while LV_{mass} index did not differ significantly in subjects with 4 or 5 risk factors, but it was still significantly increased

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Table 3. Prevalence of left ventricular hypertrophy and abnormal diastolic function in the study population.

	Controls (n=76)	3 factors (n=91)	4 factors (n=65)	5 factors (n=48)	p (trend)
LV hypertrophy (%)	4 (5)*	17 (19)[e]	13 (20)	17 (35)[e]	<0.001
Abnormal diastolic function (%)	7 (9)*	22 (24)[c]	17 (26)[e]	22 (46)[c,e]	<0.001

3 *vs.* 4 MS criteria (a<0.05, b<0.01); 3 *vs.* 5 MS criteria (c<0.05, d<0.01); 4 *vs.* 5 MS criteria (e<0.05, f< 0.01). * p<0.001 for all comparisons (0 *vs.* 3, 0 *vs.* 4 and 0 *vs.* 5 MS criteria).

Table 4. Multiple variable linear regression model of RWT, E/A ratio and DT for each component of the metabolic syndrome in metabolic syndrome group.

	RWT		E/A ratio		DT (ms)	
	β	p	β	p	β	p
Systolic BP (mmHg)	0.298	<0.001	−0.334	<0.001	0.278	<0.001
Diastolic BP (mmHg)	0.257	<0.001	−0.249	0.015	0.147	0.036
Fasting glucose (mmol/l)	0.156	0.068	−0.291	0.001	0.115	0.092
Triglycerides (mmol/l)	0.075	0.224	−0.082	0.102	0.087	0.152
HDL (mmol/l)	−0.055	0.367	0.041	0.231	0.048	0.379
Waist circumference (cm)	0.193	0.005	−0.182	0.025	0.125	0.043
Model r2		0.76		0.66		0.72

BP – blood pressure; HDL – high density lipoprotein.

when compared to the group with 3 criteria (Table 2). The parameters of systolic function obtained by tissue Doppler (s_{septal} and $s_{lateral}$) were similar in the 3 subgroups. On the other hand, parameters of left ventricular diastolic function E/A, DT, e'_{septal}, $e'_{lateral}$, E/e'_{septal}, $E/e'_{lateral}$, and $E/e'_{average}$ progressively deteriorated with an increasing number of risk factors (Table 2).

The parameters required for calculation of Tei index also changed with the increased number of risk factors. Thus, IVRT and IVCT exhibited stepwise prolongation with the increased number of criteria, while there was no significant difference in ET between the observed subgroups, except among the subgroups with 3 and 5 risk factors (Table 2). These findings showed that there was a progressive impairment in LV global function, estimated with Tei index, as the number of MS criteria increased.

Compared with the control group, all 3 subgroups with MS had a significantly higher prevalence of LV hypertrophy (Table 3). Subjects with 3 criteria had a 4-fold higher prevalence compared to the control group (OR 4.14, 95% CI: 1.33–12.88, p=0.01), subjects with 4 factors had 4.5-fold greater prevalence (OR 4.5, 95% CI: 1.39–14.59, p=0.009), while subjects with all 5 criteria of the metabolic syndrome had an almost 10-fold greater prevalence of LV hypertrophy (OR 9.87, 95% CI: 3.07–31.73, p<0.001).

Among the patients with MS we noticed that subjects with all 5 risk factors had a higher incidence of LV hypertrophy in relation to the remaining 2 groups (Table 3). However,

subjects with 3 or 4 risk factors have a similar risk of left ventricular hypertrophy, while subjects with 5 risk factors were 2.5 times more likely to have LV hypertrophy than subjects with 3 risk factors (OR 2.39, 95% CI: 1.08–5.27, p=0.038). Patients with 5 components have a similar risk of left ventricular hypertrophy as subjects with 4 risk factors.

In relation to the control group, all 3 subgroups of MS had a significantly higher risk of left ventricular diastolic dysfunction (Table 3). Subjects with 3 factors of metabolic syndrome had a 3 times greater risk than the control group (OR 3.14, 95% CI: 1.26–7.84, p=0.013), those with 4 factors had almost 3.5 times higher risk (OR 3.49, 95% CI: 1.35–9.07, p=0.012), and subjects with all the criteria had almost 8.34 times greater risk of LV diastolic dysfunction (OR 8.34, 95% CI: 3.19–21.84, p<0.001).

Risk of LV diastolic dysfunction progressively increased from the group with 3 to the group with 5 criteria (Table 3). Subjects with 5 factors of metabolic syndrome had 2.7 times higher prevalence than persons with 3 criteria (OR 4.65, 95%CI: 1.26–5.58, p=0.013), and 2.4 times higher prevalence of LV diastolic dysfunction than those with 4 risk factors (OR 2.39, 95%CI: 1.08–5.28, p=0.045).

The multivariate linear regression analyses found that systolic and diastolic blood pressure and waist circumference were independently associated with relative wall thickness and DT, respectively (Table 4). The same analysis revealed that systolic and diastolic blood pressure, glucose level and waist circumference were also independently associated

Table 5. Multiple variable linear regression models of E/e'$_{septal}$, E/e'$_{lateral}$ and E/e'$_{average}$ for each component of the metabolic syndrome in metabolic syndrome group.

	E/e'$_{septal}$		E/e'$_{lateral}$	
	β	p	β	p
Systolic BP (mmHg)	0.383	<0.001	0.307	<0.001
Diastolic BP (mmHg)	0.116	0.076	0.082	0.086
Fasting glucose (mmol/l)	0.077	0.179	0.058	0.221
Triglycerides (mmol/l)	0.202	0.001	0.163	0.044
HDL (mmol/l)	−0.041	0.311	−0.031	0.357
Waist circumference (cm)	0.266	<0.001	0.241	0.022
Model r2		0.68		0.71

BP – blood pressure; HDL – high density lipoprotein.

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with E/A ratio (Table 4). The multiple regression models of E/e'$_{septal}$, E/e'$_{lateral}$, and E/e'$_{average}$ revealed systolic blood pressure, triglycerides level and waist circumference as independent predictors (Table 5).

DISCUSSION

Left ventricular structure in MS

A small number of clinical studies have explored the impact of different numbers of metabolic syndrome risk factors on the structure and function of the left ventricle [3,7,17,18]. This is the first study that compares the effects of the increasing number of MS components on systolic, diastolic, and global left ventricular function by using tissue Doppler imaging.

In our study, values of all the parameters of MS were significantly higher in persons with MS compared to controls, but there were no significant differences among the 3 MS subgroups. Individual factors of MS in this investigation were not equally distributed in the MS group and its subgroups.

The analysis of echocardiographic parameters of the left ventricle structure showed that there were no differences in the left ventricular diameters between the control group and the 3 subgroups with MS, which corresponds to the findings of other authors [3,18]. However, there are studies that have shown that left ventricular diameters increased proportionally with the number of MS criteria [7]. Results of the present study revealed that parameters that indicate left ventricular hypertrophy (the left ventricle relative wall thickness, the left ventricular mass indexed to height) progressively increased as the number of MS risk factors increased. Similar results were obtained in other studies [3,7,17]. The multivariate analyses of our results showed that systolic and diastolic blood pressure and waist circumference were independently associated with relative wall thickness. Other authors also found a correlation between these parameters and left ventricular hypertrophy in MS [6,19]. Additionally, Rurik et al. found that stability in body weight is a preventive factor of some components of MS, mainly diabetes, which is very important for this population of patients [20]. The prevalence of left ventricular hypertrophy significantly increased

with the increasing number of risk factors; hypertrophy was present in 19% of the subjects with 3 factors, 20% of those with 4 factors and even 35% of subjects with all 5 risk factors. This high percentage of subjects with left ventricular hypertrophy can be explained by the large proportion of patients with arterial hypertension, as well as a reasonably high percentage of patients with diabetes. The left atrium diameter also increased from the group with 3 criteria to the group with all 5 criteria of MS, which corresponds to findings from the literature [3,7].

Left ventricular systolic and diastolic function in MS

The traditional parameters of systolic left ventricular function (ejection fraction and fractional shortening) were not different among the observed groups. The parameters obtained by using tissue Doppler (s$_{septal}$ and s$_{lateral}$) also confirmed that there were no significant differences between the groups, which matches the results of Fuentes et al. [3].

Parameters of left ventricular diastolic function evidently deteriorated with the increasing number of MS factors. The E/A ratio was progressively reduced from the control group to the subjects with all 5 risk factors due to the increasing of the late diastolic transmitral velocity (A wave), which is probably the consequence of an increase in left ventricle rigidity. The multivariate analysis revealed that systolic and diastolic blood pressure, glucose level and waist circumference were independently associated with E/A ratio. Fuentes et al. showed that systolic and diastolic blood pressure and HDL are independent predictors of E/A ratio [3], while Masugata et al. found that systolic blood pressure and triglycerides were independently associated with E/A ratio [21]. The deceleration time was significantly prolonged with the growing number of risk factors, whereas flow velocities across the septal and lateral segments of the mitral annulus during early diastole measured by tissue Doppler (e'$_{septal}$, e'$_{lateral}$) were significantly and gradually reduced, which resulted in higher E/e'$_{septal}$, E/e'$_{lateral}$ and E/e'$_{average}$ ratios. Our study showed that deceleration time was independently associated with systolic and diastolic blood pressure and waist circumference, whereas systolic blood pressure, triglycerides level and waist circumference were independently associated with E/e'$_{septal}$ and E/e'$_{lateral}$,

respectively. The progressive deterioration of parameters of the left ventricular diastolic function with the increasing number of MS criteria confirmed additive and synergistic effects of MS risk factors on the left ventricle. Fuentes et al. obtained similar results, noting that they determined e'_{septal} and e'_{global} (average of 4 mitral annular sites) [3]. The same authors also found that diastolic blood pressure, triglycerides and waist circumference were independently associated with e'_{global} [3], whereas Mahmud et al. found that systolic blood pressure correlated with E/e'_{septal} [6]. The possible reason for the difference between these studies may lie in the fact that the authors used different echocardiographic parameters and, more importantly, different echocardiographic methods for estimation of systolic and particularly diastolic function of the left ventricle. In the beginning it was enough to use pulsed Doppler for determination of transmitral E/A ratio, DT, IVRT and estimation of left ventricular diastolic function. The advent of tissue Doppler imaging gave us new opportunities for more accurate estimation of left ventricular systolic and diastolic function which we and other authors in recently published studies used (s_{septal}, $s_{lateral}$, e'_{septal}, $e'_{lateral}$) [3,6].

The prevalence of left ventricular diastolic dysfunction in subgroups of MS

Azavedo et al. found that the prevalence of the left ventricle diastolic dysfunction increases from 20% to 36% starting from the group without risk factors to subjects with 4 or 5 risk factors [7], while Fuentes et al. revealed that the prevalence of diastolic dysfunction was 7–9% in the control group, 17–18% in the group with pre-metabolic syndrome (1 or 2 criteria), and 29–35% in the group with metabolic syndrome [3]. In our research, left ventricle diastolic dysfunction was observed in 9% of the controls, 24% in the group with 3 factors, 26% in the group with 4 risk factors and 46% in the group with all 5 risk factors. The slightly higher percentage of left ventricular diastolic dysfunction in this study could be explained by the higher proportion of hypertensive patients and significantly higher values of systolic and diastolic blood pressure compared to the aforementioned studies.

Global left ventricular function in MS

Global left ventricular function was estimated by Tei index [22]. The parameters needed for its calculation were significantly different among the observed groups, so the isovolumetric contraction and isovolumetric relaxation time progressively extended, while the ejection time was quite constant, which resulted in a significant increase in Tei index; in other words, stepwise and progressive worsening of global left ventricular function in subjects with MS. After determining the effects of MS on global left ventricular function, other authors did not compare mutual subgroups with the different number of MS factors, and found that global left ventricular function was significantly affected in patients with MS [19,23].

Limitations

The lack of subjects with 1 or 2 risk factors could contribute to the findings of metabolic syndrome and its influence on functional and structural damage of the left ventricle certainly is a limitation of the study. On the other hand, the best insight into the effect of metabolic syndrome on left ventricular function and structure is sought through the comparison between subjects with no MS criteria and subjects with 3, 4 or 5 criteria. Patients included in the study were recruited from primary care; however, referral bias still exists because those patients had some cardiovascular risk factor that could contribute to the impairment of LV structure and function, which also represents a limitation to this study. A small number of clinical trials have studied this issue, but even in these studies tissue Doppler imaging was not used, which could partly reduce the comparison of obtained results.

CONCLUSIONS

This research has shown that the structure of the left ventricle is significantly impaired in patients with MS, but that the left ventricular systolic function is completely preserved in patients with MS. It has also been found that the left ventricle diastolic function is impaired. Thus it can be concluded that the impaired global left ventricular function is actually the result of impairment of diastolic function. The degree of structural and functional damage increased with the number of risk factors for metabolic syndrome. Further studies recruiting subjects with 1 or 2 MS criteria are necessary for complementing the influence of MS on the left ventricular structure and function.

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