VILNIUS UNIVERSITY

Vilma Dženkevičiūtė

PECULIARITIES OF STRUCTURAL AND FUNCTIONAL CHANGES OF CENTRAL AND PERIPHERAL ARTERIES IN METABOLIC SYNDROME

Summary of doctoral dissertation

Biomedical Sciences, Medicine (06 B)

Vilnius, 2011

The dissertation was developed in 2007-2011 in the Clinic of Cardiovascular Disease of Vilnius University Faculty of medicine.

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The public defence of the dissertation will take place at the open session of the Medical Research Council at 14:00 on September 28, 2011 in the red audience of Vilnius University Hospital Santariškių clinics. Adress: Santariškių st. 2, LT-08661, Vilnius, Lithuania.

The dissertation is available at the library of Vilnius University.

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Vilma Dženkevičiūtė

CENTRINIŲ IR PERIFERINIŲ ARTERIJŲ STRUKTŪRINIŲ IR FUNKCINIŲ PAKITIMŲ YPATUMAI SERGANT METABOLINIU SINDROMU

Daktaro disertacijos santrauka

Biomedicinos mokslai, medicina (06 B)

Vilnius, 2011

Disertacija rengta 2007 – 2011 metais Vilniaus universiteto Medicinos fakulteto

Širdies ir kraujagyslių ligų klinikoje.

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Disertacija bus ginama viešame medicinos mokslo krypties tarybos posėdyje 2011 m. rugsėjo 28 d. 14 val. Vilniaus universiteto ligoninės Santariškių klinikos konferencijų Raudonojoje auditorijoje. Adresas: Santariškių g. 2, LT-08661, Vilnius, Lietuva.

Disertaciją galima peržiūrėti Vilniaus universiteto bibliotekoje.

ABBREVIATION

AH	arterial hypertension
AHA/NHLBI	American Heart Association/National Heart, Lung and Blood Institute
Aix	Augmentation index
BP	blood pressure
ATP III	Adult Treatment Panel III
CAVI	cardio-vascular ankle index
CRP	C-reactive protein
DBP	diastolic blood pressure
HDL	high density lipoprotein cholesterol
IMS	intima media thickness
BMI	body mass index
CAD	coronary artery disease
CVD	cardiovascular disease
LVMMI	left ventricular myocardial mass index
M	mean
mm	millimetre
mmHg	millimetres of mercury
MS	metabolic syndrome
LDL	low density lipoprotein cholesterol

N	sample size
NCEP	National Cholesterol Education Program
OR	odds ratio
P	significance level
PWV	pulse wave velocity
PS	pulse pressure
SBP	systolic blood pressure
SD	standard deviation
SCORE	Systemic Coronary Risk Evaluation
HR	heart rate
TG	triglycerides
MAP	mean arterial pressure
VUL SK	Vilnius University Hospital Santariskes Clinic
χ^2	chi-square criterion

1. INTRODUCTION

Cardiovascular diseases (CVD) are the main cause of death all over the Europe. Based on the data of Health Information Centre of Lithuania CVD was the most prevalent disease in Lithuania in 2010. The results of multicenter research showed that both DM and MS influence the increased rate of incidence and mortality of CVD in general population. It has been proved that MS induces early atherosclerosis, its advance and increases the rate of various atherosclerosis and diabetes mellitus-related complications of cardiovascular diseases. Recently the advance of atherosclerosis is evaluated not only based on clinical symptoms and laboratory markers, but also evaluating the changes in the thickness and stiffness of peripheral and central arteries. Currently these methods are the main non-invasive standardized methods of evaluation of atherosclerosis that allow identifying objectively the initial changes in the artery wall function and structure.

The role of MS in developing a cardiovascular disease has been analysed in numerous publications; however, there have been various opinions about it. One of the main questions remains unanswered: which are the risk factors or groups of risk factors of MS that influence the advance of cardiovascular diseases the most. Based on some of the data, MS risk factors have different influence on changes of artery structure and function. Consequently, it is only natural that patients with MS differ when it comes to emergence and advance of cardiovascular diseases due to the fact that different people have MS that consists of different combinations of risk factors. E. G., clinical research has proved that increased concentration of triglycerides and decreased concentration of DTL cholesterol (two of MS-comprising factors) had a different effect on men and women. Women with these risk factors have higher risk of cardiovascular disease than men.

Recently American Diabetes Association and European Association for the Study of Diabetes issued a joint statement, declaring that MS is not a separate risk factor and does not provide more information than separate cardiovascular risk factors or their combinations and does not forecast more accurately the risk of cardiovascular events.

However, there is another opinion based on the research, according to which MS (estimated using ATP III criteria) induces the aging of arteries and is more accurate in forecasting CVD events than its separate risk factors. Consequently a conclusion can be made that both MS and its components can influence differently the emergence of cardiovascular diseases and advance of complications in men and women. The results of the research are rather ambiguous. One study of subclinical atherosclerosis showed that MS or its separate risk factors influence more the changes in arteries in females than in males; however, the authors of this study did not differentiate the participants of the study based on their age. There was only one subclinical study of atherosclerosis carried out and published in 2010: SardiNIA, which evaluated MS in different age groups of males and females. Based on the data of this study, metabolic syndrome speeds up the aging of arteries of both men and women at any age. Thus, in this Thesis we tried to evaluate the relation of functional and structural changes of arteries, as well as the changes in left ventricle myocardial mass index to age, gender and MS, bearing in mind not only the MS, but also the independent influence of separate cardiovascular risk factors on cardiovascular complications. Furthermore, we tried to estimate the number of separate components constituting MS that can have the most significant influence on functional and structural changes in cardiovascular arteries and increase of the left ventricle myocardial mass index. The particularity of changes in different arterial stiffness indicators in patients with MS has not been determined yet in the literature, as well as prognostic value of MS when initiating early disorders in arterial structure and function and left ventricular hypertrophy.

1.1. The Goal of the Research

To determine the importance of metabolic syndrome and its individual cardiovascular risk factors for morphologic and functional changes of central and peripheral arteries and left ventricular myocardial hypertrophy in men and women.

1.2. The Objectives of the Research

1. To evaluate the differences in changes of arterial function and structure as well as changes in left ventricular myocardial mass in groups of patients with and without metabolic syndrome based on age and gender.

2. To evaluate the prognostic risk of cardiovascular damage in men and women with metabolic syndrome.
3. To determine the independent influence of metabolic syndrome and individual cardiovascular risk factors on arterial stiffness, thickening of the wall, emergence of atherosclerotic plaques and left ventricular hypertrophy.
4. To evaluate the quantitative significance of cardiovascular risk factors of metabolic syndrome in functional and structural cardiovascular changes.
5. To evaluate the particularity of changes in indicators of stiffness of peripheral and central arteries in patients with metabolic syndrome.
6. To determine the normal limits of pulse wave velocity in different age groups of patients with metabolic syndrome.

1.3. The Novelty of the Research

Complex evaluation of patients with high risk of cardiovascular disease with and without MS was carried out in Lithuania for the first time. Both functional and structural changes of arteries were evaluated, as well as left ventricular myocardial mass index based on gender and age of the patients. We have carried out large-scale research, thus normal limits of pulse wave velocity in different age groups reflecting higher arterial stiffness of patients were established. For the first time specificity of changes of arterial stiffness indicators in patients with metabolic syndrome was evaluated based on the size and structure of the arteries. Prognostic value of metabolic syndrome anticipating possible disorders in structure and function of arteries, as well as left ventricular hypertrophy was determined.

2. STUDY SUBJECTS AND METHODS

The research was carried out in 2007-2010 in Vilnius University Santariškės Clinics (VUL SK). In order to carry out the research, the approval No. 158200-05-179-056LP18 of Committee of Ethics of Research in Biomedicine of Vilnius region was obtained.

2.1 Selection and grouping of participants

Data of 3058 patients who visited Department of Primary Preventive Cardiology of VUL SK in 2006-2010 on pursuance of "Program of funding of screening and preventive measures for subjects of high cardiovascular risk group" („Asmenų, priskirtų širdies ir kraujagyslių ligų didelės rizikos grupei, atrankos ir prevencijos priemonių finansavimo programą") were used in the research. All patients with established high risk of cardiovascular disease (CVD) were included in the research and scheduled tests were performed. High risk of CVD is determined when:

- Total probability of vascular disease based on SCORE is 11 per cent and more;
- Metabolic syndrome or diabetes mellitus (diagnosed not earlier than 6 months ago) is diagnosed
- Asymptomatic atherosclerosis is discovered in other areas
- Family history of early coronary disease
- Total cholesterol plasma level is higher than 7.5 mmol/L
- Low density lipoprotein cholesterol blood serum level is higher than 6 mmol/L or familial dyslipidaemia is suspected

Age of the participants: males from 40 to 55 years and females from 50 to 65 years. Two groups were formed: *case* group, consisting of patients with MS, and *control* group, consisting of patients without MS. MS was evaluated according to modified criteria of National Cholesterol Education Program (NCEP), 2005. Patients with rhythm disturbances were not included into the research in order to avoid false evaluation of pulse wave velocity (PWV) due to high minute variation of cardiac minute output causing uneven changes of diameter of arteries during systole-diastole and difficulties in recording ECG synchronized with R wave.

2.2 Course of the Research

History of CVD risk factors, other diseases and medications used was obtained during the interview of participant. Height, body mass, arterial blood pressure of all patients was measured, as well as samples of venous blood were taken for biochemical tests. During the same visit all patients underwent arterial stiffness evaluation, ultrasound examination of carotids and echocardiography.

Tests and procedures were performed in the morning. Participants were recommended to not eat at least 12 hours before tests. Also, patients should not smoke and, drink alcohol or tea before testing. Patients were recommended not to use any vasoactive medications that affect arterial wall structure and function (e. g., angiotensin receptor inhibitors, calcium channel blockers and others). Tests were performed by experienced analysts in Blood Vessel Subdivision of the Department of Non-invasive Cardiology of Santariškės Clinics in a room where a steady temperature of 22º C was maintained.

2.3. Study methods

2.3.1. Cardiovascular risk factors and anthropometric data

Height and weight of all the participants was measured. Both body mass and height was measured using standardized and calibrated medical electronic scales and height meter SECA 704 (SECA GmbH& Co, Germany). Measurements were rounded to whole numbers. Body mass index (BMI) was estimated using the following formula: weight, kg / height m².

History of early coronary heart disease was considered positive in case primary relatives had had myocardial infarction or there was sudden death in males younger than 55, and in females younger than 65.

Arterial blood pressure (ABP) was measured according to recommendations for correct ABP measurement based on the Guidelines of the European Society of Hypertension, 2007. After patient was seated for approximately 5 minutes in quiet environment standard cuff is put on his forearm at heart level. Blood pressure was measured twice

using automated oscillometric device SCHILLER Argis VCM (Switzerland) while patient was seated with his feet flat on the floor. Mean of two arterial blood pressure measurements was calculated, and it was used for the analysis. Arterial hypertension was determined when arterial blood pressure was ≥ 140 mmHg or diastolic blood pressure was ≥ 90 mmHg, or when antihypertensive medications were used. Mean ABP was calculated using the following formula: Mean ABP = 1/3 systolic blood pressure + 2/3 diastolic blood pressure. Pulse pressure (PP) = systolic blood pressure - diastolic blood pressure.

Waist circumference was measured. Measurements were performed at median line of waist between the lower rib margin and wing of ileum was measured while patient held his/her breathe.

Blood samples were taken at the Centre for Laboratory diagnostics of VUL Santariškių Clinics. Fasting plasma glucose levels, C-reactive protein (CRP) plasma concentration, total cholesterol (TC), high density lipoprotein cholesterol (HDL-C) and triglyceride (TG) levels were measured. Low density lipoprotein cholesterol (LDL-C) blood level was calculated using the Friedewald formula. Lipid level was evaluated according to the standards recommended by the European Society of Hypertension, 2007: dislypidaemia is considered when TC >5 mmol/l or LDL-C >3 mmol/l, or HDL-C <1 mmol/l, or TG >1.7 mmol/l.

C-reactive protein was evaluated using high-sensitivity method. The analysis of C-reactive protein, as common inflammatory indicator, was performed using the standardized turbidimetry method. The evaluation of its amount is based on the antigen-antibody reaction (anti-CRP antibodies reacts with CRP on latex slide, and agglutination reaction takes place). Later absorption is evaluated which proportional to the amount of C-reactive protein affected by 572 nm wavelength. Obtained concentration of C-reactive protein was evaluated according to relative risk criteria established by Centre for Disease Control and Prevention and the American Heart Association: low – C-reactive protein < 1 mg/L**,** moderate – 1-3 mg/L, and high - ≥3 mg/L. When level of C-reactive protein was ≥10 mg/L, such finding was not involved in study.

Oral glucose tolerance test (OGTT) was performed in patients with plasma glucose level ≥ 5.6 mmol/L. Oral glucose tolerance test was performed according to the recommendations of American Diabetes Association (ADA) and World Health Organization (WHO). Patients were given to drink standard solution of 75 g of glucose. Disorder of glucose tolerance was diagnosed according ADA recommendations. When fasting plasma glucose level was ≥7.0 mmol/L and in 2 hours after OGTT >11.1 mmol/L diabetes was diagnosed; when fasting plasma glucose level was 5.6-6.9 mmol/L and in 2 hours after OGTT 7.8-11.0 mmol/L impaired glucose tolerance was diagnosed. Impaired fasting glycemia > 5.6 mmol/L, and normal response to OGTT was < 5.6 mmol/L.

Subjects' history of risk factors was obtained and assessed. Smoking was considered as risk factor in case subject smoked at least one cigarette per day and smoked at least one month. Non-smokers were considered patients who were not smoking at least for 1 year.

2.3.2 Assessment of cardiovascular risk

Risk of all patients involved in this study was calculated according to SCORE risk assessment scale. Score system (Systemic Coronary Risk Evaluation) is a new model of the evaluation of cardiovascular risk, published in European Cardiovascular Disease Prevention Guidelines in 2003. Patient's gender, smoking, total cholesterol blood level, age, systolic blood pressure at the day of examination are evaluated in this scale. SCORE defines risk to die from cardiovascular disease within 10 years (for 40-65 year old subjects). Subject's risk to die from cardiovascular disease within 10 years is expressed in per cent (e.g., risk of 40 years old non-smoker female, with 120 mm Hg systolic blood pressure, risk equals 0%). Risk scale colour-map includes risk from < 1 per cent to > 15 per cent. Risk ≥ 5 per cent considered was regarded as increased.

2.3.3 Assessment of metabolic syndrome

MS was assessed according to National Cholesterol Education Program (NCEP, 2005) III modified criteria. Subjects were included in MS group when at least three symptoms of listed below were diagnosed:

1. waist circumference in males > 102 cm, in females > 88 cm;
2. systolic blood pressure > 130 mm Hg and/or diastolic blood pressure > 85 mm Hg or hypertensive medications are used;
3. blood glucose level (fasting) > 5.6 mmol/L; or type 2 diabetes mellitus is diagnosed;
4. triglycerides (TG) > 1.7 mmol/L or special treatment to lower TG level is applied;
5. high density lipoprotein cholesterol (DTL) < 1 mmol/L in males and < 1.2 mmol/L in females.

Arterial stiffness was evaluated using two research techniques: applanation tonometry technique when pulse wave is registered using tonometer SphygmoCor (SphugmoCor version 8.0 with AtCor Medical Pty. Ltd. Software); and cardio-ankle vascular index (CAVI) technique using VaSera VS 1000 (Fukuda Denshi, Tokyo, Japan) device.

2.3.4 Applanation tonometry technique

Using special computer software subject data are entered: age, height, weight, systolic and diastolic blood pressure. According to the selected program distal (radial, brachial and femoral arteries) and proximal (carotid artery) pulse waves are registered in turns together with ECG signal. Only tests with performance quality higher than 85 per cent of quality index calculated by Sphygmo-Cor® software were evaluated. During atypical arterial pulse wave analysis (PWA) Sphygmo-Cor® software automatically calculated calibrated central shape of blood pressure wave of ascending aorta, augmentation index (AIx) and heart rate (HR), aorta central arterial blood pressure (CABP), pulse pressure, central systolic and diastolic pressure. AIx is calculated as difference between second and first systolic peak and is expressed as percentage of pulse

pressure. Measured AIx of every subject was automatically adjusted to heart rate of 75/min (AIx/HR) because this index highly depends on HR.
When carotid artery and femoral artery pulse curves were registered Sphygmo-Cor® software also automatically calculated pulse wave velocity: brachial-carotid pulse wave velocity and femoral artery (aorta)-carotid artery pulse wave velocity.

2.3.5 Measurement of cardio-ankle vascular index (CAVI).

Cardio-ankle vascular index (CAVI) was determined using VaSera VS-1000 (Fukuda Denshi, Tokyo, Japan) device with version 08-01 software. After subject lay down for 10 minutes, his feet and hands were put on pillows. Blood pressure measuring cuffs with pletismographic sensors were put on his four extremities: on both forearms and ankles. ECG leads are put on both wrists; phonocardiography sensor is positioned at the right side of sternum at the level of 2nd intercostals space. Vases device calculates Cardio-ankle vascular index (CAVI) automatically using two main parameters: β-parameter of arterial stiffness and cardio-ankle index; the following formula is used for calculations: $CAVI = a\{(2\rho/\Delta P) \ln (SBP/DBP)PWV^2\} + b$; where ΔP is the difference between systolic blood pressure (SBP) and diastolic blood pressure (DBP); ρ is blood viscosity; a and b are constants equal to PWV. This equation was derived from Bramwell-Hill equation and β-coefficient of arterial stiffness. To calculate cardio-ankle index ECG, phonocardiography data were used, and signals of curves of forearm and ankle pulse waves were used to calculate β-parameter of arterial stiffness. Cardio-ankle vascular index (CAVI) is a new index of arterial stiffness that does not depend on arterial blood pressure. All these calculations are performed simultaneously. Mean deviation of calculation suing this device is 3.8 per cent.

2.3.6 Ultrasound examination of carotid arteries

Ultrasound examination of carotid arteries was performed using high definition *Art Lab Esaote ALOKA* (Italy) ultrasound machine with automated wall track system that comprises composite sensor (Doppler signal and 128 radiofrequency signal). After patient for 10 minutes rests on his back, sensor is allocated on his stretched neck,

and optimal picture of carotid artery obtained. Adjacent arterial wall thickening more than 50 per cent or > 1.5 mm thickness of intima-media is recognized as atherosclerotic plaque. Thickness of intima-media layer of carotid arteries is measured in the lower wall of the common carotid artery 1-2 cm from bifurcation employing 2D live picture involving 4 cm radiofrequency automatic tracking. Live image recording with ECG of 6 seconds in duration is obtained. Resolution of radiofrequency signal measuring intima-media layer thickness is 0.21 μm.

2.4. Methods of statistical analysis

Data were analysed using statistical software package SPSS (version 17.0 for Windows). Descriptive and analytical statistical methods were used. Two independent groups were compared using common Student t-test statistics: $t = \frac{\overline{X}_1 - \overline{X}_2}{S_{\overline{X}_1 - \overline{X}_2}}$, (where $\overline{X}_1, \overline{X}_2$ are first- and second-order arithmetic mean, and $S_{\overline{X}_1 - \overline{X}_2}$ is standard deviation, i.e.,

$$\overline{X}_1 = \frac{X_{11} + X_{12} + \ldots + X_{1n_1}}{n_1}, \overline{X}_2 = \frac{X_{21} + X_{22} + \ldots + X_{2n_1}}{n_2}$$

and

$$S_{\overline{X}_1 - \overline{X}_2} = \sqrt{\left(\frac{1}{n_1} + \frac{1}{n_2}\right) \frac{\sum_{i=1}^{n_1} (X_{1i} - \overline{X}_1)^2 + \sum_{i=1}^{n_2} (X_{2i} - \overline{X}_2)^2}{n_1 + n_2 - 2}}$$. Student's t-test was used to compare mean of the same characteristic in two groups, when characteristic distribution was normal.

When normality presumption was not met, non-parametric Mann-Whitney test was used instead of Student's t-test. Categorical variables were analysed using Chi-square of exact Fisher's test. Chi-square statistics $Q_P = \sum_{j,k} \frac{(n_{jk} - m_{jk})^2}{m_{jk}}$ proposed by Pearson was used. Group mean and dispersions were compared using analysis of variance (ANOVA).

In order to find associations and predict associations of atherosclerotic plaques with individual risk factors we used logistic regression method assessing odds ratio and 95% confidential interval (CI). Odds ratio was considered to be significant when figure of one was not included into 95% confidential interval. Quantitative variables dependence from other factors was analysed using multiple linear regression models. Significance level of $p < 0,05$ was selected to test hypotheses and to determine statistical significance of association. Independent variable was included into regression equation when its significance was not higher than 0,05. Correlations coefficients were also calculated to examine linear dependence of variables.

Descriptive statistic is presented as mean and standard deviation. Significance level is fixed and equals 0,05. Two-sided p-values are presented elsewhere.

3. RESULTS

3.1 General characteristics of study subjects

Final study analysis involved 3058 study subjects. In order to evaluate significance of metabolic syndrome in morphological and functional changes of central and peripheral arteries and left ventricle hypertrophy, all subjects were allocated in two groups: subjects with metabolic syndrome and subjects without metabolic syndrome. Metabolic syndrome was diagnosed in 1998 (65.3%) subjects, and 1060 (34.7%) subjects had no metabolic syndrome. Age of involved subjects ranged from 45 to 64 years. Females comprised majority of study population: 1946 (63.64%). Distribution of cardiovascular risk factors is presented in Table 1 and Table 2.

Analysis of Table 1 and Table 2 showed, that cardiovascular risk factors comprising metabolic syndrome were different in different groups. Hypertension ($p = 0.0001$) and diabetes mellitus ($p = 0.0001$) were more often in metabolic syndrome group. Subjects with metabolic syndrome statistically significantly had bigger waste circumference ($p = 0.001$), higher fasting glycemia ($p = 0.0001$), triglyceride level ($p = 0.0001$), and lower high-density lipoprotein cholesterol level ($p = 0.02$). Low-density lipoprotein cholesterol level was significantly lower in metabolic syndrome group ($p =$

0.0001). However, there were no differences between groups in the following risk factors: subject mean age, total blood cholesterol level, gender, and smoking.

Table 1. Distribution of quantitative cardiovascular risk factors and their comparison between groups.

Variables	Subject groups		P-value
	MS- (n=1060)	MS+ (n=1998)	
Age (years)	54.02 ± 6.06	53.85 ± 6.14	0.47
BMI (kg/m²)	27.20 ± 4.14	32.08 ± 4.92	0.0001
Waist circumference (cm)	93.97 ± 11.45	106.55 ± 11.00	0.0001
Systolic blood pressure (mmHg)	146.02 ± 18.54	158.72 ± 20.39	0.0001
Diastolic blood pressure (mmHg)	90.92 ± 10.48	97.45 ± 11.31	0.0001
HR (bpm)	65.38 ± 11.28	67.92 ± 11.90	0.0001
Cardiovascular risk according SCORE	2.22 ± 2.44	2.64 ± 2.14	0.0001
Blood plasma glucose level (mmol/L)	5.35 ± 0.57	6.30 ± 1.75	0.0001
Total cholesterol level (mmol/L)	6.99 ± 1.28	7.00 ± 2.32	0.891
HDLC level (mmol/L)	1.59 ± 0.39	1.41 ± 3.54	0.02
LDLC level (mmol/L)	4.80 ± 1.19	4.49 ± 1.27	0.0001
Triglyceride blood serum level (mmol/L)	1.31 ± 0.57	2.70 ± 3.34	0.0001
C-reactive protein (mmol/L)	2.53 ± 8.68	3.60 ± 5.53	0.0001

Abbreviations and explanations: * Subjects with metabolic syndrome (MS+); Subject without metabolic syndrome (MS-); BMI – body mass index; HR- heart rate; HDLC – high density lipid cholesterol; LDLC – low density lipid cholesterol. Data presentation: mean ± SD; one-way analysis of variance (ANOVA) was used to compare groups.

After analysis of scientific allowed us to make an assumption that metabolic syndrome in males and females promotes occurrence and development of cardiovascular diseases in different ways. Supposedly, sex differences specific to our population exist that determines different cardiovascular structure and function disorders in males and females. To justify our assumption further analysis was performed separately for males and females, and comparison between case group and control group was performed.

Table 2. Distribution of qualitative cardiovascular risk factors and their comparison between groups.

Variables		Subject groups		
		MS- (n=1060)	**MS+ (n=1998)**	**P-value**
Gender	females	688 (64.9%)	1.258 (63.0%)	0.288
	males	372 (35.1%)	740 (37.0%)	
Arterial hypertension	absent	263 (26.9%)	166 (8.3%)	0.0001
	present	713 (73.1%)	1.832 (91.7%)	
Smoking	non-smoker	770 (78.9%)	1.514 (75.8%)	0.059
	smoker	206 (21.1%)	484 (24.2%)	
Diabetes mellitus	absent	927 (96.0%)	1.611 (81.2%)	0.0001
	present	39 (4.0%)	374 (18.8%)	

Abbreviations and explanations: * Subjects with metabolic syndrome (MS+); Subject without metabolic syndrome (MS-); Chi-square (χ^2) was used to compare groups.

Comparison of general characteristics and laboratory findings in female groups are presented in Table 3 and Table 4. Comparison of general characteristics in male groups is presented in Table 5 and Table 6.

It was established, that there were statistically significant age differences (p = 0.031) between female groups, however, median difference between groups is smaller than 1 year. Statistical differences occurred likely due to high number of subjects and low dispersion. There were differences between groups in risk factors comprising metabolic syndrome: waist circumference (p = 0.0001), body mass index (p = 0.0001), systolic (p = 0.0001) and diastolic (p = 0.0001) blood pressure, triglyceride level (p =

0.0001), high density lipoprotein cholesterol level (p = 0.002), glucose plasma level (p = 0.0001). There were no differences between groups in total cholesterol level (p = 0.377). Level of inflammation marker, C-reactive protein, plasma level was also higher in subjects with MS (p = 0.0001), compared with subjects without MS, as well as heart rate was also higher in MS group (p = 0.0001). Data presented in Table 3 show that cardiovascular risk factors are more expressed in subjects with MS, and therefore it is not surprising, that mean cardiovascular diseases SCORE sum was higher in subjects with metabolic syndrome (p = 0.0001) compared with subjects without metabolic syndrome.

Table 3. Comparison of quantitative variables between females.

Variables	Groups of female subjects		P value
	MS- (n=688)	MS+ (n=1258)	
Age (years)	56.87 ± 4.15	57.30 ± 4.16	0.031
BMI (kg/m²)	27.24 ± 4.44	32.15 ± 5.19	0.0001
Waste circumference (cm)	92.24 ± 12.13	104.11 ± 10.66	0.0001
Systolic blood pressure (mmHg)	146.23 ± 19.81	159.01 ± 20.95	0.0001
Diastolic blood pressure (mmHg)	89.85 ± 10.27	96.22 ± 10.88	0.0001
Aortal pulse pressure	49.61 ± 10.04	51.96 ± 11.17	0.06
Mean arterial blood pressure (mmHg)	97.69 ± 10.45	100.16 ± 10.14	0.05
HR (bpm)	65.66 ± 10.77	67.95 ± 11.77	0.0001
Total cholesterol level (mmol/L)	7.18 ± 1.25	7.10 ± 1.90	0.377
HDLC level (mmol/L)	1.70 ± 0.37	1.44 ± 2.84	0.02
LDLC level (mmol/L)	4.91 ± 1.20	4.70 ± 1.25	0.0001
Triglyceride serum concentration (mmol/L)	1.22 ± 0.38	2.27 ± 2.91	0.0001
C-reactive protein (mmol/L)	2.39 ± 9.79	3.48 ± 4.93	0.0001
Plasma glucose level (mmol/L)	5.26 ± 0.43	6.20 ± 1.92	0.0001
Cardiovascular risk according to SCORE	2.07 ± 2.46	2.45 ± 1.70	0.0001

Abbreviations and explanations: * - mean and standard deviations are presented (M ± SD); subjects with metabolic syndrome (MS+); subjects without metabolic syndrome (MS-); BMI – body mass index; HR- heart rate; HDLC – high density lipid cholesterol; LDLC – low density lipid cholesterol; TG - triglycerides.

Analysis of frequencies of risk factor presentations showed that females with metabolic syndrome more frequently had increased blood pressure (p = 0.0001), diabetes mellitus (p= 0.0001), they smoked more frequently (p = 0.007), and increase of C-reactive protein level ≥ 3 mmol/L and heart rate higher than 70 bpm were also more frequent (p = 0.0001 and p = 0.01, respectively).

Table 4. Comparison of qualitative variables in females.

Variables		**Groups of female subjects**		
		MS- (n=688)	**MS+ (n=1258)**	**P values**
Arterial hypertension	absent	176 (26.9%)	98 (7.8%)	0.0001
	present	479 (73.1%)	1.160 (92.2%)	
Smoking	non-smoker	589 (89.9%)	1.076 (85.5%)	0.007
	smoker	66 (10.1%)	182 (14.5%)	
Diabetes mellitus	absent	631 (97.2%)	1.010 (80.9%)	0.0001
	present	18 (2.8%)	239 (19.1%)	
CRP (mmol/L)	>3	549 (85.4%)	815 (65.9%)	0.0001
	3+	94 (14.6%)	422 (34.1%)	
HR (bpm)	<= 70.00	458(70.5%)	817(65.2%)	0.01
	71.00+	192(29.5%)	436(34.8%)	

Abbreviations and explanations: * subjects with metabolic syndrome (MS+); subjects without metabolic syndrome. Chi-square (χ^2) was used to compare groups. CRP – C-reactive protein; HR – heart rate.

Comparison of risk factors and laboratory findings in male groups showed that there were no differences in age (p = 0.22), total cholesterol level (p = 0.092), high density lipoprotein cholesterol level (p = 0.869); however, similarly to females differences in risk factors comprising metabolic syndrome were observed: waist

circumference (p = 0.0001), body mass index (p = 0.0001)systolic (p = 0.0001) and diastolic (p = 0.0001) blood pressure, triglyceride level (p = 0.0001), plasma glucose concentration (p = 0.0001). Higher hart rate (p = 0.01), higher C-reactive protein level (p = 0.0001), and higher cardiovascular diseases SCORE sum (p = 0.0001) were also observed.

Table 5. Comparison of quantitative variables in males.

Variables	**Groups of male subjects**		
	MS- **n= 372**	**MS+** **n=740**	**P value**
Age (years)	48.74 ± 5.48	47.99 ± 4.24	0.22
BMI (kg/m²)	27.14 ± 3.46	31.95 ± 4.43	0.0001
Waist circumference (cm)	97.53 ± 8.96	110.69 ± 10.31	0.0001
Systolic blood pressure (mmHg)	145.60 ± 15.63	158.23 ± 19.40	0.0001
Diastolic blood pressure (mmHg)	93.10 ± 10.59	99.54 ± 11.73	0.0001
HR (bpm)	64.81 ± 12.25	67.86 ± 12.14	0.0001
Cardiovascular risk according to SCORE	2.55 ± 2.36	2.94 ± 2.71	0.024
Plasma glucose level (mmol/L)	5.54 ± 0.74	6.45 ± 1.41	0.0001
Total cholesterol level (mmol/L)	6.61 ± 1.27	6.83 ± 2.89	0.092
HDLC level (mmol/L)	1.37 ± 0.31	1.34 ± 4.48	0.869
LDLC cholesterol level (mmol/L)	4.57 ± 1.14	4.14 ± 1.24	0.0001
Serum triglyceride level (mmol/L)	1.48 ± 0.80	3.43 ± 3.88	0.0001
C-reactive protein (mmol/l)	2.81 ± 5.78	3.81 ± 6.43	0.017

Abbreviations and explanations: * - mean and standard deviations are presented (Av ± SD); subjects with metabolic syndrome (MS+); subjects without metabolic syndrome (MS-); BMI – body mass index; HR- heart rate; LDLC – low density lipid cholesterol; HDLC – high density lipid cholesterol; TG - triglycerides.

Analysis of distribution of variables frequencies showed that frequencies of diabetes mellitus (p = 0.0001), increase in C-reactive protein > 3 mmol/L (p = 0.0001), increase in HR > 70bpm (p = 0.0001) in group of subjects with metabolic syndrome

were higher compared with frequencies in group of subjects without metabolic syndrome.

Summarizing results of analysis of both genders it could be stated that it is not always possible to control secondary variables in groups. We brought this to notice and therefore we applied statistical measures to control secondary variables in our later calculations (e.g., not only Student's t-test and Mann-Whitney test to compare groups, but also analysis of covariance).

Table 6. Comparison of qualitative variables in males.

Variables		**Groups of male subjects**		**P value**
		MS-	**MS+**	
Arterial hypertension	absence	87 (27.1%)	68 (9.2%)	0.0001
	presence	234 (72.9%)	672 (90.8%)	
Smoking	non-smoker	181 (56.4%)	438 (59.2%)	0.395
	smoker	140 (43.6%)	302 (40.8%)	
Diabetes mellitus	absence	296 (93.4%)	601 (81.7%)	0.0001
	presence	21 (6.6%)	135 (18.3%)	
CRP (≥3 mmol/L)	< 3	244 (77.2%)	472 (64.5%)	0.0001
	3+	72 (22.8%)	260 (35.5%)	
HR (≥70bpm)	< 70	234 (73.8%)	463 (62.8%)	0.001
	70 +	83 (26.2%)	274 (37.2%)	

Abbreviations and explanations: * subjects with metabolic syndrome (MS+); subjects without metabolic syndrome (MS-); PWV –pulse wave velocity; LVMMI – left ventricular myocardial mass index; CRP – C-reactive protein; HR – heart rate. Chi-square (χ^2) was used to compare groups.

3.2 Differences in changes of structure and function of arteries and changes in left ventricular myocardial mass in patients with and without metabolic syndrome

The first objective of this study was to evaluate significance of metabolic syndrome for changes of arterial function and structure and changes in left ventricular myocardial mass considering age and gender. This problem was examined in two stages:

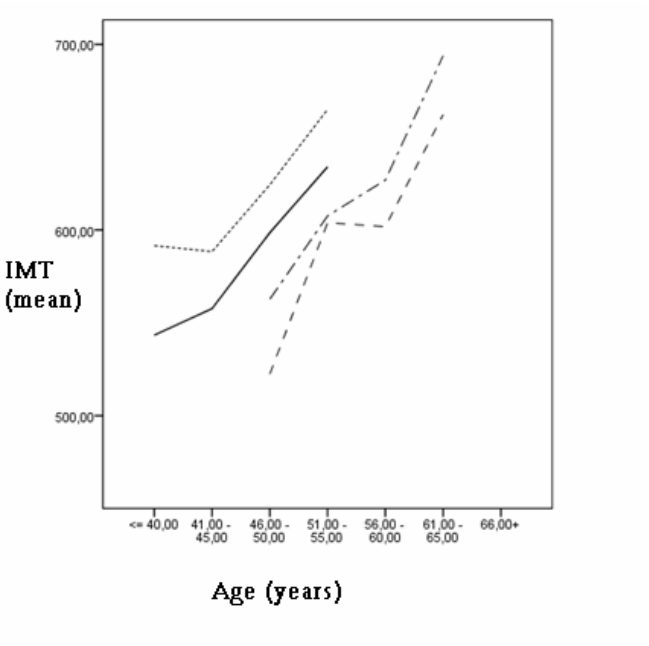
1. we calculated correlations between age and structure and function of arteries and left ventricular myocardial mass index;
2. we compared control and case groups dividing them by gender and age.

In order to perform more detailed analysis of changes of structure and function of arteries and left ventricular myocardial mass in both groups we allocated subjects to 5-year age groups.

Obtained results evaluating significance of metabolic syndrome for changes of arterial function and structure and changes in left ventricular myocardial mass considering age and gender are presented in Figure 1-6. Significant Pearson correlation between changes in blood vessels walls and age was found: intima-media thickness $r = 0.176$, $p = 0.0001$; femoral - carotid arteries PWV $r = 0.225$, $p = 0.0001$; CAVI $r = 0.126$, $p = 0.001$; LV MMI $r = 0.136$, $p = 0.0001$, augmentation index $r = 0.193$, $p = 0.004$. Meanwhile, changes in brachial-carotid PWV with age were insignificant, $r = 0.054$, $p = 0.433$.

We used two-way analysis of variance to analyse age groups differences in males in females with and without MS. We established that intima-media thickness ($p = 0.0001$), femoral-carotid arteries pulse wave velocity ($p = 0.0001$), cardio-ankle vascular index (CAVI) ($p = 0.0001$), left ventricular myocardial mass index ($p = 0.0001$) and augmentation index ($p = 0.003$) increase with the increase of age in all age groups (Figures 1, 2, 3, 4, 6). Age did not influence forearm-carotid PWV ($p = 0.054$) (Figure 5). In subjects with metabolic syndrome intima-media thickness ($p = 0.0001$), femoral-carotid arteries pulse wave velocity ($p = 0.0001$) and left ventricular myocardial mass index ($p = 0.0001$) increase was faster. Meanwhile, increase in augmentation index ($p = 0.513$), cardio-ankle vascular index (CAVI) ($p = 0.491$) and brachial-carotid PWV ($p = 0.054$) did not depend on the presence of metabolic syndrome. Brachial-carotid artery PWV ($p = 0.0001$) and femoral-carotid PWV ($p = 0.0001$), as well as cardio-ankle vascular index (CAVI) ($p = 0.0001$), left ventricular myocardial mass index ($p = 0.0001$), intima-media thickness ($p = 0.001$) in females were lower compared with males, and augmentation index ($p = 0.0001$) in females was higher than in males.

Figure 1. Carotid intima-media thickness dependence on age, gender and metabolic syndrome.

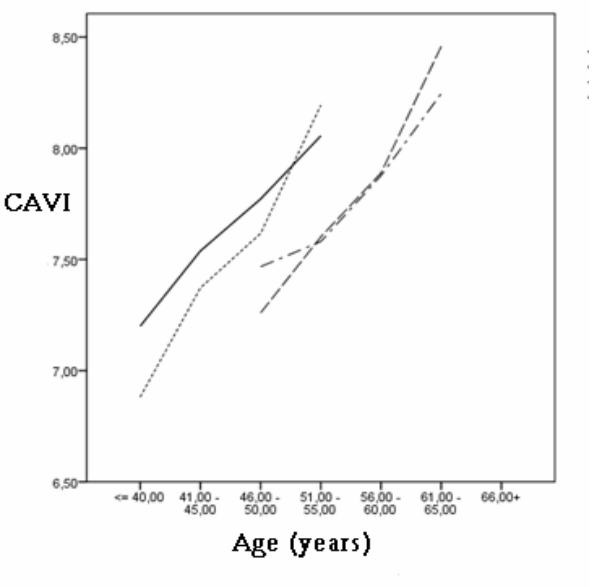


IMT- intima media thickness; ─ ─ women with metabolic syndrome (MS+); ─·─· women without metabolic syndrome (MS-); ····· Man with metabolic syndrome (MS+); ——— men without metabolic syndrome (MS-);

Figure 2. Carotid-femoral artery pulse wave velocity dependence on age, gender and metabolic syndrome.

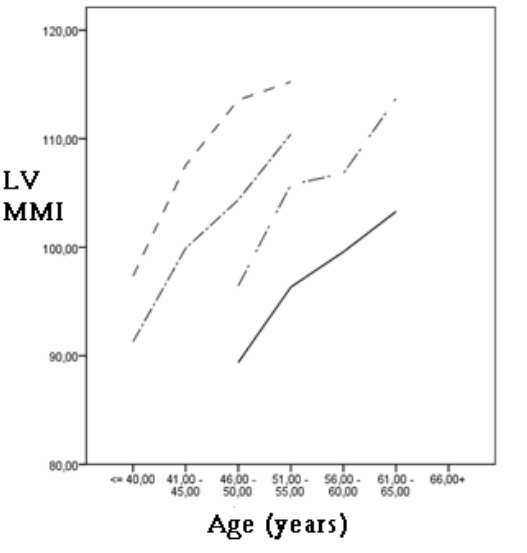
PWV - femoral-carotid pulse wave velocity; ─ ─ women with metabolic syndrome (MS+); ─·─· women without metabolic syndrome (MS-); ····· Man with metabolic syndrome (MS+); ——— men without metabolic syndrome (MS-);

Figure 3. Cardio-ankle vascular index (CAVI) dependence on age, gender and metabolic syndrome.



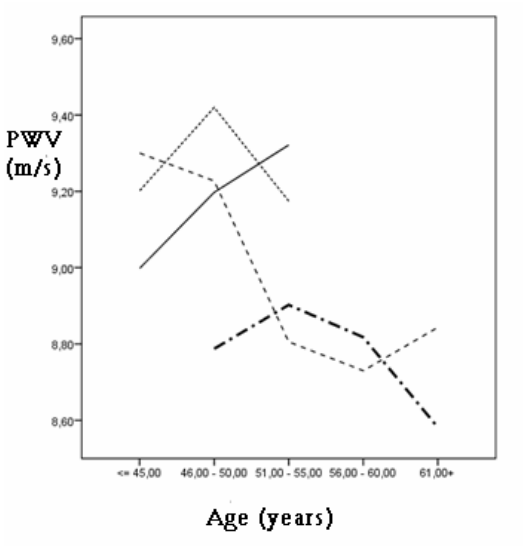
CAVI – cardio-ankle vascular index; ─ ─ women with metabolic syndrome (MS+); ─·─· women without metabolic syndrome (MS-); ····· Man with metabolic syndrome (MS+); ——— men without metabolic syndrome (MS-);

Figure 4. Left ventricular myocardial mass index dependence on age, gender and metabolic syndrome.



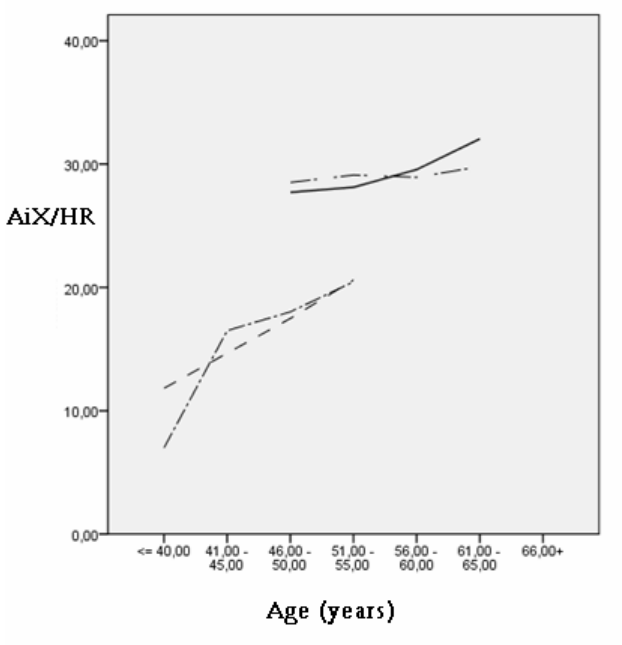
LVMMI- left ventricular myocardial mass index; ─ ─ women with metabolic syndrome (MS+); ─·─· women without metabolic syndrome (MS-); ····· Man with metabolic syndrome (MS+); ——— men without metabolic syndrome (MS-);

Figure 5. Brachial-carotid pulse wave velocity dependence on age, gender and metabolic syndrome.



Abbreviations and explanations: PWV- pulse wave velocity in brachial-carotid artery; ─ ─ women with metabolic syndrome (MS+); ─·─· women without metabolic syndrome (MS-); ····· Man with metabolic syndrome (MS+); ——— men without metabolic syndrome (MS-);

Figure 6. Augmentation index dependence on age, gender and metabolic syndrome.



Abbreviations and explanations: AiX/HR – adjusted augmentation index; ─·─ women with metabolic syndrome (MS+); ——— women without metabolic syndrome (MS-); ─ ─ Man with metabolic syndrome (MS+); ─·─· men without metabolic syndrome (MS-);

Data presented in Table 7 show that number of atherosclerotic plaques statistically significantly (r = 0.269, p = 0.0001) increase and number of subjects without atherosclerotic plaques decrease with age.

Table 7. Atherosclerotic plaques in carotid artery dependence of age.

Age groups	**≤ 45 m.**	**46–50 m.**	**51–55 m.**	**56–60 m.**	**≥ 60 m.**	**P value**
No plaques	78.2 %.	71.5 %	64.8%	68.9 %	59.8 %	0.0001
One plaque	17.7 %	19.3 %	27.1 %	19.7 %	23.2 %	
Two plaques	4.1 %	9.2 %	8.1 %	11.4 %	16.9 %	

Qualitative variables are presented as percentage.

3.3. Prognostic risk of cardiovascular disorders in subjects with metabolic syndrome

Obtained results stimulated to assess incidence of cardiovascular lesions in males and females with metabolic syndrome and later to determine risk of these lesions. We assumed that major lesion of arteries is associated with more advanced atherosclerotic process and presumably is associated with greater risk cardiovascular diseases. We established the following lesion margins: intima-media thickness > 900 μm, femoral-carotid arteries PWV > 12 m/s, left ventricular myocardial mass index in females' > 95 g/m^2, in males' > 115 g/m^2. Analysis of incidence of lesion margins when cardiovascular disease risk increases is presented in Tables 8-11. Data in table 8 show that in females increase of left ventricular myocardial mass was observed rather frequently, whereas increase in femoral-carotid arteries pulse wave velocity and in intima-media thickness were fairly rare. When comparing females groups, statistically significant changes were observed only in frequency of the threshold level of left ventricular myocardial mass index. Meanwhile, there were no differences in incidence of changes in mean intima-media thickness and disorders of femoral-carotid arteries pulse wave velocity in females groups.

Table 8. Comparison of incidence of lesions of arterial walls and left ventricular myocardial mass between female groups.

Variables		Subjects groups, females		P value
		MS- (n=688)	MS+ (n=1258)	
IMT	< 900 (μmm)	441 (96%)	794 (95 %)	0.47
	>900 (μmm)	18 (3.9 %)	40 (5 %)	
PWV (femoral-carotid arteries)	<12 (m/s)	194 (97 %)	874 (94 %)	0.123
	>12 (m/s)	6 (3 %)	52 (5.6 %)	
LVMMI	<95 (g/m²)	386 (56.3 %)	510 (40.6 %)	0.0001
	>95 (g/m²)	301 (43.7 %)	845 (59.4 %)	

Abbreviations and explanations: * IMT – intima-media thickness, AIx/HR – augmentation index corrected by heart rate, PWV – pulse wave velocity, CAVI- cardio-ankle vascular index, LVMMI- left ventricular myocardial mass index.

Data on number of atherosclerotic plaques in carotid arteries are presented in Table 9. It was established that atherosclerotic plaques in carotid arteries were more frequent in females with metabolic syndrome compared with females without metabolic syndrome.

Table 9. Comparison of plaques in female groups.

Variables		Subject groups, females		P values
		MS- (n=688)	MS+ (n=1258)	
Number of plaques	0	331 (72.1 %)	542 (64. 8%	0.001
	1	86(18.7 %)	190 (22.7 %)	
	2	42 (9.2 %)	105 (12.5 %)	

Abbreviations and explanations: * subjects with metabolic syndrome (MS+); subjects without metabolic syndrome (MS-). Chi-square (χ^2) was used to compare groups.

Analysis of Table 10 showed that there are significant differences between male groups in indices evaluated, such as incidence of disorders of intima-media thickness,

pulse wave velocity and left ventricular myocardial mass index. The most common disorder was the increase of left ventricular myocardial mass, i.e., hypertrophy of the left ventricle.

Table 10. Comparison between males groups of incidence of disorders of arterial walls and left ventricular myocardial mass.

Variables		**Subject groups, males**		**P values**
		MS- (n=372)	**MS+ (n=740)**	
IMT	<900.00 (μmm)	230(99.1 %)	492 (95.6 %)	0.018
	>900.00 (μmm)	2 (0.9 %)	21 (4.5 %)	
PWV (femoral-carotid arteries)	<12.00 (m/s)	130 (100 %)	536 (95.9 %)	0.019
	>12.00 (m/s)	0	23 (4.1 %	
LVMMI	<115 (g/m²)	295 (79.7 %)	479 (64.7 %)	0.0001
	>115 (g/m²)	75 (20.3 %)	261 (35.3 %)	

Abbreviations and explanations: * IMT – intima-media thickness, PWV – pulse wave velocity, CAVI- cardio-ankle vascular index, LVMMI- left ventricular myocardial mass index.

Table 11. Comparison of incidence of plaques between male groups.

Variables		**Subject groups, males**		**P value**
		MS- (n=372)	**MS+ (n=740)**	
Number of plaques	0	150 (64.9 %)	338 (65.8 %)	0.865
	1	55 (23.8 %)	114 (22.2 %)	
	2	26 (11.3 %)	62 (12.1 %)	

Abbreviations and explanations: * subjects with metabolic syndrome (MS+); subjects without metabolic syndrome (MS-). Chi-square (χ^2) was used to compare groups.

Meanwhile comparison of incidence of atherosclerotic plaques in carotid arteries did not revealed any differences between male groups (table11).

We intended not only determine incidence of lesions of arterial walls and disorders of left ventricle, but also evaluate risk of development of these disorders. To do this logistic regression models were developed, and odds ratio was evaluated. Results of comparison between groups are presented in Tables 12 and 13. Analysis of Table 12 showed that there were no statistically significant differences in risk of disorders of intima-media thickness and pulse wave velocity in females with metabolic syndrome compared with females without metabolic syndrome. Statistically significant differences were observed only in predicting hypertrophy of left ventricle. Odds ratio of the disorder of left ventricular myocardial mass was statistically significant and equal 1.873, i.e., likelihood of development of hypertrophy of left ventricle in females with metabolic syndrome is 1.873 times higher than in females without metabolic syndrome. Whereas metabolic syndrome in females is associated with higher incidence of atherosclerotic plaques in carotid arteries, we calculated odds ratio for subjects with metabolic syndrome to have at least one atherosclerotic plaque in carotid artery. Calculated odds ratio was 1.401, i.e., likelihood of at least one atherosclerotic plaque in female with metabolic syndrome is approximately 1.4 times higher compared with females without metabolic syndrome.

Table 12. Risk of disorders of intima-media thickness, femoral-carotid pulse wave velocity and left ventricular myocardial mass index in females with metabolic syndrome.

Variables	**Odds ratio for MS groups (MS+ vs. MS-)***	**Sensibility**	**Specificity**	**P value**
IMT (≥900 μmm)	1.234 (0.699;2.179)	4.7 %	96.1 %	0.468
PWV(≥12m/s)	1.924 (0.815;4.545)	5.6 %	97 %	0.136
LVMMI (≥95 g/m²)	1.873 (1.552;2.261)	59.4 %	56.2 %	<0.001
Atherosclerotic plaques	1.401 (1.097; 1.796)	35.1 %	72.2 %	0.008

Abbreviations and explanations: * within brackets: 95% confidential interval; ** p value is to examine hypothesis that odds ratio statistically significantly differs from 1; subjects with metabolic syndrome (MS+); subjects without metabolic syndrome (MS-); PWV – pulse wave velocity; IMT – intima-media thickness; LVMMI – left ventricular myocardial mass index.

Analysis of the results in males showed that in males with metabolic syndrome odds ratio for intima-media thickness ≥ 900 μmm is higher 4.909 times, and odds ratio for left ventricular myocardial mass index ≥ 115 g/m^2 is 2.143 times higher compared with males without metabolic syndrome. Risk of atherosclerotic plaques was not examined, because there were no statistically significant differences in development of atherosclerotic plaques between male groups.

Table 13. Risk of disorders of intima-media thickness, femoral-carotid pulse wave velocity and left ventricular myocardial mass index in males with metabolic syndrome.

Variables	**Odds ratio for MS groups (MS+ vs. MS-)***	**Sensitivity**	**Specificity**	**P value**
IMT (≥900μmm)	4.909 (1.141;21.111)	4.1 %	99.1 %	0.033
PWV (≥12m/s)	-	-	-	-
LVMMI (≥115g/m²)	2.143 (1.596;2.878)	35.3 %	79.7 %	<0.001

Abbreviations and explanations: * within brackets: 95% confidential interval; ** p value is to examine hypothesis that odds ratio statistically significantly differs from 1; subjects with metabolic syndrome (MS+); subjects without metabolic syndrome (MS-); PWV – pulse wave velocity; IMT – intima-media thickness; LVMMI – left ventricular myocardial mass index.

3.4. Independent influence of metabolic syndrome and individual cardiovascular risk factors on arteries stiffening, arterial wall thickening, occurrence of atherosclerotic plaques and hypertrophy of left ventricle

During this study we sought to evaluate influence of specific cardiovascular risk factors on parameters of arterial wall and left ventricular myocardial mass index. For this purpose we used stepwise linear regression method for quantitative variables, and for rank (qualitative) variables we used logistic regression method. We developed individual model for every index of arterial wall and left ventricular myocardial mass, where this index was used as dependent variable, while independent variables were where the following risk factors: age, mean arterial blood pressure, waist circumference, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, triglycerides, C-reactive protein, heart rate, plasma glucose level. In logistic regression

model atherosclerotic plaque was dependent variable, and age, mean arterial blood pressure, waist circumference, total cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, triglycerides, C-reactive protein, heart rate, and plasma glucose level were independent variables. Males and females were analyzed separately. Results of analysis are presented in Tables 14-17.

Table 14. Models of stepwise linear regression in females determining independent influence of cardiovascular risk factors on pulse wave velocity, intima-media thickness and left ventricular myocardial mass index.

Dependent variable*	**Independent variables**	**Regression coefficient**	**β**	**P value**
PWV * (femoral-carotid arteries) (R^2=0.259, adjusted R^2=0.255, P<0.0001)	Mean BP	0.054	0.351	0.0001
	Age	0.081	0.214	0.0001
	Waist circumference	0.023	0.149	0.0001
	HR	0.016	0.112	0.0001
IMT * (R^2=0.072, adjusted R^2=0.068 P<0.0001)	Age	2.377	0.211	0.0001
	Waist circumference	4.296	0.169	0.0001
LVMMI*(R^2=0.224, adjusted R^2=0.05 P<0.0001)	Mean BP	0.582	0.198	0.0001
	HR	-0.202	-0.075	0.025
	Waist circumference	0.214	0.071	0.035

Abbreviations and explanations: * – determination coefficient R^2, adjusted determination coefficient R^2 and p value are presented together with dependent variable; β - linear regression coefficient for standardized data; PWV – pulse wave velocity; IMT – intima-media thickness; LVMMI – left ventricular myocardial mass index; HR – heart rate; BP – blood pressure.

Results of the last step of stepwise regression model in females with metabolic syndrome are presented in Table 14. The highest influence of cardiovascular risk factors was on pulse wave velocity (26 percent), left ventricular myocardial mass index (22 percent), and intima-media thickness (7 percent) (risk factors' influence on intima-media thickness was the lowest).

Age, mean blood pressure, waist circumference and heart rate statistically significantly increase femoral-carotid arteries pulse wave velocity. Mean ABP and, waist circumference increase left ventricular myocardial mass index, and HR lowers it. Intima-media thickness is increasing with the increase of age and waist circumference.

Table 15. Results of logistic regression. Associations of cardiovascular risk factors and atherosclerotic plaques in carotid artery in females.

Independent variables	**Regression coefficient**	**Odds ratio (CI, 95 %)**	**P value**
Age	0.078	1.081 (1.032-1.132)	<0.001
LDL C	0.12	1.128 (1.002-1.27)	0.047
Smoking	0.55	1.733 (1.15 – 2.6)	0.008

Abbreviations and explanations: * LDL C - CI - 95% confidential interval.

Evaluating risk factors influence on atherosclerotic plaques logistic regression model showed that in females with metabolic syndrome occurrence of atherosclerotic plaques is associated with age, LDL cholesterol and smoking.

Similar analysis was also performed in males. As in females, the highest influence of cardiovascular risk factors was on pulse wave velocity (26 percent), left ventricular myocardial mass index (12 percent), and intima-media thickness (8 percent) (risk factors' influence on intima-media thickness was the lowest). Mean ABP, waist circumference, triglyceride blood level statistically significantly increase left ventricular myocardial mass index in male with metabolic syndrome, and heart rate and total cholesterol blood level lowers it. Intima-media thickness is increasing with the increase of age, mean blood pressure and C-reactive protein. Similar to females with metabolic syndrome results were obtained evaluating pulse wave velocity and cardiovascular risk

factors. Age, mean blood pressure, waist circumference and heart rate increase femoral-carotid arteries pulse wave velocity in males with metabolic syndrome.

Table 16. Modes of stepwise linear regression in males determining independent influence of cardiovascular risk factors on pulse wave velocity, intima-media thickness and left ventricular myocardial mass index.

Dependent variable*	**Independent variables**	**Regression coefficient**	**β**	**P value**
PWV (R^2=0.272, adjusted R^2=0.266, P<0.0001)	Mean BP	0.056	0.369	0.000
	Age**	0.086	0.231	0.000
	Waist circumference	0.016	0.110	0.003
	HR	0.014	0.106	0.004
IMT (R^2=0.088. adjusted R^2=0.078 P<0.0001)	Age**	5.323	0.185	0.0001
	Mean BP	1.85	0.165	0.001
	C-reactive protein	2.387	0.115	0.024
LVMMI (R^2=0.139. adjusted R^2=0.128 P<0.0001)	Mean ABP	0.411	1.86	0.0001
	Age**	0.92	0.175	0.0001
	Triglyceride blood level	1.186	0.165	0.0001
	Total cholesterol	-0.864	-0.12	0.003
	Waist circumference	0.27	0.126	0.003
	HR	-0.19	-0.101	0.014

Abbreviations and explanations: * – determination coefficient R^2, adjusted determination coefficient R^2 and p value are presented together with dependent variable; β - linear regression coefficient for standardized data; PWV – pulse wave velocity; IMT – intima-media thickness; LVMMI – left ventricular myocardial mass index; HR – heart rate; BP – blood pressure.

Evaluating risk factors influence on atherosclerotic plaques model showed that in males with metabolic syndrome occurrence of atherosclerotic plaques is associated with age, LDL cholesterol and arterial hypertension.

Table 17. Results of logistic regression. Associations of cardiovascular risk factors and atherosclerotic plaques in carotid artery in males.

Independent variables	Regression coefficient	Odds ratio (CI, 95%)	P value
Age	0.058	1.06 (1.01-1.111)	0.015
LDL C	0.275	1.37 (1.114-1.557)	0.001
Triglycerides	0.110	1.116 (1.039-1.2)	0.003
Arterial hypertension	0.992	2.698 (1.157-6.29)	0.022

Abbreviations and explanations: * – determination coefficient R^2, adjusted determination coefficient R^2, CI - 95% confidential interval and are presented together with dependent variable are presented together with dependent variable; β - linear regression coefficient for standardized data; LDL C– low density lipoprotein cholesterol.

3.4.1 Influence of metabolic syndrome on changes of arterial wall characteristics and left ventricular myocardial index

When we found out that cardiovascular risk factors influences arterial wall characteristics and left ventricular myocardial mass index from 7 to 26 percent, we made an assumption that metabolic syndrome could *per se* influence increase in arterial wall characteristics and left ventricular myocardial mass index thus increasing risk of development of cardiovascular diseases. However, we could not deny probability that in MS current differences in risk factors between groups determined higher stiffness of central arteries, thicker intima-media, and higher LV myocardial mass index. In order to make sure that these secondary variables do not influence results obtained and to confirm that metabolic syndrome changes thickness of intima-media, pulse wave velocity and left ventricular myocardial mass index we performed analysis of covariance. Factors specifically influencing intima-media thickness, pulse wave velocity and left ventricular myocardial index were involved into analysis; these factors are age, waist circumference, mean arterial blood pressure, heart rate, C-reactive protein. Results of analysis are presented in Tables 18-23.

Analysis of female groups presented in Tables 18-20 showed that in all cases there were no significant differences between groups, and general difference between mean was caused by risk factors' differences. That implies that these variables are associated predominantly with cardiovascular risk factors as a whole.

Table 18. Mean of pulse wave velocity in females in the absence of influence of specific risk factors.

		95% CI		P value
	Mean ± SD	Lowest limit	Highest limit	
MS-	8.80 ± 1.05	8.595	9.006	0.0752
MS+	9.007 ± 0.048	8.913	9.101	

Abbreviations and explanations: * - mean and standard deviations are presented (mean±SD),MS – subjects without metabolic syndrome; MS+ - subjects with metabolic syndrome, CI – confidential interval.

Table 19. Mean of intima-media thickness in females in the absence of influence of specific risk factors.

		95% CI		P value
	Mean ± SD	Lowest limit	Highest limit	
MS-	613.057 ± 10.701	592.035	634.079	0.62
MS+	618.929 ± 4.979	609.149	628.709	

Abbreviations and explanations: * - mean and standard deviations are presented (Avgas.±SD),MS – subjects without metabolic syndrome; MS+ - subjects with metabolic syndrome, CI – confidential interval.

Table 20. Mean of left ventricular myocardial mass index in females in the absence of influence of specific risk factors.

		95% CI		P value
	Mean ± SD	Lowest limit	Highest limit	
MS-	105.498 ± 2.458	100.674	110.322	0.607
MS+	104.085 ± 1.089	101.947	106.223	

Abbreviations and explanations: * - mean and standard deviations are presented (M±SD), MS – subjects without metabolic syndrome; MS+ - subjects with metabolic syndrome, CI – confidential interval.

Analysis showed that similar to females, metabolic syndrome in males had no statistically significant influence on arterial walls characteristics (Tables 21, 22), as well as on the increase of left ventricular myocardial mass (Table 22). Theses findings again confirm that changes in arterial wall characteristics and left ventricular myocardial mass index should be directly associated only with cardiovascular risk factors as a whole.

Table 21. Mean of pulse wave velocity in males in the absence of influence of specific risk factors.

		95 % CI		P value
	Mean ± SD	**Lowest limit**	**Highest limit**	
MS-	8.8±0.105	8.566	9.101	0.075
MS+	9.007±0.048	8.616	8.857	

Abbreviations and explanations: * - mean and standard deviations are presented (M±SD),MS – subjects without metabolic syndrome; MS+ - subjects with metabolic syndrome, CI – confidential interval.

Table 22. Mean of left ventricular myocardium mass in males in the absence of influence of specific risk factors.

		95 % CI		P value
	Mean ± SD	**Lowest limit**	**Highest limit**	
MS-	107.568±0.136	103.285	111.852	0.644
MS+	108.700±0.980	106.775	110.626	

Abbreviations and explanations: * - mean and standard deviations are presented (M±SD),MS – subjects without metabolic syndrome; MS+ - subjects with metabolic syndrome, CI – confidential interval.

23 lentelė. Mean of intima-media thickness in males in the absence of influence of specific risk factors.

		95 % CI		P value
	Mean ± SD	**Lowest limit**	**Highest limit**	
MS-	596.889 ± 13.91	569.545	624.233	0.442
MS+	608.6985 ± 6.380	596.154	621.243	

Abbreviations and explanations: * - mean and standard deviations are presented (M±SD),MS – subjects without metabolic syndrome; MS+ - subjects with metabolic syndrome, CI – confidential interval.

3.5. Influence of number of cardiovascular risk factors possibly comprising metabolic syndrome on characteristics of arterial wall characteristics and left ventricular myocardial mass

Our second task was to evaluate quantitative influence of metabolic syndrome and comprising risk factors on functional and structural changes of cardiovascular system. We tried to find out what is the highest number of individual MS components may most of all influence functional and structural changes of cardiovascular system and increase of left ventricular myocardial mass. Taking into

account that only one index of arterial stiffness differed significantly between groups, quantitative influence of risk factors we analyzed only for femoral-carotid arteries pulse wave velocity with the parallel analysis of changes in intima-media thickness, left ventricular myocardial mass index and atherosclerotic plaques. Individual analyses for both genders were performed. Results are presented in Tables 24-25 and Figure 7.

Evaluating quantitative influence of risk factors comprising metabolic syndrome in females we found out pulse wave velocity and intima-media thickness statistically significantly increases with the increase of number of risk factors comprising metabolic syndrome from 3 to 5. Meanwhile, left ventricular myocardial mass index increased when number of risk factors comprising metabolic syndrome increased from 3 to 4, and when there were more than 4 influencing risk factors it did not change any more ($p = 0.398$).

Table 24. Quantitative influence of risk factors comprising metabolic syndrome on arterial wall characteristics and left ventricular myocardial mass index in females.

Number of MS components	**0**	**1**	**2**	**3**	**4**	**5**	**P value**
Femoral-carotid arteries PWV (m/s)	8.40 ± 00	7.55 ± 1.16	8.74 ± 1.58	8.80 ± 1.58	9.17 ± 1.52	9.86 ± 5.62	0.0001
IMT (μmm)	592.50 ± 111.81	583.51 ± 97.44	627.36 ± 129.83	626.02 ± 136.97	630.53 ± 121.34	658.01 ± 154.16	0.0001
LVMMI (g/m²)	88.10 ± 18.95	93.04 ± 20.29	102.27 ± 22.67	103.56 ± 24.40	111.49 ± 40.05	110.29 ± 25.71	0.0001

Abbreviations and explanations: * - mean and standard deviations are presented (M±SD),IMT – intima-media thickness, PWV – pulse wave velocity, LVMMI – left ventricular myocardial mass index.

Based on differences found we can make an assumption that components of metabolic syndrome work synergistically, and stiffness of arteries, intima-media thickness and left ventricular myocardial mass index significantly I increase with the increase of number components of metabolic syndrome.

Analyzing of influence of number of risk factors comprising metabolic syndrome on arterial wall characteristics and left ventricular myocardial mass index in males we found out that not all variables show statistically significant differences. Only femoral-

carotid arteries pulse wave velocity statistically significantly increased with the increase of number of components of metabolic syndrome. Intima-media thickness also increased; however, difference was not statistically significant (Table 25). Left ventricular myocardial mass index increased when number of risk factors increased from 3 to 4, and when there were more than 4 influencing risk factors it did not change any more (p = 0.579)

Table 25. Quantitative influence of risk factors comprising metabolic syndrome on arterial wall characteristics and left ventricular myocardial mass index in males.

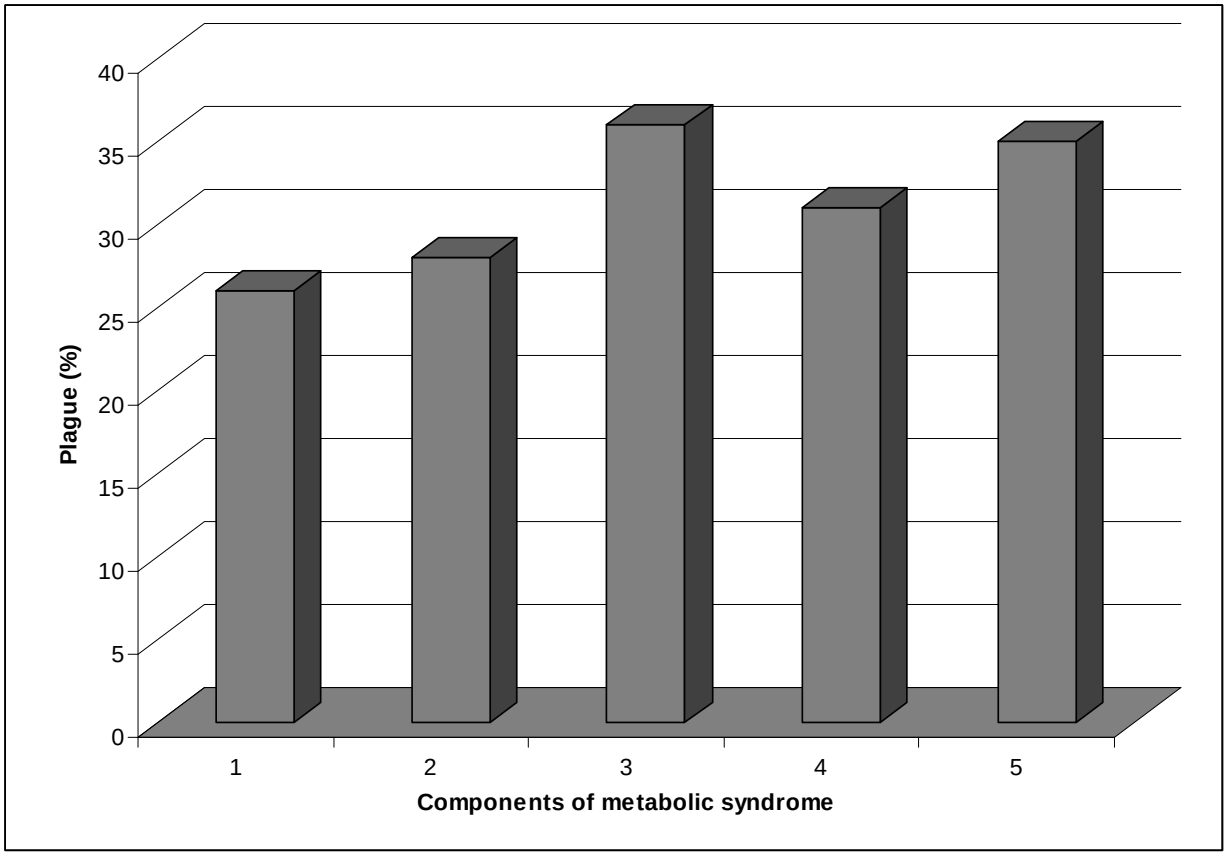
Number of MS components	**0**	**1**	**2**	**3**	**4**	**5**	**P value**
Femoral-carotid arteries PWV (m/s)	7.50± 1.12	8.24 ± 1.11	8.48 ± 1.35	8.67 ± 1.63	8.97 ± 1.59	8.79 ± 1.57	0.04
IMT (μmm)	593.85± 75.19	594.96 ± 111.48	601.63 ± 107.47	623.09 ± 136.19	633.94 ± 148.01	630.10 ± 110.75	0.089
LVMMI (g/m²)	106.40± 19.66	102.40 ± 20.62	106.42 ± 22.20	109.43 ± 25.30	113.50 ± 25.49	113.94 ± 24.71	0.0001

Abbreviations and explanations: * - mean and standard deviations are presented (M±SD),IMT – intima-media thickness, PWV – pulse wave velocity, LVMMI – left ventricular myocardial mass index.

Comparisons of MS risk factors influence on atherosclerotic plaques were performed only in females; analysis was not performed in males because initial analysis did not show statistically significant differences in incidence of atherosclerotic plaques. Data of analysis in females are presented in Figure 7.

Summarizing this result we came up to conclusion that number of atherosclerotic plaques increase in females with metabolic syndrome, though number of its components do not influence further increase of their number (p = 0.078).

Figure 7. Association between the number of components of metabolic syndrome and atherosclerotic plaques in females.



3.6. Changes in specificity of characteristics of peripheral and central arteries in subjects with metabolic syndrome

Taking into account the fact that both in females and males with metabolic syndrome femoral-carotid arteries mean PWV were higher, we made an assumption, that only central arteries, but not peripheral are being affected. We tested this hypothesis using logistic regression model. As we have already known that there are differences between case groups, developing our models we applied control mean for secondary variables: age, gender and blood pressure influence was rejected in this model. We established that

in subjects with MS only increase of femoral-carotid arteries PWV was statistically significant (beta = 0.22), and other indices of stiffness of peripheral arteries remained unchanged (Table 26).

Table 26. Metabolic syndrome influence on arterial stiffness indices.

Dependent variable *	Independent variables	Regression coefficient	β	P value
Metabolic syndrome (R^2=0.016, adjusted R^2=0.0255; P<0.0001)	Femoral artery PWV	0.22	1.247	0.0001
	Brachial artery PWV	-0.088	0.916	0.11
	AIx/HR	-0.013	0.987	0.091
	CAVI	-0.036	0.965	0.454

Logistic regression model rejecting influence of age, gender and arterial blood pressure presented. Abbreviations and explanations: * AIx/HR – augmentation index adjusted by heart rate; PWV – pulse wave velocity; CAVI – cardio-ankle vascular index.

3.7. Femoral-carotid arteries pulse wave normal limits in metabolic syndrome

Considering that recommended normal limits of pulse wave velocity are rarely detected in our study population in the last step of our study we sought to determine normal limits of femoral-carotid arteries pulse wave velocity and develop calculation algorithm enabling evaluate blood vessels stiffness characteristics in our study population. We did this in several steps. First, in order to establish normal limits of pulse wave velocity we calculated 75 and 95 percentiles for males and females according to their age groups. These limits are lesion marks. Results are presented in Table 27 and Table 28.

Table 27. Margins of disturbance of pulse wave velocity in females with metabolic syndrome.

Age groups		Females, MS (+)	
		Percentile 75	Percentile 95
46.00 - 50.00	PWV (m/s)	9.00	9.90
51.00 - 55.00	PWV (m/s)	9.60	11.30
56.00 - 60.00	PWV (m/s)	10.10	12.10
61.00 - 65.00	PWV (m/s)	10.60	12.70

Abbreviations and explanations: PWV – pulse wave velocity.

Table 28. Margins of disturbance of pulse wave velocity in males with metabolic syndrome.

Age groups		Males, MS (+)	
		Percentile 75	Percentile 95
<= 40.00	PWV (m/s)	8.20	9.30
41.00 - 45.00	PWV (m/s)	9.40	11.30
46.00 - 50.00	PWV (m/s)	9.65	11.60
51.00 - 55.00	PWV (m/s)	10.00	12.60

Abbreviations and explanations: PWV – pulse wave velocity.

Considering that age, mean blood pressure, waist circumference and HR influence femoral-carotid arteries pulse wave velocity we developed regression equation that enable in the absence of special equipment calculate pulse wave velocity in males and females.

Female regression equation enabling to calculate of femoral-carotid arteries pulse wave velocity.

PWV = 0.054 * mean ABP + 0.081 * age + 0.023*waist circumference + 0.016 * HR - 4.44

Male regression equation enabling to calculate of femoral-carotid arteries pulse wave velocity.

PWV = 0.056 * mean ABP + 0.086 * age + 0.016 * waist circumference + 0.014 * HR – 3.804

During the last step we developed standard charts for pulse wave velocity. To make these tables more applicable in practical use pulse wave velocity we colored in different colors representing normal values of pulse wave velocity calculated based on 75 percentile and 95 percentile margins for different age groups.

Conclusions

1. In subjects with metabolic syndrome irrespectively their gender and age higher intima-media thickness, femoral-carotid arteries pulse wave velocity and left ventricular myocardial mass index were found. However, higher number of atherosclerotic plaques in carotid artery was found only in females.

2. Risk of cardiovascular disorders in males and females with metabolic syndrome is different: in males probability of hypertrophy of left ventricle is 2.14 times higher, and probability of thickening of intima-media is 4.9 higher. In females metabolic syndrome does not increase risk of intima-media thickening; however, MS obviously increase risk of hypertrophy of left ventricle (1.83 times) and risk of occurrence of atherosclerotic plaques (1.4 times).

3. Nor in males, neither in females metabolic syndrome had no direct influence on pulse wave velocity, intima-media thickness, hypertrophy of left ventricle and occurrence of atherosclerotic plaques. Traditional cardiovascular risk factors determined changes in theses parameters.

4. Femoral-carotid arteries pulse wave velocity and left ventricular myocardial mass index directly depends on the number of cardiovascular risk factors comprising metabolic syndrome both in males and females. Meanwhile, only in females intima-media thickness is associated with increasing number of risk factors.

5. Metabolic syndrome affects central and peripheral arteries in different ways. Irrespective of age it increases velocity in central arteries and does not affect peripheral arteries hemodynamic.

6. Pulse wave velocity calculation algorithm depends on gender, age, heart rate, mean blood pressure and waist circumference.

SUMMARY IN LITHUANIAN

ĮVADAS

Širdies ir kraujagyslių ligos (ŠKL) yra pagrindinė mirties priežastis visoje Europoje. Lietuvos sveikatos informacijos centro duomenimis 2010 metais Lietuvos gyventojai dažniausiai sirgo ŠKL. Literatūroje plačiai, tačiau nevienareikšmiai aptarta MS svarba širdies kraujagyslių ligų atsiradimui. Neatsakyta į vieną iš pagrindinių klausimų: kurie MS sudarantys rizikos veiksniai ar jų grupės daugiausia lemia širdies ir kraujagyslių ligų progresavimą. Kai kurie autoriai teigia, kad MS sudarantys rizikos veiksniai skirtingai lemia arterijų struktūros ir funkcijos kitimus. Todėl natūralu, kad sergančiųjų MS širdies ir kraujagyslių ligų atsiradimas ir progresavimas turėtų tarpusavyje skirtis, nes skirtingų žmonių MS sudaro nevienodi rizikos veiksnių deriniai. Taip pat pasigirsta nuomonių, kad MS nėra atskiras rizikos veiksnys, jis nesuteikia daugiau informacijos ir nenumato širdies bei kraujagyslių ligų įvykių rizikos tiksliau negu atskiri širdies ir kraujagyslių rizikos veiksniai ar jų deriniai. Atliktų tyrimų rezultatai gana prieštaringi. Taip pat vieni kliniškai dar nesireiškiančios aterosklerozės tyrimai parodė, kad MS arba atskiri jo rizikos veiksniai didesnę įtaką turi moterų nei vyrų arterijų kitimams. Tačiau šie autoriai neskirstė tiriamųjų asmenų pagal amžiaus grupes.

Tyrimo tikslas

Nustatyti vyrų ir moterų metabolinio sindromo ir jį sudarančių širdies ir kraujagyslių ligų rizikos atskirų veiksnių reikšmę centrinių ir periferinių arterijų morfologiniams ir funkciniams kitimams bei kairiojo skilvelio miokardo hipertrofijai.

Darbo uždaviniai

7. Įvertinti sergančių ir nesergančių metaboliniu sindromu skirtingo amžiaus ir lyties asmenų arterijų funkcijos ir struktūros bei kairiojo skilvelio miokardo masės pakitimų skirtumus.
8. Nustatyti sergančių metaboliniu sindromu vyrų ir moterų širdies ir kraujagyslių pažeidimo prognostinę riziką.
9. Nustatyti metabolinio sindromo ir atskirų širdies ir kraujagyslių ligų rizikos veiksnių nepriklausomą įtaką arterijų standumui, sienelės storėjimui, aterosklerozinių plokštelių atsiradimui ir kairiojo skilvelio hipertrofijai.
10. Įvertinti metabolinį sindromą sudarančių širdies ir kraujagyslių rizikos veiksnių kiekybinę reikšmę širdies ir kraujagyslių funkciniams bei struktūriniams pakitimams.
11. Įvertinti periferinių ir centrinių arterijų standumo rodiklių kitimų specifiškumą sergantiesiems metaboliniu sindromu.
12. Nustatyti pulsinės bangos greičio normines ribas skirtingo amžiaus ligoniams, sergantiems metaboliniu sindromu.

Darbo naujumas

Pirmą kartą Lietuvoje kompleksiškai įvertinti širdies ir kraujagyslių ligų didelės rizikos grupės asmenys, sergantys ir nesergantys MS. Pagal lytį, amžių, širdies ir kraujagyslių rizikos veiksnių kiekį įvertinti ne tik arterijų funkcijos ir struktūros pakitimai, bet ir kairiojo skilvelio miokardo masės indeksas. Atliktame tyrime dalyvavo daug tiriamųjų, todėl atskirose amžiaus grupėse buvo nustatytos pulsinės bangos greičio norminės ribos, rodančios tiriamųjų asmenų arterijų didesnį standumą. Pirmą kartą sergantiesiems metaboliniu sindromu įvertintas skirtingo dydžio ir struktūros arterijų standumo rodiklių kitimų specifiškumas. Nustatyta metabolinio sindromo prognostinė reikšmė numatant galimus arterijų struktūros ir funkcijos sutrikimus bei kairiojo skilvelio hipertrofiją.

TIRIAMIEJI IR TYRIMO METODIKA

Tyrimui atlikti panaudoti 3058 ligonių duomenys, kurie 2006–2010 m. apsilankė VUL Santariškių klinikų pirminės kardiologijos prevencijos skyriuje pagal ***Asmenų, priskirtų širdies ir kraujagyslių ligų didelės rizikos grupei, atrankos ir prevencijos priemonių finansavimo programą***. Į tyrimą buvo įtraukti visi pacientai, kuriems buvo nustatyta didelė širdies ir kraujagyslių ligų (ŠKL) rizika ir atlikti numatyti tyrimai.

Sudarytos dvi tiriamųjų grupės: *atvejo* – kuriems nustatytas MS ir *kontrolinė* – be MS. Metabolinis sindromas vertintas pagal 2005 m. Nacionalinės cholesterolio mokymo programos III Suaugusiųjų gydymo rekomendacijų (NCEP ATP III) modifikuotus kriterijus.

Anamnezės duomenys apie ŠKL rizikos veiksnius, kitas ligas ir vartojamus vaistus surinkti apklausiant tiriamuosius. Visiems asmenims buvo išmatuotas ūgis, kūno masė, arterinis kraujo spaudimas ir paimti veninio kraujo pavyzdžiai biocheminiams tyrimams. To paties apsilankymo metu pacientams buvo atliekami arterijų standumo, ultragarsinis miego arterijų tyrimai bei širdies echokardioskopija.

REZULTATAI

Į galutinę tyrimo analizę įtraukti 3058 asmenų rezultatai. Tiriamieji suskirstyti į dvi grupes: su MS ir be MS. Metabolinis sindromas nustatytas 1998 (65,3 %), likę 1060 (34,7 %) metabolinio sindromo požymių neturėjo. Tirtų asmenų amžius svyravo nuo 45 iki 64 metų . Tyrimo populiacijos daugumą sudarė moterys – 1946 (63,64 %). Grupės skyrėsi metabolinį sindromą sudarančiais širdies ir kraujagyslių rizikos

Analizuodami vyrų ir moterų su MS ir be MS skirtumus pagal amžiaus grupes nustatėme, kad visose amžiaus grupėse miego arterijos intimos medijos storis (p=0,0001), šlaunies miego arterijų pulsinės bangos greitis (p= 0,0001), širdies kulkšnies indeksas (CAVI) (p= 0,0001), kairiojo skilvelio miokardo masės indeksas (p=0,0001) ir augmentacijos indeksas (p= 0,003) didėjo priklausomai nuo amžiaus. Žasto-miego arterijos PBG amžius neturėjo įtakos (p=0,054). Dėl metabolinio sindromo buvo spartesnis miego arterijos intimos medijos storio (p=0,0001), šlaunies

miego arterijų pulsinės bangos greičio (p= 0,0001), kairiojo skilvelio miokardo masės indekso didėjimas (p=0,0001) Tuo tarpu augmentacijos indekso (p= 0,513), širdies-kulkšnies indekso (CAVI) (p= 0,491) ir žasto-miego arterijos PBG didėjimas nepriklausė (p= 0,221) nuo metabolinio sindromo. Moterims visose amžiaus grupėse nustatytas mažesnis žasto-miego arterijos PBG (p= 0,0001) ir šlaunies–miego arterijos PBG (p= 0,0001), širdies kulkšnies indeksas (CAVI) (p= 0,0001), kairiojo skilvelio miokardo masės indeksas (p=0,0001), intimos medijos storis (p= 0,001) ir didesnis augmentacijos indeksas (p= 0,0001) nei vyrams.

Tyrimo rezultatai rodo, kad didėjant asmenų amžiui statistiškai patikimai (r= 0,269; p=0,0001) didėja aterosklerozinių plokštelių skaičius miego arterijose ir mažėja asmenų skaičius be aterosklerozinių plokštelių.

Moterims su metaboliniu sindromu intimos medijos storio ir pulsinės bangos greičio pažeidimų rizika nebuvo statistiškai patikimai didesnė nei moterims be metabolinio sindromo. Kairiojo skilvelio miokardo masės indekso pažeidimo galimybių santykis buvo statistiškai reikšmingas ir lygus 1,873, t.y. moterims su metaboliniu sindromu galimybė atsirasti kairiojo skilvelio hipertrofijai yra apie 1,873 karto didesnė nei moterims be metabolinio sindromo. Moterims metabolinis sindromas yra susijęs ir su dažnesniu aterosklerozinių plokštelių atsiradimu miego arterijose, apskaičiuotas galimybių santykis buvo lygus 1,401 t.y. moterims su metaboliniu sindromu galimybė turėti bent vieną aterosklerozinę plokštelę yra apie 1,4 kartus didesnė nei moterims be metabolinio sindromo.

Vyrų grupės tyrimų rezultatai rodo, kad vyrams su metaboliniu sindromu galimybių santykis turėti intimos medijos storį ≥900 μm yra 4,909 karto didesnis, kairiojo skilvelio miokardo masės indeksą ≥115 g/m² – 2,143 karto didesnis nei vyrams be metabolinio sindromo. Aterosklerozinių plokštelių rizika nenagrinėta, nes pradinėje analizėje negauta statistiškai reikšmingo aterosklerozinių plokštelių atsiradimo skirtumo tarp vyrų grupių.

Moterųsu metaboliniu sindromu pulsinės bangos greitį 26 % įtakoja širdies ir kraujagyslių ligų rizikos veiksniai, kairiojo skilvelio miokardo masės indeksą - 22 %, ir intimos medijos storį – 7 % .

Šlaunies miego arterijos pulsinės bangos greitį statistiškai patikimai didina amžius, vidutinis kraujo spaudimas, liemens apimtis ir širdies susitraukimų dažnis. Kairiojo skilvelio miokardo masės indeksą statistiškai patikimai didina vidutinis AKS, liemens apimtis, mažina – širdies susitraukimo dažnis. Intimos medijos storis didėja didėjant amžiui ir liemens apimčiai. Vertinant rizikos veiksnių poveikį aterosklerozinėms plokštelėms logistinės regresijos modelis parodė, kad moterims su metaboliniu sindromu aterosklerozinių plokštelių atsiradimas susijęs su amžiumi, MTL cholesteroliu (MTL-ch) ir rūkymu.

Analogiška analizė atlikta ir lyginant vyrų grupes, širdies ir kraujagyslių ligų rizikos veiksniai daugiausia veikia vyrų pulsinės bangos greitį – 26 %, kairiojo skilvelio miokardo masės indeksą – 12 % ir intimos medijos storį – 8 %. Vyrams su metaboliniu sindromu kairiojo skilvelio miokardo masės indeksas statistiškai patikimai buvo didesnis tų asmenų, kurių didesnis buvo vidutinis AKS, liemens apimtis, trigliceridų kiekis kraujuje. Intimos medijos storis didėja didėjant amžiui, vidutiniam kraujo spaudimui, C reaktyviajam baltymui. Vyrų su metaboliniu sindromu grupėje šlaunies miego arterijos pulsinės bangos greitį didina amžius, vidutinis kraujo spaudimas, liemens apimtis ir širdies susitraukimų dažnis. Vertinant rizikos veiksnių poveikį aterosklerozinėms plokštelėms vyrų su metaboliniu sindromu grupėje modelis parodė, kad aterosklerozinių plokštelių atsiradimas susijęs su amžiumi, MTL cholesteroliu ir arterine hipertenzija.

Atlikę kovariacinę analizę metabolinio sindromo įtakos arterijos sienelės parametams ir kairio skilvelio miokardo masės indekso kitimams nustatyti moterų ir vyrų grupėse aptikome, kad visais atvejais tiriamiamųjų grupės tarpusavyje statistiškai reikšmingai nesiskyrė ir bendras vidurkių skirtumas buvo nulemtas rizikos veiksnių skirtumų. Tai rodo, kad šie pakitimai daugiau sietini su širdies ir kraujagyslių ligų rizikos veiksnių poveikio visuma.

Vertindami metabolinį sindromą sudarančių rizikos veiksnių kiekybinę įtaką moterų širdies ir kraujagyslių sistemai nustatėme, kad didėjant metabolinį sindromą sudarančių rizikos veiksnių skaičiui nuo 3 iki 5, statistiškai patikimai didėja pulsinės bangos greitis ir intimos medijos storis. Tuo tarpu kairiojo skilvelio miokardo masės

indeksas didėjo kintant MS sudarančių rizikos veiksnių skaičiui nuo 3 iki 4; esant daugiau nei 4 rizikos veiksniams KSMMI daugiau nekito (p=0,398). Moterims aterosklerozinių plokštelių skaičius didėja atsiradus metaboliniam sindromui, bet jo komponentų skaičius tolesniam kitimui neturi įtakos (p=0,078).

Vyrų šlaunies-miego arterijų pulsinės bangos greitis statistiškai reikšmingai didėjo daugėjant metabolinį sindromą sudarančių komponentų. Didėjo ir intimos medijos storis, tačiau negauta statistiškai reikšmingo skirtumo (p=0,089). Kairiojo skilvelio miokardo masės indeksas didėjo daugėjant rizikos veiksnių nuo 3 iki 4; esant daugiau nei 4 rizikos veiksniams KSMMI nebekito (p=0,579).

Pritaikę logistinės regresijos modelį nustatėme, kad esant MS statistiškai patikimai (p=0,0001) padidėjo tik šlaunies miego arterijos PBG (β=0,22) ir nepakito kiti periferinių arterijų standumo rodikliai.

Vertindami ir žinodami kaip šlaunies-miego arterijų pulsinės bangos greitį veikia amžius, vidutinis kraujo spaudimas, liemens apimtis ir ŠSD, mes sudarėme regresines lygtis, leidžiančias be specialios įrangos apskaičiuoti pulsinės bangos greitį moterims:

PBG = 0.054 × vidutinis AKS + 0.081 × amžius + 0.023 × liemens apimtis + 0.016 × ŠSD – 4.44

ir vyrams:

PBG = 0.056 × vidutinis AKS+0.086 × amžius + 0.016 × liemens apimtis + 0.014 × ŠSD – 3.804

Paskutiniajame etape sudarėme pulsinės bangos greičio normines lenteles. Siekdami šias lenteles padaryti patogesnes praktiniam naudojimui, pulsinės bangos greitį nuspalvinome skirtingomis spalvomis, kurios atspindi pulsinės bangos norminę vertę, apskaičiuotą pagal 75 ir 95 centilių ribas atskiroms amžiaus grupėms.

IŠVADOS

1. Sergantiesiems metaboliniu sindromu nepriklausomai nuo lyties ir amžiaus rastas didesnis intimos medijos storis, šlaunies-miego arterijų pulsinės bangos

greitis ir kairiojo skilvelio miokardo masės indeksas. Miego arterijoje aterosklerozinių plokštelių daugiau nustatyta tik moterims.

2. Širdies ir kraujagyslių pažeidimų rizika sergantiems metaboliniu sindromu vyrams ir moterims yra skirtinga. Vyrams su MS yra 2,14 karto didesnė kairiojo skilvelio hipertrofijos ir 4,9 karto – intimos medijos sustorėjimo tikimybė. Moterims metabolinis sindromas nesukelia intimos medijos storio padidėjimo rizikos, bet akivaizdžiai (1,83 karto) padidina kairiojo skilvelio hipertrofijos ir 1,4 karto – aterosklerozinių plokštelių atsiradimo tikimybę.

3. Moterims ir vyrams metabolinis sindromas nedaro tiesioginės įtakos pulsinės bangos greičiui, intimos medijos storiui, kairiojo skilvelio hipertrofijos ir aterosklerozinių plokštelių atsiradimui. Šių parametrų kitimus daugiausia lemia tradiciniai širdies ir kraujagyslių ligų rizikos veiksniai.

4. Šlaunies-miego arterijų pulsinės bangos greitis, kairiojo skilvelio miokardo masės indeksas tiek vyrams, tiek moterims tiesiogiai priklauso nuo metabolinį sindromą sudarančių širdies ir kraujagyslių ligų rizikos veiksnių skaičiaus. Tuo tarpu intimos medijos storio didėjimas tik moterims siejamas su didėjančiu rizikos veiksnių skaičiumi.

5. Metabolinis sindromas skirtingai veikia centrines ir periferines arterijas. Nepriklausomai nuo lyties jis padidina centrinių arterijų pulsinės bangos greitį, tačiau neveikia periferinių arterijų hemodinamikos.

6. Pulsinės bangos greičio apskaičiavimo algoritmas priklauso nuo lyties, amžiaus, širdies susitraukimų dažnio, vidutinio kraujo spaudimo ir juosmens apimties.

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