

# Cardiovascular risk factors in menopausal women and the intima-media thickness

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**Abstract:** The aim of this study was analysis of the relationship between cardiovascular risk factors and intima-media thickness (I-M) at menopause. 27 women aged 53.4±3.7 years with hypertension were examined by means of the Doppler examination of carotid arteries. The Holter method was used to measure 24-hour arterial blood pressure. C-reactive protein (CRP) was determined. A correlation was found between I-M and the percentage of abnormal diastolic pressure values ( $r=0.423$ ,  $p<0.05$ ). CRP correlated with the I-M ( $r=0.50$ ,  $p<0.05$ ). The measurements of the intima-media complex should be regarded as a diagnostic factor in patients with subclinical atherosclerosis.

**Key words:** coronary risk factors, menopause, intima-media complex, C-reactive protein, hypertension

## INTRODUCTION

The functioning of the endothelium and damage to it are responsible for the gradual development of atherosclerosis and narrowing of the vascular lumen. The early changes concern the intima and media thickness. Measurements of the intima-media thickness described as intima-media complex (I-M) are one of the significant factors in discovering subclinical changes and predicting severe vascular events. The risk of a severe vascular event increases with the rise of the intima-media complex, as shown in the Rotterdam Study in which 7,983 people took part, and other population studies [1-3]. The increased value of I-M is connected with subclinical atherosclerosis, not only within the examined artery itself, but also other arteries, especially the coronary artery.

The aim of the study was analysis of the relationship between cardiovascular risk factors, sex hormones, the C-reactive protein level (CRP), and the scale of the intima-media complex I-M values in menopausal women.

## MATERIALS AND METHOD

The examined women were patients in the Cardiological Clinic. The interview and physical examination were registered by means of a questionnaire. 27 women with arterial hypertension and other cardiovascular risk factors were qualified for the study. Criteria for the qualification for the study were women aged 40-60 approaching the menopause with arterial hypertension, newly or earlier diagnosed. Hypertension was diagnosed if the systolic pressure level reached:  $RR_s \geq 140$  mmHg, and/or diastolic pressure reached:  $RR_d \geq 90$  mmHg. Criteria for

exclusion from the study: myocardial ischaemia with severe vascular events diagnosed earlier, stroke diagnosed earlier, cardiac failure, peripheral vessels diseases, severe systemic and organ diseases, hormonal replacement therapy.

The examined patients and the control group had the following measurements taken: Lipid levels (LDL: cholesterol-LDL, HDL: cholesterol-HDL, TG: triglycerides) was calculated by the enzymatic method using the bioMerieux kit, while glucose level fasting was determined by the enzymatic method with glucose oxidase. Estradiol ( $E_2$ ), testosterone (T), DHEA-S and sex hormone binding globulin (SHBG) levels were determined using the RIA method by means of gamma radiation meter Berthold Technologist LBIS 501. CRP levels by the quantitative turbidimetric method using Konelab 301 were analysed. Free testosterone index (FTI) and free estradiol index ( $FE_2I$ ) were calculated as:  $FTI = T$  (nmol/l)  $\times$  100/SHBG (nmol/l),  $FE_2I = E_2$  (pmol/l)  $\times$   $10^{-3}$   $\times$  100/SHBG (nmol/l). Free testosterone (FT) concentrations were measured according to the calculation method using the Sodergard formula [4] with the assumption of a constant albumin level in blood. The testosterone level calculated by this method in postmenopausal women showed a significant correlation with free testosterone [4-6]. Doppler examination of the carotid and vertebral arteries was performed using an ACUSON X300 kit with a linear probe and a changing frequency of 5-10 MHz. The intima-media complex (I-M) measurements were taken bilaterally, 1 cm from a patient's finger tip. A 24-hour measurement of arterial blood pressure was performed by means of the Holter method.

**Statistics.** The material was statistically worked out using the Statistica 5.0 computer programme. To compare mean values, the parametric Student T test was used. Relations between variables were evaluated on the basis of Pearson's linear correlation, calculating r coefficient and on the basis of multiple regression analysis, calculating beta coefficient.  $P<0.05$  was considered as significant.

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## RESULTS

The average age of the patients was  $53.4 \pm 3.7$  years. The patients had been suffering from arterial hypertension for  $7.5 \pm 5.07$  years, on average. Mean values of BMI in the examined group reached:  $29.0 \pm 4.9$ , of lipidogram: TG- $126.6 \pm 89.6$  mg/dl, TCh- $220.0 \pm 56.5$  mg/dl, LDL- $140.3 \pm 53.9$  mg/dl. Mean values of CRP reached  $4.07 \pm 3.7$  mg/dl. In the Holter examination, maximum systolic blood pressure was  $153.8 \pm 14.1$  mmHg, on average, whereas diastolic pressure was  $98.9 \pm 11.3$  mmHg. Abnormal values of systolic blood pressure during the day comprised 16.1% of the measurements, diastolic blood pressure 18.3%, whereas at night systolic blood pressure reached 16.8% and diastolic blood pressure 8.7%.

The scale of the intima-media complex in the right carotid artery (RCA) was  $0.73 \pm 0.25$  mm, while in the left one (LCA) –  $0.77 \pm 0.21$  mm. The thickness of the right carotid artery wall (RCA) was  $0.86 \pm 0.36$  mm and of the left (LCA) –  $0.89 \pm 0.36$  mm. The scale of the I-M complex increased with the percentage of abnormal arterial blood pressure measurements. There was a significant positive correlation between the scale of the IM complex and the percentage of abnormal arterial blood pressure measurements, and diastolic blood pressure throughout the night ( $r=0.423$ ,  $p<0.05$ ). The I-M complex increased with the rise of CRP. There was a positive correlation between CRP and the scale of the I-M complex of the right carotid artery ( $r=0.50$ ,  $p<0.05$ ), and a correlation of the I-M complex of the left carotid artery (LCA) ( $r=0.43$ ,  $p<0.05$ ).

Mean level of sex hormones: DHEA-S –  $119.6 \pm 58.5$  ug/100ml, estradiol –  $143.7 \pm 250.7$  pmol/l, SHBG –  $54.9 \pm 25.8$  nmol/l, testosterone –  $1.45 \pm 0.52$  nmol/l, FT- $0.0207 \pm 0.0089$  nmol/l,  $FE_2 I$  –  $0.03039 \pm 0.053$ , FAI –  $3,250 \pm 1,857$ . The correlations between the intima-media complex and sex hormone levels were statistically insignificant.

## DISCUSSION

Early diagnosis, appropriate prevention and treatment for vascular atherosclerosis in women can decrease the incidence of coronary artery disease and the rate of mortality caused by it. The scale of the intima-media complex within the arteries accessible for examination, including the carotid arteries, can be regarded as an indication of early vascular atherosclerosis. The I-M complex median for adults is 0.5-1 mm. The I-M complex value increases with age. It is higher in men than in women. The population studies show that people with intima-media thickness exceeding 2 mm constitute less than 5% of the population. For most authors, the measurement value exceeding 1 mm is abnormal, while for others it is 1.2 mm. In the examined population of women with arterial hypertension, values exceeding 1mm were registered in  $\frac{1}{4}$  of the patients (22.2% of the patients). In the examination of the Framingham Heart Study, described by Wang *et al.* [7], the measurements of the intima-media complex are regarded as a sensitive diagnostic factor in patients with developed subclinical atherosclerosis [8]. Moreover, this complex may prove helpful in estimating the global cardiovascular risk [2]. The Framingham Hart Study [9] provided information concerning the relationship between the scale of the intima-media complex and the inflammatory markers, including the CRP protein. A similar relationship between the scale of

intima-media complex and the protein level was observed in our population. According to other authors, the scale of the I-M measurement is less connected to the CRP level than its dependence on ageing, age, and other cardiovascular risk factors. Makit *et al.* [10] claim that in a general population, CRP can be a supplementary and quantitative factor for the development of atheromatous plaque in men, whereas it does not play such a role in women. According to Kawamoto *et al.* [11], the interdependence between CRP and the scale of intima-media measurement I-M was significantly different between patients with and without diabetes. The CRP level in patients with arterial hypertension can be considered a factor predisposing to arterial atherosclerosis. Its value is similar to arterial blood or systolic blood pressure [8]. In the epidemiological research Bernini *et al.* [12], there is a connection between the scale of the intima-media complex and endogenic sex hormones – negative correlation with DHEA-S, androstendione, and free testosterone. The authors claim that physiological androgen and DHEA-S levels are associated with lower atherosclerosis risk of the carotid vessels. Higher total testosterone and SHBG accompanying less advanced atherosclerosis in carotid arteries were observed by Gulden *et al.* [13]. According to Debing *et al.* [14] and other researchers [15], endogenic sex hormones are associated with atherosclerosis of the internal carotid arteries in women at natural menopause. A significant reverse correlation was shown between free testosterone, androstenedione, and the presence of severe atherosclerosis of the carotid arteries. Higher, yet physiological androgen levels in menopausal women are of protective significance in the development of atherosclerosis. This favourable metabolic effect of higher, yet physiological hormone levels, and the beneficial effect of the hormonal replacement therapy described by numerous authors, can result from a long-term advantageous impact on cardiovascular risk factors (lipids level, arterial hypertension, abdominal obesity, insulin resistance). Simultaneously, the studies of Tremollieres *et al.* [16] conducted on menopausal women aged 45-65, receiving and not receiving hormonal replacement therapy, prove that long-term treatment leads to a significant decrease in the total cholesterol level. The scale of the intima-media complex was significantly lower in carotid artery in older women undergoing hormonal replacement therapy, compared with women not receiving the treatment. Such observations give rise to the suggestion that long-term therapy has a protective result [16]. A number of publications by Signorelli *et al.* [15, 17-18] lead to the conclusion that the intima-media complex correlates with age, cardiovascular risk factors another duration of menopause, especially in women with arterial hypertension.

Our studies concerning women with hypertension and other cardiovascular risk factors did not show any statistically significant associations between sex hormones and the scale of the intima-media complex, which may be connected with the size of the examined population. Nevertheless, there was a strong correlation between the thickness of vascular wall and the percentage of abnormal diastolic blood pressure values, and a weaker correlation for mean values of systolic blood pressure.



## CONCLUSION

In patients with arterial hypertension, there is a connection between the thickness of vascular wall and the frequency of rises in arterial blood pressure during 24-four hours. The intima-media complex measurements should be regarded as a sensitive diagnostic factor in patients with advanced subclinical atherosclerosis.

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