The influence of mean blood pressure on arterial stiffening and endothelial dysfunction in women with rheumatoid arthritis and systemic lupus erythematosus

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***Key words**: rheumatoid arthritis; systemic lupus erythematosus; arterial stiffness; endothelial function; atherosclerosis.*

***Summary.** Objective. To investigate the carotid-radial pulse wave velocity, augmentation index, and flow-mediated dilation of the brachial artery and factors possibly influencing them in women with rheumatoid arthritis and systemic lupus erythematosus.*

Material and methods. A total of 63 women with rheumatoid arthritis, 31 with systemic lupus erythematosus, and 72 controls, aged 18–55 years, were examined. Parameters of arterial stiffness, augmentation index and carotid-radial pulse wave velocity, were obtained by applanation tonometry (Sphygmocor (v.7.01) AtCor Medical). Flow-mediated dilatation of the brachial artery, reflecting endothelial function was determined by ultrasound system (Logiq 7, General Electric).

Results. The groups of women with rheumatoid arthritis and systemic lupus erythematosus lupus differed from controls regarding augmentation index ($P<0.001$; $P=0.008$) and did not differ between each other. Women with systemic lupus erythematosus differed from controls regarding pulse wave velocity ($P=0.018$), while women with rheumatoid arthritis – did not. Flow-mediated dilatation in both the groups of diseases was not different from controls. In rheumatoid arthritis patients, mean blood pressure was the main explanatory factor for augmentation index and pulse wave velocity; vessel diameter and high-density lipoprotein cholesterol – for flow-mediated dilatation. In women with systemic lupus erythematosus, pulse wave velocity was not related to any of the pending parameters; augmentation index was dependent on organ damage index, age, and mean blood pressure, and flow-mediated dilatation on vessel diameter, body mass index, and disease duration.

Conclusions. The mean blood pressure was the major and the only one risk factor of arterial stiffening in rheumatoid arthritis, while the disease damage index played the most important role in the systemic lupus erythematosus group. The mean blood pressure in the systemic lupus erythematosus group was not as important as in the rheumatoid arthritis group, though may have a partial influence.

Introduction

The increased prevalence of premature atherosclerosis in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) is well established. Patients with RA are at the increased risk of development premature cardiovascular disease that shortens life by 3 to 18 years (1). The incidence of myocardial infarction is 5 times as high in patients with SLE if compared to general population, and in young women, the age-specific incidence is increased by a factor of as much as 50 (2). It may be assumed that cardiovascular events and functional impairment of the arteries, inflammation, or side effects of the treatment added to traditional risk factors go together or possibly the latter preceding the other.

Noninvasive detection of endothelial dysfunction,

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increased arterial stiffness, the important assessment in the diagnosis of early atherosclerosis, recently have been described widely in patients with RA and SLE (3–11). Nevertheless, data about damage of arterial function in inflammatory rheumatic diseases are not consistent, and their prognostic value is not well established. Great attention has been paid to the underlying mechanisms of early atherosclerosis in RA and SLE patients; however, the functioning of large elastic arteries was the main object of researches. Several studies demonstrated that inflammation is considered the major cause of endothelial dysfunction and arterial stiffening in both patients' groups. C-reactive protein (CRP) and some of circulating and endothelium-derived factors, including nitric oxide, von Willebrand factor (vWF), excess of adhesive molecules, endothelin-1 may influence the elasticity of large arteries providing so-called "functional" regulation of arterial stiffness (12–14). Not only active chemical compounds but also disease itself may harm endothelium and induce arterial stiffening. Chronic autoimmune inflammation or drugs used to treat it, such as corticosteroids, or other not described risk factors may play role in the development of early atherosclerosis. This study was designed to improve and extend our previous studies by examining the functioning not only of the central elastic but also peripheral muscular arteries and by comparing the risk factors of subclinical vascular disease in RA (4–6) and SLE (15). The aim of this study was to determine the carotid-radial pulse wave velocity (PWV), aortic augmentation index (AIx) as a derivate marker of arterial wall dysfunction and endothelium-dependent flow-mediated dilatation (FMD) and factors possibly influencing them in middle-aged RA and SLE women without significant organ damage and to compare them to healthy controls.

Patients and methods

Study population. One hundred sixty-six women aged between 18 and 55 years without clinically apparent cardiovascular disease were enrolled into the study: 63 with an established RA, 31 with SLE, and 72 controls. The patients fulfilled strict diagnostic criteria for the presence of RA (16) and SLE (17), and they were recruited from the Department of Rheumatology and examined at the Department of Cardiology and Angiology of Vilnius University Hospital. In addition to demographical data, the disease activity index in RA patients was measured by the Disease Activity Score (DAS28), a validated score including tender and swollen joint count, erythrocyte sedimentation rate, and a patient global assessment of disease activity (18). In SLE patients, the disease activity index by SLEDAI score (19) and damage by the SLICC damage index (20) and in parallel Raynaud's syndrome, and antiphospholipid syndrome were evaluated. Renal impairment in SLE patients was considered when proteinuria was more than 0.5 g up to 3.4 g per 24 hours and/or hematuria of more than 5 erythrocytes in the visual area. In both groups of patients, the current therapy was documented. Blood samples were obtained in the morning after 12 hours' fasting for the following tests: erythrocyte sedimentation rate, high-sensitivity C-reactive protein (hsCRP) by immunonephelometry, serum lipid profile, serum glucose, and creatinine. Seventy-two healthy women were consequently involved into the study when they were undergoing the preventive inspection at the same hospital.

Subjects were excluded from the study in cases of a previous history of coronary artery disease or stroke, arrhythmias, infectious diseases, neoplasia, kidney or liver insufficiency, smoking, or alcohol abuse. Hypertension (defined by blood pressure of >140/90 mm Hg), history of severe hyperlipidemia (total cholesterol, >6.2 mmol/L; low-density lipoprotein [LDL] cholesterol, >4.1 mmol/L) or obesity (body mass index [BMI], >30 kg/m^2), and diabetes mellitus (fasting glucose, ≥7.0 mmol) were also considered as exclusion criteria. Approval was obtained from the Lithuanian Bioethics Committee, and written informed consent was obtained from each participant.

Noninvasive assessment of arterial stiffness. Subjects were refrained from eating, drinking alcohol, coffee, or tea at least 12 hours before the study. To ensure the stability of the measurement, the test of arterial stiffness was performed in the supine position after 10 minutes resting in a quiet, temperature controlled room (22–24˚C) in the early morning hours. Blood pressure was recorded in the left arm using an automatic blood pressure monitor.

PWV was determined by measuring the carotid-to radial pulse wave transit time. Carotid and radial pulse waves were obtained noninvasively by applanation tonometry using a high-fidelity micromanometer (Sphygmocor, v.7.01, AtCor Medical Pty. Ltd 1999–2002). Pulse waves obtained consecutively from the radial and carotid arteries were referenced to a simultaneously recorded ECG, and transit time was computed from the time difference between the carotid and radial waveforms. The distance between the surface markings of the sternal notch and the radial artery was used to estimate the difference in path

between the carotid and radial arteries, and PWV adjusted for mean blood pressure was calculated. AIx adjusted for the heart rate of 75 beats per minute was calculated from radial pulse waves of nondominant arm (21). Validated transfer function from peripheral pulse wave analysis was used to generate a corresponding central waveform. From this, aortic AIx was calculated by using the integrated software. The systolic part of the central arterial waveform is characterized by two pressure peaks. The first peak is caused by left ventricular ejection, whereas the second peak is a result of pulse wave reflection. The difference between both the pressure peaks reflects the degree to which central arterial pressure is augmented by wave reflection. AIx, a measure of systemic arterial stiffness, is calculated as the difference between the second and the first systolic peaks expressed as a percentage of pulse pressure.

Flow-mediated dilatation measurement. The endothelium-dependent flow-mediated dilatation test in a brachial artery was performed according to the method described by Celermajer et al. and adapted according to the international recommendations (22, 23) and technical equipment of our department. The diameter of brachial artery was measured on B-mode imaging by the ultrasound system (Logiq 7, General Electric) with a high-resolution 12-MHz linear-array transducer.

The computerized software program for image acquisition (CVI Acquisition) and semi-automatic analysis software were used (Vascular Analysis Tools [Vascular Converter CVI and Brachial Analyzer], Medical Imaging Application, 1998–2003 LLC Iowa City, IA 52246, USA). The arterial diameter was measured between the intima/lumen interfaces of the anterior and posterior wall at the end of diastole (synchronized with the beginning of the R wave on the continuously recorded ECG). Scans were taken in the longitudinal plane 1–8 cm above the *antecubital fossa*.

Measurements were performed at rest and during reactive hyperemia. Ten-to-fifteen resting scans were obtained, and resting arterial flow velocity was measured by means of a pulsed Doppler signal at the 60˚ angle to the vessel, with the range gate in the center of the artery. Increased flow was induced by the inflation of a pneumatic tourniquet to a 100 mm Hg suprasystolic pressure for 5 minutes. A second scan was taken continuously for 3 minutes after cuff deflation, including a repeated flow velocity measurement within the first 15 seconds after cuff release. During image acquisition, a stereotactic probe-holding device was used to ensure hand stability.

Statistical analysis. Data were analyzed with the SPSS software for Windows (version 16.0, Chicago, Illinois). Continuous variables were compared with one-way ANOVA. Post hoc comparisons were made using Scheffe statistics. In order to adjust for other confounding factors, a stepwise linear regression was applied. For each measure of arterial wall function, two models we designed. Models of the first type included two binary variables used to model the impact of separate diseases (control group was considered as a reference group). Models of the second type included one binary variable used to discriminate between patients (RA, SLE) and controls. The complete list of independent predictors was based on findings of other studies. To avoid multicolinearity, correlations between independent predictors were taken into account before including them into the initial list of independent predictors. A variable was included into the model if its significance was less or equal to 0.05, and it was excluded from the model if its significance was greater than 0.1. For continuous variables, descriptive statistics were presented as mean (SD). Level of significance was set at 0.05. One-sided *P* values were not used.

Results

Demographic characteristics. Summary of comparisons among the groups with respect to demographic characteristics is presented in Table 1. The groups did not differ in body mass index (BMI) and cholesterol levels; however, there were differences in other characteristics. To keep it short, we do not present here pairwise comparisons since the variables were included as independent predictors into the linear stepwise regression models (see next section) when looking for influence of different variables on arterial wall parameters.

Comparison of groups regarding parameters of arterial wall. The direct comparison of arterial wall function parameters has shown a difference in AIx and PWV among the groups (Table 1). Post hoc tests revealed that the RA and SLE groups did not differ (*P* value for comparison with respect to AIx was equal to 0.286; *P* value for comparison with respect to PWV was equal to 0.450). However, both of them differed from the control group with respect to AIx ($P_{\text{SLE vs controls}}$=0.008; $P_{\text{RA vs controls}}$<0.001), and only SLE group differed from controls regarding PWV ($P_{\text{SLE vs controls}}$=0.018; $P_{\text{RA vs controls}}$=0.150). There was no difference in FMD comparing the groups.

In order to adjust for other confounding factors, a linear stepwise regression was employed. Each of

Table 1. Demographic characteristics of study population and direct comparison of arterial wall parameters among all groups

Variable	RA (n=63)	SLE (n=31)	Controls (n=72)	*P* value
Age, years	41.48 (10.77)	37.23 (9.09)	37.42 (9.15)	0.034
Height, cm	164.76 (5.86)	166.23 (6.17)	166.51 (5.58)	0.201
Body mass index, kg/m^2	23.52 (4.31)	23.59 (4.25)	23.75 (3.39)	0.941
Systolic blood pressure, mm Hg	119.43 (10.59)	124.35 (16.52)	114.65 (16.42)	0.007
Diastolic blood pressure, mm Hg	75.25 (7.70)	81.90 (11.63)	74.00 (8.10)	0.004
Mean blood pressure, mm Hg	92.29 (8.85)	96.74 (12.95)	88.44 (9.61)	0.001
Total cholesterol, mmol/L	4.81 (0.96)	5.26 (1.37)	4.95 (0.88)	0.263
High-density lipoproteins, mmol/L	1.55 (0.41)	1.44 (0.49)	1.53 (0.32)	0.446
Low-density lipoproteins, mmol/L	2.74 (0.82)	2.93 (0.96)	3.00 (0.73)	0.165
Triglycerides, mmol/L	1.14 (0.46)	2.00 (1.00)	0.91 (0.53)	<0.001
C-reactive protein, mg/L	31.89 (40.44)	5.80 (5.56)	1.64 (3.18)	<0.001
Creatinine, μmol/L	64.24 (19.59)	75.14 (23.38)	66.06 (9.94)	0.018
Blood vessel diameter, mm	3.12 (0.48)	3.17 (0.42)	2.95 (0.29)	0.007
AIx, %	24.71 (11.52)	20.81 (12.29)	13.24 (10.44)	<0.001
PWV, m/s	8.41 (0.98)	8.76 (1.87)	7.98 (1.15)	0.012
FMD, %	8.27 (3.85)	8.95 (5.32)	9.68 (3.24)	0.115

The results are presented as mean (standard deviation).
PWV, pulse wave velocity; AIx, augmentation index; FMD, flow-mediated dilation; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus.

measures of arterial wall function was treated as a dependent variable, and models of two types were designed. Models of the first type included two binary variables used to model the impact of each of diseases (control group was treated as a reference group), meanwhile models of the second type included only one binary variable, which indicated disease status (control or patient), i.e. in both of the models, a usual binary coding was applied. Other independent variables used in the initial step of model building were as follows: age, BMI, high-density lipoproteins (HDL), triglycerides (TG), CRP, total cholesterol, and creatinine. For AIx and PWV, MBP was also added, meanwhile for FMD, the diameter of blood vessel was added. LDL was not included into the list of predictors since it strongly correlated with total cholesterol (r=0.9; P<0.001). We do not present here final models since the main task of this procedure was to compare the groups with adjustment for other confounding factors. We briefly report that after adjustment for additional factors, only RA subgroup significantly differed from controls and only in respect of AIx (P<0.001). Merged RA and SLE subgroups did not differ from controls.

Predictors of arterial wall damage in RA and SLE subgroups. We used a linear stepwise regression to find out independent predictors of arterial wall damage in RA and SLE subgroups separately. We considered the following additional variables: SLEDAI, disease duration, Raynaud's syndrome, antiphospholipid syndrome, and SLICC when analyzing the SLE group and DAS28 in the RA group. Other independent variables were the same in both the groups: age, disease duration, BMI, HDL, TG, CRP, total cholesterol, creatinine, MBP (for AIx and PWV), blood vessel diameter (for FMD). Results of this analysis are summarized in Tables 2 and 3. The mean blood pressure was the major and the only one risk factor of arterial stiffening in RA women, while disease activity had no effect on arterial functioning. The disease damage index and not activity index played the most important role in the SLE group. To some extent, increased MBP and older age was shown to increase the AIx. It may be assumed that higher MBP goes in parallel with increased AIx in both diseases explored in this study. Disease duration in SLE was important in endothelial dysfunction, showing that with an increase in age, the elasticity of the arteries tends to decrease.

Discussion

Chronic inflammatory conditions, such as RA and SLE, are associated with premature atherosclerosis, and the causes of cardiovascular mortality may be multi-factorial, but cannot be explained merely by conventional risk factors such as age, gender, hyperlipidemia, hypertension, smoking, or excess weight.

In recent decade, many similarities have emerged between the paradigm of the inflammation in pathogenesis of atherosclerosis and the well-established mechanisms of inflammation in the pathogenesis of RA and SLE. Premature atherosclerosis has been

Table 2. Influence of different factors on arterial wall parameters in patients with rheumatoid arthritis*

Dependent variable	Predictor	Regression coefficient (SE)	Beta	*P* value
AIx (r^2=0.376; r^2(adj.)=0.365; P_{ANOVA}<0.001)	Mean blood pressure	0.779 (0.133)	0.613	<0.001
PWV (r^2=0.249; r^2(adj.)=0.235; P_{ANOVA}<0.001)	Mean blood pressure	0.054 (0.012)	0.499	<0.001
FMD (r^2=0.376; r^2(adj.)=0.354; P_{ANOVA}<0.001)	Blood vessel diameter	–4.129 (0.840)	–0.523	<0.001
	High density lipoprotein	–3.845 (1.035)	–0.395	<0.001

*The multivariate stepwise linear regression model was used for RA patients; r^2, the coefficient of determination; *P* value close to the coefficient of determination indicates the presence of regression as the whole;
The complete list of independent predictors is as follows: age, BMI, HDL, TG, CRP, total cholesterol, creatinine, MBP (for AIx and PWV), blood vessel diameter (for FMD), DAS28, disease duration.

Table 3. Influence of different factors on arterial wall parameters in patients with systemic lupus erythematosus*

Dependent variable	Predictor	Regression coefficient (SE)	Beta	*P* value
AIx (r^2=0.567; r^2(adj.)=0.508; P_{ANOVA}<0.001)	Mean blood pressure	0.319 (0.184)	0.285	0.097
	SLICC	3.458 (1.291)	0.414	0.014
	Age	0.529 (0.210)	0.380	0.019
PWV**	–	–	–	–
FMD (r^2=0.714; r^2(adj.)=0.673; P_{ANOVA}<0.001)	Blood vessel diameter	–11.511 (1.658)	–0.868	<0.001
	Disease duration	–0.265 (0.081)	–0.403	0.004
	Body mass index	0.547 (0.223)	0.315	0.023

*The multivariate stepwise linear regression model was used for SLE patients. r^2, the coefficient of determination; *P* value close to the coefficient of determination indicates the presence of regression as the whole;
** The complete list of independent predictors is as follows: age, BMI, HDL, TG, CRP, total cholesterol, creatinine, MBP (for AIx and PWV), blood vessel diameter (for FMD), SLICC, disease duration, Raynaud's syndrome (0 – absent, 1 – present), antiphospholipid antibodies (0 – absent, 1 – present), SLEDAI.

repeatedly shown to be prevalent and the age of onset reduced in RA and SLE patients if compared to matched population (3, 4, 7–11). It may be assumed that impaired arterial stiffness plays an independent pathogenetic role in atherosclerosis (24) and may be responsible for premature atherosclerosis in RA and SLE and atherosclerotic lesions.

This study showed that aortic AIx, the marker of early atherosclerosis, the parameter systemic arterial stiffness, is modified in RA and SLE patients, and a significant difference was detected in both diseases as compared with controls. To less extend parameter of regional vessel flexibility, the carotid-radial PWV in SLE patients also significantly differed from controls, but in RA patients did not. On the other hand, the FMD, the parameter of endothelial dysfunction, was not shown to be serious damaged in middle-aged RA and SLE women if compared to healthy controls.

To avoid the summing effect of traditional and disease-related risk factors, this study compared middle-aged RA and SLE women group without traditional risk factors and without a clinically apparent cardiovascular disease with a healthy control group. Organ insufficiency was also considered as an exclusion criterion for this study. In multivariate regression model, age, MBP, and RA were found to be associated with AIx. In the cohort of solely RA patients, only mean blood pressure was an important predictive factor for increased AIx. Meanwhile in SLE women, disease damage index (SLICC), age, and mean blood pressure remained as the most important predictive factors for AIx. Our study echoes with the study by Laurent et al. that proved aging and the blood pressure to be the two major determinants of arterial stiffness in the cohort of patients with cardiovascular disease (24). Based on this, we assume that monitoring and controlling the blood pressure may have a beneficiary effect on the outcome of diseases. In addition, in SLE women, SLICC appears to be an independent and potentially treatable influencing factor of functional status of arteries, so the adequate treatment of lupus patients can help to protect all arterial tree system.

Several studies investigated the structural and functional reformation of the arteries in RA, but the data are still controversial. Our study echoes with the study by Roman et al. (3) that arterial stiffness index AIx from applanation tonometry was significantly greater in RA and SLE patient populations than in the

control group. In the study by Klocke et al., the AIx of middle-aged RA patients (mean age, 42 years) was significantly higher in the RA group than in the control group (9). In the study of Maki-Petaja et al. (7) where the mean age of study population was about 57 years, no difference was found in AIx between the RA and control groups, although the carotid-radial PWV was found to be significantly higher in RA patients as compared to controls. This study confirmed the previous findings of Čypienė et al. (5) comparing the arterial wall parameters of RA patients aged about 40 years where the mean AIx was significantly higher in RA patients while carotid-radial PWV did not differ between the groups. It may be concluded from the above-mentioned studies that differences in AIx and carotid-radial PWV are more expressed at younger ages when inflammation plays the major role and are less prominent in older years when age adds to the profile of influencing factors.

Data on SLE is in harmony with the studies focusing on SLE and arterial wall functioning, namelythe studies by Brodszki et al. (25) and Roman et al. (3). These studies demonstrated an increased arterial stiffness and signs of premature vascular aging in SLE patients without manifest cardiovascular disease and without significant atherosclerotic lesions. The authors agree that other mechanisms beside atherosclerosis might be involved in the pathogenesis of arterial stiffening in SLE patients. The association of arterial stiffening with disease duration and circulating levels of CRP and IL-6 implicates chronic inflammatory conditions being important mediators of this process (3). SLE-specific variables were more important among younger women than in senior ones when traditional risk factors and age were added to the context of disease (26).

Conversely, the study by Bjarnegard et al. did not find differences in AIx and carotid-radial PWV in SLE women compared to controls (8). Nevertheless, the authors concluded that women with SLE had increased stiffness of their elastic central arteries judging on carotid-femoral PWV that was still higher in SLE women and was positively associated to CRP and complement factor 3 (8).

In our study, we did not find a significant difference in FMD between RA, SLE patients and controls. However, after adjusting for various risk factors, we found that the presence of SLE is related to endothelial dysfunction and it depends on disease duration. In previous studies, RA was associated with endothelial dysfunction (7, 26), which can be reversed with immunomodulatory therapy (7, 26). Therefore, our finding about the absence of a significant difference in FMD between RA patients and controls may be partially explained by the fact that 15 of 63 RA women in our study received anti-TNF-α therapy (infliximab) and methotrexate in parallel. Our findings also confirm the data of Van Doornum et al. (27). Their study did not demonstrate any difference in endothelial function between RA patients and controls. Several other studies (28, 29) have shown the presence of endothelial dysfunction in RA patients. It is important that in these studies, an invasive assessment of endothelial function was applied. Therefore, our failure to detect the difference in FMD may be also related to the limitations specific to the methods we used. Unfortunately, there are no studies comparing the sensitivity of several methods for detection of endothelial function.

Several studies approaching endothelial function of the brachial artery in SLE women differently from our findings indicate an impaired FMD (10, 11). The patients enrolled in the quoted studies were older or smokers or diseased with other important diseases such as diabetes or coronary artery disease, which may result in alterations of FMD. It may be assumed that differently from AIx increasing early in the disease, the endothelial dysfunction may evolve later in the course of disease. Interestingly, not SLE itself, not even SLEDAI as a composite measure of disease activity or renal impairment, had any impact on artery wall functioning. Concomitantly Raynaud syndrome or antiphospholipid syndrome had no impact on arterial wall or endothelium as well. Moreover, triglycerides and hsCRP, which are commonly considered as predictors of cardiovascular risk in general population and are significantly higher in RA and SLE groups, did not show any influence on AIx, PWV, or FMD.

This study did not omit the limitations. We excluded patients with known cardiovascular risk factors, serious organ damage, which resulted in a relatively small sample size of SLE patients. Furthermore, we cannot exclude the possibility that treatment might have contributed to our results. The effect of treatment in "vascular rheumatology" remains uncertain till now, that was described by Szekanecz and Koch (30). Anti-inflammatory treatment may be either proatherogenic or antiatherogenic. Corticosteroids are atherogenic by augmenting dyslipidemia, hypertension, and long exposure to corticosteroid therapy is associated with the development of atherosclerosis. Glucocorticoids may exert a bimodal action as they are atherogenic but, on the other hand, also anti-inflammatory. There is evidence that the above-described inflammatory

factors associated with more active disease may exert higher risk for atherosclerosis than anti-inflammatory treatment. In contrast to corticosteroids, antimalarial drugs such as chloroquine and hydroxychloroquine may exert evident antiatherogenic properties. Antimalarials may reduce LDL cholesterol, LDL cholesterol, and triglyceride production in corticosteroid-treated patients. Methotrexate exerts bipolar effects on atherosclerosis in RA: on one hand, methotrexate treatment increases plasma levels of homocysteine, but on the other hand, methotrexate controls several other mediators of inflammation and thus may beneficially influence the net outcome of cardiovascular diseases in RA. Concomitant folate supplementation prevented the increase of homocysteine production and reduced cardiovascular mortality in methotrexate-treated patients. Regarding the importance of treatment, our studies investigating the influence of biological therapy on arteries functioning in RA clearly demonstrated the reduction of carotid-radial PWV in young RA patients after infliximab infusion (5, 6). Based on this, treatment effects may be extremely important in RA and SLE patients as well. In this study, we achieved a good matching between the RA, SLE and control groups for all pending variables, except for mean blood pressure, which was significantly lower in the control group. The results of our study were evidential – the mean blood pressure was an explanatory factor for AIx and carotid-radial PWV in RA patients. Therein we think that monitoring and controlling of blood pressure should be started from the beginning of RA and potentially in SLE to prevent vascular damage in future. Though controlling the mean blood pressure seems to be logical to prevent from artery stiffening, some other important factors may be missing and their influence underestimated.

Conclusions

The study showed that the mean blood pressure was the major independent risk factor for both arterial stiffness parameters (augmentation index and carotid-radial pulse wave velocity) in rheumatoid arthritis patients and to some extent in systemic lupus erythematosus patients. The parameters of arterial stiffness were influenced the same direction by the mean blood pressure, showing that with an increase in the mean blood pressure, the arterial stiffness increased. In addition, augmentation index was affected by rheumatoid arthritis as an autoimmune disease itself and importantly by disease damage index in systemic lupus erythematosus patients. Endothelial function expressed by flow-mediated dilatation was exceptionally influenced by the duration of systemic lupus erythematosus, showing that with an increase in disease duration, the elasticity of the arteries tends to decrease.

The assessment of augmentation index, the parameter of systemic arterial stiffness, carotid-radial pulse wave velocity, the parameter of regional muscular vessel flexibility, and flow-mediated dilatation in the brachial artery, reflecting endothelial function in the preatherosclerotic stage, may have a beneficial diagnostic, prognostic, and therapeutic relevance.

Vidutinio kraujospūdžio įtaka arterijų standėjimui ir endotelio disfunkcijai moterims, sergančioms reumatoidiniu artritu ir sistemine raudonąja vilklige

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Raktažodžiai: reumatoidinis artritas, sisteminė raudonoji vilkligė, arterijų standėjimas, endotelio funkcija, aterosklerozė.

Santrauka. *Tyrimo tikslas*. Ištirti moterų, sergančių reumatoidiniu artritu, sistemine raudonąja vilklige, kurioms nenustatytas ryškus organų pažeidimas, miego-stipininės arterijų pulsinės bangos greitį, augmentacijos indeksą ir žasto arterijos tėkmės sąlygotą dilataciją; nustatyti veiksnius, galinčius turėti įtakos šiems parametrams.

Tyrimo medžiaga ir metodai. Ištirtos 18–55 metų moterys: 63 sergančios reumatoidiniu artritu, 31 – sistemine raudonąja vilklige, 72 – kontrolinės grupės moterys. Arterijų standumo parametrai, miego-stipininės arterijų pulsinės bangos greitis, augmentacijos indeksas užregistruoti aplanacinės tonometrijos būdu („Sphygmocor

(v.7.01) AtCor Medical“). Žasto arterijos tėkmės sąlygota dilatacija, atspindinti endotelio funkciją, nustatyta ultragarso aparatu („Logiq 7, General Electric“).

Rezultatai. Moterų, sergančių reumatoidiniu artritu ir vilklige, augmentacijos indeksas buvo didesnis palyginus su kontroline grupe ($p<0,001$; $p=0,008$), tačiau nesiskyrė tarp šių ligų. Vilklige sergančių moterų pulsinės bangos greitis skyrėsi palyginus su kontroline grupe ($p=0,018$), tačiau sergančiųjų reumatoidiniu artritu nesiskyrė. Tėkmės sąlygota dilatacija abiejų ligų atveju nesiskyrė nuo kontrolinės grupės. Pagrindinis veiksnys, turintis įtakos sergančiųjų reumatoidiniu artritu augmentacijos indeksui ir pulsinės bangos greičiui, buvo vidutinis arterinis kraujospūdis, o tėkmės sąlygotai dilatacijai – kraujagyslės diametras ir didelio tankio lipoproteinų cholesterolis. Vilklige sergančiųjų pulsinės bangos greičiui įtakos neturėjo nė vienas tirtas parametras, o augmentacijos indeksas priklausė nuo organų pažeidimo indekso, amžiaus ir vidutinio arterinio kraujospūdžio; tėkmės sąlygota dilatacija – nuo kraujagyslės spindžio, kūno masės indekso bei ligos trukmės.

Išvados. Vidutinis arterinis kraujospūdis – pagrindinis rizikos veiksnys, turintis įtakos arterijų standėjimui moterims, sergančioms reumatoidiniu artritu ir sistemine raudonąja vilklige. Reumatoidinis artritas, kaip liga bei organų pažeidimo indeksas, sergant vilklige, siejami su pagreitėjusiu arterijų standėjimu. Sisteminės raudonosios vilkligės trukmė yra svarbi endotelio disfunkcijai pasireikšti.

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