Intima media thickness measurement as a marker of subclinical atherosclerosis in SLE patient

Andrea Smrzovaa, Pavel Horaka, Martina Skacelovaa, Zuzana Hermanovab, Katerina Langovac, Josef Zadrazilb, Dalibor Novotnyd

Aim. Accelerated atherosclerosis in systemic lupus erythematosus (SLE) is an important cause of morbidity and mortality. The pathophysiology of accelerated atherosclerosis in SLE is mediated by factors such as inflammatory processes in the vascular wall, specific antibodies, dyslipoproteinemia, endothelial dysfunction and the high prevalence of traditional risk factors for cardiovascular diseases. In this context, we evaluated the clinical significance of ultrasound examination of the carotic arteries in the early diagnosis of atherosclerosis.

Methods. The study included 63 patients with SLE (female: male 53:10, mean age 38.4±12.7 years, mean disease duration 143.0±82.6 months), 24 patients had lupus nephritis. The control group consisted of 24 volunteers (female: male 20:4 mean age 31.04±8.59). Intima media thickness (IMT) was measured by ultrasound on both sides. The results were correlated with markers of lipid spectrum, anti-dsDNA, antinucleosomal and anticardiolipin antibodies, lupus anticoagulant and complement components. Clinical disease activity and damage were evaluated by SLEDAI and SLICC indices. Lifestyle and other important factors were examined per protocol and by questionnaire.

Results. A significant difference of IMT (P≤0.03) was found between the lupus patients and sex-age adjusted healthy controls with an in mean IMT in SLE patients of 0.569±0.11 mm, in control group 0.495±0.05 mm. A significant correlation between IMT and disease duration, age, positivity of lupus anticoagulant, use of ACE inhibitors, glomerular filtration and serum creatinine were found. No difference in IMT was found between patients with or without lupus nephritis.

Conclusion. IMT measurement could be used as a clinical predictor of risk of accelerated atherosclerosis in lupus patients.

Key words: systemic lupus erythematodes, atherosclerosis, intima media thickness

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INTRODUCTION

Accelerated atherosclerosis (AT) is one of the major late complications of systemic lupus erythematosus (SLE) and is recognized as a major cause of morbidity and mortality in lupus patients. The first reports of early atherosclerotic involvement appeared in 1975 (ref.1). One year later, a study described bimodal “twin-peaks” pattern of mortality rate related to SLE, the first peak being associated with active lupus, the second with acute myocardial infarction or other cardiovascular diseases 10-15 years after initial diagnosis2. The probability of a 10-year survival of lupus patients is now more than 90% (ref.3). The impact of previous frequent causes of death like high activity of auto inflammatory process, renal insufficiency, infection and sepsis have been diminished but not eliminated while cardiovascular diseases as a cause of lupus mortality have increased considerably. Patients with SLE have more than six times higher risk of AT than the general population4. In studies, this relative risk ranges from 5.0-10.0 depending on the design of the observation and the odds ratio lays between 4.8 and 9.8 (ref.4,5). Two retrospective studies on traditional risk factors for CVD mortality showed that patients with SLE had a ten times higher incidence of nonfatal myocardial infarction and seventeen times higher mortality due to coronary heart disease independently of their traditional CVD risk factor profile6. The data from the General Practice Research Database in the UK showed 2.67 times more common acute myocardial infarction in SLE patients than in controls7. Subclinical AT is present in up to 40% of lupus patients8. The vast majority of these publications show that higher prevalence of traditional risk factor cannot be the only explanation for these alarming findings and that the complex inflammatory character of SLE with numerous consequences plays a crucial role9.

In this study, the selected risk factors of AT were investigated in the group of SLE patients followed up at the department of rheumatology and compared with ultrasound evaluation of intima media thickness of the common carotid artery.
MATERIALS AND METHODS

Sixty three patients with SLE, 53 females and 10 males, all fulfilling four or more criteria of the American College of Rheumatology for the disease and who had given informed consent, were examined in the out-patient lupus clinic and the clinical and laboratory parameters were assessed in the period from September 2010 to December 2011 (ref. 10). The inclusion criteria were diagnosis of SLE with all types of organ damage. Patients with a previous history of atherosclerosis (before manifestation of SLE) were excluded. Measurement of IMT, laboratories parameters and information from questionnaires were collected in the same time in one visit. The mean age was 38.4±12.7 years (18-72), mean duration of the disease 143.0±82.6 months (0-342), age of onset of SLE was 28.0±12.0 years (median 25.0, 9 minimum, 60 maximum). The sub-group of lupus nephritis (LN) patients comprised 24 in all, but in two renal diseases was not confirmed by histology of the kidney biopsy. In the remaining two cases, the diagnosis of lupus nephritis was based merely on clinical data (proteinuria and nephrotic syndrome) as renal biopsy would be associated with substantial risk due to thrombocytopenia. Whereas the mean age of patient in LN group was 33.71 years and in patients without LN 41.3 years, the age matched subgroup (32.1 years) of lupus patients without LN was used for comparison of IMT values.

The clinical examination included a detailed history of the disease, hypertension, diabetes, smoking, family history of premature cardiovascular disease (before the age of 55 for men or 60 for women in first-degree relatives), nutrition and sport activities or sedentary lifestyle assessment by simple questionnaire and further on, standardized measurement of systolic and diastolic blood pressure, obesity defined by body mass index and waist circumference and complete physical examination at study entry.

In each patient, the cumulative dose of glucocorticoids (equivalent of prednisone) and eventually of hydroxychloroquine (if ever given) were calculated. The data on use of other drugs possibly interfering with atherosclerosis such as ACEi (angiotensin converting inhibitors), statins and anticoagulation or antiaggregation were collected.

The SLE Disease Activity Index (SLEDAI) was used for evaluation of clinical disease activity and Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) index for assessment of disease damage 11, 12.

The levels of C3 and C4 components of the comple- ment were measured using nephelometry (Analyzer BNII Dade Behring) with diagnostic antiburum (Orion Diagnostica Company, Espoo, Finland). The normal limits for the C3 component of the complement are 0.98-1.97 g/L and 0.120-0.4 g/L for the C4 component. Anti-double-stranded DNA (anti-dsDNA) and antinucleosomal antibodies were detected by ELISA (Organtec Diagnostika GmbH, Mainz, Germany). The producer expected normal values less than 15 IU/mL for anti-dsDNA and less than 20 UI/mL for antinucleosomal antibodies.

Anticardiolipin antibodies (ACLA IgG, IgM) were tested by ELISA (Aeskulisa Cardiolipin-GM, Wendelsheim, Germany) with normal limits between 0-10 GPL-UI/mL for ACLA IgG and 0-15 GPL-UI/mL for IgM. Lupus anticoagulant was measured by routine method with determination of lac screen ration (LSR) 0-15 for negativity. High sensitivity C reactive protein was measured by nephelometry (Roche/Hitachi 912, Modular P analyzers, Germany) with expected normal levels of 0-5 mg/L. Complete lipid spectrum was assessed by nephelometry (Roche/Hitachi , Germany). Normal value of cholesterol was 2.90-5.00 mmol/L, triglycerides 0.45-1.70 mmol/L, HDL 1.00-2.10 mmol/L, LDL 1.20-3.00 mmol/L, lipoprotein (a) 0-0.3 g/L, apolipoprotein A-1 1.15-1.60 g/L, apolipoprotein B 0-1.20 g/L and creatinine 64-104 μmol/L. Glomerular filtration was calculated using formula of MDRD (Modification of Diet in Renal Disease).

The B-mode ultrasound scan of the common carotid artery was performed in all participants including controls by the standard protocol. Five scans were measured on each side and the mean was calculated. The far wall common carotid intima media thickness (IMT) measurements were made at a predefined site 1cm from the carotid bulb free of plaques defined according to Touboul 13. All measurements were performed by the same trained ultrasound operator. The intima media thickness index was measured also in the age and sex matched control group of 24 healthy volunteers (female: male: 20:4, mean age 31.04±8.59 years).

Descriptive statistics, regression, correlation, Mann–Whitney, Kruskal-Wallis test, t-tests and Levene’s Test for Equality of variance and Chi-Square Tests were used for statistical evaluation of the results. ANOVA software was used for the calculations and statistic graphs.

RESULTS

The characteristic of SLE group and prevalence of cardiovascular risk factors is summarized in the Table 1, which also summarizes the correlation of these parameters with IMT. The treated arterial hypertension was present in 25 patients (39.7%) and criteria for diabetes mellitus were met in 15 patients (23.8%). Twenty six (41.3%) patients admitted current or past cigarette smoking in the last five years. The positive family history of CVD was prevalent in 4.7% (3 respondents), hypertension at an early age (before 55 in males and before 60 in females) in 25% (16 patients). Two third of patients (40 respondents) did not comply with a diet containing predefined amounts of vegetables 14. According to the questionnaire, a sedentary life style (threshold defined as aerobic exercise 30 min 5 times a week) prevailed among the examined patients (n=43, 68.3%) (ref. 14). Use of alcohol beverages more than 20 mg per day or absolute abstinence was present in 6.3% respectively 42.9% (4 resp. 27 patients). The mean BMI was 24.79±5.1 (16.93-39.45), the waist circumference 84.95±14.1 cm (61-121 cm), hip circumference 99.11±11.9 cm (78-130 cm).

**Table 1.** Characteristic of group of 63 lupus patients and results of IMT (intima-media thickness) measurement and statistical evaluation by sig 2 tailed.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mean (SD) or %</th>
<th>Range</th>
<th>Correlation coefficient</th>
<th>Sig. (2-tailed)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients (n)</td>
<td>63</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Women (n, %)</td>
<td>53 (84.1)</td>
<td></td>
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<tr>
<td>Number of patients (n)</td>
<td>63</td>
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</tr>
<tr>
<td>Women (n, %)</td>
<td>53 (84.1)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>38.38±12.7</td>
<td>18-72</td>
<td>0.666</td>
<td>&gt; 0.001</td>
</tr>
<tr>
<td>Duration of SLE (months)</td>
<td>143.14±82.6</td>
<td>0-292</td>
<td>0.329</td>
<td>0.008</td>
</tr>
<tr>
<td>Age in diagnosis SLE (years)</td>
<td>28.04±12.0</td>
<td>9.7-60.9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension (n, %)</td>
<td>25 (39.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes (n, %)</td>
<td>15 (23.8)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking cigarette (n, %)**</td>
<td>26 (41.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Family history of CVD or hypertension in early age****</td>
<td>3.16 (4.7, 25.4)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Healthy food (n, %)</td>
<td>40 (66.7)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smoking cigarette (n, %)**</td>
<td>26 (41.3)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Using hydroxychlorochin, cumulative dose (g) (n=35, 55.5%)</td>
<td>387.09±632.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Using of ACEi (n, %)</td>
<td>31 (49.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Using of statins (n, %)</td>
<td>13 (20.6)</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Using of ACEi (n, %)</td>
<td>31 (49.2)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Using of statins (n, %)</td>
<td>13 (20.6)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SLICC/ACR/DI</td>
<td>1.17±1.4</td>
<td>0-5</td>
<td>0.093</td>
<td>NS</td>
</tr>
<tr>
<td>SLEDAI</td>
<td>7.22±5.4</td>
<td>0-20</td>
<td>0.027</td>
<td>NS</td>
</tr>
<tr>
<td>C3 (g/L)</td>
<td>0.99±0.3</td>
<td>0.42-1.62</td>
<td>0.100</td>
<td>NS</td>
</tr>
<tr>
<td>C4 (g/L)</td>
<td>0.15±0.1</td>
<td>0.05-0.49</td>
<td>0.223</td>
<td>NS</td>
</tr>
<tr>
<td>Anti ds DNA (UI/mL)</td>
<td>98.37±105.3</td>
<td>3-300</td>
<td>0.010</td>
<td>NS</td>
</tr>
<tr>
<td>ANUC (UI/mL)</td>
<td>124.54±79.5</td>
<td>13-300</td>
<td>-0.084</td>
<td>NS</td>
</tr>
<tr>
<td>Positivity ACLA IgG (n, %)</td>
<td>10 (15.9)</td>
<td>1-300</td>
<td>-0.187</td>
<td>NS</td>
</tr>
<tr>
<td>Positivity ACLA IgM (n, %)</td>
<td>7 (11.1)</td>
<td>1-101</td>
<td>-0.164</td>
<td>NS</td>
</tr>
<tr>
<td>LSR</td>
<td>1.4</td>
<td>0.38-4.64</td>
<td>-0.258</td>
<td>0.041</td>
</tr>
<tr>
<td>hsCRP g/L</td>
<td>5.14±6.2</td>
<td>0-27</td>
<td>0.092</td>
<td>NS</td>
</tr>
<tr>
<td>TC mmol/L</td>
<td>5.15±1.17</td>
<td>3.58-9.65</td>
<td>0.227</td>
<td>NS</td>
</tr>
<tr>
<td>TG mmol/L</td>
<td>1.72±1.0</td>
<td>0.49-5.16</td>
<td>0.088</td>
<td>NS</td>
</tr>
<tr>
<td>HDL mmol/L</td>
<td>1.38±0.4</td>
<td>0.75-2.91</td>
<td>0.114</td>
<td>NS</td>
</tr>
<tr>
<td>LDL mmol/L</td>
<td>3.02±1.1</td>
<td>1.28-7.18</td>
<td>0.158</td>
<td>NS</td>
</tr>
<tr>
<td>TC/HDL</td>
<td>3.97±1.2</td>
<td>1.92-6.6</td>
<td>0.075</td>
<td>NS</td>
</tr>
<tr>
<td>Apo lipoprotein A-1 (g/L)</td>
<td>1.50±0.4</td>
<td>0.77-2.85</td>
<td>0.059</td>
<td>NS</td>
</tr>
<tr>
<td>Apo lipoprotein B (g/L)</td>
<td>0.93±0.3</td>
<td>0.53-1.83</td>
<td>0.047</td>
<td>NS</td>
</tr>
<tr>
<td>Lipoprotein a (g/L)</td>
<td>0.39±0.5</td>
<td>0.03-1.76</td>
<td>0.113</td>
<td>NS</td>
</tr>
<tr>
<td>Creatinine (μmol/L)</td>
<td>71.32±20.5</td>
<td>41-133</td>
<td>0.321</td>
<td>0.010</td>
</tr>
<tr>
<td>Glomerular filtration rate (mL/s)</td>
<td>1.58±0.5</td>
<td>0.26-2.42</td>
<td>0.002</td>
<td></td>
</tr>
</tbody>
</table>

*Smoking - current smoker, ex-fumator in the last 5 years
** Positive family history - for first-stepwise relative in women over 65 years in men over 55 years
***Sedentary life style - aerobic exercise less than 30 min 5times a week
****Alcohol - abstainer / more than the recommended daily dose
Only three patients were glucocorticoids naïve. The rest of the patients (n=61, 97%) were taking glucocorticoids with a mean cumulative dose of 27.87±25.2 g Prednisone or its equivalent (0.24-132 g), mean daily dose was 14.90±18.9 mg (3.1-131.3), mean duration of therapy was 97.80±7.7 months (2-285). Some patients had been taking glucocorticoids before diagnosis of SLE; the dose was included in the calculation. Thirty five patients were current or past users of hydroxychlorochine or chlorochine (55.5%) with mean cumulative dose of 387.09±632.2 g (6-3765), mean daily dose was 205.69±64.8 mg (16-500 mg) in duration of 54.97±49.2 months (1-251). Thirty one patients (49.2%) were taking ACE inhibitors, 13 patients (20.6%) statins, 24 patients (38.1%) were on anticoagulation therapy with warfarin (n=16, 25.4%) or low molecular weight heparin (n=8, 12.7%) and 23 patients (36.5%) were taking antiaggregation therapy.

The mean SLICC/ACR damage index reached 1.17±1.4 (0-5) and disease activity assessed by SLEDAI was 7.22±5.4 (0-20).

Serum levels of C3 complement component was 0.99±0.3 g/L (0.42-1.62), C4 was 0.15±0.1 g/L (0.05-0.49). The mean concentration of anti-dsDNA antibodies was 98.37±105.3 IU/mL and of antinucleosomal antibodies 124.54±79.5 IU/mL. Twenty patients (31.75%) were negatively tested for anti-dsDNA Ab and nine patients (14.2%) were negative for antinucleosomal antibodies and ten patients were negative for both at the time of examination.

Anticardiolipin antibodies (ACLA) IgG were positive in 10 patients (15.9%), ACLA IgM in seven patients (11.1%); lupus anticoagulant (LSR) over 1.15 was present in 23 patients (36.5%). Positivity of ACLA and lupus anticoagulants was following: Positive ACLA IgG plus positive LSR was present in eight respondents (12.7%), positive ACLA IgM plus positive LSR in four patients (6.3%), and finally three patients expressed ACLA IgM, IgG plus LSR (4.8%).

The mean serum levels of high sensitivity C-reactive protein upon exclusion of infection were 5.14±6.2 mg/L (0.3-27). The lipid profile was as follows: total cholesterol was 5.15±1.2 mmol/L (3.58-9.65), triglycerides 1.72±1.0 mmol/L (0.49-5.16), HDL 1.38±0.4 mmol/L (0.75-2.91), LDL 3.02±1.0 mmol/L (0.49-5.16), CH/HDL ration 3.97±1.2 (1.92-6.72), serum levels of apolipoprotein A-1 were 1.50±0.4 g/L (0.77-2.85 g/L), apolipoprotein B 0.93±0.3 g/L (0.53-1.83 g/L) and lipoprotein (a) 0.39±0.5 g/L (0.03-1.76).

Mean levels of serum creatinine were 71.32±20.5 μmol/L (41-133) and glomerular filtration (calculation by Modification of Diet in Renal Disease – MDRD) 1.58±0.47 mL/s (0.26-2.42).

All patients underwent ultrasound examination by high sensitivity B-mode scan IMT. The mean value of IMT on left side was 0.579±0.12 mm (0.38-1.02 mm), on right side 0.561±0.10 mm (0.39-0.95) and the calculated mean was 0.569±0.11 mm (0.39-0.95). Healthy controls had IMT on left side 0.502±0.06 mm (0.41-0.65 mm), on right side 0.489±0.05 mm (0.418-0.602 mm) and mean was 0.495±0.049 mm (0.414-0.627 mm). We prefer distribution to groups with absolute number of IMT, plaques was not detected.

Lupus nephritis defined by histology was present in 24 (38.1%) patients in our group. None of the patients had minimal mesangial lupus nephritis (Class I) or sclerotizing nephritis (Class VI), while Class II (mesangial proliferative lupus nephritis) was present in 6.3%; focal segmental lupus nephritis (Class III) in 17.5%, diffuse proliferative lupus nephritis (Class IV) was detected in 7.9% and membranous lupus nephritis (Class V) in 4.8% (ref.1). In two patients the clinical manifestation of lupus nephritis with nephrotic syndrome was present but biopsy was contraindicated by clinicians. The IMT in group of patients with LN on left side was 0.548±0.052 mm (0.43-0.67 mm), on right side 0.538±0.059 mm (0.44-0.664 mm); mean was 0.538±0.054 mm (0.46-0.67 mm). IMT in all patients without LN was measured within 0.38 mm to 1.02 mm on left side with a mean of 0.60±0.15 mm and from 0.34 to 0.91 mm on the right side with a mean of 0.578±0.12 mm, and calculated mean of both sides was 0.589±0.13 mm (0.37-0.945). After adjustment for age, the IMT of lupus nephritis patients was 0.529±0.07 mm (0.38-0.73) on left, 0.518±0.07 mm (0.39-0.66) on right and calculated mean was 0.524±0.07 mm (0.387-0.661).

**CONCLUSION**

The IMT values differed significantly between the lupus patients and healthy controls using a t-test, Ps0.03 (Fig. 1). No significant difference was found between patients with and without lupus nephritis (Fig. 2).
Fig. 2. Correlation of IMT (mm) in age-matched 23 patient with lupus nephritis, 23 patient without lupus nephritis and 24 healthy control respondens.

Fig. 3. Correlation of IMT (mm) and waist circumference (cm) in a group of 63 lupus patients.

Fig. 4. Correlation of IMT (mm) and glomerular filtration in a group of 63 lupus patients.

Fig. 5. Significant different of IMT ($P=0.003$) between patients treated with ACEi (n=31, 49.2%) and without ACEi medication (n=32, 50.8%).

The IMT correlated positively and significantly with age ($P<0.001$), duration of disease ($P=0.008$), with BMI ($P=0.014$), waist and hip circumference ($P<0.001$ reps. $P=0.014$, Fig. 3) and with decrease of renal function impacting the serum creatinine ($P=0.01$) or glomerular filtration rate calculated by MDRD ($P=0.02$, Fig. 4). The medication of ACEi showed a negative correlation to the IMT index ($P=0.056-0.07$), however none of these factors met statistical significance at $P=0.05$.

DISCUSSION

Advances in the diagnosis and treatment of systemic lupus erythematosus (SLE) in the last fifty years has enabled patients to survive to the late phases of disease, which are characterized by different pattern of manifestation than the early disease with increase in cardiovascular diseases, infections, tumors and osteoporosis. The presence of AT associated with SLE seems to be even higher than in diabetes mellitus approaching the rate of Cushing’s syndrome and sharing comparable risk with other high risk disease like renal insufficiency, familiar hyperlipoproteinemia or states after organ transplantation.

The pathogenesis of atherosclerosis in SLE is complex. Atherosclerosis often presents even before the 40th year of age, commonly with angina, myocardial infarction.
or sudden death. The ATS in SLE can be confirmed by histology up in 54% of cases\textsuperscript{40}. Relative risk of accelerated atherosclerosis is 8.1 in young females with SLE, the risk is up to 50 times greater than in an age adjusted healthy population\textsuperscript{21}. Autoimmune systemic diseases are characterized by a broad spectrum of clinical manifestations, by variable course and are associated with a spectrum of laboratory abnormalities, some of which can be used for diagnosis, assessment of organ involvement; follow up of disease activity or for prognosis. The research of parameters related to increased risk of ATS and its relation to the disease activity and other clinical manifestations could be of the great importance for the management of the early phases of atherosclerosis development in SLE and could assist in widening the time frame for early intervention. In other rheumatic diseases too, cardiovascular mortality and morbidity are significantly higher than in the general population. The relative risk for rheumatoid arthritis is 1.28-3.0, for ankylosing spondylitis 1.5-1.93 (ref.\textsuperscript{22,23}). In aggressive types of psoriatic arthritis with early joint damage, the cardiovascular risk is associated especially closely with high activity of inflammatory processes, disease duration and early radiographic lesions\textsuperscript{24}. Dysfunction of endothelium and micro- and macrovascular damage also leads to accelerated atherosclerotic process in systemic sclerosis with involvement of anti-endothelial antibodies and adhesive molecules like ICAM-1 (intercellular adhesion molecule 1) (ref.\textsuperscript{25}). The presence of anti-SSA/Ro antibodies and dyslipoproteinemia with low levels and dysfunction of HDL is related to AT in Sjögren’s syndrome\textsuperscript{26}. The endothelial dysfunction seen in primary vasculitis is very close to the dysfunction in atherosclerosis and this aside, dyslipoproteinemia, activation of macrophages and ANCA antibodies also play a major role\textsuperscript{27}.

This study has shown the very high prevalence of common atherosclerotic risk factors such as smoking, obesity, hypertension, diet, diabetes and sedentary life style in the studied group of lupus patients, confirming findings of other authors describing higher rates in SLE than in a general aged matched population. The metabolic syndrome manifested in 28 (44%) of patients\textsuperscript{28}. While a review of several epidemiological studies showed the distribution of metabolic syndrome in the general population to be 1.2-60%, comparable with the 40% prevalence among SLE patients, a Chinese study presented the prevalence of metabolic syndrome in 16.3% of 123 lupus patients in comparison with 9.6% in control age- and sex matched group (odds ratio 3.11) (ref.\textsuperscript{29,30}). The presence of metabolic syndrome had more often higher carotid IMT and higher Agatston calcium score as detected in coronary arteries by computed tomography scan, higher levels of hsCRP and homocysteine\textsuperscript{31}. In another study on 162 lupus females, the prevalence of metabolic syndrome was 32.1% and was associated with negative course of disease with increased proteinuria, higher modified SLEDAI-2k activity score, worse damage index score (SLICC/ACR), and were more often treated with cyclophosphamide\textsuperscript{32}.

A large number of studies report a high prevalence of hypertension in SLE patients; in some cohorts in up in 74% of those aged between 18-74 years of age, the prevalence is 36.3%, while among young healthy women between 20 and 44 years of age it is 2.7 to 14% only\textsuperscript{33,34}.

In Volkman’s study, a sedentary lifestyle was associated with higher IMT and the presence of atherosclerotic plaques, with proinflammatory HDL, representing a crucial disharmony in protective mechanisms\textsuperscript{35}.

The presence of preclinical atherosclerosis could be measured by several methods including invasive examinations such as coronarography, highly specific and sensitive, but unsuitable for prevention trials. The analysis of arterial stiffness, ankle-brachial index, exercise treadmill testing, segmental limb pressures, segmental volume plethysmography, magnetic resonance imaging, computer tomography or duplex ultrasonography could be used as non-invasive methods for determining AT (ref.\textsuperscript{13,36}). The advantage of ultrasound is the non-invasivity and simplicity and the fact that the method has been validated in several studies in different populations. Our study showed that the IMT index is significantly higher in patients with SLE in comparison to healthy age- and sex- matched controls and correlates with age, duration of the disease, body mass index as well as with waist and hip circumference showing a pattern similar to atherosclerosis unrelated to SLE. A similar pattern of distribution was also apparent in a meta-analysis of 68 relevant studies of carotid intima media thickness in rheumatic disease and also in a population of SLE patients\textsuperscript{37}. In some studies, significant correlation with cardiovascular event and risk factors with plaques, more plaques over time, minimal in two years\textsuperscript{38,39}. This is our secondary plan in future.

This study showed no significant correlation to classical parameters of SLE activity such as SLEDAI index, levels of C3, C4 components of complement, anti-dsDNA or antinucleosome antibodies, or to parameters of lipid metabolism, which could be explained by the heterogeneity of the lupus patients and by the influence of concomitant treatments (glucocorticoids, hydroxychlorochine, ACEi, statins, anticoagulation and antiaggregation therapies used). It seems to be virtually impossible to constitute a group of probands with lupus with significant duration of the disease free of these factors.

The role of the glucocorticoids in the pathogenesis of atherosclerosis is controversial\textsuperscript{40}. This study found no significant relation of the prednisone cumulative dose and IMT index. Some other studies have even demonstrated a protective effect of glucocorticoid use on intimal wall in SLE with strong additive affect if combined with hydroxychlorochine\textsuperscript{41}. Studies in rheumatoid arthritis have not shown any negative effect of therapy on the metabolic syndrome, confirming that glucocorticoids can improve glucose intolerance and dyslipoproteinemia in patients with chronic inflammatory diseases\textsuperscript{42}.

ACE inhibitors have significant influence on deceleration of the atherosclerosis process in the general population as well as in SLE patients. In this study the use of ACEi correlated negatively with the IMT which indicates the possible protective role of these drugs for atherosclerosis.

In the Thompson study, progression of intimal thickness was associated with poor renal function, lower serum
Arthritis 45. IMT measurement could be used as one of the risk adopting similar recommendation as for rheumatoid also include measurement to decrease the cardiovascular systematic intervention. Care for lupus patients should evaluation of risk factors and the importance of early and necessity of awareness of atherosclerosis in SLE and active sclerosis which also correlated with other risk factors of a very complex process. The study showed the role of lupus anticoagulant was associated with significantly higher IMt indicating the importance of the antiphospholipid syndrome and maybe particularly of lupus anticoagulant in the development of atherosclerosis. Cardiovascular events in patients with positivity of lupus anticoagulants are more common with an odds ratio of 5.3 for IM and even 43.1 for ischemic stroke. Combination of this risk factor with smoking elevated this odds ratio to 33.7, respectively to 87 according to this odds ratio to 33.7, respectively to 87 according to Urbanus 44. Accelerated atherosclerosis in patients with SLE is a very complex process. The study showed the role of measurement of IMt as the parameter of early atherosclerosis which also correlated with other risk factors of accelerated atherosclerosis. The study highlights the necessity of awareness of atherosclerosis in SLE and active evaluation of risk factors and the importance of early and systematic intervention. Care for lupus patients should also include measurement to decrease the cardiovascular risk adopting similar recommendation as for rheumatoid arthritis 45. IMT measurement could be used as one of the clinical predictors of risk of accelerated atherosclerosis in lupus patients. 

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