

## Arterial stiffness and peripheral arterial disease in patients with systemic lupus erythematosus

Konstantinos Tziomalos<sup>1</sup>  · Ioannis Gkougkourelas<sup>2</sup> · Alexandros Sarantopoulos<sup>2</sup> · Eleni Bekiari<sup>2</sup> · Evangelia Makri<sup>1</sup> · Nikolaos Raptis<sup>1</sup> · Konstantinos Tselios<sup>2</sup> · Marianna Pantoura<sup>2</sup> · Apostolos I. Hatzitolios<sup>1</sup> · Panagiota Boura<sup>2</sup>

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**Abstract** Systemic lupus erythematosus (SLE) is associated with increased cardiovascular risk. We aimed to evaluate arterial stiffness and the ankle brachial index (ABI), two markers of subclinical cardiovascular disease, in SLE. We studied 55 patients with SLE (12.7% males, age  $53.3 \pm 15.3$  years) and 61 age- and gender-matched controls. Arterial stiffness was evaluated by measuring pulse wave velocity (PWV), augmentation index (AIx) and central systolic, diastolic, pulse and mean blood pressure (BP). Peripheral arterial disease was defined as  $ABI \leq 0.90$ . Regarding markers of arterial stiffness, patients with SLE had lower PWV and AIx than controls ( $p < 0.01$  and  $p < 0.05$ , respectively). However, after adjusting for differences in cardiovascular risk factors between patients with SLE and controls, PWV and AIx did not differ between the two groups. Central systolic, diastolic, pulse and mean BP also did not differ between the two groups. In patients with SLE, PWV correlated independently with systolic BP ( $B = 0.05$ ,  $p < 0.001$ ) and waist/hip ratio ( $B = 6.72$ ,  $p < 0.05$ ). Regarding ABI, the lowest ABI was lower in patients with SLE than in controls ( $p < 0.005$ ). However, after adjusting for differences in cardiovascular risk factors between patients with SLE and controls, the lowest ABI did not differ between the two groups. The prevalence of PAD also did not differ between patients with SLE and controls

(10.0 and 5.4%, respectively;  $p = \text{NS}$ ). Markers of arterial stiffness and the ABI do not appear to differ between patients with SLE and age- and gender-matched controls. However, given the small sample size, larger studies are needed to clarify whether SLE promotes arterial stiffness and PAD.

**Keywords** Systemic lupus erythematosus · Arterial stiffness · Peripheral arterial disease · Ankle brachial index · Pulse wave velocity · Augmentation index

### Introduction

Systemic lupus erythematosus (SLE) is one of the commonest connective tissue diseases [1, 2]. In recent decades, cardiovascular disease (CVD) has emerged as a leading cause of morbidity and mortality in SLE [1, 3]. Several studies showed that patients with SLE are at higher risk of cardiovascular events than the general population [4, 5]. Both traditional cardiovascular risk factors and disease-related factors appear to contribute to the increased incidence of CVD in SLE [1, 6]. Indeed, hypertension, smoking, type 2 diabetes mellitus (T2DM) and atherogenic dyslipidemia (i.e., the combination of high-density lipoprotein cholesterol (HDL-C) levels, elevated triglyceride (TG) levels and small-dense low-density lipoprotein cholesterol (LDL-C) particles) are more prevalent in patients with SLE [7–9]. Moreover, subclinical inflammation and oxidative stress are more pronounced in SLE and also play a role in the pathogenesis of CVD [8, 10].

Given the elevated cardiovascular risk in patients with SLE, several markers of subclinical CVD have been evaluated in this population, aiming at improving cardiovascular risk stratification and preventing cardiovascular events [6].

✉ Konstantinos Tziomalos  
ktziomalos@yahoo.com

<sup>1</sup> First Propedeutic Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, AHEPA Hospital, 1 Stilponos Kyriakidi Street, 54636 Thessaloniki, Greece

<sup>2</sup> Clinical Immunology Unit, Second Department of Internal Medicine, Medical School, Aristotle University of Thessaloniki, Hippokraton Hospital, Thessaloniki, Greece

One of these markers is arterial stiffness, which is associated with increased cardiovascular risk in the general population [11, 12]. In patients with SLE, arterial stiffness is associated with left ventricular dysfunction [13, 14], left ventricular hypertrophy [14, 15] and carotid atherosclerosis [16]. Pulse wave velocity (PWV), the gold-standard for evaluating arterial stiffness, has been assessed in a number of studies in patients with SLE [17–20]. However, most of these reports included selected patients with SLE (i.e., without cardiovascular risk factors) and did not adjust for differences in established and emerging cardiovascular risk factors between patients with SLE and controls [17–20]. Moreover, there is a paucity of data on other markers of arterial stiffness, including augmentation index (AIx) and central blood pressure (BP), in patients with SLE [17, 21]. Another noninvasive marker of subclinical CVD is the ankle brachial index, which is a sensitive and specific method for diagnosing peripheral arterial disease (PAD) and predicts cardiovascular events in the general population [22–24]. However, there are very limited data on the prevalence and determinants of abnormal ABI in patients with SLE [25–28]. Four previous studies evaluated the ABI in this population, but three of them did not include a control population [26–28], and the only controlled study applied a cutoff ABI value of 1.00 to identify PAD [25] instead of the recommended cutoff of 0.90 [22].

The aim of the present study was to compare markers of arterial stiffness and the ABI between patients with SLE and healthy controls and to identify the major determinants of arterial stiffness and ABI in SLE.

## Patients and methods

We studied consecutive patients with SLE who attended a regular follow-up visit at the Clinical Immunology Unit of the Second Department of Internal Medicine, at Hippokratia Hospital, Thessaloniki, Greece, between April of 2013 and March of 2015. We then studied consecutive age- and gender-matched controls who visited for routine checkups the Internal Medicine Outpatient Clinic of the First Propedeutic Department of Internal Medicine, at AHEPA Hospital, Thessaloniki, Greece, between October and December of 2015. Patients and controls with cancer or chronic inflammatory diseases were excluded from the study.

In all subjects, demographic data (age, sex), history of cardiovascular risk factors [hypertension, type 2 diabetes mellitus, atrial fibrillation, smoking, alcohol consumption and family history of CVD] and history of concomitant CVD (coronary heart disease, ischemic stroke) were recorded. Anthropometric parameters (weight, height, waist and hip circumference) and systolic and diastolic BP were also measured. The body mass index (BMI) was calculated

by dividing the weight (in kilograms) by the square of the height (in meters), and the waist/hip ratio (WHR) was calculated by dividing the waist circumference by the hip circumference.

Laboratory investigations were performed after overnight fasting and included full blood count, erythrocyte sedimentation rate (ESR), plasma levels of fibrinogen and serum levels of glucose, total cholesterol, HDL-C, TG, creatinine, uric acid and C-reactive protein levels. LDL-C levels were calculated using Friedewald's formula [29]. Glomerular filtration rate (GFR) was estimated using the Modification of Diet in Renal Disease (MDRD) equation [30]. Chronic kidney disease was defined as estimated GFR (eGFR) <60 ml/min/1.73 m<sup>2</sup>. Serum levels of antinuclear antibodies and related epitopes, antibodies against double-stranded DNA and anti-Scl-70 antibodies were measured only in patients with SLE.

The following markers of arterial stiffness were recorded with the SphygmoCor device (Atcor Medical, Sydney, Australia): PWV, AIx, central systolic BP, central diastolic BP, central pulse pressure and central mean pressure. All measurements were taken in the morning, in supine position, at the right side, after at least 10 min of rest and after fasting for at least 4 h [31]. The ABI was measured according to current guidelines immediately after the evaluation of arterial stiffness [22]. The ABI was measured in both legs, and the lowest ABI was used in the statistical analyses. Peripheral arterial disease was defined as ABI ≤ 0.90 in either leg [22].

## Statistical analysis

Data are presented as percentages for categorical variables and as mean and standard deviation for continuous variables. Differences in categorical and continuous variables between groups were assessed with the Chi-square test and the independent samples *t* test, respectively. Correlations between parameters were assessed with Pearson's correlation. Linear logistic regression analysis was used to identify independent correlations between clinical/laboratory characteristics and markers of arterial stiffness/ABI. Linear logistic regression analysis was also used to identify whether markers of arterial stiffness and the ABI differed between patients with SLE and controls after adjusting for differences between the two groups in other clinical and laboratory characteristics. In all cases, a two-tailed *p* < 0.05 was considered significant. All data were analyzed with the statistical package SPSS (version 17.0; SPSS, Chicago, IL, USA).

## Results

We studied 55 consecutive patients with SLE (12.7% males, age 53.3 ± 15.3 years) and 61 age- and gender-matched

**Table 1** Clinical characteristics of patients with systemic lupus erythematosus (SLE) and controls

	Patients with SLE ( <i>n</i> = 55)	Controls ( <i>n</i> = 61)	<i>p</i>
Age (years)	53.3 ± 15.3	55.4 ± 8.1	NS
Males [ <i>n</i> (%)]	7 (12.7)	5 (8.2)	NS
Systolic blood pressure (mmHg)	127 ± 19	121 ± 14	NS
Diastolic blood pressure (mmHg)	75 ± 10	72 ± 9	NS
Body mass index (kg/m <sup>2</sup> )	27.0 ± 6.3	27.2 ± 4.4	NS
Waist (cm)	90 ± 17	100 ± 10	<0.001
Waist/hip ratio	0.88 ± 0.08	0.96 ± 0.06	<0.001
Hypertension [ <i>n</i> (%)]	18 (32.7)	18 (29.5)	NS
Type 2 diabetes mellitus [ <i>n</i> (%)]	4 (7.3)	1 (1.6)	NS
Duration of type 2 diabetes mellitus (years)	15.2 ± 14.5	2 ± 0	NS
Smoking [current/past, <i>n</i> (%)]	17 (30.9)/10 (18.2)	25 (41.0)/7 (11.5)	NS
Package-years	20 ± 18	24 ± 35	NS
Alcohol (units/week)	2.3 ± 2.0	0.4 ± 1.3	<0.01
Atrial fibrillation [ <i>n</i> (%)]	2 (3.6)	0 (0.0)	NS
Family history of cardiovascular disease [ <i>n</i> (%)]	1 (1.8)	3 (4.9)	NS
Coronary heart disease [ <i>n</i> (%)]	2 (3.6)	0 (0.0)	NS
Ischemic stroke [ <i>n</i> (%)]	3 (5.5)	3 (4.9)	NS
Family history of cardiovascular disease [ <i>n</i> (%)]	1 (1.8)	3 (4.9)	NS
Chronic kidney disease [ <i>n</i> (%)]	11 (20.4)	4 (6.7)	NS
Overweight/obese [ <i>n</i> (%)]	26 (47.3)/15 (27.3)	19 (31.1)/30 (49.2)	NS

All values are expressed as mean ± SD unless otherwise specified

**Table 2** Laboratory characteristics of patients with systemic lupus erythematosus (SLE) and controls

	Patients with SLE ( <i>n</i> = 55)	Controls ( <i>n</i> = 61)	<i>p</i>
White blood cell (/μl)	7052 ± 3021	7067 ± 2278	NS
Hemoglobin (g/dl)	12.8 ± 1.5	12.9 ± 1.7	NS
Platelets (/μl)	236,310 ± 77,358	252,590 ± 101,532	NS
Glucose (mg/dl)	92 ± 16	92 ± 16	NS
LDL cholesterol (mg/dl)	116 ± 39	115 ± 41	NS
HDL cholesterol (mg/dl)	57 ± 14	60 ± 16	NS
Triglycerides (mg/dl)	120 ± 50	95 ± 37	<0.05
Uric acid (mg/dl)	4.2 ± 1.4	3.9 ± 0.9	NS
Estimated GFR (ml/min/1.73 m <sup>2</sup> )	80 ± 22	92 ± 23	<0.05
Erythrocyte sedimentation rate (mm/h)	24.0 ± 18.4	16.9 ± 7.9	<0.05
C-reactive protein (mg/dl)	3.5 ± 8.8	5.3 ± 7.0	NS
Fibrinogen (mg/dl)	350 ± 91	270 ± 65	< 0.05

All values are expressed as mean ± SD

LDL low-density lipoprotein, HDL high-density lipoprotein, GFR glomerular filtration rate

controls (8.2% males, age 55.4 ± 8.1 years). No patient or control refused to participate in the study. Clinical and laboratory characteristics of patients with SLE and controls are shown in Tables 1 and 2. Patients with SLE had smaller waist circumference and WHR than controls (<0.001 for both comparisons). On the other hand, patients with SLE reported higher alcohol intake (*p* < 0.01) and had higher serum TG levels, lower eGFR, higher plasma fibrinogen levels and higher ESR than controls (*p* < 0.05 for all

comparisons). Other clinical and laboratory characteristics did not differ between patients with SLE and controls.

Markers of arterial stiffness in patients with SLE and controls are shown in Table 3. Patients with SLE had lower PWV than controls (*p* < 0.01). The AIx was also lower in patients with SLE (*p* < 0.05). However, after adjusting for differences in waist circumference, WHR, alcohol consumption, TG and fibrinogen levels, eGFR and ESR between patients with SLE and controls, PWV and AIx did

**Table 3** Markers of arterial stiffness and ankle brachial index in patients with systemic lupus erythematosus (SLE) and controls

	Patients with SLE ( <i>n</i> = 55)	Controls ( <i>n</i> = 61)	<i>p</i>
Pulse wave velocity (m/s)	6.3 ± 1.8	7.3 ± 1.8	<0.01
Augmentation index (%)	28.7 ± 12.2	32.8 ± 8.8	<0.05
Central systolic blood pressure (mmHg)	112 ± 19	113 ± 14	NS
Central diastolic blood pressure (mmHg)	73 ± 11	74 ± 9	NS
Central mean blood pressure (mmHg)	89 ± 14	91 ± 10	NS
Central pulse pressure (mmHg)	38 ± 15	39 ± 11	NS
Ankle brachial index	1.04 ± 0.09	1.10 ± 0.13	<0.005

All values are expressed as mean ± SD

not differ between the two groups ( $B = 0.542$ ,  $p = 0.107$  and  $B = 0.446$ ,  $p = 0.319$ , respectively). Central systolic, diastolic, pulse and mean BP did not differ between patients with SLE and controls in both univariate and multivariate analyses.

In patients with SLE, PWV correlated with age ( $r = 0.557$ ,  $p < 0.001$ ), systolic BP ( $r = 0.581$ ,  $p < 0.001$ ), diastolic BP ( $r = 0.502$ ,  $p < 0.001$ ), waist circumference ( $r = 0.467$ ,  $p < 0.001$ ), WHR ( $r = 0.417$ ,  $p < 0.005$ ), BMI ( $r = 0.381$ ,  $p < 0.01$ ), hemoglobin ( $r = 0.369$ ,  $p < 0.01$ ), fibrinogen levels ( $r = 0.328$ ,  $p < 0.05$ ) and eGFR ( $r = -0.402$ ,  $p < 0.005$ ). In linear logistic regression analysis, PWV correlated independently with systolic BP ( $B = 0.05$ ,  $p < 0.001$ ) and WHR ( $B = 6.72$ ,  $p < 0.05$ ).

The lowest ABI among the two legs was lower in patients with SLE than in controls ( $p < 0.005$ ; Table 3). However, after adjusting for differences in waist circumference, WHR, alcohol consumption, TG and fibrinogen levels, eGFR and ESR between patients with SLE and controls, the lowest ABI did not differ between patients with SLE and controls ( $B = -0.249$ ,  $p = 0.479$ ). The prevalence of PAD also did not differ between patients with SLE and controls (10.0 and 5.4%, respectively;  $p = \text{NS}$ ). In patients with SLE, the ABI did not correlate with any clinical or laboratory parameter.

## Discussion

The main finding of the present study is that markers of arterial stiffness and the ABI do not differ between patients with SLE and age- and gender-matched controls. However, given the small number of patients and controls, larger studies are needed to confirm or refute these findings. On the other hand, in patients with SLE, the main determinants of arterial stiffness are systolic BP and WHR.

Pulse wave velocity did not differ between patients with SLE and controls in our study. In contrast, previous studies reported higher PWV in patients with SLE than in age-matched controls [17–20]. However, most of the former

studies excluded patients with cardiovascular risk factors, introducing selection bias in their results [18–20]. In addition, most studies reported only unadjusted comparisons of PWV between patients with SLE and controls [18–20]. In our study, PWV was lower in patients with SLE than in controls, but this difference became nonsignificant when adjustment for differences in obesity, renal function, obesity and markers of inflammation was performed. Moreover, WHR, which emerged as an independent predictor of PWV in our population, was not evaluated in any of the studies that evaluated PWV in patients with SLE [17–20]; therefore, differences in WHR between patients with SLE and controls might have affected the findings of these reports. On the other hand, the lack of association between SLE and PWE in our study might be due to the small sample size and the low statistical power of adjusted analyses to identify differences.

In the present study, other markers of arterial stiffness besides PWV, i.e., AIx and central systolic BP, diastolic BP, pulse pressure and mean BP, did not differ between patients with SLE and controls. To the best of our knowledge, only one early study evaluated AIx and central systolic BP, diastolic BP and pulse pressure in 27 patients with SLE and 27 age-matched controls and did not identify any differences between the two groups [17]. In a more recent study in 30 patients with SLE and 66 age-matched controls, the AIx was also similar in the two groups [21]. The lack of difference in these markers of arterial stiffness between patients with SLE and controls in these smaller studies further supports our findings that arterial stiffness is comparable in patients with SLE and controls when differences in cardiovascular risk factors between the two groups are accounted for. However, the small sample size of the present study also suggests the possibility of a type II statistical error in the comparison of markers of arterial stiffness between patients with SLE and controls.

In the present study, the only independent predictors of PWV in patients with SLE were systolic BP and the WHR. Previous studies also reported a correlation between PWV and systolic BP [19, 20, 32]. In the general population, BP

is also a major determinant of arterial stiffness [33]. In contrast, the association between WHR and arterial stiffness has not been evaluated before in patients with SLE. In the general population, the WHR is more strongly associated with both arterial stiffness and cardiovascular risk than BMI [34, 35]. Our findings suggest that WHR, an easily measured and inexpensive marker of abdominal obesity, is also closely related to increased arterial stiffness in patients with SLE.

In our study, the ABI and the prevalence of PAD did not differ between patients with SLE and controls. Nevertheless, the large numerical difference in the prevalence of PAD between the two groups (10.0 and 5.4%, respectively) again suggests that our study had limited power to identify significant differences between patients with SLE and controls. Only one previous study compared the ABI between patients with SLE and controls and also did not identify any difference in the prevalence of PAD between the two groups [25]. Given this paucity of data on the association between SLE and PAD and the increased cardiovascular risk of both diseases, it is clear that more research is needed to clarify whether SLE increases the risk of PAD. In previous uncontrolled studies in patients with SLE, the major determinants of abnormal ABI were age and smoking [26–28]. In the present study, we did not identify any correlations between ABI and clinical or laboratory parameters, potentially due to the low prevalence of PAD and the narrow range of ABI values.

In conclusion, markers of arterial stiffness and the ABI do not appear to differ between patients with SLE and age- and gender-matched controls. However, the small size of our population suggests that our results are inconclusive rather than negative and that larger studies are needed to confirm or refute them. Systolic BP and the WHR, two easily obtained and inexpensive clinical parameters, are the most important determinants of PWV in patients with SLE. Therefore, they could be useful as indirect markers of arterial stiffness in settings where dedicated devices for measurement of arterial stiffness are not available.

#### Compliance with ethical standards

**Conflict of interest** All authors declare that they have no conflict of interest.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

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## References

1. D’Cruz DP, Khamashta MA, Hughes GR (2007) Systemic lupus erythematosus. *Lancet* 369:587–596
2. Danchenko N, Satia JA, Anthony MS (2006) Epidemiology of systemic lupus erythematosus: a comparison of worldwide disease burden. *Lupus* 15:308–318
3. Nossent J, Cikes N, Kiss E, Marchesoni A, Nasonova V, Mosca M, Olesinska M, Pokorny G, Rozman B, Schneider M, Vlachoyiannopoulos PG, Swaak A (2007) Current causes of death in systemic lupus erythematosus in Europe, 2000–2004: relation to disease activity and damage accrual. *Lupus* 16:309–317
4. Ward MM (1999) Premature morbidity from cardiovascular and cerebrovascular diseases in women with systemic lupus erythematosus. *Arthritis Rheum* 42:338–346
5. Fischer LM, Schlienger RG, Matter C, Jick H, Meier CR (2004) Effect of rheumatoid arthritis or systemic lupus erythematosus on the risk of first-time acute myocardial infarction. *Am J Cardiol* 93:198–200
6. Tziomalos K, Sivanadarajah N, Mikhailidis DP, Boumpas DT, Seifalian AM (2008) Increased risk of vascular events in systemic lupus erythematosus: is arterial stiffness a predictor of vascular risk? *Clin Exp Rheumatol* 26:1134–1145
7. Asanuma Y, Oeser A, Shintani AK, Turner E, Olsen N, Fazio S, Linton MF, Raggi P, Stein CM (2003) Premature coronary-artery atherosclerosis in systemic lupus erythematosus. *N Engl J Med* 349:2407–2415
8. Nuttall SL, Heaton S, Piper MK, Martin U, Gordon C (2003) Cardiovascular risk in systemic lupus erythematosus—evidence of increased oxidative stress and dyslipidaemia. *Rheumatology (Oxford)* 42:758–762
9. El Magadmi M, Ahmad Y, Turkie W, Yates AP, Sheikh N, Bernstein RM, Durrington PN, Laing I, Bruce IN (2006) Hyperinsulinemia, insulin resistance, and circulating oxidized low density lipoprotein in women with systemic lupus erythematosus. *J Rheumatol* 33:50–56
10. De Leeuw K, Freire B, Smit AJ, Bootsma H, Kallenberg CG, Bijl M (2006) Traditional and non-traditional risk factors contribute to the development of accelerated atherosclerosis in patients with systemic lupus erythematosus. *Lupus* 15:675–682
11. Vlachopoulos C, Aznaouridis K, O’Rourke MF, Safar ME, Baou K, Stefanadis C (2010) Prediction of cardiovascular events and all-cause mortality with central haemodynamics: a systematic review and meta-analysis. *Eur Heart J* 31:1865–1871
12. Vlachopoulos C, Aznaouridis K, Stefanadis C (2010) Prediction of cardiovascular events and all-cause mortality with arterial stiffness: a systematic review and meta-analysis. *J Am Coll Cardiol* 55:1318–1327
13. Yip GW, Shang Q, Tam LS, Zhang Q, Li EK, Fung JW, Yu CM (2009) Disease chronicity and activity predict subclinical left ventricular systolic dysfunction in patients with systemic lupus erythematosus. *Heart* 95:980–987
14. Roldan CA, Alomari IB, Awad K, Boyer NM, Qualls CR, Greene ER, Sibbitt WL Jr (2014) Aortic stiffness is associated with left ventricular diastolic dysfunction in systemic lupus erythematosus: a controlled transesophageal echocardiographic study. *Clin Cardiol* 37:83–90
15. Pieretti J, Roman MJ, Devereux RB, Lockshin MD, Crow MK, Paget SA, Schwartz JE, Sammaritano L, Levine DM, Salmon JE (2007) Systemic lupus erythematosus predicts increased left ventricular mass. *Circulation* 116:419–426
16. Selzer F, Sutton-Tyrrell K, Fitzgerald S, Tracy R, Kuller L, Manzi S (2001) Vascular stiffness in women with systemic lupus erythematosus. *Hypertension* 37:1075–1082

17. Bjarnegråd N, Bengtsson C, Brodzki J, Sturfelt G, Nived O, Länne T (2006) Increased aortic pulse wave velocity in middle aged women with systemic lupus erythematosus. *Lupus* 15:644–650
18. Morreale M, Mulè G, Ferrante A, D'ignoto F, Cottone S (2016) Early vascular aging in normotensive patients with systemic lupus erythematosus: comparison with young patients having hypertension. *Angiology* 67:676–682
19. Sabio JM, Vargas-Hitos JA, Martínez-Bordonado J, Navarrete-Navarrete N, Díaz-Chamorro A, Olvera-Porcel C, Zamora M, Jiménez-Alonso J (2015) Association between low 25-hydroxyvitamin D, insulin resistance and arterial stiffness in nondiabetic women with systemic lupus erythematosus. *Lupus* 24:155–163
20. Sacre K, Escoubet B, Pasquet B, Chauveheid MP, Zennaro MC, Tubach F, Papo T (2014) Increased arterial stiffness in systemic lupus erythematosus (SLE) patients at low risk for cardiovascular disease: a cross-sectional controlled study. *PLoS ONE* 9:e94511
21. Cypiene A, Kovaite M, Venalis A, Dadoniene J, Ruziene R, Petruilioniene Z, Ryliskyte L, Laucevicius A (2009) Arterial wall dysfunction in systemic lupus erythematosus. *Lupus* 18:522–529
22. Aboyans V, Criqui MH, Abraham P, Allison MA, Creager MA, Diehm C, Fowkes FG, Hiatt WR, Jönsson B, Lacroix P, Marin B, McDermott MM, Norgren L, Pande RL, Preux PM, Stoffers HE, Treat-Jacobson D, American Heart Association Council on Peripheral Vascular Disease, Council on Epidemiology and Prevention, Council on Clinical Cardiology, Council on Cardiovascular Nursing, Council on Cardiovascular Radiology and Intervention, and Council on Cardiovascular Surgery and Anesthesia (2012) Measurement and interpretation of the ankle-brachial index: a scientific statement from the American Heart Association. *Circulation* 126:2890–2909
23. Collaboration Ankle Brachial Index, Fowkes FG, Murray GD, Butcher I, Heald CL, Lee RJ, Chambless LE, Folsom AR, Hirsch AT, Dramaix M, deBacker G, Wautrecht JC, Kornitzer M, Newman AB, Cushman M, Sutton-Tyrrell K, Fowkes FG, Lee AJ, Price JF, d'Agostino RB, Murabito JM, Norman PE, Jamrozik K, Curb JD, Masaki KH, Rodríguez BL, Dekker JM, Bouter LM, Heine RJ, Nijpels G, Stehouwer CD, Ferrucci L, McDermott MM, Stoffers HE, Hooi JD, Knottnerus JA, Ogren M, Hedblad B, Witteman JC, Breteler MM, Hunink MG, Hofman A, Criqui MH, Langer RD, Fronck A, Hiatt WR, Hamman R, Resnick HE, Guralnik J, McDermott MM (2008) Ankle brachial index combined with Framingham Risk Score to predict cardiovascular events and mortality: a meta-analysis. *JAMA* 300:197–208
24. Tziomalos K, Athyros VG, Karagiannis A, Mikhailidis DP (2010) The role of ankle brachial index and carotid intima-media thickness in vascular risk stratification. *Curr Opin Cardiol* 25:394–398
25. June RR, Scalzi LV (2013) Peripheral vascular disease in systemic lupus patients. *J Clin Rheumatol* 19:367–372
26. Kay SD, Poulsen MK, Diederichsen AC, Voss A (2016) Coronary, carotid, and lower-extremity atherosclerosis and their interrelationship in Danish patients with systemic lupus erythematosus. *J Rheumatol* 43:315–322
27. Erdozain JG, Villar I, Nieto J, Ruiz-Irastorza G (2014) Peripheral arterial disease in systemic lupus erythematosus: prevalence and risk factors. *J Rheumatol* 41:310–317
28. Theodoridou A, Bento L, D'Cruz DP, Khamashta MA, Hughes GR (2003) Prevalence and associations of an abnormal ankle-brachial index in systemic lupus erythematosus: a pilot study. *Ann Rheum Dis* 62:1199–1203
29. Friedewald WT, Levy RI, Fredrickson DS (1972) Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 18:499–502
30. Levey AS, Bosch JP, Lewis JB, Greene T, Rogers N, Roth D (1999) A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 130:461–470
31. Van Bortel LM, Laurent S, Boutouyrie P, Chowienczyk P, Cruickshank JK, De Backer T, Filipovsky J, Huybrechts S, Mattace-Raso FU, Protogerou AD, Schillaci G, Segers P, Vermeersch S, Weber T, Artery Society, European Society of Hypertension Working Group on Vascular Structure and Function, European Network for Noninvasive Investigation of Large Arteries (2012) Expert consensus document on the measurement of aortic stiffness in daily practice using carotid-femoral pulse wave velocity. *J Hypertens* 30:445–448
32. Selzer F, Sutton-Tyrrell K, Fitzgerald SG, Pratt JE, Tracy RP, Kuller LH, Manzi S (2004) Comparison of risk factors for vascular disease in the carotid artery and aorta in women with systemic lupus erythematosus. *Arthritis Rheum* 50:151–159
33. Cecelja M, Chowienczyk P (2009) Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertension: a systematic review. *Hypertension* 54:1328–1336
34. Wohlfahrt P, Somers VK, Cifkova R, Filipovsky J, Seidlerova J, Krajcoviechova A, Sochor O, Kullo IJ, Lopez-Jimenez F (2014) Relationship between measures of central and general adiposity with aortic stiffness in the general population. *Atherosclerosis* 235:625–631
35. Yusuf S, Hawken S, Ounpuu S, Bautista L, Franzosi MG, Commerford P, Lang CC, Rumboldt Z, Onen CL, Lisheng L, Tanomsup S, Wangai P Jr, Razak F, Sharma AM, Anand SS, INTERHEART Study Investigators (2005) Obesity and the risk of myocardial infarction in 27,000 participants from 52 countries: a case-control study. *Lancet* 366:1640–1649