LUPUS SCIENCE & MEDICINE™

Prevalence of coronary artery calcification in young patients with SLE of predominantly Hispanic and African–American descent

Yevgeniya Gartshteyn,[1] Genna Braverman,[2] Sharan Mahtani,[3] Laura Geraldino-Pardilla,[1] Sabahat Bokhari,[4] Anca Askanase[1]

To cite: Gartshteyn Y, Braverman G, Mahtani S, *et al*. Prevalence of coronary artery calcification in young patients with SLE of predominantly Hispanic and African–American descent. *Lupus Science & Medicine* 2019;**6**:e000330. doi:10.1136/lupus-2019-000330

Received 8 March 2019
Revised 20 May 2019
Accepted 10 June 2019

[1]Department of Rheumatology, Columbia University College of Physicians and Surgeons, New York, New York, USA
[2]Department of Medicine, Columbia University College of Physicians and Surgeons, New York, New York, USA
[3]Department of Medicine, University of Edinburgh College of Medicine and Veterinary Medicine, Edinburgh, , UK
[4]Division of Cardiology, and Nuclear Cardiology Laboratory, Columbia University College of Physicians and Surgeons, New York, New York, USA

Correspondence to
Dr Yevgeniya Gartshteyn; yg2372@cumc.columbia.edu

ABSTRACT

Objectives Cardiovascular disease (CVD) is a leading cause of death in SLE. Coronary artery calcium (CAC) scores predict CVD events, independent of traditional risk factors. Patients with SLE aged >45 years have an increased prevalence of CAC in a predominantly white population. Little is known about CAC in younger patients with SLE. We evaluated CAC in younger patients with SLE of predominantly African–American and Hispanic ancestry, compared with healthy controls.

Methods We identified 76 patients with SLE meeting 1997 American College of Rheumatology classification criteria, without known coronary artery disease and who had a non-contrast chest CT performed as part of their clinical care, with images retrievable for calculation of CAC scores. Demographics, disease characteristics and comorbidities were ascertained and adjusted for.

Results 42.1% of patients with SLE (mean age 40±13 years, 90% female, 33% Hispanic and 40% African–American) had CAC>0, 32% for age ≤45 years and 61.6% for age >45. Patients with SLE with CAC>0 were older and had more comorbid hypertension. Women with SLE aged ≤45 years, had a 12.6-fold higher adjusted odds of CAC>0 compared with age-matched and sex-matched controls (95% CI 5.2 to 30.7, p<0.001). Furthermore, 29% of patients with SLE aged 18–32 years (median disease duration of 5 years) had CAC>0.

Conclusion Patients with SLE aged ≤45 years have an increased prevalence of detectable CAC compared with the general population. Our data suggest that subclinical atherosclerosis in SLE develops early and warrants timely screening and cardioprotective interventions.

INTRODUCTION

SLE is a chronic, autoimmune disease with variable organ involvement and clinical course. Cardiovascular disease (CVD) is a leading cause of mortality in SLE.[1] Traditional CVD risk assessments do not fully account for the increased risk in SLE, and 10-year risk calculators underperform in younger patients where events are unlikely to occur within 10 years, even in high-risk individuals.[2] Improved strategies for estimating CVD risk in SLE are needed.

CAC scores quantify the presence and extent of calcified plaque in the coronary arteries. A CAC>0 in the general population is an independent predictor of CVD mortality.[3] The prevalence of detectable CAC in a cohort of 65 patients with SLE was three to four times higher compared with non-SLE controls (mean age 40±12 years, 72% white race).[4] Similarly, Kiani *et al* showed a 2.8 times higher prevalence of CAC in women with SLE aged 45–54 years, 65% white and 31% African–American.[5] This study was initiated to assess the prevalence of CAC in younger patients with SLE of predominantly Hispanic and African–American ancestry.

MATERIALS AND METHODS

Cohorts

The study included 76 patients, aged 18–64 years, from the Columbia University Lupus Cohort. Patients met the 1997 American College of Rheumatology (ACR) classification criteria,[6] had no history of coronary artery disease (CAD) based on self-report and chart review, and had a chest CT performed for routine care with images retrievable for CAC scoring. The Coronary Artery Risk Development in Young Adults (CARDIA) cohort participants, aged 33–45 years, were used as population controls.[7] The raw CARDIA data with available CAC results were used in our analysis.

CAC scoring

CAC scores for the Columbia University Lupus Cohort were calculated from images of non-gated chest multidetector CT (MDCT). A cardiologist with expertise in cardiovascular imaging visually estimated the CAC,

Table 1 Characteristics of patients with SLE

	Total (n=76)	CAC=0 (n=44)	CAC>0 (n=32)	P value
Age, years	40±13	37±12	45±15	**0.01**
Female, n (%)	68 (90%)	41 (93%)	27 (84%)	0.22
Race/ethnicity				
White, n (%)	12 (16%)	7 (16%)	5 (16%)	0.97
Hispanic, n (%)	25 (33%)	15 (34%)	10 (31%)	0.80
Black, n (%)	30 (40%)	15 (34%)	15 (47%)	0.26
Disease duration, years	7 (2–13)	7 (1–13)	8 (3–12)	0.69
Katz SLE Severity Disease Index	5 (3–8)	6 (4–8)	5 (3–8)	0.50
SLICC Damage Index	1 (1–2)	1 (1–2)	2 (1–3)	0.17
Lupus nephritis, n (%)	35 (46%)	22 (50%)	13 (41%)	0.37
APS, n (%)	8 (11%)	5 (11%)	3 (9%)	0.76
Antibodies				
ANA, n (%)	76 (100%)			–
ds-DNA antibody, n (%)	49 (64%)	31 (70%)	18 (56%)	0.20
SSA antibody, n (%)	32 (42%)	19 (43%)	13 (41%)	0.76
SSB antibody, n (%)	11 (15%)	7 (16%)	4 (13%)	0.65
Sm antibody, n (%)	33 (43%)	21 (48%)	12 (38%)	0.33
RNP antibody, n (%)	41 (54%)	25 (57%)	16 (50%)	0.48
Antiphospholipid antibodies, n (%)	28 (37%)	18 (41%)	10 (31%)	0.43
Hypertension, n (%)	33 (43%)	15 (34%)	18 (56%)	**0.05**
Diabetes, n (%)	8 (10.5%)	5 (11%)	3 (9%)	0.98
Ever smoker n (%)	11 (15%)	5 (11%)	6 (19%)	0.37
BMI, kg/m^2	27.5±8	26.7±8	28.5±8	0.36
Total cholesterol, mg/dL	186±74	189±89	182±84	0.37
HDL, mg/dL	51±19	53±18	47±20	0.24
LDL, mg/dL	104±47	103±54	106±32	0.81
Aspirin use, n (%)	22 (29%)	10 (23%)	12 (38%)	0.16
Statin use, n (%)	10 (13%)	4 (9%)	6 (19%)	0.22
Immunomodulatory medication use				
Antimalarials, n (%)	73 (96%)	42 (96%)	31 (97%)	0.75
Non-biologic DMARDs, n (%)	62 (82%)	36 (82%)	26 (81%)	0.95
Cyclophosphamide, n (%)	23 (30%)	13 (30%)	10 (31%)	0.87
Biologics, n (%)	24 (32%)	15 (34%)	9 (28%)	0.58
Glucocorticoids, n (%)	68 (90%)	38 (86%)	30 (94%)	0.30

Characteristics are expressed as n (%), mean±SD or median (IQR). Values in bold are considered significant (∝<0.05).
APS, antiphospholipid antibody syndrome; BMI, body mass index; CAC, coronary artery calcium; DMARD, disease-modifying antirheumatic drug, including azathioprine, methotrexate and mycophenolate mofetil; HDL, high-density lipoprotein; LDL, low-density lipoprotein; RNP, ribonucleoprotein; SLICC, systemic lupus International collaborative clinics; SSA, Sjogren's syndrome-related antigen; SSB, Sjogren's syndrome-related antigen B; Sm, Smith.

classifying patients as having an estimated Agatston Score of 0, 1–99, 100–399 or ≥400.[8 9]

The CAC scoring protocol for the CARDIA cohort was previously described.[7] Briefly, two CT scans were obtained for each participant using electron beam CT (EBM-CT) or gated MDCT. Scans were read by trained readers at each CARDIA study site and the Agatston Score was averaged from the two scans.

Assessment of covariates

Patient characteristics

Demographics and smoking history were self-reported. Hypertension (HTN) was defined as a systolic blood pressure of ≥140 mm Hg or a diastolic blood pressure of ≥90 mm Hg, or the use of antihypertensive medications. Diabetes was defined as a glycated haemoglobin of ≥6.4% or antidiabetic medications use.

SLE disease severity and accrued organ damage were measured by the Katz Severity Index[10] and the Systemic Lupus International Collaborative Clinics/ACR Damage Index (SDI).[11] We chose the Katz Severity Index and the SDI to quantify the cumulative SLE disease exposure.

Laboratory covariates, including lipid panels, C3, C4, anti-dsDNA, anti-Sjogren's syndrome-related antigen/Ro and Sjogren's syndrome-related antigen B/La, anti-Smith, antiribonucleoprotein and antiphospholipid (aPL) antibodies were measured at New York Presbyterian clinical laboratories.

Statistical analysis

CAC was analysed as a dichotomous variable defined by any detectable CAC>0 or as a categorical variable 0, 1–99, 100–399 and ≥400. Univariate analyses were performed using a two-sided Student t-test or Mann-Whitney U test and χ^2 or Fisher's exact test. Prevalence of CAC>0 was stratified by age, and the prevalence in patients with SLE aged ≤45 years was compared with the CARDIA controls. Adjusted odds ratios were obtained using logistic regression to control for covariates, identified on the basis of the univariate analysis. Calculations were performed in Stata/IC V.15.1.

RESULTS

Patient characteristics

Seventy-six patients with SLE, aged 18–64 years, with available CT chest images were identified. The average age was 40±13 years, and 90% were women. Thirty-three per cent were Hispanic and 40% were African–American.

Patients met on average 6±2 ACR-SLE classification criteria; all had positive ANA titres, and 64% had elevated dsDNA. Average SLE Katz Severity Index[10] was 5±3 (consistent with moderate disease), 46% had lupus nephritis and 37% tested positive for aPL antibodies. Forty-three per cent had HTN, 10% had diabetes and 15% had a history of smoking. Sixty-four patients had a lipid panel: total cholesterol and high-density lipoprotein (HDL) were 186±74 and 51±19 mg/dL, respectively. Ninety per cent of patients had a history of systemic glucocorticoid use. Aspirin and statins were used by 29% and 13% of the patients, respectively (table 1).

Coronary artery calcifications in patients with SLE

A CAC>0 was present in 32 patients (42.1%). Patients with SLE with CAC>0 were older (45±15 vs 37±12 years, p=0.01) and had more frequent comorbid HTN (56% vs 34%, p=0.05). No association was seen between the presence of CAC-specific and SLE-specific characteristics (table 1).

An increasing prevalence of CAC>0 with advancing age was noted: CAC>0 was seen in 29.0%, 42.1% and 61.6% of patients with SLE aged 18–32, 33–44 and 45–64 years, respectively. Overall, 30% had low CAC scores in the 1–99 range, 8% had medium CAC scores in the 100–399 range and 4% had CAC scores≥400 (figure 1).

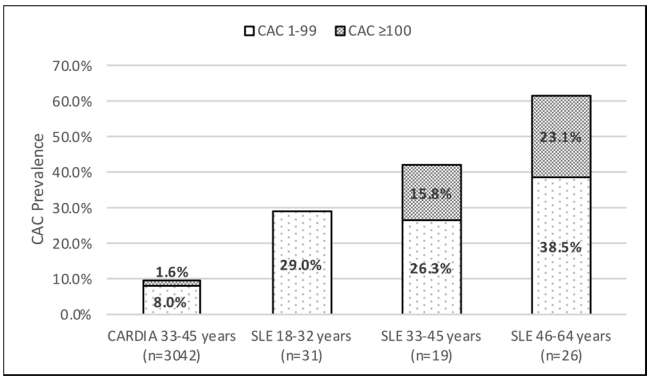

Figure 1 Prevalence and extent of CAC in patients with SLE and CARDIA controls, shown by age group. Prevalence of CAC>0 was seen in 9.6% of CARDIA participants and 29.0%, 42.1% and 61.6% of patients with SLE aged 18–32, 33–45 and 46–64 years, respectively. CAC scores 1–99 vs ≥100 were seen in 8.0% and 1.6% of the CARDIA participants, and 29.0%, 26.3% and 38.5% and 0%, 15.8%, and 23.1% of patients with SLE aged 18-32, 33-45, and 46-64 respectively. CAC, coronary artery calcium; CARDIA, Coronary Artery Risk Development in Young Adults.

Comparison of patients with SLE aged ≤45 years with patients in the CARDIA cohort

CAC data from 50 patients with SLE aged ≤45 years were compared with those of 3042 CARDIA controls (table 2). Patients with SLE were younger (32±8 vs 40±4 years, p<0.001) and were mostly female (92% vs 54%, p<0.001). More patients identified with being white in the CARDIA cohort (6% vs 55%, p<0.001), whereas more Hispanics were part of the SLE cohort (32% vs none in CARDIA). Patients with SLE had more comorbid HTN (44% vs 23%, p<0.001) and higher aspirin use (32% vs 7%, p<0.001), whereas the patients in the CARDIA cohort were more likely to smoke (4% vs 56%, p<0.001).

Patients with SLE aged ≤45 years had a higher prevalence of CAC>0 compared with patients in the CARDIA cohort (32.0% vs 9.6%, p<0.001, OR 4.5, 95% CI 2.4 to 8.2). We could not adjust for sex, white race and smoking status, given too few patients in these subgroups. Restricting the analysis to women and adjusting for age, HTN, total cholesterol levels and aspirin use, the odds of having CAC>0 in women with SLE aged ≤45 years was 12.6 times higher than those in women in the CARDIA cohort (95% CI 5.2 to 30.7).

DISCUSSION

Our study assessed the prevalence of CAC>0 in patients with SLE aged 18–64 years and without clinical CAD. Forty-two per cent of the patients had a CAC>0. The prevalence of CAC>0 increased with age, present in 29.0%, 42.1% and 61.6% of patients aged 18–32, 33–45 and 46–64 years, respectively. Patients with CAC>0 were older and were more likely to have HTN. In patients aged ≤45 years, we found a significantly higher prevalence of CAC>0 compared with CARDIA controls (32.0% vs 9.6%, p<0.0001). Importantly, this high prevalence of CAC>0

Table 2 Characteristics of patients with SLE aged ≤45 years compared with patients in the CARDIA cohort

	SLE ≤45 years (n=50)	CARDIA (n=3042)	P value	Women with SLE aged ≤45 years (n=46)	Women in the CARDIA cohort (n=1659)	P value
Age, years	32±8	40±4	**<0.001**	32±8	40±4	**<0.001**
Female, n (%)	46 (92%)	1659 (54%)	**<0.001**	–	–	–
Race/ethnicity						
White, n (%)	3 (6%)	1666 (55%)	**<0.001**	3 (7%)	859 (52%)	**<0.001**
Hispanic, n (%)	16 (32%)	–	–	14 (30%)	–	–
Black, n (%)	24 (48%)	1376 (45%)	0.70	23 (50%)	800 (48%)	0.81
Hypertension, n (%)	22 (44%)	705 (23%)	**<0.001**	22 (48%)	274 (17%)	**<0.001**
Diabetes, n (%)	3 (6%)	305 (10%)	0.87	3 (7%)	125 (8%)	0.85
Ever smoker, n (%)	2 (4%)	1718 (56%)	**<0.001**	2 (4%)	884 (53%)	**<0.001**
BMI, kg/m^2	27.8±9	28.4±6	0.49	28.2±9	28.8±7	0.59
Total cholesterol, mg/dL	183±88	183±41	0.99	191±90	178±40	0.07
HDL, mg/dL	49±19	50±16	0.69	50±19	54±16	0.10
LDL, mg/dL	100±52	111±36	0.05	106±52	107±33	0.92
Aspirin use, n (%)	16 (32%)	213 (7%)	**<0.001**	14 (30%)	78 (5%)	**<0.001**

Characteristics are expressed as n (%) or as the mean±SD. Values in bold are considered significant (∝<0.05).
Data for all patients (left) and women only (right) are shown.
BMI, body mass index; CARDIA, Coronary Artery Risk Development in Young Adults; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

in patients with SLE ≤45 years is similar to that reported in diabetic patients aged ≤40 years (32% vs 43%, respectively).[12]

CAC is an established surrogate for future CVD events in the general population.[3] Asanuma *et al* reported increased CAC in SLE compared with controls (31% vs 9%); however, their population consisted of predominantly white patients, and only two patients under the age of 40 had CAC>0.[4] Similarly, the prevalence of CAC>0 was higher in women with SLE aged 45–64 years compared with age-matched and sex-matched controls (58% vs 28%).[5] We now describe, in a predominantly Hispanic and African–American SLE cohort, an increased prevalence of CAC>0 in patients aged ≤45 years, with detectable CAC present as early as 21 years of age.

CVD event risk increases with higher CAC scores. In our cohort CAC scores≥100, corresponding to a 10 year event rate of >7.5%,[13] were seen in 16% and 23% of patients with SLE ages 33–45 and 46–64, respectively. Patients with SLE ages 18–32 had CAC scores 1–99. However, estimates of annual CAC progression suggest an increase of 20 Agatston units per year.[14 15] At this rate, a patient with a CAC 1–99 in her twenties could be expected to reach a CAC>300 by age 50, corresponding to a subsequent 10 year event risk of 13%–25%.[13]

A limitation of the study is the difference in the populations being compared. The patients with SLE were enrolled from a single-centre cohort as compared with the multicentre CARDIA cohort. Additionally, we enrolled patients with SLE who had a chest CT performed as part of routine care. This could introduce selection bias and the risk of overestimating the CAC prevalence in the SLE population. Reassuringly, the prevalence of CAC>0 in patients with SLE aged >45 years is similar to that reported by Kiani *et al*,[5] suggesting relative precision and reproducibility. Another limitation is that CAC in CARDIA was assessed by EBM-CT or electrocardiography-gated MDCT, whereas we relied on CAC estimated from non-gated MDCT. The non-gated scan can introduce blurring of the coronary arteries and/or gaps or duplications in the images, which can affect calcium scoring. However, we have shown that the estimates of CAC from the non-gated MDCT have a strong correlation with the traditional CAC scoring methods.[9]

In conclusion, we found an increased prevalence of CAC>0 in patients with SLE, detectable at a young age. The high prevalence in this young, predominantly female, minority population is disquieting and warrants further investigation and longitudinal follow-up.

Contributors YG, GB, SM, LG-P and AA contributed to the design and the analysis of the results and the writing of the manuscript. SB performed the CAC analysis and manuscript preparation.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval The study was approved by the Columbia University Institutional Review Board, which deemedit appropriate to waive the requirement for informed consent.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

1. Fors Nieves CE, Izmirly PM. Mortality in systemic lupus erythematosus: an updated review. *Curr Rheumatol Rep* 2016;18.
2. Bonow RO. Should coronary calcium screening be used in cardiovascular prevention strategies? *N Engl J Med* 2009;361:990–7.
3. Detrano R, Guerci AD, Carr JJ, *et al*. Coronary calcium as a predictor of coronary events in four racial or ethnic groups. *N Engl J Med* 2008;358:1336–45.
4. Asanuma Y, Oeser A, Shintani AK, *et al*. Premature coronary-artery atherosclerosis in systemic lupus erythematosus. *N Engl J Med* 2003;349:2407–15.
5. Kiani AN, Magder LS, Post WS, *et al*. Coronary calcification in SLE: comparison with the multi-ethnic study of atherosclerosis. *Rheumatology* 2015;54:1976–81.
6. Hochberg MC. Updating the American College of rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1725;1997.
7. Loria CM, Liu K, Lewis CE, *et al*. Early adult risk factor levels and subsequent coronary artery calcification. *Journal of the American College of Cardiology* 2007;49:2013–20.
8. Agatston AS, Janowitz WR, Hildner FJ, *et al*. Quantification of coronary artery calcium using ultrafast computed tomography. *Journal of the American College of Cardiology* 1990;15:827–32.
9. Einstein AJ, Johnson LL, Bokhari S, *et al*. Agreement of visual estimation of coronary artery calcium from low-dose CT attenuation correction scans in hybrid PET/CT and SPECT/CT with standard Agatston score. *Journal of the American College of Cardiology* 2010;56:1914–21.
10. Katz JD, Senegal J-L, Rivest C, *et al*. A simple severity of disease index for systemic lupus erythematosus. *Lupus* 1993;2:119–23.
11. Gladman D, Ginzler E, Goldsmith C, *et al*. The development and initial validation of the systemic lupus international collaborating clinics/American College of rheumatology damage index for systemic lupus erythematosus. *Arthritis & Rheumatism* 1996;39:363–9.
12. Daga N, Nasir K, Hamirani Y, *et al*. Prevalence and severity of coronary artery calcium in young persons with diabetes. *Journal of Cardiovascular Computed Tomography* 2013;7:241–7.
13. Budoff MJ, Young R, Burke G, *et al*. Ten-year association of coronary artery calcium with atherosclerotic cardiovascular disease (ASCVD) events: the multi-ethnic study of atherosclerosis (MESA). *Eur Heart J* 2018;39:2401–8.
14. Budoff MJ, Young R, Lopez VA, *et al*. Progression of coronary calcium and incident coronary heart disease events: MESA (multi-ethnic study of atherosclerosis). *J Am Coll Cardiol* 2013;61:1231–9.
15. Chung CP, Giles JT, Kronmal RA, *et al*. Progression of coronary artery atherosclerosis in rheumatoid arthritis: comparison with participants from the multi-ethnic study of atherosclerosis. *Arthritis Res Ther* 2013;15.