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Progression of Noncalcified and Calcified Coronary Plaque by CT Angiography in SLE

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INTRODUCTION

The National Inpatient Sample in 1998 showed that there were 5,000 hospitalizations, in the United States, among patients with systemic lupus erythematosus, due to coronary artery disease [1], of which 1,763 were due to acute myocardial infarction. In women less than fifty years of age, approximately 300 hospitalizations were due to myocardial infarction. It has been shown that the risk of cardiovascular events is increased 2.66 fold in the SLE population [2].

Traditional stress tests used to diagnose coronary artery disease only detect flow-limiting stenosis and may miss early coronary atherosclerosis. Noninvasive imaging of coronary plaques resulted in major advances in our understanding of atherosclerosis and its

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Compliance with Ethical Standards

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- 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.
- Informed consent: Informed consent was obtained from all individual participants included in the study.

pathogenesis. Coronary CT angiography is one such tool that can be integrated into the management of patients with known or suspected coronary atherosclerosis. It can assess the coronary lumen as well as volume and composition of coronary atherosclerotic plaque. Coronary CT angiography, unlike invasive coronary angiography, also gives detailed information about nonobstructive atherosclerosis within the coronary blood vessel wall. This is most helpful as we know that acute coronary syndromes are frequently caused by non-obstructive coronary plaques [3].

A mature atherosclerotic plaque is composed of a lipid/macrophage-rich atheromatous material with an overlying fibrous cap. The cap may rupture and – in the right context – may trigger an acute coronary syndrome [4]. Plaque instability is related to the degree of ongoing inflammation [5] and plaque composition [6]. Coronary atherosclerotic plaques can be classified as calcified, noncalcified or mixed [7, 8, 9]. Often, noncalcified atherosclerotic plaques are more metabolically active than heavily calcified plaques and are associated with increased risk of acute coronary syndromes [10]. Noncalcified coronary plaque and the total plaque burden of the coronary arteries, even of only one segment, are associated with an increased risk of cardiovascular events [11]. Noncalcified coronary plaques can even be found in individuals who have zero coronary calcium scores [11]. Although the coronary artery calcium score serves as a surrogate for total coronary atherosclerotic burden, and correlates with risk of mortality [12], it does not consider noncalcified plaque, which may be more relevant for risk assessment [13, 14, 15, 16]. Patients without any coronary atherosclerotic disease by CTA have exceedingly low risk of subsequent major adverse cardiovascular events and thus, require no short or intermediate term follow-up for concerns of coronary artery disease [17].

Increased prevalence of subclinical measures of coronary atherosclerosis including noncalcified plaque is seen in chronic diseases including HIV [18] and autoimmune diseases including rheumatoid arthritis [19]. In a study of 150 rheumatoid arthritis patients without prior symptoms or diagnosis of coronary artery disease and 150 controls, rheumatoid arthritis patients had a higher prevalence of noncalcified coronary plaque [19]. We have previously studied noncalcified coronary plaque cross-sectionally in SLE. We found that 54% of patients with SLE had noncalcified coronary plaque [20].

This is the first study of serial measurement of NCP in SLE. The aim of our study was to determine the frequency of progression and to evaluate the risk factors that lead to progression of noncalcified coronary plaque in patients with SLE, by serial CTA.

METHODS

This is an observational longitudinal prospective study nested in the Johns Hopkins lupus cohort. Consecutive patients who consented to participate were assessed for NCP at baseline, and again 2 to 8 years later. Patients who were pregnant, allergic to contrast or had a serum creatinine level equal to or more than 1.2 mg/dL were excluded as previously described [20]. As part of the Hopkins Lupus Cohort, all patients were seen quarterly for the assessment of disease activity by physician's global assessment (PGA) on a visual analogue scale of zero to three, and SELENA-SLEDAI [21,22]. Laboratory tests including complete

blood count, erythrocyte sedimentation rate (ESR), fasting lipid profile, homocysteine, serum creatinine, urinalysis, urine protein/creatinine ratio, complement C3 and C4, anti-dsDNA, anticardiolipin and lupus anticoagulant (by dRVVT) were done at each visit. Cardiovascular risk factors including weight, mean systolic blood pressure, and history of smoking were assessed.

CT acquisition and Image Reconstruction

CT images were acquired using a 320 × 0.5 mm-detector row CT system (Aquilion ONE, Toshiba Medical Systems, Otawara, Japan). Patient preparation included oral (75–150 mg) metoprolol. Fifty to seventy mL of iodinated contrast (Iopamidol 370 mg iodine/mL) was injected intravenously at 4.0–6.0 mL/sec for prospectively ECG-triggered acquisitions (typically 75% of the R-R interval). If coronary calcification was evident on angiographic images, a non-contrast CT acquisition was added to quantify calcium for the Agatston score. CT angiographic data were reconstructed to generate 0.5-mm slice thickness images with a 0.25-mm increment using both a standard (FC43) and a sharp (FC05) convolution kernel. Reconstructed images were transferred to a dedicated workstation for further analysis (Vitrea™ FX version 3.0 workstation, Vital Images, Minnetonka, MN, USA).

Coronary Atherosclerotic Plaque Analysis

All images were interpreted by a physician, blinded to any clinical information, with extensive experience (level III certified) in the interpretation of coronary CT angiography. The left anterior descending coronary artery, left circumflex coronary artery, and right coronary artery were divided into proximal, mid, and distal segments respectively according to standard segmentation guidelines [23]. The left main coronary artery was evaluated separately, resulting in 10 segments evaluated in total. Each segment was assessed for the presence and severity of atherosclerotic plaques on a semi-quantitative scale. Furthermore, plaque characteristics, including remodeling, were noted for each segment. These metrics were integrated for a total plaque severity score as previously described [24]. Briefly, the NCP score was the sum of plaque severity multiplied by plaque composition, divided by the number of vessels examined. Severity was calculated as 0 = absent, 1 = mild, 2 = moderate, and 3 = severe for each coronary artery segment, according to the American Heart Association classification [25, 26]. Plaque composition was calculated as 0 = 0%, 1 = 1%–25%, 2 = 26%–50%, 3 = 51%–75%, and 4 = 76%–100% in the noncalcified portion of coronary plaque for each coronary artery segment. Mild stenosis was defined as < 25%, moderate 25%–49%, and severe ≥ 50%. Coronary artery side branches were not included in the analysis for practical reasons, because the main branches have the bulk of disease. Non-interpretable coronary segments were excluded from our analysis. A segment was determined non-evaluable when either motion or poor contrast-to-noise ratio deemed detection of plaque impossible in the segment. Using this approach scores ranged from 0 to 1.7. For ease of description, we classified NCP as none, low (<0.5) or high (0.5+).

CAC was quantified by the Agatston score. CAC was classified as none, low if the Agatston score was 1–99, moderate if it was 100–299 or high if it was 300 and above [27].

Statistical analysis

To quantify the clinical experience of patients between the two NCP assessments, we calculated the weighted mean value of the clinical variables measured during that period. The weights were calculated based on the interval between assessments so that the means calculated are interpretable as the average height of the curve based on a trapezoidal approach. This is equivalent to the method used to calculate the “adjusted mean SLEDAI” applied to other clinical variables [28]. We then estimated the association between these exposures and changes in the NCP score using linear regression, adjusting for the duration between NCP assessments.

RESULTS

Thirty-six patients with a diagnosis of SLE were included in this study. The 36 SLE pts were 75% female. They were 75% Caucasians, 17% African-Americans, and 8% other races/ethnicities. The age at the first assessment ranged from 22 to 75 with a mean of 46.6 years. Table 1 shows the ACR-11 criteria satisfied by our sample. Table 2 shows the percentage of patients using the different immunosuppressive drugs at the time of baseline and then at the time of follow-up scan.

A follow-up assessment of NCP was performed from 2 to 8 years after the baseline assessment. Thirty-six scans allowed repeat assessment for noncalcified plaque and thirty-five for coronary artery calcium. Of these follow-up assessments, 5 (14%) were performed in 2–3 years, 18 (50%) were performed in 3–4 years, and 13 (36%) were performed more than 4 years after baseline.

Twenty-four of 36 (75%) of the SLE patients had evidence of noncalcified coronary plaque (NCP) at the first assessment. In contrast, only 12/35 (34%) had evidence of calcified plaque (a baseline measure of calcified plaque was missing for one patient). Those with noncalcified plaque were more likely to have calcified plaque than those without (11/23, 48% vs 1/12, 8%, $P=0.027$).

Table 3 shows the results seen at follow-up in groups defined by baseline NCP. The pre and post scores were classified in the same category for 19 of 36 patients (53%). Progression occurred in 12/36 (33%) patients, and 5/36 (14%) patients showed plaque regression, implying that noncalcified coronary plaque levels were variable over a period of 2 to 8 years.

Table 4 shows the baseline and follow-up CTA results for calcified coronary artery plaque. For calcified coronary plaque, the pre-post scores were in the same category for 32 of 35 patients (91%). Calcified coronary plaque progression occurred in 2/35 (5.71%) patients, and 1/35 (2.85%) patients showed regression of calcified plaque. This suggests that calcified coronary plaque levels remained relatively stable over a period of 2 to 8 years.

To identify predictors of NCP progression, we quantified clinical exposures experienced between the two NCP measures and assessed their association with changes in NCP score adjusting for time between assessments. Table 5 shows the results. There was a significant association between duration of time between assessments and increases in NCP (mean

increase in NCP score per year: 0.09, 95% confidence limits 0.02–0.17, $P = 0.038$). There was not a strong association between any of the clinical variables considered and changes in NCP. There was some evidence ($P = 0.06$) of an association between immunosuppressant use and less progression of NCP.

DISCUSSION

This study showed that calcified coronary plaque remained relatively stable over a period of 2–8 years, compared to noncalcified plaque, which was more variable. Neither traditional cardiovascular risk factors nor lupus related disease activities were significantly associated with changes in NCP. There was some evidence that immunosuppressive drugs have a protective effect.

In our previous Lupus Atherosclerosis Prevention Study (LAPS), two hundred SLE patients participated in a placebo-controlled trial of 40 mg atorvastatin [29]. It was shown that some SLE patients did have an increase in coronary calcified plaque burden over 2 years. Progression of calcified coronary plaque was shown to be associated with age, current smoking status, and total serum cholesterol, in the multivariate analyses. It was not associated with SLE disease activity, hypertension or anti-dsDNA [30]. Atorvastatin did not reduce calcified plaque in our LAPS trial [29], nor in the pediatric trial [31] or in a murine model [32].

In a cross-sectional study among patients in the Hopkins lupus cohort, one hundred and forty-seven patients underwent semiquantified assessment of noncalcified coronary plaque by 64-slice multi-detector computed tomography [24]. This included the baseline samples of the patients reported here. Patient age ($P = 0.0001$), current methotrexate use ($P = 0.0005$), history of anti-dsDNA positivity ($P = 0.019$) and obesity (assessed by body mass index, $P = 0.058$) were associated with the presence of noncalcified coronary plaque, in the multivariate model. Use of hydroxychloroquine and prednisone had no effect on the quantification of noncalcified coronary plaque [24].

In contrast, a protective effect of methotrexate has been shown in rheumatoid arthritis patients. In a study of forty patients with rheumatoid arthritis, treatment of one year with methotrexate, led to a decrease in carotid intima media thickness, shown by an overall decrease in atherosclerosis [33]. In a systematic literature review of 2420 abstracts, the use of methotrexate was associated with a decreased risk of cardiovascular events in patients diagnosed with rheumatoid arthritis [34]. In a study of 613 rheumatoid arthritis patients who were using disease-modifying anti-rheumatic drugs, especially methotrexate, a decreased risk of cardiovascular events was observed, when compared to rheumatoid arthritis patients who did not use methotrexate, hydroxychloroquine, or sulfasalazine [35].

A protective effect of mycophenolate mofetil on atherosclerosis was studied in *gld.apoE* $-/-$ mice. These seven-week old mice were given a high-cholesterol Western diet for twelve weeks, with or without mycophenolate mofetil. Decreased atherosclerosis and decreased lupus phenotype were seen in the mice receiving mycophenolate mofetil, compared to controls [36].

We do not have sufficient numbers of patients in this study to subdivide immunosuppressive use into methotrexate or mycophenolate mofetil. Immunosuppressive drug use in SLE is predominantly methotrexate and mycophenolate mofetil. The protective effect (that was nearly statistically significant, $P=0.06$) of use of immunosuppressive drugs reflects mycophenolate mofetil use in the majority.

Our current study is the first to look at noncalcified coronary plaque over time in patients with SLE. Neither SLE disease activity, traditional cardiovascular risk factors nor lupus serologies predicted progression of noncalcified coronary plaque over time. There was no evidence that a history of smoking or current smoking status, mean systolic blood pressure, total serum cholesterol, or BMI were associated with the progression of noncalcified coronary atherosclerotic plaque. Similarly, SLE-related risk factors including Physician's Global Assessment, mean SLEDAI, lupus anticoagulant (by dRVVT), proportion of time with low C3 or C4, and positive anti-dsDNA were not associated with an increase in NCP score. Use of prednisone or hydroxychloroquine did not predict change in NCP.

This longitudinal study has enabled us to estimate rates of progression of noncalcified coronary plaque and to provide better evidence and greater resolution for identifying risk factors for plaque. However, given the small sample size, we cannot rule out the possibility that some subsets are associated with progression. Study of larger numbers of patients may allow identification of further predictors. Most importantly, we did find a near significant protective effect of immunosuppressive use (mostly mycophenolate) on progression, consistent with animal models.

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References

1. Thorburn CM, Ward MM. Hospitalizations for coronary artery disease among patients with systemic lupus erythematosus. *Arthritis Rheum.* 2003; 48:2519–2523. [PubMed: 13130471]
2. Magder LS, Petri M. Incidence of and risk factors for adverse cardiovascular events among patients with systemic lupus erythematosus. *Am J Epidemiol.* 2012; 176:708–719. [PubMed: 23024137]
3. Priester TC, Litwin SE. Measuring progression of coronary atherosclerosis with computed tomography: searching for clarity among shades of gray. *J Cardiovasc Comput Tomogr.* 2009; 3:S81–90. [PubMed: 20129521]
4. Virmani R, Burke AP, Farb A, Kolodgie FD. Pathology of the vulnerable plaque. *J Am Coll Cardiol.* 2006; 47:C13–8. [PubMed: 16631505]
5. Hunt BJ. The endothelium in atherogenesis. *Lupus.* 2000; 29:189–93.
6. Falk E, Shah PK, Fuster V. Coronary plaque disruption. *Circul.* 1995; 92:657–71.
7. Achenbach S, Ropers D, Hoffmann U. Assessment of coronary remodeling in stenotic and nonstenotic coronary atherosclerotic lesions by multidetector spiral computed tomography. *J Am Coll Cardiol.* 2004; 43:842–7. [PubMed: 14998627]
8. Leber AW, Knez A, Becker A. Accuracy of multidetector spiral computed tomography in identifying and differentiating the composition of coronary atherosclerotic plaques: a comparative study with intra-vascular ultrasound. *J Am Coll Cardiol.* 2004; 3:1241–7.

9. Achenbach S, Moselelewski F, Ropers D, Ferencik M, Hoffmann U, MacNeill B, et al. Detection of calcified and noncalcified coronary atherosclerotic plaque by contrast enhanced submillimeter multidetector spiral computed tomography: a segmented based comparison with intravascular ultrasound. *Circul.* 2004; 109:14–7.
10. Motoyama S, Ito H, Sarai M, Kondo T, Kawai H, Nagahara Y, et al. Plaque Characterization by Coronary Computed Tomography Angiography and the Likelihood of Acute Coronary Events in Mid-Term Follow-Up. *J Am Coll Cardiol.* 2015; 66:337–346. [PubMed: 26205589]
11. Plank F, Friedrich G, Dichtl W, Klauser A, Jaschke W, Franz WM, et al. The diagnostic and prognostic value of coronary CT angiography in asymptomatic high-risk patients: a cohort study. *Open Heart.* 2014; 1:e000096. [PubMed: 25332810]
12. Budoff MJ, Shaw LJ, Liu ST, Weinstein SR, Mosler TP, Tseng PH, et al. Long-term prognosis associated with coronary calcification: observations from a registry of 25,253 patients. *J Am Coll Cardiol.* 2007; 49:1860–70. [PubMed: 17481445]
13. Motoyama S, Sarai M, Harigaya H, Anno H, Inoue K, Hara T, et al. Computed tomographic angiography characteristics of atherosclerotic plaques subsequently resulting in acute coronary syndrome. *J Am Coll Cardiol.* 2009; 54:49–57. [PubMed: 19555840]
14. Virmani R, Burke AP, Farb A, Kolodgie FD. Pathology of the vulnerable plaque. *J Am Coll Cardiol.* 2006; 47:C13–8. [PubMed: 16631505]
15. Calvert PA, Obaid DR, O'Sullivan M, Shapiro LM, McNab D, Densem CG, et al. Association between IVUS findings and adverse outcomes in patients with coronary artery disease: the VIVA (VH-IVUS in Vulnerable Atherosclerosis) Study. *JACC Cardiovasc Imaging.* 2011; 4:894–901. [PubMed: 21835382]
16. Stone GW, Ellis SG, Cox DA, Hermiller J, O' Shaughnessy C, Mann JT, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med.* 2004; 350:221–31. [PubMed: 14724301]
17. Wilson SR, Lin FY, Min JK. Role of coronary artery calcium score and coronary CT angiography in the diagnosis and risk stratification of individuals with suspected coronary artery disease. *Curr Cardiol Rep.* 2011; 13:271–9. [PubMed: 21647575]
18. Post WS, Budoff M, Kingsley L, Palella FJ, Witt MD, Li X, et al. Associations between HIV infection and subclinical coronary atherosclerosis. *Ann Int Med.* 2014; 160:458–67. [PubMed: 24687069]
19. Karpouzas GA, Malpeso J, Choi TY, Li D, Munoz S, Budoff MJ. Prevalence, extent and composition of coronary plaque in patients with rheumatoid arthritis without symptoms or prior diagnosis of coronary artery disease. *Ann Rheum Dis.* 2014; 73:1797–804. [PubMed: 23887286]
20. Kiani AN, Vogel-Claussen J, Magder LS, Petri M. Noncalcified coronary plaque in systemic lupus erythematosus. *J Rheumatol.* 2010; 37:579–84. [PubMed: 20110529]
21. Petri M, Kim MY, Kalunian KC, Grossman J, Hahn BH, Sammaritano LR, et al. OC-SELENA Trial. Combined oral contraceptives in women with systemic lupus erythematosus. *N Engl J Med.* 2005; 353:2550–8. [PubMed: 16354891]
22. Gladman D, Ginzler E, Goldsmith C, Fortin P, Liang M, Urowitz M, 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 Rheum.* 1996; 39:363–9. [PubMed: 8607884]
23. Raff GL, Abidov A, Achenbach S, Berman DS, Boxt LM, Budoff MJ, et al. SCCT guidelines for the interpretation and reporting of coronary computed tomographic angiography. *J Cardiovasc Comput Tomogr.* 2009; 3:122–36. [PubMed: 19272853]
24. Kiani AN, Vogel-Claussen J, Arbab-Zadeh A, Magder LS, Lima J, Petri M, et al. Semiquantified noncalcified coronary plaque in systemic lupus erythematosus. *J Rheumatol.* 2012; 39:2286–2293. [PubMed: 23027889]
25. Nakanishi K, Fukuda S, Shimada K, Ehara S, Inanami H, Matsumoto K, et al. Non-obstructive low attenuation coronary plaque predicts three-year acute coronary syndrome events in patients with hypertension: multidetector computed tomographic study. *J Cardiol.* 2012; 59:167–75. [PubMed: 22245100]

26. Leber AW, Knez A, White CW. Composition of coronary atherosclerotic plaques in patients with acute myocardial infarction and stable angina pectoris determined by contrast-enhanced multislice computed tomography. *Am J Cardiol.* 2003; 91:714–8. [PubMed: 12633805]
27. Agatston AS, Janowitz WR, Hildner FJ, Zusmer NR, Viamonte M Jr, Detrano R. Quantification of coronary artery calcium using ultrafast computed-tomography. *J Am Coll Cardiol.* 1990; 15:827–32. [PubMed: 2407762]
28. Ibañez D, Urowitz MB, Gladman DD. Summarizing disease features over time: I. Adjusted mean SLEDAI derivation and application to an index of disease activity in lupus. *J Rheumatol.* 2003; 30:1977–1982. [PubMed: 12966601]
29. Petri MA, Kiani AN, Post W, Christopher-Stine L, Magder LS. Lupus atherosclerosis prevention study (LAPS). *Ann Rheum Dis.* 2011; 70:760–5. [PubMed: 21177297]
30. Kiani AN, Post WS, Magder LS, Petri M. Predictors of progression in atherosclerosis over 2 years in systemic lupus erythematosus. *Rheumatol.* 2011; 50:2071–2079.
31. Schanberg LE, Sandborg C, Barnhart HX, Ardoin SP, Yow E, Evans GW, et al. Use of atorvastatin in systemic lupus erythematosus in children and adolescents. *Arthritis Rheum.* 2012; 64:285–96. [PubMed: 22031171]
32. van Leuven SI, Mendez-Fernandez YV, Wilhelm AJ, Wade NS, Gabriel CL, Kastelein JJ, et al. Mycophenolate mofetil but not atorvastatin attenuates atherosclerosis in lupus-prone LDLr (–/–) mice. *Ann Rheum Dis.* 2012; 71:408–14. [PubMed: 21953346]
33. Georgiadis AN, Voulgari PV, Argyropoulou MI, Alamanos Y, Elisaf M, Tselepis AD, et al. Early treatment reduces the cardiovascular risk factors in newly diagnosed rheumatoid arthritis patients. *Semin Arthritis Rheum.* 2008; 38:13–19. [PubMed: 18191989]
34. Westlake SL, Colebatch AN, Baird J, Kiely P, Quinn M, Choy E, et al. The effect of methotrexate on cardiovascular disease in patients with rheumatoid arthritis: a systematic literature review. *Rheumatol.* 2010; 49:295–307.
35. van Halm VP, Nurmohamed MT, Twisk JW, Dijkmans BA, Voskuyl AE. Disease-modifying antirheumatic drugs are associated with a reduced risk for cardiovascular disease in patients with rheumatoid arthritis: a case control study. *Arthritis Res Ther.* 2006; 85:R151.
36. Richez C, Richards RJ, Duffau P, Weitzner Z, Andry CD, Rifkin IR, et al. The effect of mycophenolate mofetil on disease development in the gld.apoE (–/–) mouse model of accelerated atherosclerosis and systemic lupus erythematosus. *PloS One.* 2013; 8:e61042. [PubMed: 23577189]

Key Messages

- Noncalcified coronary plaque is more likely to undergo progression compared to calcified coronary plaque.
- Traditional cardiovascular risk factors nor SLE disease activity do not predict progression of noncalcified coronary plaque.
- Immunosuppressive drugs have a protective effect on the progression of noncalcified coronary plaque.

Table 1

Distribution of the cumulative American College of Rheumatology revised classification criteria for SLE in this population

American College of Rheumatology revised classification criteria	Patient Population (n=36)
Malar rash	25 (69%)
Discoid rash	20 (56%)
Photosensitivity	24 (67%)
Oral ulcers	17 (47%)
Arthritis	32 (89%)
Serositis	24 (67%)
Proteinuria	28 (78%)
Neurologic disorder	11 (31%)
Hematologic disorder	31 (86%)
Immunologic disorder	34 (94%)
ANA positivity	36 (100%)

Usage of immunosuppressive drugs at the time of baseline and follow-up scan in the patient population

Table 2

Immunosuppressive Drug	Number of patients using at time of baseline scan-	Percentage of patients using at time of baseline scan	Mean dose being used by patients at time of baseline scan	Number of patients using at follow-up Scan-Mean dose	Percentage of patients using at follow-up Scan-Mean dose	Mean dose being used by patients at time of follow-up scan
No immunosuppressant	20/36	(56%)	0 mg per week	23/36	(64%)	0 mg per week
Methotrexate	2/36	(5.5%)	22.5 mg per week	1/36	(2.7%)	25 mg per week
Mycophenolate mofetil	9/36	(25%)	2111.1 mg per day	6/36	(16.7%)	1500 mg per day
Azathioprine	4/36	(11%)	115 mg per day	4/36	(11%)	112.5 mg per day
Prednisone	10/36	(28%)	9.5 mg per day	5/36	(14%)	9 mg per day

Table 3Number (%) with NCP at follow-up by baseline level[/]

		Follow-up		
		None	Low	High
Baseline	None	4 (33%)	3 (25%)	5 (42%)
	Low	1 (6%)	13 (72%)	4 (22%)
	High	0 (0%)	4 (67%)	2 (33%)

[/]“None” defined as an NCP score of 0, “Low” defined as an NCP score greater than 0 and less than 0.5, “High” defined as an NCP score of 0.5 or more.

Table 4Number (%) with CAC at follow-up by baseline level^I

		Follow-up		
		None	Low	Moderate/High
Baseline	None	23 (96%)	1 (4%)	0 (0%)
	Low	1 (20%)	3 (60%)	1 (20%)
	Moderate/High	0 (0%)	0 (0%)	6 (100%)

^I“None” defined as an CAC score of 0, “Low” defined as a CAC score greater than 0 but less than 100, “Moderate/High” was defined as a CAC score of 100 or more.

Table 5

Mean change in noncalcified coronary plaque score by various clinical variables, adjusted for time between assessments

Clinical Variable	Mean Change ²	P-value
Years between assessments	0.09 (per year)	0.04
SLEDAI at the time of follow-up assessment	0.01 (per 1 unit change)	0.82
PGA at the time of follow-up assessment	-0.16 (per 1 unit change)	0.28
Mean ¹ SLEDAI	-0.02 (per 1 unit change)	0.63
Mean ¹ Physician Global Assessment	-0.19 (per 1 unit change)	0.20
Mean ¹ Systolic Blood Pressure	-0.08 (per 10 mmHg change)	0.19
Mean ¹ Total Serum Cholesterol	-0.08 (per 25 mm/dl change)	0.26
Mean ¹ Body Mass Index	0.01 (per 1 unit change)	0.43
History of Smoking	-0.12	0.49
Current Smoking	-0.33	0.17
Mean ¹ Lupus Anticoagulant (by dRVVT)	0.01 (per second)	0.61
Proportion of time ¹ with Low C3	0.06 (per 0.5 difference)	0.66
Proportion of time ¹ with Low C4	-0.01 (per 0.5 difference)	0.95
Proportion of time ¹ with positive anti-dsDNA	0.11 (per 0.5 difference)	0.33
Mean ¹ Daily Prednisone Dose	-0.19 (per 10 mg/d difference)	0.38
Proportion of time ¹ on Hydroxychloroquine	-0.07 (per 0.5 difference)	0.71
Proportion of time ¹ on Immunosuppressants	-0.13 (per 0.5 difference)	0.06

¹The means and proportions of the clinical variables were calculated during the interval of time between the two NCP assessments.

²The numbers in this column are interpretable as the mean change in NCP score per unit change in the clinical predictors, after adjustment for time between NCP assessments.