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Depression and Progression of Subclinical Cardiovascular Disease in Systemic Lupus Erythematosus

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Abstract

Objective—Women with SLE have an increased incidence of premature CVD. A relationship between depression and increased inflammation leading to CVD has been proposed. The aim of this study was to evaluate the relationship between depression and the progression of subclinical atherosclerosis in women with SLE.

Methods—In this prospective case-control study, 149 participants with SLE and 126 controls were followed over 5 years. Evaluation included laboratory studies, assessment of CVD risk factors, depression screening, ultrasound evaluations of CIMT and carotid plaque, and assessment of SLE disease activity for the SLE cases.

Results—The SLE group had a higher rate of depression, 29% compared with 11% in the control group (p 0.003). When controlling for traditional CVD risk factors, the presence of baseline depression correlated with increased progression of CIMT in the SLE group, but not in the control group. The mean increase in CIMT was 0.026mm in the SLE group without depression versus 0.064mm in the depressed SLE group (p=0.0096).There was no association between depression and carotid plaque in either group, with the calculated OR for plaque progression in the depressed SLE group of 1.118 (95% CI 0.476–2.623) in the adjusted model.

Conclusion—Women with SLE and concomitant depression have an increased risk of developing subclinical atherosclerosis, as measured by CIMT, but not by carotid plaque. The data suggest that depression, a potentially modifiable risk factor, may contribute to the increased risk of subclinical atherosclerosis in women with SLE.

Patients with Systemic Lupus Erythematosus (SLE) are known to have a higher incidence of cardiovascular disease (CVD) when compared with healthy peers. CVD is a leading cause of mortality in patients with long-standing SLE, and patients with SLE are at risk for premature morbidity and mortality related to cardiovascular events. The etiology of this increased burden of CVD in patients with SLE is a matter of ongoing investigation. This has been attributed in part to a higher incidence of traditional CVD risk factors, including hypertension, sedentary lifestyle, and diabetes in patients with SLE, but these factors do not completely explain the higher incidence of CVD.[1] Chronic inflammation associated with

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SLE disease activity may also be a contributing factor. However, this relationship is not fully understood. There is some suggestion that psychological factors such as depression may also play a role in the increased risk of CVD in the general population.[2]

Clinical depression has been shown to be more common in patients with SLE than in the general population.[3] This relationship is complex and may be bidirectional; SLE activity may contribute to depression but depression may also contribute to increased SLE disease activity.[4] Patients with depression have been shown to have lower medication adherence and lower compliance with medical recommendations, which may explain some of this association. There may also be a role of increased inflammation associated with depression, which contributes to SLE activity and damage.

The relationship between depression and psychological stress and increased inflammation is controversial and not well established. Some small studies have shown higher levels of high-sensitivity C-reactive protein (CRP) and interleukin 6 in patients with depression.[5,6] These inflammatory markers are also associated with risk of cardiovascular disease progression. There is limited data regarding a possible association between depression in patients with SLE and their development of CVD. Studies of the general population have found mixed results regarding depression and the progression of subclinical atherosclerosis, as measured by coronary artery calcium (CAC) and carotid atherosclerosis. Multiple studies in the general population have shown that depression in women was associated with increased incidence and severity of CAC, aorta calcium, and carotid plaque.[7,8] In one study, this correlation was partially mediated by waist to hip ratio.[7] However, in the Multiethnic Study of Atherosclerosis (MESA) in the general population, there were no identified differences in CAC between patients with different measures of psychological distress including depression as measured by Centre for epidemiologic studies depression scale (CES-D).[9] Different findings from these studies may be related to the method of assessing for depression and whether current or historical depression was assessed.

To our knowledge, only two studies have been performed to date evaluating this possible relationship between depression in patients with SLE and the risk of developing CVD. In one study by Greco et al, depression, as measured by the CES-D, correlated with increased severity of CAC. However, this association was mediated by increased body-mass index (BMI).[10] Another study from the same group also showed that depression was correlated with increased CAC and carotid plaque.[11] The aim of this present study was to evaluate the association between depression and progression of subclinical cardiovascular disease as measured by carotid artery plaque and carotid intima-medial thickness (CIMT) in a population of women with SLE. Our hypothesis was that women with SLE would have a higher incidence of depression and this would correlate with increased progression of CIMT and carotid plaque compared with control patients without SLE.

Materials and Methods

Study Population

This study is an ancillary project of the Study of Lupus Vascular and Bone Long-term Endpoints (SOLVABLE). The study population is the SOLVABLE cohort, which includes

women with SLE, who meet at least 4 of the American College of Rheumatology classification criteria for definite SLE and are greater than or equal to 18 years of age, as well as matched controls. This cohort has been described previously.[12,13] 185 SLE patients and 186 matched controls were enrolled into the SOLVABLE cohort. The controls are women without SLE from the general population who are matched to patients by age (+/− 5 years), ethnicity, and residence zip code.

Data Collection

This study was approved by the Institutional Review Boards at Northwestern University and the University of Illinois at Chicago. All participants provided informed consent. These study participants were each followed for 5 years over the time span from 2004 through 2013, with study visits at baseline, 36 months, and 60 months. This ancillary study focuses on 60 month follow up data. 149 patients and 126 controls completed all visits through 60 months of follow up. At each visit, the study participants filled out a self-administered questionnaire, they were interviewed, a physical examination was performed by trained physicians, and blood and urine samples were collected for laboratory tests. They also underwent imaging to assess for subclinical cardiovascular disease. This included carotid ultrasound to measure intima media thickness and the presence of plaque.

SLE Related Factors

Baseline measurements of lupus disease activity and damage were determined by using the validated Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and the Systemic Lupus International Collaborating Clinics Damage Index (SLICC/ACR DI).[14,15] Trained physicians completed these measures at each visit. These physicians were Rheumatology fellows-in-training who were taught to perform these disease assessment tools for over one year in clinical practice before performing the disease activity assessment for the SOLVABLE cohort. Information regarding medication use for SLE was obtained at each visit by self-reported use from study participants, including glucocorticoids, hydroxychloroquine, and immunosuppressive agents. For glucocorticoids, details were obtained about cumulative past and current use. The immunosuppressive medications included azathioprine, cyclophosphamide, cyclosporine, methotrexate, mycophenolate mofetil, and tacrolimus.[13] For 10% of the study participants, the self-reported medication list was compared to the medications listed in the electronic medical record, and there was found to be 100% consistency. Additional laboratory tests associated with SLE including the antiphospholipid antibodies lupus anticoagulant and anti-cardiolipin were performed.

Depression

Study participants were screened at each visit for depression using the Centre for Epidemiologic Studies Depression Scale (CES-D). A positive screen for depression was defined by a score of 16 or greater.[16]

Traditional CVD Risk Factors

Information regarding traditional risk factors for cardiovascular disease was obtained from the self-administered questionnaires and objective measurements. Self-reported data

included age, race/ethnicity, tobacco use history, menopausal status, family history of CVD, and history of angina pectoris. BMI was determined from standard height and weight measurements at clinic visits. Blood pressure was also measured at clinic visits, and hypertension was defined as systolic blood pressure (BP) greater than 140mmHg or diastolic BP greater than 90 mmHg. Fasting lipid panels were obtained (including total cholesterol, high-density lipoprotein (HDL) cholesterol, and triglycerides), and low-density lipoprotein (LDL) was measured using the standard Friedewald equation. Plasma fasting glucose levels were measured as well. Self-reported data regarding use of aspirin and statins were obtained from patient questionnaires. Personal history of CVD events including myocardial infarction, percutaneous coronary angioplasty +/− stenting, coronary artery bypass graft (CABG) surgery, congestive heart failure, transient ischemic attack, and cerebrovascular accident (CVA) were also obtained from the questionnaire.

Subclinical Cardiovascular Disease Outcomes Measures

Study participants were assessed for carotid plaque and carotid intima media thickness from carotid ultrasounds. These studies were performed at baseline visits and then were repeated at 60 months of follow up.

For the measurement of carotid plaque, the presence of plaque was assessed in four bilateral locations for a total of eight sites, including the common carotid artery, carotid bulb, external carotid artery, and proximal internal carotid artery. Plaque was defined as a distinct focal area protruding into the lumen that was ≥50% greater than the thickness of the adjacent intima-media layer.[17] For each site, the degree of plaque was graded between 0 (no observable plaque) to 3 (plaque covering 50% or more of the vessel diameter). The grades from each of the eight sites were summed to create the plaque index.[18] The agreement for carotid plaque assessment between sonographers was good to excellent (kappa statistic, κ=0.78).[17] Progression was defined by an increased plaque grade at follow up when compared to baseline. A decrease in plaque grade or no change over time was counted as no progression. For CIMT, measurements were obtained in eight sites including the bilateral near and distal walls of the common carotid artery, the bilateral distal wall of the carotid bulb, and the internal carotid artery. Average CIMT was obtained from these eight measurements. Progression of CIMT was determined by the change in mean CIMT measurements from baseline to follow up.[13,19,20]

Statistical Analysis

Descriptive statistics including means, standard deviations, and ranges were calculated for patient characteristics, laboratory values, SLE-related indices, traditional CVD risk factor variables, and measurements of carotid plaque and CIMT. Logistic and linear regressions were performed to estimate the relationships between baseline depression and the progression of CVD outcome measures, carotid plaque and CIMT, respectively. The multivariate analyses were adjusted for baseline values of traditional CVD risk factors including age, BMI, total cholesterol to HLD ratio, hypertension, and diabetes, as well as corticosteroid use. Statistical differences between groups were determined using a significance level of 0.05.

Results

Of the 185 women with SLE enrolled in this study, 36 did not have a follow-up visit. Of these participants without follow-up, 20 refused participation, three did not respond, two were unable to be reached, two relocated, and nine were deceased. Of the nine deceased participants with SLE, causes of death were known in five: two died from heart failure, one died from lung cancer, one died from unknown cancer, and one died from infectious complications. One of the aforementioned had cardiovascular events (stroke) prior to enrollment. Of the 186 controls enrolled, 60 did not have a follow-up visit; one control was deceased from an unknown cancer and others refused participation or were unable to be reached. Baseline characteristics between the recruited participants and those included in the five-year study analyses varied only by age for both cases and controls and varied by baseline SLEDAI-2K scores and baseline CES-D scores for SLE cases. The SLE group included in the five-year analysis was older than the initially recruited SLE participants (mean age 48.6 vs 46.2 years, p=0.006), and the included control group was older than the initially recruited control participants (mean age 52.2 vs 50.0 years, p= 0.0003). The mean baseline SLEDAI-2K score was lower for the five-year follow-up SLE group compared to the initially recruited SLE participants (2.72 vs 4.22, p=0.03). The mean baseline CES-D score was lower for the five-year SLE group compared to the initially recruited SLE participants (11.5 vs 16.1, p=0.02). 149 SLE subjects and 126 controls were followed longitudinally and included in the subsequent analysis. The mean ± SD time to follow-up re-examination was 5.35 ± 0.60 years in cases and 5.62 ± 0.66 years for controls.

As seen in table 1, the SLE and control groups did not differ by race, BMI, smoking status, total cholesterol to HDL cholesterol ratio, creatinine level, or statin use. The cases were younger than controls, with mean age +/− SD 48.6 +/− 10.1 years for SLE cases and 52.2 +/− 10.1 years for controls (p=0.003). The control group had slightly higher baseline blood pressure, but rates of hypertension were similar in both groups and were low (mean +/− SD systolic blood pressure at baseline of 118.9 +/− 15.7 mmHg for SLE group versus 114.0 +/− 15.1 mmHg for the control group, p=0.01). The SLE group had a higher frequency of diabetes (14 cases, 9.4%) than the control group (1 case, 0.8%) (p=0.02). The SLE group had a higher rate of aspirin usage, 31 cases (20.8%) compared with 9 (7.1%) of the controls (p=0.001). In the SLE group, 56 were taking corticosteroids at baseline, and the mean dose was 12.0 mg of prednisone (SD 8.66).

As seen in Table 1, 29% of participants with SLE had depression at baseline, as measured by a positive CES-D score, and the control group had 11% incidence of baseline depression (p=0.003). The mean CES-D score for the SLE group was 11.5 versus 7.7 for the control group. Of the SLE cases with depression, the mean BMI +/− SD (30.98 +/− 9.09) was higher than the mean BMI of the SLE cases without depression at baseline (27.38 +/− 7.47) (P=0.014). There were no other significant differences of traditional CVD risk factors between the SLE cases with and without depression, as seen in table 2. There were no significant differences between the mean SLEDAI-2K or SLICC/ACR DI scores between the SLE cases with and without depression. A greater portion of the depressed SLE group was taking corticosteroids at baseline when compared with the SLE group without depression (53.5% vs 31.1%, p=0.011).

As seen in table 3, the mean CIMT for SLE cases was 0.61mm (SD 0.13) at baseline and 0.64mm (SD 0.12) at 5 years. The mean CIMT for controls was 0.63mm (SD 0.13) at baseline and 0.66mm (SD 0.13) at 5 years. Over the 5 year study period, there was net progression of mean CIMT in both the controls and the SLE cases, and this was seen in participants with and without depression. There was no difference between baseline mean CIMT in the depressed SLE group compared with the not-depressed SLE group (0.60mm vs 0.61mm, p= 0.50). However, as seen in table 5, in both the unadjusted and adjusted models, the presence of baseline depression correlated with increased progression of CIMT in the SLE group. There was a mean increase in CIMT of 0.026mm (95% CI 0.012–0.041)in the SLE group without depression and of 0.064mm (95% CI 0.041–0.087) in the SLE group with depression (p=0.0096). This correlation was not seen in the control group.

As seen in table 4, at baseline, 55 (36.9%) of SLE cases had carotid plaque as detected by B mode ultrasound. At 5 years, 67 (45.0%) of SLE cases had carotid plaque. Of the controls, 51 (40.5%) had carotid plaque at baseline, and 47 (37.3%) had carotid plaque at 5 years. Over the 5 year study period, 47 (31.5%) of women with SLE had progression of carotid plaque compared with 19 (15.1%) of the control group (p=0.038). There was no difference between the presence of plaque in the depressed SLE group versus the not-depressed SLE group either at baseline or at five years (p=1.0 and p=0.10, respectively). As seen in table 5, there was not a significant association between depression and mean progression of carotid plaque in the SLE group, with the calculated OR for plaque progression in SLE cases with depression of 1.118 (95% CI 0.476–2.623) in the adjusted model. There was no association between depression and progression of carotid plaque in the control group, 0.314 (95% CI 0.037–2.661).

Discussion

Patients with SLE have increased risk of developing atherosclerosis and premature CVD.[20,21] As previously shown in the SOLVABLE cohort, these patients have increased progression of subclinical CVD, as measured by CIMT and carotid plaque, when compared to healthy controls.[12] However, the associated factors and pathogenic mechanisms for this increased risk are not fully understood. This present study evaluated whether the presence of concomitant depression is a factor that contributes to this increased progression of subclinical atherosclerosis in patients with SLE.

Our results show that women with SLE have higher rates of depression than healthy peers, which is consistent with prior studies.[22,23] This relationship between SLE and depression is complex. Several factors including coping with chronic illness, pain, reduced physical functionality, and the use of corticosteroids may all contribute to the increased risk of depression in women with SLE.[24,25] The presence of depression has been shown to negatively impact other comorbidities including the traditional CVD risk factors diabetes, HTN, and obesity in the general population.[2] In our SLE group, participants with SLE and depression had higher mean BMI than the non-depressed SLE group. However, the increased progression of CIMT in the depressed SLE group was independent of BMI. Overall, despite the complex relationship between traditional CVD risk factors, SLE, and

depression, the presence of depression in the SLE group independently correlated with progression of CIMT in our study.

We have shown that women with SLE and depression have increased progression of CIMT, but not carotid plaque, when compared with women with SLE who are not depressed. This association was independent of baseline values of traditional cardiovascular risk factors, including age, BMI, cholesterol level, hypertension, diabetes status, and corticosteroid usage. Compared to CIMT, carotid plaque may represent a later stage in the progression of atherosclerosis.[19] Therefore, our findings demonstrating a significant change in CIMT but not in carotid plaque may represent a subtle association between depression and the progression of subclinical atherosclerosis in women with SLE. The increased burden of depression in women with SLE may therefore explain some of the excess CVD seen in SLE patients. Additional studies in larger cohorts could further evaluate these findings.

There are several strengths and limitations to acknowledge for this study. This was a small cohort, and we did not have sufficient numbers of patients with a positive smoking history to control for the known cardiovascular risk factor of tobacco use. We also did not control for kidney disease, which could additionally have an impact on the progression of atherosclerosis. Our follow up time was restricted to 5 years, and this may not have been long enough to detect changes in carotid plaque progression. However, the mean change in CIMT that we identified over five years of follow up was comparable to other studies of subclinical CVD progression in the general population.[26] Additionally, our assessment of carotid plaque with use of the plaque index is one of several validated methods that can be used to quantify the extent of carotid plaque. We did not measure total plaque area or total plaque volume which have also been validated.[27] However, to our knowledge these different methods of plaque assessment have not been directly compared in lupus patients. Another consideration is that there may be bias associated with loss of follow up in our study. Our population included in the final analysis was older and appeared to have less active lupus (based on lower SLEDAI-2K scores) and less depression (lower CES-D scores) than the initially recruited group. This may limit the generalizability of our results, but it is unlikely that these differences led to overestimation of the effect size. Additionally, we utilized a validated measure of depression, the CES-D, but we did not account for the treatment of depression in our analysis. Further studies could evaluate the impact of the treatment of depression on modifying this risk in patients with SLE.

Our SLE group had relatively low lupus disease activity and damage as measured by SLEDAI-2K and ACR/SLICC scores. Therefore, these results may not be representative of patients with more severe lupus. However, it may be hypothesized that patients with more severe/active lupus would have more advanced progression of atherosclerosis. Additional studies which include a population with higher SLE disease activity would be beneficial to further evaluate the factors associated with progression of atherosclerosis in patients with SLE, including depression.

This study uniquely evaluated the relationship between depression and the progression of atherosclerosis in women with SLE. The mechanism behind this association is not proven at this time. We hypothesize that depression may mediate behavioral factors, such as

medication adherence and negative lifestyle behaviors such as inactivity, as well as biologic factors including increased systemic inflammation. We did not find this same association with baseline depression and progression of subclinical CVD in healthy controls. This may suggest that the presence of concomitant depression potentiates other pro-atherosclerotic factors that are unique to women with SLE. Overall, our findings suggest that depression may be a potentially modifiable risk factor that contributes to the increased risk of subclinical CVD in women with SLE. Treating physicians should be aware of the importance of identifying depression in women with SLE.

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References

1. Bichile T, Petri M. Prevention and management of co-morbidities in SLE. Presse Med. 2014; 43:e187–e195. [PubMed: 24855047]
2. Nemeroff CB, Goldschmidt-Clermont PJ. Heartache and heartbreak—the link between depression and cardiovascular disease. Nature Reviews Cardiology. 2012; 9:526–539. [PubMed: 22733213]
3. Kozora E, Ellison MC, West S. Depression, fatigue, and pain in systemic lupus erythematosus (SLE): relationship to the American College of Rheumatology SLE neuropsychological battery. Arthritis and Rheumatism. 2006; 55(4):628–635. [PubMed: 16874786]
4. Exel E, Jacobs J, Korswagen L, Voskuyl AE, Stek M, Dekker J, Bultink IE. Depression in systemic lupus erythematosus, dependent on or independent of severity of disease. Lupus. 2012; 22(14): 1462–1469.
5. Miller GE, Stetler CA, Carney RM, Freedland KE, Banks WA. Clinical depression and inflammatory risk markers for coronary heart disease. The American Journal of Cardiology. 2002; 90(12):1279–1283. [PubMed: 12480034]
6. Steptoe A, Hamer M, Chida Y. The effects of acute psychological stress on circulating inflammatory factors in humans: a review and meta-analysis. Brain, Behavior, and Immunity. 2007; 21(7):901–912.
7. Agatisa PK, Matthews KA, Bromberger JT, Edmundowicz D, Chang Y, Sutton-tyrrell K. Coronary and Aortic Calcification in Women with a History of Major Depression. Archives of Internal Medicine. 2005; 165:1229–1236. [PubMed: 15956001]
8. Haas DC, Davidson KW, Schwartz DJ, Rieckmann N, Roman MJ, Pickering TG, Schwartz JE. Depressive symptoms are independently predictive of carotid atherosclerosis. The American Journal of Cardiology. 2005; 95(4):547–550. [PubMed: 15695154]
9. Diez Roux A, Ranjit L, Powell L, Jackson S, Lewis T, Shea S, Wu C. Annals of Internal Medicine Article Psychosocial Factors and Coronary Calcium in Adults without Clinical. Annals of Internal Medicine. 2006; 144:822–831. [PubMed: 16754924]
10. Greco CM, Kao AH, Sattar A, Danchenko N, Maksimowicz-McKinnon KM, Edmundowicz D, Sutton-Tyrrell K, Tracy RP, Kuller LH, Manzi S. Association between depression and coronary artery calcification in women with systemic lupus erythematosus. Rheumatology (Oxford, England). 2009; 48(5):576–581.
11. Greco CM, Li T, Sattar A, Kao AH, Danchenko N, Edmundowicz D, Manzi S. Association between depression and vascular disease in systemic lupus erythematosus. The Journal of Rheumatology. 2012; 39(2):262–268. [PubMed: 22174200]
12. Lertratanakul, A.; Wu, P.; Dyer, A.; Pearce, W.; Barinas-Mitchell, E.; Thompson, T.; Ramsey-Goldman, R. Risk Factors for Changes in Subclinical Atherosclerosis as Measured by Carotid Intima Media Thickness (IMT) and Plaque over Five Years in Women with Systemic Lupus

Erythematosus (SLE) [abstract]. Arthritis & Rheumatology Abstract Supplement: 2014 ACR/AHRP Annual Meeting; 2014 November 14–19; Boston, MA. 2014 Oct. Abstract number 862

13. Wu PU, Rhew EY, Dyer AR, Dunlop DD, Langman CB, Price H, Sutton-Tyrrell K, McPherson DD, Edmundowicz D, Kondos GT. 25-hydroxyvitamin D and cardiovascular risk factors in women with systemic lupus erythematosus. Arthritis and Rheumatism. 2009; 61(10):1387–1395. [PubMed: 19790113]
14. Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000. J Rheumatol. 2002; 29:288–291. [PubMed: 11838846]
15. Gladman DD, Urowitz MB, Goldsmith CH, et al. The reliability of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index in patients with systemic lupus erythematosus. Arthritis Rheum. 1997; 40:809–813. [PubMed: 9153540]
16. Radloff LS. The CES-D Scale: A Self-Report Depression Scale for Research in the General Population. Applied Psychological Measurement. 1977 Jun; 1(3):385–401.
17. Thompson T, Sutton-Tyrrell K, Wildman RP, et al. Progression of carotid intima-media thickness and plaque in women with systemic lupus erythematosus. Arthritis and rheumatism. 2008; 58:835–842. [PubMed: 18311797]
18. Sutton-Tyrrell K, Kuller LH, Matthews KA, et al. Subclinical atherosclerosis in multiple vascular beds: an index of atherosclerotic burden evaluated in postmenopausal women. Atherosclerosis. 2002; 160:407–416. [PubMed: 11849665]
19. Naqvi TZ, Lee MS. Carotid intima-media thickness and plaque in cardiovascular risk assessment. JACC. Cardiovascular Imaging. 2014; 7(10):1025–1038. [PubMed: 25051948]
20. Kao A, Lertratanakul A, Elliot J, Sattar A, Santelices L, Shah P, Birru M, Avram Z, Thompson T, Sutton-Tyrrell K, Ramsey-Goldman R, Manzi S. Relation of Carotid Intima-Media Thickness and Plaque With Incident Cardiovascular Events in Women With Systemic Lupus Erythematosus. Am J Cardiology. 2013; 112(7):1025–1032.
21. Lertratanakul A, Wu P, Dyer AR, Kondos G, Edmundowicz D, Carr J, Ramsey-Goldman R. Risk factors in the progression of subclinical atherosclerosis in women with systemic lupus erythematosus. Arthritis Care & Research. 2014; 66(8):1177–1185. [PubMed: 24376005]
22. Julian LJ, Gregorich SE, Tonner C, Yazdany J, Trupin L, Criswell LA, Yellen E, Katz P. Using the Center for Epidemiologic Studies Depression Scale to screen for depression in systemic lupus erythematosus. Arthritis Care & Research. 2011; 63(6):884–890.
23. Julian LJ, Tonner C, Yelin E, Yazdany J, Trupin L, Criswell LA, Katz P. Cardiovascular and disease-related predictors of depression in systemic lupus erythematosus. Arthritis Care & Research. 2011; 63(4):542–549. [PubMed: 21452266]
24. Warrington P, Bostwick JM. Psychiatric Adverse Effects of Corticosteroids. 2006; 81(10):1361–1367.
25. Skare T, da Silva Magalhães VD, Siqueira RE. Systemic lupus erythematosus activity and depression. Rheumatology International. 2014; 34(3):445–446. [PubMed: 23263497]
26. Berry JD, Liu K, Folsom AR, Lewis CE, Carr JJ, Polak JF, Lloyd-Jones DM. Prevalence and progression of subclinical atherosclerosis in younger adults with low short-term but high lifetime estimated risk for cardiovascular disease: the coronary artery risk development in young adults study and multi-ethnic study of atherosclerosis. Circulation. 2009; 119(3):382–389. [PubMed: 19139385]
27. Eder L, Gladman DD, Ibanez D, Urowitz MB. The correlation between carotid artery atherosclerosis and clinical ischemic heart disease in lupus patients. Lupus. 2014; 23:1142–1148. [PubMed: 24876099]

Significance and Innovations

- Women with SLE have an increased burden of premature atherosclerosis and CVD-related mortality, and the mechanisms for this increased risk are not fully understood.
- Depression is a common comorbidity in women with SLE.
- This study adds new information evaluating the potential association between depression and subclinical atherosclerosis in patients with SLE and identifies depression as a potential modifiable risk factor for CVD.

Table 1

Baseline Demographics of Participants with SLE and controls

	SLE Cases N=149	Controls N=126	p value
Traditional CVD Risk Factors			
Age (years), mean (SD)	48.6 (10.1)	52.2 (10.1)	**0.003**
African American, n (%)	42 (28.2%)	27 (21.4%)	0.290
Body Mass Index (kg/m^2), mean (SD)	28.4 (8.1)	29.8 (10.9)	0.260
Current Smoker, n (%)	10 (6.8%)	8 (6.4%)	0.890
Systolic Blood Pressure (mmHg), mean (SD)	114.0 (15.1)	118.9 (15.7)	**0.010**
Hypertension, n (%)	86 (58.7%)	40 (31.8%)	**<.0001**
Diabetes, n (%)	10 (6.7%)	1 (0.79%)	**0.013**
Total cholesterol: HDL ratio, mean (SD)	3.69 (1.42)	3.54 (1.05)	
Statin use, n (%)	29 (19.5%)	17 (13.5%)	0.186
Aspirin use, n (%)	37 (24.8%)	19 (15.1%)	**0.045**
Prednisone use, n (%)	56 (37.6%)	N/A	N/A
Prednisone dose (mg), mean (SD) *	12.06 (8.66)	N/A	N/A
Serum creatinine (mg/dL), mean (SD)	0.93 (1.16)	0.75 (0.13)	0.053
SLE-Related Factors			
SLICC/ACR-DI, mean (SD)	2.7 (3.3)	N/A	N/A
SLEDAI-2K, mean (SD)	2.3 (2.3)	N/A	N/A
Depression-related factors			
CES-D ≥ 16, n (%)	43 (28.9%)	14 (11.1%)	**<0.001**

* Of 56 patients taking prednisone at baseline visit

Table 2

Baseline Demographics of SLE Cases with and without Depression

	SLE Cases Not Depressed N=106	SLE Cases Depressed N=43	p value
Traditional CVD Risk Factors			
Age (years), mean (SD)	48.28 (10.86)	49.36 (7.96)	0.504
African American, n (%)	26 (24.53%)	16 (37.21%)	0.189
Body Mass Index (kg/m^2), mean (SD)	27.38 (7.47)	30.98 (9.09)	**0.014**
Current Smoker, n (%)	6 (5.71%)	4 (9.30%)	0.477
Systolic Blood Pressure (mmHg), mean (SD)	113.08 (14.60)	116.30 (16.13)	0.239
Diabetes, n (%)	6 (5.66%)	4 (9.30%)	0.475
Total cholesterol: HDL ratio, mean (SD)	3.60 (145)	3.90 (1.33)	0.250
Serum creatinine, mean (SD)	0.98 (1.36)	0.83 (0.22)	0.296
Statin use, n (%)	22 (20.75%)	7 (16.28%)	0.532
Aspirin use, n (%)	22 (20.75%)	15 (34.88%)	0.071
Prednisone use, n (%)	33 (31.1%)	23 (53.5%)	0.011
Prednisone dose, mean (SD) *	13.4 (9.83)	10.1 (6.34)	0.135
SLE-Related Factors			
SLICC/ACR-DI, mean (SD)	2.62 (2.83)	2.95 (1.81)	0.640
SLEDAI-2K, mean (SD)	2.21 (2.41)	2.60 (1.81)	0.293
Depression-related factors			
CES-D , mean (SD)	5.75 (4.59)	25.70 (8.25)	**<.0001**

* Of 23 depressed and 33 not depressed patients taking prednisone at baseline visit

Table 3

Carotid IMT at Baseline and Follow Up

Group	Depressed Status	n	Baseline mean (SD)	5 years mean (SD)	Mean change from baseline to 5 years (SD)
SLE	Not Depressed	106	0.61 (0.13)	0.64 (0.12)	0.03 (0.07)
	Depressed	43	0.60 (0.12)	0.66 (0.12)	0.06 (0.08)
	All	149	0.61 (0.13)	0.64 (0.12)	0.04 (0.08)
Controls	Not Depressed	112	0.63 (0.13)	0.65 (0.14)	0.03 (0.10)
	Depressed	14	0.66 (0.13)	0.68 (0.11)	0.02 (0.07)
	All	126	0.63 (0.13)	0.66 (0.13)	0.02 (0.10)

Table 4

Presence of Carotid Plaque at Baseline and Follow Up

Group	Depressed Status	n	Number with plaque at baseline (%)	Number with plaque at 5 years (%)	Total Participants with Progression at 5 years
SLE	Not Depressed	106	39 (36.8%)	43 (40.6%)	31 (29.3%)
	Depressed	43	16 (37.2%)	24 (55.8%)	16 (37.2%)
	All	149	55 (36.9%)	67 (45.0%)	47 (31.5%)
Controls	Not Depressed	112	43 (38.4%)	37 (33.0%)	18 (16.1%)
	Depressed	14	8 (57.1%)	7 (50.0%)	1 (7.1%)
	All	126	51 (40.5%)	47 (37.3%)	19 (15.1%)

Table 5

Progression of Carotid Plaque and CIMT at 5 Years

		Odds ratio of carotid plaque progression comparing depressed vs not depressed (95% CI)	IMT mean change (mm) from baseline to 5 years (95% CI)		
			Depressed	Not Depressed	p value
Cases (n= 149)	**Unadjusted**	1.434 (0.680, 3.025)	0.061 (0.039, 0.084)	0.028 (0.014, 0.042)	0.016
	Adjusted *	1.118 (0.476, 2.623)	0.064 (0.041, 0.087)	0.026 (0.012, 0.041)	0.0096
Controls (n=126)	**Unadjusted**	0.402 (0.049, 3.266)	0.019 (−0.033, 0.071)	0.026 (0.007, 0.044)	0.82
	Adjusted **	0.314 (0.037, 2.661)	0.020 (−0.033, 0.074)	0.025 (0.007, 0.044)	0.854

* Adjusted for Baseline Age, BMI, Total Cholesterol/HDL ratio, Diabetes, Hypertension, Corticosteroid use

** Adjusted for Baseline Age, BMI, Total Cholesterol/HDL ratio, Hypertension

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