HHS Public Access

Author manuscript

Arthritis Care Res (Hoboken). Author manuscript; available in PMC 2020 January 01.

Published in final edited form as:

Arthritis Care Res (Hoboken). 2019 January ; 71(1): 126–133. doi:10.1002/acr.23576.

Obesity Independently Associates with Worse Patient-Reported Outcomes in Women with Systemic Lupus Erythematosus

Sarah L Patterson[1], **Gabriela Schmajuk**[1,2], **Kashif Jafri**[1], **Jinoos Yazdany**[1], and **Patricia Katz**[1]

[1]University of California San Francisco

[2]San Francisco VA Hospital

Abstract

Background—We aimed to determine whether obesity in women with systemic lupus erythematosus (SLE) independently associates with worse patient-reported outcomes (PROs).

Methods—Data derive from a prospective study of adult women who carried a diagnosis of SLE verified by medical record review. Two established definitions for obesity were used: fat mass index (FMI) ≥ 13 kg/m^2 and BMI ≥ 30 kg/m^2. Dependent variables included 4 validated PROs: disease activity via Systemic Lupus Activity Questionnaire (SLAQ), depressive symptoms via Center for Epidemiologic Studies Depression Scale (CES-D), pain via Short Form 36 Health Survey (SF-36) Pain Subscale, and fatigue via SF-36 Vitality Subscale. We used multivariable linear regression to evaluate the associations of obesity with PROs while controlling for potential confounders (age, race, education, income, smoking, disease duration, disease damage, and prednisone use).

Results—The analysis included 148 participants; 32% were obese. In the multivariate regression model, obesity associated with worse scores on each PRO. Mean adjusted scores for SLAQ and CES-D comparing obese versus non-obese participants were 14.8 versus 11.1 (p=0.01) and 19.8 versus 13.1 (p<0.01), respectively. The obese group also reported worse mean adjusted scores for pain (38.7 vs. 44.2, p<0.01) and fatigue (39.6 vs. 45.2, p=0.01).

Conclusion—In a representative sample of women with SLE, obesity (by FMI and BMI) independently associated with worse patient reported outcomes, including disease activity, depressive symptoms, and symptoms of pain and fatigue. Obesity may represent a modifiable target for improving outcomes in this patient population.

Introduction

Patients with SLE experience a detriment in health-related quality of life (HRQoL) and other patient-reported outcomes (PROs) relative to both healthy individuals (1–9) and those with

Corresponding Author: Patricia Katz, PhD, University of California, San Francisco, 3333 California Street, San Francisco, CA 94143-0936, patti.katz@ucsf.edu.
DR. GABRIELA SCHMAJUK (Orcid ID : 0000-0003-2687-5043)
DR. KASHIF JAFRI (Orcid ID : 0000-0002-9717-7827)

Competing interests: The authors have no financial disclosures.

other chronic conditions such as rheumatoid arthritis and non-inflammatory rheumatic disease (10). The prevalence of poor PROs in lupus relative to other disease states has been established, but the cause of unfavorable results for the most impactful PROs in this patient population—namely pain, fatigue, and depressive symptoms—is not completely understood (1, 11–13). For example, clinical measures of disease activity and damage do not fully explain the observed severity of these symptoms (1). Multiple studies show the impact of sociodemographic factors such as poverty on PROs, but again, much of the variation in PROs remains unexplained (14). Studies in other inflammatory conditions have shown an association between excess adiposity and worse PROs (15–17), but prior research to understand the contribution of obesity to PROs in SLE is scant and conflicting (18, 19).

In this study, we aimed to investigate the relationship between excess fat mass and PROs in individuals with SLE. We conducted a cross-sectional observational study of women with SLE to measure the association of obesity with four PROs: self-reported disease activity, fatigue, pain, and depressive symptoms.

Patients and Methods

Study Design and Participants

The sample for the present study was drawn from participants in the University of California at San Francisco (UCSF) Lupus Outcomes Study (LOS). Participants in the LOS had formerly participated in a study of genetic risk factors for SLE outcomes (20, 21), and were recruited from both clinical- and community-based sources, including UCSF-affiliated clinics (22%), non-UCSF rheumatology offices (11%), lupus support groups and conferences (26%), and newsletters, web sites, and other forms of publicity (41%). SLE diagnoses using the American College of Rheumatology (ACR) criteria were verified by medical record review. LOS participants who lived in the greater San Francisco Bay area were recruited for an in-person assessment, which included measurement of body composition, in the UCSF Clinical and Translational Science Institute's Clinical Research Center (CRC). Exclusion criteria were non-English-speaking, age < 18 years, current oral prednisone dose ≥ 50 mg, current pregnancy, uncorrected vision problems that would interfere with reading ability, and joint replacement within 1 year.

A total of 325 individuals were asked to participate, of whom 74 (22.8%) were ineligible (35 lived too far away, 25 were too ill, 9 had recent surgery, 2 were pregnant, 2 had poor English skills, and 1 had cognitive problems). Of the 251 eligible individuals, 84 (33.5%) declined participation. Reasons for declining were primarily related to transportation (n = 12) and scheduling difficulties (n = 39). A total of 163 individuals completed study visits, and body composition data was obtained from 145 participants. Because of the substantial differences in body composition between men and women and the small number of men in the sample, only women were included in these analyses (n = 145). Additionally, three participants met the criterion for being underweight (body mass index [BMI] < 18.5 kg/m^2). Because being underweight may also be associated with poor outcomes, but for reasons that differ from that of obesity (e.g., cachexia from very active disease), the 3 underweight women were excluded, resulting in a sample size of 142 for the present analysis. The study received approval from the UCSF Committee on Human Research and was completed in accord with

the ethical guidelines outlined by the Helsinki Declaration. All subjects provided written informed consent.

Measures

Body composition measures—Height was measured with a wall-mounted stadiometer. Weight was measured with subjects wearing light indoor clothing and no shoes. BMI was calculated as weight (kg) divided by height (m^2). Body composition was further assessed using a Lunar Prodigy dual-energy x-ray absorptiometry (DXA) system. DXA has been validated as a method of assessing body composition in both younger and older persons, has good reported reproducibility, is sensitive to small changes in body composition, and can be used to measure fat mass with a precision error (1 SD) of 1 kg (22–25). Fat mass index (FMI), a measure of total fat mass adjusted for height, is calculated as fat mass (kg) divided by height (m^2). Two established definitions for obesity were used: FMI ≥13 kg/m^2 (26) and BMI ≥30 kg/m^2 (27).

Patient-reported Outcomes—Patient reported outcomes were assessed at the study visit using validated questionnaires. We assessed 4 different PROs: patient-reported disease activity, depressive symptoms, pain, and fatigue. Patient-reported disease activity was measured using the Systemic Lupus Activity Questionnaire (SLAQ), which has been shown to have good reliability (Cronbach's alpha 0.87) and validity in observational studies (28–30). The SLAQ assesses SLE disease activity by way of 24 items in 9 organ systems, with total scores ranging from 0 to 44, where higher scores indicate greater disease activity. Depressive symptoms were measured with the Center for Epidemiologic Studies Depression Scale (CES-D), a validated 20-item scale used to evaluate depressive symptom severity; scores range from 0 to 60 (31). Symptoms of pain and fatigue were measured using the Short Form 36 (SF-36) Health Survey bodily pain and vitality subscales, respectively. Though the SF-36 includes a total of 8 subscales, we focused on the two subscales measuring pain and fatigue as prior research has identified these symptoms as the most commonly reported symptoms and greatest area of unmet need in SLE (1, 11–13). The SF-36 subscales have demonstrated excellent reliability and validity in previous studies, and are the PROs most commonly used in studies of SLE (32). They are scored on a scale of 0–100, where higher scores reflect better status (e.g., less pain and fatigue).

SLE-specific disease factors—Disease duration was obtained by self-report. The Brief Index of Lupus Damage (BILD) was used to measure lupus-related cumulative organ damage (33, 34). The BILD was developed from the Systemic Lupus International Collaborating Clinics Damage Index (SDI) and includes items for important comorbid conditions such as cardiovascular events and diabetes. Participants were also queried regarding current immunomodulatory medications and glucocorticoids, including dosage and frequency.

Other variables—Sociodemographic characteristics included age, race, educational attainment (education beyond high school or not), and poverty status (household income ≤ or > 125% of the federal poverty level (35)). Participants were also asked about smoking status, with potential answers that included current, former, or never.

Statistical analysis

Differences in characteristics of obese and non-obese participants were tested with t-tests and chi-square analyses. Bivariate linear regression was used to quantify the cross-sectional association between obesity and each PRO. Multiple linear regression was then used to model each of the PROs as a function of obesity adjusting for age, race, educational attainment, poverty status, smoking, disease duration, disease damage, and moderate prednisone use (defined as ≥ 7.5 mg/day). Several procedures were used to ensure the integrity of the model: the normality assumption was evaluated visually with boxplots and normal probability plots; collinearity was assessed by calculating a variance inflation factor (VIF) for each covariate and removing collinear variables based on VIF ≥ 10 from the final model; and homoscedasticity was confirmed by plots of fitted values versus residuals. We also conducted sensitivity analyses in which additional measurements of adiposity were used as the dependent variable—including BMI ≥ 30 kg/m^2, BMI as a continuous measure, FMI as a continuous measure, and percent body fat—in order to determine whether the relationship between adiposity and each PRO varied depending on the measure of adiposity used. We then calculated adjusted means for each outcome based on the multivariable regression. All analyses were performed using Stata 14.

Results

Sample Characteristics

The demographic and disease-specific characteristics of study participants are presented in Table 1. Thirty two percent and 30% of participants met criteria for obesity by the FMI and BMI definitions, respectively. Five participants were obese by FMI but not BMI (4%), while 2 participants were obese by BMI and not by FMI (1%), and the remaining 95% demonstrated concordance across the two definitions. Study participants who were obese were more likely to be black, living at or below poverty level income, and have low education. Additionally, more participants in the obese group were on treatment for diabetes and had elevated levels for serum C-reactive protein.

Bivariate associations of obesity with patient reported outcomes

In bivariate regression analyses, obesity defined by FMI was significantly associated with higher disease activity as measured by SLAQ (β=4.55, $p<0.001$), greater symptoms of depression (β=7.74, $p<0.001$), and higher levels of pain (β=−7.16, $p<0.001$) and fatigue (β=−6.98, $p=0.001$) (Table 2). These relationships remained stable when we repeated the analysis using alternative definitions for obesity and adiposity, including the traditional obesity definition of BMI ≥ 30 kg/m^2.

Multivariate analysis

In the multivariate regression model, obesity defined by FMI was associated with significantly worse scores on each PRO after adjustment for age, race, educational attainment, poverty status, smoking, disease duration, disease damage (BILD), and glucocorticoid use (Table 3). Patient-reported disease activity was higher in the obese group: the mean adjusted SLAQ score was 14.8 (CI 12.7–16.9) versus 11.5 (CI 10.1–12.9) among

non-obese participants. Using CES-D to compare severity of depressive symptoms, the mean adjusted score was 19.8 (CI 16.1–23.4) for the obese group versus 13.1 (10.6–15.6) for the rest of the cohort. Similarly, the obese group reported a significantly higher burden of pain (p=0.005) and fatigue (p=0.01) as assessed by the SF-36 sub-scales. The same independent relationship between obesity and each PRO was observed after repeating the analyses using the BMI ≥ 30 kg/m^2 cut-off. The associations for obesity and each covariate with each PRO from the bivariate and multivariate regression analyses are presented in Tables 4 and 5.

Discussion

Among a representative sample of women with SLE, one-third of participants were obese. The obesity prevalence reported here is consistent with other reports in the limited literature on this topic. One study found a 39% prevalence of obesity among a group of women with lupus (36), while a more recent estimate reported a prevalence of 29–50% depending on the method of ascertainment (37). The proportion of obese in this lupus cohort was slightly lower than that of the general population in the United States during the same time frame. According to the Center for Disease Control National Health and Nutrition Examination Survey, obesity prevalence among women was 35.8% across all age groups, 31.9% among women ages 20–39, and 42.3% among women 60 or older (38).

We investigated the impacts of obesity in SLE and found a significant independent association with worse patient-reported outcomes, including self-reported disease activity, depressive symptoms, and symptoms of pain and fatigue. The raw differences in scores for the PROs between the obese and overweight/normal BMI groups were more than half the standard deviation of the mean for each measure, suggesting a difference that is clinically meaningful (39). After adjusting for relevant variables, the association between obesity and all four PROs remained statistically significant.

Body composition, and specifically excess adiposity, has been recognized as an important predictor of worse PROs in the general population and several rheumatic diseases. We now understand that adipose tissue is an active endocrine tissue that secretes pro-inflammatory cytokines and adipokines (including leptin, adiponectin, and resistan) into systemic circulation with the potential to impact joint disease (40–43). A study in patients with osteoarthritis of the shoulder found that greater synovial fluid adiponectin and leptin independently associated with greater patient-reported shoulder-specific pain (44), supporting the hypothesis that adiposity contributes to pain in OA via both local mechanical and systemic biomechanical mechanisms. A meta-analysis designed to assess the impact of obesity on outcomes in RA found that obese patients had significantly worse Health Assessment Questionnaire (HAQ) scores and higher pain scores at follow-up relative to non-obese patients even after controlling for relevant covariates (15). Similarly, studies evaluating the relationship between obesity and PROs in sarcoidosis and axial spondyloarthritis have demonstrated an independent association between the presence of obesity and worse PROs including pain, fatigue, and indices of global health status (16, 17).

This study builds on a limited literature with inconsistent findings on the relationship between obesity and PROs in SLE, and is the first to demonstrate a significant independent

association between obesity and greater levels of pain and fatigue in this patient population. Oeser et al examined these relationships using a sample of 100 patients with SLE, and though they observed an association between obesity and pain in the bivariate analysis, the relationship was not statistically significant in the adjusted multivariable model (19). We adjusted for a greater number of covariates and yet achieved statistically significant results in the multivariable regression for obesity on pain. Similarly, two previous studies on obesity in SLE (18, 19) found significant associations with fatigue in the bivariate—but not the multivariate—regression models. Our finding of a more robust association between obesity and both pain and fatigue may be due to differences in power (larger sample size), measurement tools (e.g., Fatigue Severity Scale versus SF-36 Vitality Subscale), or the composition of the multivariable models. Our multivariable regression model was crafted to include all major covariates with potential for confounding while eliminating those that demonstrated colinearity. The results remained consistent after testing multiple iterations of the model.

The primary limitation of this study is the cross-sectional design, which precludes the ability to infer causation or directionality between variables. We hypothesize that obesity adversely impacts PROs via both physiologic and psychosocial mechanisms. However, it is also possible that individuals who report greater disease activity and symptom burden are more sedentary, and therefore more likely to become obese. In the future, longitudinal data evaluating the relationship between obesity and changes in PROs over time will be helpful for elucidating the most proximal variable in these relationships. Additionally, future work should address whether the association between obesity and worse outcomes in this population includes less favorable scores on physician-reported instruments or whether the association is limited to PROs.

As with most human studies, there is a risk of selection bias. Less than half of the initially screened individuals were eligible and agreed to participate. The requirement that participants be well enough to attend study visits, as well as self-selection, may have resulted in a sample skewed toward women with less severe disease. Also, because this analysis included only female participants, the results are not generalizable to men with SLE. It is also possible that analysis of other PROs may yield different results.

The limitations of this study are outweighed by several strengths. The independent variable was measured using multiple definitions of obesity, including both body mass index and fat mass index. Though BMI has been the traditional measure of obesity and is easy to perform in clinical practice, it comes with limitations, including inability to distinguish between fat and lean mass (45). We overcame this limitation by using fat mass index as measured by DXA—which allows for distinction between fat and lean mass—as our primary measure of obesity. Additionally, the sample included participants with physician-confirmed lupus who were recruited from a variety of practice settings and represented a diverse range of racial and socioeconomic groups.

In conclusion, we found that excess adiposity is common in SLE and independently associates with greater symptom burden and self-reported disease activity. This finding has important clinical implications, as the symptoms assessed in our study are known to have

profound effects on quality of life and remain an area of unmet need for the majority with the disease. The relationship observed here between body composition and PROs further underscores the need to examine the impact of lifestyle interventions for lupus patients who are overweight. In addition to reducing the risk of important comorbidities such as cardiovascular disease, such interventions may reduce the severity of debilitating symptoms experienced by patients with SLE.

Acknowledgments

Funding: NIH T32 5T32AR007304-38 (SP)

References

1. Schmeding A, Schneider M. Fatigue, health-related quality of life and other patient-reported outcomes in systemic lupus erythematosus. Best Pract Res Clin Rheumatol. 2013; 27(3):363–75. [PubMed: 24238693]
2. Alarcon GS, McGwin G Jr, Uribe A, Friedman AW, Roseman JM, Fessler BJ, et al. Systemic lupus erythematosus in a multiethnic lupus cohort (LUMINA). XVII. Predictors of self-reported health-related quality of life early in the disease course. Arthritis Rheum. 2004; 51(3):465–74. [PubMed: 15188335]
3. Almehed K, Carlsten H, Forsblad-d'Elia H. Health-related quality of life in systemic lupus erythematosus and its association with disease and work disability. Scand J Rheumatol. 2010; 39(1): 58–62. [PubMed: 20132072]
4. Barta Z, Harrison MJ, Wangrangsimakul T, Shelmerdine J, Teh LS, Pattrick M, et al. Health-related quality of life, smoking and carotid atherosclerosis in white British women with systemic lupus erythematosus. Lupus. 2010; 19(3):231–8. [PubMed: 20007814]
5. Dobkin PL, Da Costa D, Fortin PR, Edworthy S, Barr S, Esdaile JM, et al. Living with lupus: a prospective pan-Canadian study. J Rheumatol. 2001; 28(11):2442–8. [PubMed: 11708416]
6. Rinaldi S, Doria A, Salaffi F, Ermani M, Iaccarino L, Ghirardello A, et al. Health-related quality of life in Italian patients with systemic lupus erythematosus. I. Relationship between physical and mental dimension and impact of age. Rheumatology (Oxford). 2004; 43(12):1574–9. [PubMed: 15353611]
7. Strand V, Aranow C, Cardiel MH, Alarcon-Segovia D, Furie R, Sherrer Y, et al. Improvement in health-related quality of life in systemic lupus erythematosus patients enrolled in a randomized clinical trial comparing LJP 394 treatment with placebo. Lupus. 2003; 12(9):677–86. [PubMed: 14514130]
8. Campbell R Jr, Cooper GS, Gilkeson GS. Two aspects of the clinical and humanistic burden of systemic lupus erythematosus: mortality risk and quality of life early in the course of disease. Arthritis Rheum. 2008; 59(4):458–64. [PubMed: 18383420]
9. Mahieu MA, Ahn GE, Chmiel JS, Dunlop DD, Helenowski IB, Semanik P, et al. Fatigue, patient reported outcomes, and objective measurement of physical activity in systemic lupus erythematosus. Lupus. 2016; 25(11):1190–9. [PubMed: 26869353]
10. Wolfe F, Michaud K, Li T, Katz RS. EQ-5D and SF-36 quality of life measures in systemic lupus erythematosus: comparisons with rheumatoid arthritis, noninflammatory rheumatic disorders, and fibromyalgia. J Rheumatol. 2010; 37(2):296–304. [PubMed: 20032098]
11. Pettersson S, Lovgren M, Eriksson LE, Moberg C, Svenungsson E, Gunnarsson I, et al. An exploration of patient-reported symptoms in systemic lupus erythematosus and the relationship to health-related quality of life. Scand J Rheumatol. 2012; 41(5):383–90. [PubMed: 22646821]
12. Moses N, Wiggers J, Nicholas C, Cockburn J. Prevalence and correlates of perceived unmet needs of people with systemic lupus erythematosus. Patient Educ Couns. 2005; 57(1):30–8. [PubMed: 15797150]
13. Danoff-Burg S, Friedberg F. Unmet needs of patients with systemic lupus erythematosus. Behav Med. 2009; 35(1):5–13. [PubMed: 19297299]

14. Trupin L, Tonner MC, Yazdany J, Julian LJ, Criswell LA, Katz PP, et al. The role of neighborhood and individual socioeconomic status in outcomes of systemic lupus erythematosus. J Rheumatol. 2008; 35(9):1782–8. [PubMed: 18634153]
15. Liu Y, Hazlewood GS, Kaplan GG, Eksteen B, Barnabe C. Impact of Obesity on Remission and Disease Activity in Rheumatoid Arthritis: A Systematic Review and Meta-Analysis. Arthritis Care Res (Hoboken). 2017; 69(2):157–65. [PubMed: 27159376]
16. Lee YX, Kwan YH, Png WY, Lim KK, Tan CS, Lui NL, et al. Association of obesity with patient-reported outcomes in patients with axial spondyloarthritis: a cross-sectional study in an urban Asian population. Clin Rheumatol. 2017
17. Gvozdenovic BS, Mihailovic-Vucinic V, Vukovic M, Lower EE, Baughman RP, Dudvarski-Ilic A, et al. Effect of obesity on patient-reported outcomes in sarcoidosis. Int J Tuberc Lung Dis. 2013; 17(4):559–64. [PubMed: 23485390]
18. Chaiamnuay S, Bertoli AM, Fernandez M, Apte M, Vila LM, Reveille JD, et al. The impact of increased body mass index on systemic lupus erythematosus: data from LUMINA, a multiethnic cohort (LUMINA XLVI) [corrected]. J Clin Rheumatol. 2007; 13(3):128–33. [PubMed: 17551377]
19. Oeser A, Chung CP, Asanuma Y, Avalos I, Stein CM. Obesity is an independent contributor to functional capacity and inflammation in systemic lupus erythematosus. Arthritis Rheum. 2005; 52(11):3651–9. [PubMed: 16258902]
20. Freemer MM, King TE Jr, Criswell LA. Association of smoking with dsDNA autoantibody production in systemic lupus erythematosus. Ann Rheum Dis. 2006; 65(5):581–4. [PubMed: 16150789]
21. Thorburn CM, Prokunina-Olsson L, Sterba KA, Lum RF, Seldin MF, Alarcon-Riquelme ME, et al. Association of PDCD1 genetic variation with risk and clinical manifestations of systemic lupus erythematosus in a multiethnic cohort. Genes Immun. 2007; 8(4):279–87. [PubMed: 17344889]
22. Heymsfield SB, Wang J, Heshka S, Kehayias JJ, Pierson RN. Dual-photon absorptiometry: comparison of bone mineral and soft tissue mass measurements in vivo with established methods. Am J Clin Nutr. 1989; 49(6):1283–9. [PubMed: 2729167]
23. Mazess RB, Barden HS, Bisek JP, Hanson J. Dual-energy x-ray absorptiometry for total-body and regional bone-mineral and soft-tissue composition. Am J Clin Nutr. 1990; 51(6):1106–12. [PubMed: 2349926]
24. Visser M, Pahor M, Tylavsky F, Kritchevsky SB, Cauley JA, Newman AB, et al. One- and two-year change in body composition as measured by DXA in a population-based cohort of older men and women. J Appl Physiol (1985). 2003; 94(6):2368–74. [PubMed: 12598481]
25. Wang J, Heymsfield SB, Aulet M, Thornton JC, Pierson RN Jr. Body fat from body density: underwater weighing vs. dual-photon absorptiometry. Am J Physiol. 1989; 256(6 Pt 1):E829–34. [PubMed: 2735405]
26. Kelly TL, Wilson KE, Heymsfield SB. Dual energy X-Ray absorptiometry body composition reference values from NHANES. PLoS One. 2009; 4(9):e7038. [PubMed: 19753111]
27. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000; 894:i–xii. 1–253. [PubMed: 11234459]
28. Karlson EW, Daltroy LH, Rivest C, Ramsey-Goldman R, Wright EA, Partridge AJ, et al. Validation of a Systemic Lupus Activity Questionnaire (SLAQ) for population studies. Lupus. 2003; 12(4):280–6. [PubMed: 12729051]
29. Romero-Diaz J, Isenberg D, Ramsey-Goldman R. Measures of adult systemic lupus erythematosus: updated version of British Isles Lupus Assessment Group (BILAG 2004), European Consensus Lupus Activity Measurements (ECLAM), Systemic Lupus Activity Measure, Revised (SLAM-R), Systemic Lupus Activity Questionnaire for Population Studies (SLAQ), Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI–2K), and Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI). Arthritis Care Res (Hoboken). 2011; 63(Suppl 11):S37–46. [PubMed: 22588757]
30. Yazdany J, Yelin EH, Panopalis P, Trupin L, Julian L, Katz PP. Validation of the systemic lupus erythematosus activity questionnaire in a large observational cohort. Arthritis Rheum. 2008; 59(1): 136–43. [PubMed: 18163398]

31. Smarr KL, Keefer AL. Measures of depression and depressive symptoms: Beck Depression Inventory-II (BDI-II), Center for Epidemiologic Studies Depression Scale (CES-D), Geriatric Depression Scale (GDS), Hospital Anxiety and Depression Scale (HADS), and Patient Health Questionnaire-9 (PHQ-9). Arthritis Care Res (Hoboken). 2011; 63(Suppl 11):S454–66. [PubMed: 22588766]
32. Ware JE Jr, Gandek B. Overview of the SF-36 Health Survey and the International Quality of Life Assessment (IQOLA) Project. J Clin Epidemiol. 1998; 51(11):903–12. [PubMed: 9817107]
33. Katz P, Trupin L, Rush S, Yazdany J. Longitudinal validation of the Brief Index of Lupus Damage. Arthritis Care Res (Hoboken). 2014; 66(7):1057–62. [PubMed: 24376263]
34. Yazdany J, Trupin L, Gansky SA, Dall'era M, Yelin EH, Criswell LA, et al. Brief index of lupus damage: a patient-reported measure of damage in systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2011; 63(8):1170–7. [PubMed: 21584946]
35. McCormick N, Trupin L, Yelin EH, Katz PP. Socioeconomic Predictors of Incident Depression in Systemic Lupus Erythematosus. Arthritis Care Res (Hoboken). 2017
36. Petri M. Detection of coronary artery disease and the role of traditional risk factors in the Hopkins Lupus Cohort. Lupus. 2000; 9(3):170–5. [PubMed: 10805483]
37. Katz P, Gregorich S, Yazdany J, Trupin L, Julian L, Yelin E, et al. Obesity and its measurement in a community-based sample of women with systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2011; 63(2):261–8. [PubMed: 20824801]
38. Ogden CL, Carroll MD, Kit BK, Flegal KM. Prevalence of obesity in the United States, 2009–2010. NCHS Data Brief. 2012; (82):1–8.
39. Farivar SS, Liu H, Hays RD. Half standard deviation estimate of the minimally important difference in HRQOL scores? Expert Rev Pharmacoecon Outcomes Res. 2004; 4(5):515–23. [PubMed: 19807545]
40. Bokarewa M, Nagaev I, Dahlberg L, Smith U, Tarkowski A. Resistin, an adipokine with potent proinflammatory properties. J Immunol. 2005; 174(9):5789–95. [PubMed: 15843582]
41. Gandhi R, Takahashi M, Smith H, Rizek R, Mahomed NN. The synovial fluid adiponectin-leptin ratio predicts pain with knee osteoarthritis. Clin Rheumatol. 2010; 29(11):1223–8. [PubMed: 20349258]
42. Lago R, Gomez R, Otero M, Lago F, Gallego R, Dieguez C, et al. A new player in cartilage homeostasis: adiponectin induces nitric oxide synthase type II and pro-inflammatory cytokines in chondrocytes. Osteoarthritis Cartilage. 2008; 16(9):1101–9. [PubMed: 18261936]
43. Toussirot E, Streit G, Wendling D. The contribution of adipose tissue and adipokines to inflammation in joint diseases. Curr Med Chem. 2007; 14(10):1095–100. [PubMed: 17456023]
44. Gandhi R, Perruccio AV, Rizek R, Dessouki O, Evans HM, Mahomed NN. Obesity-related adipokines predict patient-reported shoulder pain. Obes Facts. 2013; 6(6):536–41. [PubMed: 24335140]
45. Okorodudu DO, Jumean MF, Montori VM, Romero-Corral A, Somers VK, Erwin PJ, et al. Diagnostic performance of body mass index to identify obesity as defined by body adiposity: a systematic review and meta-analysis. Int J Obes (Lond). 2010; 34(5):791–9. [PubMed: 20125098]

Significance and Innovations

- This is one of the first studies of systemic lupus erythematosus (SLE) to evaluate the impact of excess adiposity on patient reported outcomes (PROs) and the first to use DXA to quantify fat mass in the investigation of these relationships.
- Among adult women with SLE, obesity was common (32% of the cohort), and independently associated with worse PROs, including self-reported disease activity, depressive symptoms, and symptoms of pain and fatigue.
- The association between excess adiposity and worse PROs remained stable using multiple measurements of adiposity and definitions of obesity.
- These findings highlight the need for lifestyle interventions targeting lupus patients who are overweight given the potential to reduce both cardiovascular risk and debilitating symptoms common in this disease.

Table 1

Characteristics of Patients with SLE According to Obesity Category (N(%)

	Overall	Not Obese	Obese[a]	P
Number (%)	142	96 (66.9)	47 (33.1)	
Demographic				
Age, mean ± SD	47.9 ± 12.3	47.3 ± 12.7	48.9 ± 11.7	0.47
Race				0.03
White	92 (64.8)	68 (71.6)	24 (51.1)	
Black	20 (14.1)	9 (9.5)	11 (23.4)	
Asian	18 (12.7)	14 (14.7)	4 (8.5)	
Latino	25 (17.6)	15 (15.8)	10 (21.3)	
Unspecified or other	4 (2.8)	1 (1.1)	3 (6.4)	
Education beyond high school	123 (86.6)	86 (90.5)	37 (78.7)	0.05
Poverty level income[b]	21 (15.3)	8 (8.7)	13 (28.9)	0.002
Health related				
Cardiovascular Disease[c]	5 (3.5)	3 (3.2)	2 (4.3)	0.74
Diabetes Mellitus on treatment	8 (5.6)	2 (2.1)	6 (12.8)	0.01
SLE disease duration, years	15.5 ± 8.9	14.9 ± 8.4	16.9 ± 9.9	0.21
C-reactive protein, mean ± SD	4.2 ± 7.6	3.2 ± 7.0	6.2 ± 8.4	<0.01
Smoking, current	8 (5.6)	6 (6.3)	2 (4.3)	0.62
Smoking, ever	53 (37.6)	37 (39.0)	16 (34.8)	0.63
Medication Use[d]				
Glucocorticoid	63 (45.3)	42 (45.2)	21 (45.7)	0.96
Prednisone dose ≥ 7.5 mg/day	29 (20.1)	18 (19.4)	11 (23.9)	0.53
Hydroxychloroquine	63 (44.4)	44 (46.3)	19 (40.4)	0.51
Oral DMARD[e]	50 (35.2)	35 (36.8)	15 (31.9)	0.56
Cyclophosphamide	7 (4.9)	7 (7.4)	0 (0.0)	0.06
Rituximab	5 (3.5)	5 (5.3)	0 (0.0)	0.12

Except where indicated otherwise, values are number (%). P-values were calculated using chi-squared test for categorical measures, t-test for normally distributed continuous measures, and Wilcoxon-rank sum for skewed continuous measures.

[a] Defined as fat mass index ≥ 13 kg/m^2.

[b] Household income ≤ 125% of the federal poverty level.

[c] History of transient ischemic attack, stroke, or myocardial infarction.

[d] Report of use within the last 12 months.

[e] Disease Modifying Antirheumatic Drugs – includes azathioprine, mycophenolate mofetil, methotrexate, and tacrolimus.

Table 2

Raw Medians for Patient Reported Outcomes by Obesity Status

	Total	Obese*	Not Obese	P
Disease Activity (SLAQ)	12.0 (8.0, 18.0)	15.0 (11.0, 19.0)	10.0 (5.0, 15.0)	<0.001
Depression (CES-D)	13.5 (5.0, 23.0)	20.0 (11.0, 31.0)	10.0 (4.0, 21.0)	<0.001
Pain (SF-36 Pain) †	41.4 (33.4, 50.3)	37.2 (33.0, 41.4)	46.1 (33.4, 55.4)	<0.001
Fatigue (SF-36 Vitality) †	42.7 (33.4, 52.1)	36.5 (30.2, 45.8)	45.8 (36.5, 55.2)	<0.001

Values are median (interquartile range). P-values calculated with Wilcoxon rank-sum test.

*Obese defined as fat mass index ≥ 13 kg/m^2

†Higher scores reflect better status (less pain/fatigue)

SLAQ – Systemic Lupus Activity Questionnaire (range: 0–44)

CES-D – Center for Epidemiologic Studies Depression Scale (range: 0–60)

SF-36 – Short Form 36 Health Survey (range 0–100)

Table 3

Adjusted* Means for Patient Reported Outcomes by Obesity Status

	Obese by FMI ≥ 13 kg/m^2			Obese by BMI ≥ 30 kg/m^2		
	Yes	**No**	**P**	**Yes**	**No**	**P**
Disease Activity (SLAQ)	14.8 (12.7–16.9)	11.5 (10.1–12.9)	0.01	14.7 (12.6–16.9)	11.6 (10.2–13.1)	0.02
Depression (CES-D)	19.8 (16.1–23.4)	13.1 (10.6–15.6)	0.004	20.3 (16.5–24.0)	13.1 (10.7–15.5)	0.003
Pain (SF-36 Pain) †	38.7 (35.7–41.7)	44.2 (42.2–46.3)	0.004	38.2 (35.1–41.3)	44.2 (42.1–46.1)	0.003
Fatigue (SF-36 Vitality) †	39.6 (36.2–43.0)	45.2 (42.9–47.6)	0.01	38.0 (34.5–41.4)	45.7 (43.4–47.9)	<0.001

*Adjusted means calculated based on multivariate linear regression adjusted for age, race, education, income, smoking, disease duration, disease damage (Brief Index of Lupus Damage score), and prednisone use. P-values by Wilcoxon rank-sum test.

†Higher scores reflect better status (less pain/fatigue)

SLAQ – Systemic Lupus Activity Questionnaire

CES-D – Center for Epidemiologic Studies Depression Scale

SF-36 – Short Form 36 Health Survey

Arthritis Care Res (Hoboken). Author manuscript; available in PMC 2020 January 01.

Table 4

Bivariate Relationships for Obesity and Covariates with Patient Reported Outcomes

	SLAQ β (P)	CES-D β (P)	SF-36 Pain β (P)	SF-36 Vitality β (P)
Body Composition				
Obese by FMI ≥ 13 kg/m^2	**4.55 (<0.001)**	**7.74 (<0.001)**	**−7.16 (<0.001)**	**−6.98 (0.001)**
Obese by BMI ≥ 30 kg/m^2	**4.54 (0.001)**	**8.17 (<0.001)**	**−7.30 (<0.001)**	**−8.66 (<0.001)**
Covariates				
Age	0.02 (0.68)	−0.01 (0.90)	−0.07 (0.31)	−0.11 (0.17)
Race	−0.78 (0.55)	2.76 (0.20)	0.77 (0.68)	−2.91 (0.15)
Low education[1]	1.27 (0.48)	2.67 (0.38)	−2.95 (0.26)	−2.90 (0.31)
Poverty level income[2]	**4.26 (0.01)**	**8.87 (0.001)**	**−5.49 (0.02)**	**−5.35 (0.04)**
Smoking, current	**5.13 (0.04)**	2.18 (0.62)	−5.29 (0.16)	−2.15 (0.60)
Smoking, ever	0.79 (0.53)	−1.01 (0.64)	**−3.90 (0.04)**	0.23 (0.91)
Disease Duration	−0.09 (0.16)	−0.01 (0.90)	−0.05 (0.61)	0.02 (0.81)
BILD Score	0.57 (0.055)	0.46 (0.36)	**−1.22 (0.01)**	−0.83 (0.08)
Prednisone Use (yes/no)	2.20 (0.08)	1.47 (0.49)	−3.31 (0.07)	−2.41 (0.23)
Prednisone Dose	0.18 (0.08)	0.09 (0.60)	−0.25 (0.10)	−0.04 (0.81)
Prednisone > 7.5 mg/day	**4.64 (0.002)**	4.20 (0.11)	**−5.70 (0.01)**	−2.92 (0.23)
Oral DMARD[3]	−0.52 (0.69)	2.16 (0.32)	−2.53 (0.18)	**−4.80 (0.02)**
Immunosuppression[4]	−0.48 (0.70)	3.23 (0.13)	−2.74 (0.14)	**−5.13 (0.01)**

SLAQ, Systemic Lupus Activity Questionnaire; CES-D, Center for Epidemiologic Studies Depression Scale; SF-36 Pain, Short Form 36 Health Survey Pain Subscale (higher scores indicate less pain); SF-36 Vitality, Short Form 36 Vitality Subscale (higher scores indicate less fatigue); FMI, fat mass index; BMI, body mass index; BILD, Brief Index of Lupus Damage; DMARD, Disease-modifying antirheumatic drugs.

[1] No education beyond high school.

[2] Household income ≤ 125% of the federal poverty level.

[3] Includes azathioprine, mycophenolate mofetil, methotrexate, and tacrolimus.

[4] Includes oral DMARDs listed above plus cyclophosphamide and rituximab.

Table 5

Multivariate Relationships for Obesity and Covariates with Patient Reported Outcomes

	SLAQ β (P)	CES-D β (P)	SF-36 Pain β (P)	SF-36 Vitality β (P)
Obese by FMI ≥ 13 kg/m2	**3.33 (0.01)**	**6.67 (0.004)**	**−5.55 (0.004)**	**−5.66 (0.01)**
Age	0.11 (0.06)	0.02 (0.82)	−0.16 (0.05)	**−0.20 (0.03)**
Race	0.82 (0.52)	**5.96 (0.01)**	−1.62 (0.38)	**−4.77 (0.02)**
Low education[1]	−0.64 (0.72)	−2.57 (0.41)	−0.45 (0.86)	−1.00 (0.73)
Poverty level income[2]	3.01 (0.10)	**8.67 (0.01)**	−3.06 (0.24)	**−6.39 (0.03)**
Smoking, current	3.91 (0.14)	0.80 (0.86)	−2.95 (0.44)	−0.24 (0.96)
Disease Duration	**−0.19 (0.01)**	−0.01 (0.92)	0.08 (0.45)	0.18 (0.15)
BILD Score	**0.69 (0.02)**	0.51 (0.31)	**−1.23 (0.004)**	−0.90 (0.06)
Prednisone > 7.5 mg/day	**3.33 (0.03)**	2.65 (0.31)	**−5.73 (0.01)**	−2.38 (0.33)
Model F value (df)	3.72	2.98	3.98	3.28
Model R^2	0.21	0.18	0.23	0.19
Model Adjusted R^2	0.16	0.12	0.17	0.13

SLAQ, Systemic Lupus Activity Questionnaire; CES-D, Center for Epidemiologic Studies Depression Scale; SF-36 Pain, Short Form 36 Health Survey Pain Subscale (higher scores indicate less pain); SF-36 Vitality, Short Form 36 Vitality Subscale (higher scores indicate less fatigue); FMI, fat mass index; BILD, Brief Index of Lupus Damage; DMARD, Disease-modifying antirheumatic drugs.

[1] No education beyond high school.

[2] Household income ≤ 125% of the federal poverty level.