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Muscle Strength Predicts Changes in Physical Function in Women with Systemic Lupus Erythematosus

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Abstract

Objective—Cross-sectional studies have observed that muscle weakness is associated with worse physical function among women with systemic lupus erythematosus (SLE). The present study examines whether reduced upper and lower extremity muscle strength predict declines in function over time among adult women with SLE.

Methods—One hundred forty-six women from a longitudinal SLE cohort participated in the study. All measures were collected during in-person research visits approximately 2 years apart. Upper extremity muscle strength was assessed by grip strength. Lower extremity muscle strength was assessed by peak knee torque of extension and flexion. Physical function was assessed using the Short Physical Performance Battery (SPPB). Regression analyses modeled associations of baseline upper and lower extremity muscle strength with follow-up SPPB scores controlling for baseline SPPB, age, SLE duration, SLE disease activity (Systemic Lupus Activity Questionnaire [SLAQ]), physical activity level, prednisone use, body composition, and depression. Secondary analyses tested whether associations of baseline muscle strength with follow-up in SPPB scores differed between intervals of varying baseline muscle strength.

Results—Lower extremity muscle strength strongly predicted changes over 2 years in physical function even when controlling for covariates. The association of reduced lower extremity muscle strength with reduced future physical function was greatest among the weakest women.

Conclusions—Reduced lower extremity muscle strength predicted clinically significant declines in physical function, especially among the weakest women. Future studies should test whether therapies that promote preservation of lower extremity muscle strength may prevent declines in function among women with SLE.

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INTRODUCTION

Reduced muscle strength is associated with decreased physical function in various study populations, including elders and individuals with osteoarthritis (1–10). Among populations with rheumatic disease, data are emerging that describe similar associations between muscle structure and function and physical function. Prior observational studies have demonstrated strong associations between muscle density, a measure of muscle integrity and fatty infiltration, and physical function among individuals with rheumatoid arthritis (RA) (11–13). Individuals with SLE frequently experience reduced physical function (14–16). However, only limited data exist describing the relationship between muscle strength and physical function among individuals with SLE (17, 18). Using cross-sectional data, our group recently observed that, among women with SLE, low muscle strength is strongly associated with reduced self-reported physical function even when controlling for differences in muscle mass and other covariates (19).

The ability of muscle strength to predict changes in function is well-established among elderly populations (3, 4, 9, 10, 20–22). However, among younger patients with rheumatic illness, including SLE, there are few published studies that examine the longitudinal relationships between muscle strength and physical function. Given our prior cross-sectional findings of an association between low muscle strength and self-reported physical function among women with SLE, we sought to further examine whether low muscle strength predicts changes in physical function in this same cohort.

SUBJECTS AND METHODS

Subjects

The sample for the present study was drawn from participants in the University of California, San Francisco (UCSF) Lupus Outcomes Study (LOS). Participants in the LOS had formerly participated in a study of genetic risk factors for SLE outcomes (23, 24) 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 (25) were verified by medical record review. Respondents participated in annual structured telephone interviews. Additional details regarding the LOS are reported by Yelin *et al.*(26).

For the present study, LOS participants who lived in the greater San Francisco Bay area were recruited for an in-person assessment in the UCSF Clinical and Translational Science Institute's Clinical Research Center (CRC) that included measurement of upper and lower extremity muscle strength. Exclusion criteria were non–English speaking, age <18 years, current daily oral prednisone dose of 50 mg or greater, current pregnancy, uncorrected vision problems that would interfere with reading ability, and joint replacement within 1 year.

Three hundred twenty-five individuals were potentially eligible for the CRC study and were asked to participate during one of their annual telephone interviews; 81 (24.9%) were

ineligible (35 were actually outside the recruitment area, 25 were too ill, 9 had had recent surgery, 7 were unable to complete the study procedures, 2 were pregnant, 2 had poor English proficiency, and 1 had severe cognitive problems and was unable to complete the telephone interview). Of the 251 eligible individuals, 84 (33.5%) declined participation. The most common reasons for declining were primarily related to transportation (n=12) and scheduling difficulties (n=39). One hundred fifty-seven individuals completed study visits. Eleven men were excluded because there were too few for separate analysis. One hundred and forty-six women were included in the present analysis. Participants completed assessments at baseline and then again for a follow-up visit (Supplementary Figure 1). Average time between baseline and follow-up visit was 2.4 years. This study was approved by the UCSF Committee on Human Research.

Measures

Muscle strength—Lower extremity muscle strength was assessed by knee torque. A Biodex® unit was used to measure peak isokinetic torques of knee extension and flexion at 120 degrees/second adjusted for body weight (27). Participants completed two reproducible and acceptable trials. Average maximal knee strength for extension and flexion were analyzed. Peak isokinetic knee torque was chosen because this is commonly used proxy measures for muscle strength among rheumatologic and non-rheumatologic populations (3, 4, 9, 17, 20, 28–30). Isokinetic peak knee torque measured by Biodex® has excellent test-retest reliability with a previously reported intraclass correlation coefficient of 0.95 (31). Grip strength of the participant's dominant hand was measured using a hand-held dynamometer (32).

Body Composition—Body composition and regional body muscle distribution were assessed in the CRC using a Lunar Prodigy whole-body dual energy absorptiometry (DXA) system (GE Healthcare). The DXA technique is able to differentiate bone, muscle, and fat and calculates total body mass (kg), fat mass (gm), percent fat, and lean body mass (gm), as well as the regional distribution of these components (left arm, leg, and trunk; right arm, leg, and trunk; and total arm, leg, and trunk). DXA has been used previously in determination of soft tissue mass and has been validated (33–35) as a method of assessing body composition in both younger and older individuals. It has good reported reproducibility and is sensitive to small changes in body composition (22). The precision errors ±1 SD for percent fat are 1.4% in soft tissue, 1.0 kg for fat mass, and 0.8 kg for lean tissue mass (34). DXA has previously been used successfully to assess body composition among individuals with SLE (36, 37). Height-adjusted indices were created for total lean body mass (LMI, kg/m^2, lean mass index) and fat mass (FMI, kg/m^2, fat mass index). The primary measure of body composition used in these analyses was the ratio of LMI to FMI (LMI/FMI), which was chosen in order to account for effect of height and fat mass on total lean body mass(38–43).

Physical Function—Physical function was measured using the Short Physical Performance Battery (SPPB) (20, 21, 44). The SPPB assesses primarily lower extremity function and includes 3 measures, each scored from 0 to 4 points with 0 corresponding to lower performance and 4 to higher performance. An overall performance score sums the 3 measures and ranges from 0 to 12. The standing balance test asks subjects to maintain their

feet in a side-by-side, semi-tandem stand, or tandem stand for 10 seconds. A walking speed test asks subjects to walk 4 meters at their normal pace. The chair stand test measures the time required for the subject to stand up and sit down from a standard chair 5 times with arms folded across the chest. The SPPB has excellent inter-observer reliability, test-retest reliability, and predictive validity (20, 21, 44). A change of 1 point in the overall SPPB score is considered the minimum clinically important difference (MCID) (44).

Other Variables—Sociodemographic characteristics (age, race/ethnicity, education, income) and smoking status were obtained from the baseline LOS telephone interview. Disease activity was assessed using the Systemic Lupus Activity Questionnaire (SLAQ) a validated, self-report measure of disease activity in SLE (45, 46). The SLAQ was taken from the LOS interview that most closely preceded the CRC visit (mean time to visit = 54.4 days). Glucocorticoid use was assessed at the time of the visit. Physical activity was assessed by self-report with the long form of the International Physical Activity Questionnaire (IPAQ) (47). The IPAQ has been used and validated in a number of populations (48, 49). The scoring protocol provides a cut point by which individuals' weekly energy expenditure can be categorized as low, moderate, or high. Individuals who expended fewer than 600 metabolic equivalent (MET) minutes per week were classified as inactive for these analyses (47, 48). To simplify reporting, individuals who reported 600 MET minutes per week or more were referred to as "active." Depressive symptoms were assessed using the Center for Epidemiologic Studies Depression Scale (CES-D). The CES-D is a commonly used 20-item scale to evaluate depressive symptom severity, with a score range of 0–60 (50).

Statistical Analysis

Differences in baseline characteristics between women who did and did not complete strength measures were tested with chi-squared and *t*-test analyses. Linear regression analyses were used to model the association of baseline muscle strength with follow-up SPPB score with and without adjusting for covariates (baseline SPPB score, age, SLAQ score, disease duration, prednisone use, physical activity level, and depressive symptom score). To test whether the relationship between baseline muscle strength and follow-up SPPB score differs across values of muscle strength, linear splines were used to model the association of muscle strength with follow-up SPPB score within intervals of muscle strength, again adjusting for baseline SPPB. Linear splines allowed the regression parameters to vary between intervals of muscle strength (51). The cutpoints delimiting the intervals were empirically calculated for each muscle strength measure based on that measure's distribution of values.

In additional sensitivity analyses, we examined how the observed association of muscle strength with physical function was related to missing muscle strength data. Individuals with missing baseline muscle strength data were assigned the weakest recorded value for missing measures (i.e., the lowest knee torque and grip strength values) and regression models were repeated. Statistical analyses were conducted using Stata, version 13.1 (StataCorp, College Station, TX).

RESULTS

Subject characteristics

Sociodemographic and health-related characteristics of the study sample are shown in Table 1. The overall mean ± SD peak knee torque of extension and flexion was 44.5 ± 15.7 and 29.9 ± 11.2 N-m, respectively. The overall mean ± SD grip strength was 22.7 ± 6.0 kg. The overall mean ± SD baseline SPPB score was 8.8 ± 3.1.

Of the 146 women, 24 (16%) did not complete the baseline knee torque assessment, and 24 (16%) did not complete the baseline grip strength assessment. Of these, 7 (5%) did not complete either assessment. The most common reasons for non-completion were pain or other health-related contraindications to the procedures (e.g., high or low blood pressure). Compared to women with complete strength data available, women missing either Biodex® or grip strength data, had greater mean age, SLAQ score, and depressive symptoms (CES-D Depression score); and lower relative mean muscle mass (LMI/FMI), peak knee torque, and function (SPPB score). Mean daily prednisone dose, disease duration, physical activity, and grip strength did not significantly differ between women with complete and partial strength data.

Association of strength with physical function: linear regression models

In unadjusted and adjusted models, baseline knee torque but not grip strength were statistically significantly associated with changes in SPPB score over follow-up (Table 2). For example, a 10 N-m increase in peak torque of knee flexion at baseline predicted a 0.84-point increase in SPPB score at follow-up when the effects of all covariates are held constant. The inverse interpretation is also true in that a 10 N-m decrease in peak torque of knee flexion at baseline predicted a 0.84-point decrease in SPPB score at follow-up, when adjusting for covariates. Adjusted models control for effects of age, SLAQ score, disease duration, prednisone use, LMI/FMI, physical activity level (active vs inactive), CES-D Depression score, and baseline SPPB score. Supplementary Table 1 includes all terms in the adjusted model.

Association of strength with physical function: linear spline models

We examined whether the association of baseline muscle strength with follow-up SPPB score varied depending on values of baseline muscle strength using linear spline analyses. When baseline muscle strength was divided into intervals, the association of muscle strength with follow-up SPPB score did vary between intervals of strength, with the greatest associations observed in the intervals with lower muscle strength (Fig 1 and Table 3). For example, within the interval of weakest strength (≤ 13N-m), a 10 N-M increase in peak torque of knee flexion predicted a 7.85-point increase in follow-up SPPB score ($p<0.0001$) when adjusting for covariates. Again, the inverse interpretation is also true in that a 10 N-m decrease in peak torque of knee flexion predicted a 7.85-point decrease in follow-up SPPB score when adjusting for covariates.

Sensitivity analyses

When individuals with missing strength data were assigned the weakest recorded value for missing measures, the overall associations of muscle strength with follow-up SPPB scores were equivalent (Table 4). Reduced lower extremity strength still predicted worse SPPB scores at follow-up.

DISCUSSION

We observed that, among adult women with SLE, reduced lower extremity muscle strength predicted subsequent declines in physical function even when adjusting for covariates. In addition, we demonstrated that the weakest women are the ones at increased risk of future declines. To our knowledge this is the first study to demonstrate that muscle weakness predicts future physical declines in SLE and that this relationship affects mainly women with the lowest baseline muscle strength.

This study builds upon our prior findings that muscle strength is strongly associated with self-reported physical function. In cross-sectional analyses, we observed that lower extremity strength, measured by peak knee torque and chair-stand time, was associated with scores on the SF-36 Physical Function and Valued Life Activities assessments, even when controlling for differences in lean mass and various confounders (19). The present study builds upon our prior findings by providing evidence of a longitudinal association between muscle strength and physical function among individuals with SLE. The presence of this longitudinal association suggests that differences in muscle strength may predict future changes in physical function. These findings further corroborate a conceptual pathway leading from muscle weakness to reduced physical function among individuals with SLE.

By examining the association of muscle strength with future SPPB performance within intervals of muscle strength, we were able to clarify that it is among the weakest women where this association is greatest. These findings begin to help address a fundamental gap in the current literature regarding what degree of muscle weakness is clinically meaningful. We demonstrated that women in the intervals of lowest knee torque are at greatest risk of decreased physical function in the future. This finding has potential clinical implications since interventions to increase lower extremity muscle strength and increase physical function may be most cost effective if targeted at women who exhibit particularly decreased lower extremity strength.

As we have previously argued, muscle strength is perhaps best viewed as one important factor among the various determinants of physical function in individuals with SLE. In our analyses, differences in knee torque of 10 N-m yielded small but statistically significant difference in future SPPB scores. The minimum clinically important difference on the SPPB is a change of 1 point (44). Within the interval of lowest baseline peak torque of knee flexion a 10 N-m change in torque of flexion predicted a nearly 8-point change in future SPPB score. Associations of knee torques of extension with SPPB score were more modest, with changes of 10 N-m of extension predicting changes of approximately 1 point. Thus, interventions to increase muscle strength may be most beneficial in improving physical

function when used in conjunction with interventions to improve other aspects of physical function among women with SLE, such as total body strength training or aerobic exercise.

We observed that changes in lower extremity strength (peak knee torque) had a greater association with future SPPB scores than did changes in upper extremity strength (grip strength). One possible explanation for this finding is that the SPPB assesses primarily lower extremity function, as it includes assessments of standing balance, walking speed, and standing from a chair without using one's arms. Further studies are needed to examine this hypothesis.

The present study also makes a novel contribution by using the SPPB to characterize physical function trends in a relatively younger population with a rheumatic disease: women with SLE. To our knowledge, there are no data on the mean SPPB score in the overall population. However, the SPPB has been used extensively in elderly populations, where the mean score among women in their eighth decade of life is reported to range from approximately 8 to 9 (44). In addition, among a cohort of individuals with rheumatoid arthritis with mean age 58 years, the mean SPPB score was observed as 9.8 (52). Thus the mean function scores observed in our cohort (8.8 at baseline) suggest a significant degree of physical function comparable to that of women 30 years older than those of our cohort. In addition, we previously reported that the women in our cohort demonstrate considerably reduced lower extremity muscle strength compared to healthy women, even compared to women in their eighth decade of life (19). The extent of muscle weakness and decreased physical function observed in our cohort underscores the unmet clinical need for interventions to improve physical function among individuals with SLE.

This study also highlights the difficulty inherent in objectively measuring muscle strength among individuals at-risk for weakness. Compared to women with complete muscle strength data, those with no or only partial strength data because they declined to perform the assessment (most commonly due to pain or health-related conditions) had significantly worse mean baseline SPPB scores. Women who did not complete the strength assessments were also on average older, had higher SLAQ disease activity scores, trended towards greater disease duration, reported greater depressive symptoms, and had lower muscle mass (LMI/FMI). Thus, as we have previously reported (19), women who are likely at the greatest risk for muscle weakness are unfortunately also those most likely to decline the assessment of muscle strength. As a result of this trend, our estimate of the association of muscle strength with physical function is likely biased towards the null hypothesis of no effect. The true association of reduced muscle strength with future decreased function is likely to be even greater than that which we observed.

Our study has potential limitations. This is an observational study, and we did not have data available from a control comparison group of women without SLE. As discussed above, the power of our study was limited by missing data and the tendency of more impaired women to decline the muscle strength assessments.

There are also strengths of our study. This is one of the first studies of SLE to incorporate objective measures of muscle strength and physical function in determining the longitudinal

association of muscle strength with physical function. We used standardized, objective assessments to quantify upper and lower extremity muscle strength and its relationship to physical function.

In summary, we observed that among women with SLE, having reduced muscle strength strongly predicted future declines in physical function, even when controlling for covariates. Moreover, this association of muscle strength with physical function was strongest among women with the lowest baseline muscle strength. Randomized controlled trials are needed to examine whether interventions to increase muscle strength improve physical function in SLE.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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References

1. Bouchard DR, Heroux M, et al. Association between muscle mass, leg strength, and fat mass with physical function in older adults: influence of age and sex. J Aging Health. 2011; 23(2):313–28. [PubMed: 21081704]
2. Bouchard DR, Janssen I. Dynapenic-obesity and physical function in older adults. J Gerontol A Biol Sci Med Sci. 2010; 65(1):71–7. [PubMed: 19887536]
3. Cawthon PM, Fox KM, et al. Clustering of strength, physical function, muscle, and adiposity characteristics and risk of disability in older adults. J Am Geriatr Soc. 2011; 59(5):781–7. [PubMed: 21568948]
4. Cawthon PM, Fox KM, et al. Do muscle mass, muscle density, strength, and physical function similarly influence risk of hospitalization in older adults? J Am Geriatr Soc. 2009; 57(8):1411–9. [PubMed: 19682143]
5. O'Reilly SC, Jones A, et al. Quadriceps weakness in knee osteoarthritis: the effect on pain and disability. Ann Rheum Dis. 1998; 57(10):588–94. [PubMed: 9893569]
6. Pua YH, Liang Z, et al. Associations of knee extensor strength and standing balance with physical function in knee osteoarthritis. Arthritis Care Res (Hoboken). 2011; 63(12):1706–14. [PubMed: 21905251]
7. Santos ML, Gomes WF, et al. Muscle strength, muscle balance, physical function and plasma interleukin-6 (IL-6) levels in elderly women with knee osteoarthritis (OA). Arch Gerontol Geriatr. 2011; 52(3):322–6. [PubMed: 20627334]
8. Steultjens MP, Dekker J, et al. Avoidance of activity and disability in patients with osteoarthritis of the knee: the mediating role of muscle strength. Arthritis Rheum. 2002; 46(7):1784–8. [PubMed: 12124862]
9. Visser M, Goodpaster BH, et al. Muscle mass, muscle strength, and muscle fat infiltration as predictors of incident mobility limitations in well-functioning older persons. J Gerontol A Biol Sci Med Sci. 2005; 60(3):324–33. [PubMed: 15860469]
10. Goodpaster BH, Park SW, et al. The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. J Gerontol A Biol Sci Med Sci. 2006; 61(10):1059–64. [PubMed: 17077199]

11. Giles JT, Bartlett SJ, et al. Association of body fat with C-reactive protein in rheumatoid arthritis. Arthritis Rheum. 2008; 58(9):2632–41. [PubMed: 18759279]
12. Giles JT, Bartlett SJ, et al. Association of body composition with disability in rheumatoid arthritis: impact of appendicular fat and lean tissue mass. Arthritis Rheum. 2008; 59(10):1407–15. [PubMed: 18821641]
13. Kramer HR, Fontaine KR, et al. Muscle density in rheumatoid arthritis: associations with disease features and functional outcomes. Arthritis Rheum. 2012; 64(8):2438–50. [PubMed: 22391952]
14. Katz P, Julian L, et al. Physical activity, obesity, and cognitive impairment among women with systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2012; 64(4):502–10. [PubMed: 22337564]
15. Katz P, Morris A, et al. Disability in valued life activities among individuals with systemic lupus erythematosus. Arthritis Rheum. 2008; 59(4):465–73. [PubMed: 18383406]
16. Katz P, Yazdany J, et al. Impact of obesity on functioning among women with systemic lupus erythematosus. Arthritis Care Res (Hoboken). 2011; 63(10):1357–64. [PubMed: 21702085]
17. Balsamo S, da Mota LM, et al. Low dynamic muscle strength and its associations with fatigue, functional performance, and quality of life in premenopausal patients with systemic lupus erythematosus and low disease activity: a case-control study. BMC Musculoskelet Disord. 2013; 14:263. [PubMed: 24011222]
18. Stockton KA, Kandiah DA, et al. Fatigue, muscle strength and vitamin D status in women with systemic lupus erythematosus compared with healthy controls. Lupus. 2012; 21(3):271–8. [PubMed: 22004972]
19. Andrews JS, Trupin L, et al. Muscle Strength, Muscle Mass, and Physical Disability in Women with Systemic Lupus Erythematosus. Arthritis Care Res (Hoboken). 2014
20. Guralnik JM, Ferrucci L, et al. Lower extremity function and subsequent disability: consistency across studies, predictive models, and value of gait speed alone compared with the short physical performance battery. J Gerontol A Biol Sci Med Sci. 2000; 55(4):M221–31. [PubMed: 10811152]
21. Guralnik JM, Ferrucci L, et al. Lower-extremity function in persons over the age of 70 years as a predictor of subsequent disability. N Engl J Med. 1995; 332(9):556–61. [PubMed: 7838189]
22. Visser M, Pahor M, 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]
23. Freemer MM, King TE Jr, et al. Association of smoking with dsDNA autoantibody production in systemic lupus erythematosus. Ann Rheum Dis. 2006; 65(5):581–4. [PubMed: 16150789]
24. Thorburn CM, Prokunina-Olsson L, 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]
25. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997; 40(9):1725. [PubMed: 9324032]
26. Yelin E, Trupin L, et al. Work dynamics among persons with systemic lupus erythematosus. Arthritis Rheum. 2007; 57(1):56–63. [PubMed: 17266065]
27. Sorensen TJ, Langberg H, et al. Experimental knee joint pain during strength training and muscle strength gain in healthy subjects: a randomized controlled trial. Arthritis Care Res (Hoboken). 2012; 64(1):108–16. [PubMed: 21905254]
28. Stockton KA, Wrigley TV, et al. Test-retest reliability of hand-held dynamometry and functional tests in systemic lupus erythematosus. Lupus. 2011; 20(2):144–50. [PubMed: 21303829]
29. Visser M, Kritchevsky SB, et al. Leg muscle mass and composition in relation to lower extremity performance in men and women aged 70 to 79: the health, aging and body composition study. J Am Geriatr Soc. 2002; 50(5):897–904. [PubMed: 12028178]
30. Newcomer KL, Krug HE, et al. Validity and reliability of the timed-stands test for patients with rheumatoid arthritis and other chronic diseases. J Rheumatol. 1993; 20(1):21–7. [PubMed: 8441160]
31. Feiring DC, Ellenbecker TS, et al. Test-retest reliability of the biodex isokinetic dynamometer. J Orthop Sports Phys Ther. 1990; 11(7):298–300. [PubMed: 18796902]

32. Roberts HC, Denison HJ, et al. A review of the measurement of grip strength in clinical and epidemiological studies: towards a standardised approach. Age Ageing. 2011; 40(4):423–9. [PubMed: 21624928]
33. Heymsfield SB, Wang J, et al. 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]
34. Mazess RB, Barden HS, et al. 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]
35. Wang J, Heymsfield SB, et al. Body fat from body density: underwater weighing vs. dual-photon absorptiometry. Am J Physiol. 1989; 256(6 Pt 1):E829–34. [PubMed: 2735405]
36. Kipen Y, Strauss BJ, et al. Body composition in systemic lupus erythematosus. Br J Rheumatol. 1998; 37(5):514–9. [PubMed: 9651078]
37. Kipen Y, Briganti EM, et al. Three year follow-up of body composition changes in pre-menopausal women with systemic lupus erythematosus. Rheumatology (Oxford). 1999; 38(1):59–65. [PubMed: 10334684]
38. Baker JF, Long J, et al. Men Are at Greater Risk of Lean Mass Deficits in Rheumatoid Arthritis. Arthritis Care Res (Hoboken). 2014
39. Cawthon PM, Peters KW, et al. Cutpoints for low appendicular lean mass that identify older adults with clinically significant weakness. J Gerontol A Biol Sci Med Sci. 2014; 69(5):567–75. [PubMed: 24737559]
40. Dufour AB, Hannan MT, et al. Sarcopenia definitions considering body size and fat mass are associated with mobility limitations: the Framingham Study. J Gerontol A Biol Sci Med Sci. 2013; 68(2):168–74. [PubMed: 22503991]
41. Eisner MD, Blanc PD, et al. Body composition and functional limitation in COPD. Respir Res. 2007; 8:7. [PubMed: 17261190]
42. Rolland Y, Gallini A, et al. Body-composition predictors of mortality in women aged >/=75 y: data from a large population-based cohort study with a 17-y follow-up. Am J Clin Nutr. 2014; 100(5): 1352–60. [PubMed: 25332333]
43. Sternfeld B, Ngo L, et al. Associations of body composition with physical performance and self-reported functional limitation in elderly men and women. Am J Epidemiol. 2002; 156(2):110–21. [PubMed: 12117699]
44. Guralnik JM, Simonsick EM, et al. A short physical performance battery assessing lower extremity function: association with self-reported disability and prediction of mortality and nursing home admission. J Gerontol. 1994; 49(2):M85–94. [PubMed: 8126356]
45. Karlson EW, Daltroy LH, et al. Validation of a Systemic Lupus Activity Questionnaire (SLAQ) for population studies. Lupus. 2003; 12(4):280–6. [PubMed: 12729051]
46. Yazdany J, Yelin EH, et al. Validation of the systemic lupus erythematosus activity questionnaire in a large observational cohort. Arthritis Rheum. 2008; 59(1):136–43. [PubMed: 18163398]
47. Craig CL, Marshall AL, et al. International physical activity questionnaire: 12-country reliability and validity. Med Sci Sports Exerc. 2003; 35(8):1381–95. [PubMed: 12900694]
48. Brown WJ, Trost SG, et al. Test-retest reliability of four physical activity measures used in population surveys. J Sci Med Sport. 2004; 7(2):205–15. [PubMed: 15362316]
49. Hagstromer M, Oja P, et al. The International Physical Activity Questionnaire (IPAQ): a study of concurrent and construct validity. Public Health Nutr. 2006; 9(6):755–62. [PubMed: 16925881]
50. Radloff LS. The CES-D Scale: a self-report depression measure for research in the general population. Appl Psychol Meas. 1977; 1:385–401.
51. Vittinghoff, E.; Glidden, DV., et al. Statistics for Biology and Health. 2. New York: Springer; 2012. Linear Regression. Regression Methods in Biostatistics: Linear, Logistic, Survivial, and Repeated Measures Models; p. 69-138.
52. Shin SY, Julian L, et al. The relationship between cognitive function and physical function in rheumatoid arthritis. J Rheumatol. 2013; 40(3):236–43. [PubMed: 23322467]

SIGNIFICANCE AND INNOVATIONS

- This is one of the first studies of SLE to incorporate objective measures of upper and lower extremity muscle strength and of physical function in determining the longitudinal association of muscle strength with physical function.
- Among adult women with systemic lupus erythematosus (SLE), reduced lower extremity muscle strength predicted declines in physical function approximately 2 years later as measured by the Short Physical Performance Battery (SPPB) in adjusted models.
- The association of baseline muscle strength with future SPPB scores was greatest among women who were weakest.
- These results highlight a need for clinical trials to evaluate whether interventions to increase muscle strength improve physical function for women with SLE.

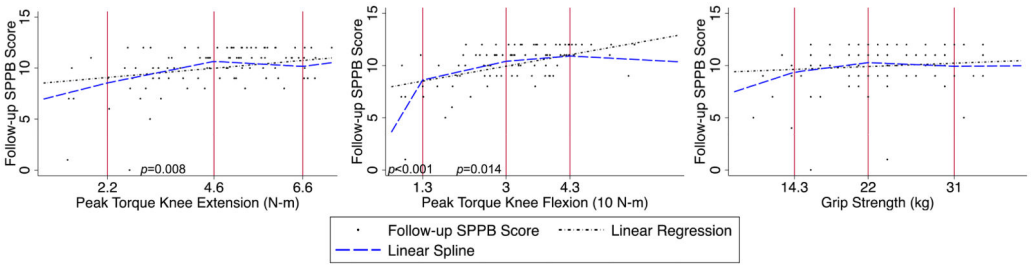

Figure 1.

Linear Regression and Linear Spline Models of the Association of Baseline Muscle Strength with Follow-up Short Physical Performance Battery Score (SPPB) in Women with SLE[#]

[#]Red vertical lines indicate the muscle strength cutpoints used to generate the linear spline. *P*-values refer to the association of muscle strength with follow-up SPPB score within each interval of strength.

Table 1

Participant Characteristics Grouped by Completeness of Strength Data[#]

		Analysis Set		
	Overall (n=146)	**Complete Strength Data (n=105)**	**Partial Strength Data (n=41)**	***p*[##]**
Age, years	47.8 ± 12.3	46.4 ± 12.9	51.2 ± 10.1	0.04
Disease Duration, years	15.5 ± 9.2	14.9 ± 9.2	17.2 ± 9.0	0.17
SLAQ Score	12.9 ± 7.4	11.4 ± 7.4	16.7 ± 6.2	0.0001
CES-D Depression Score	15.7 ± 12.3	13.6 ± 11.9	20.9 ± 12.2	0.001
Low Activity on IPAQ[+] %(n)	28.1 (41)	23.8 (25)	39.0 (16)	0.07
Prednisone use, mg/day % (n)				0.36
0	53.4 (78)	53.3 (56)	53.7 (22)	
1–4.5	6.9 (10)	4.8 (5)	12.2 (5)	
5–9.5	19.9 (29)	21.9 (23)	14.6 (6)	
10–14.5	12.3 (18)	12.4 (13)	12.2 (5)	
15–19.5	3.4 (5)	3.8 (4)	2.4 (1)	
≥ 20	2.1 (3)	1.0 (1)	4.9 (2)	
LMI/FMI[++]	1.6 ± 0.7	1.7 ± 0.7	1.3 ± 0.6	0.0005
Biodex®, N-m				
Knee Extension	44.5 ± 15.7 (n=122)	46.3 ± 15.1 (n=105)	33.4 ± 14.7 (n=17)	0.001
Knee Flexion	29.9 ± 11.2 (n=122)	30.6 ± 11.1 (n=105)	25.3 ± 11.3 (n=17)	0.07
Grip Strength, kg	22.7 ± 6.0 (n=122)	22.4 ± 5.9 (n=105)	24.4 ± 6.6 (n=17)	0.2
Short Physical Performance Battery Baseline Score	8.8 ± 3.1	9.9 ± 1.8	6.0 ± 3.9	<0.0001
Short Physical Performance Battery Follow-up Score	9.8 ± 2.4	10.2 ± 1.9	8.3 ± 3.5	0.0009
Change in Short Physical Performance Battery Score[+++] mean ± SD (range)	0.7 ± 2.4 (−8,11)	0.3 ± 1.9 (−8, 6)	1.9 ± 3.6 (−4, 11)	0.006

[#]Values are mean ± standard deviation unless otherwise indicated. Complete strength data refers to subjects for whom all Biodex® and Chair-stand measures were available. Partial strength data refers to subjects for who were missing Biodex® or grip strength data.

[##]From *t*-tests and chi-squared analyses comparing complete vs. partial.

[+]IPAQ = International Physical Activity Questionnaire

[++]LMI = lean mass index and FMI = fat mass index.

[+++]Calculated as follow-up minus baseline SPPB score.

Table 2

Regression Coefficients (95% CI) for the Association of Baseline Muscle Strength with Follow-up Short Physical Performance Battery Score in Women with SLE[#]

	Model 1[##]	Model 2[###]
Knee Extension, 10 N-m (n=93)	**0.44 (0.18, 0.69)****	**0.38 (0.10, 0.66)****
Knee Flexion, 10 N-m (n=93)	**0.79 (0.44, 1.2)*****	**0.84 (0.47, 1.2)*****
Grip Strength, kg (n=94)	0.06 (−0.01, 0.13)	0.04 (−0.03, 0.10)

[#]For ease of interpretation, knee extension and flexion values are scaled in units of 10 N-m. Higher SPPB scores (range 0–12) indicate better function.

[##]Model is adjusted only for baseline SPPB score.

[###]Model is adjusted for baseline SPPB score and the following covariates: age, SLAQ score, disease duration, prednisone use, LMI/FMI (LMI = lean mass index and FMI = fat mass index), physical activity level (active vs inactive), and CES-D Depression score.

*$p<0.05$,

**$p<0.01$,

***$p<0.001$

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Table 3

Regression Coefficients (95% CI) for the Association of Baseline Muscle Strength Grouped by Interval with Follow-up Short Physical Performance Battery Score in Women with SLE[#]

	Interval of Muscle Strength[##]			
	1st	**2nd**	**3rd**	**4th**
Knee Extension, 10 N-m (n=93)	[≤2.2] 1.10 (−1.43, 3.63)	[2.2–4.6] **0.88 (0.24, 1.53)****	[4.6–6.6] −0.25 (−0.93, 0.43)	[≥6.6] 0.57 (−4.02, 5.16)
Knee Flexion, 10 N-m (n=93)	[≤1.3] **7.85 (4.02, 11.69)*****	[1.3–3] **1.05 (0.22, 1.89)***	[3–4.3] 0.39 (−0.41, 1.19)	[≥4.3] −0.25 (−1.69, 1.19)
Grip Strength, Kg (n=94)	[≤14.3] 0.30 (−0.45, 1.05)	[14.3–22] 0.12 (−0.07, 0.31)	[22–31] −0.04 (−0.19, 0.11)	[≥31] 0.006 (−0.74, 0.75)

[#]For ease of interpretation, knee extension and flexion values are scaled in units of 10 N-m. Higher SPPB scores (range 0–12) indicate better function. Models are adjusted for baseline SPPB score and the following covariates: age, SLAQ score, disease duration, prednisone use, LMI/FMI (LMI = lean mass index and FMI = fat mass index), physical activity level (active vs inactive), and CES-D Depression score.

[##]Values in brackets are the range of muscle strength included in a given interval.

*$p<0.05$,

**$p<0.01$,

***$p<0.001$

Table 4

Regression Coefficients (95% CI) for the Sensitivity Analysis of the Effect of Missing Muscle Strength Data on the Relationship between Baseline Muscle Strength and Follow-up Short Physical Performance Battery Score in Women with SLE[#]

	Model 1[##]	Model 2[###]
Knee Extension, 10 N-m (n=106)	**0.34 (0.11, 0.56)****	**0.23 (−0.02, 0.48)**+
Knee Flexion, 10 N-m (n=106)	**0.62 (0.28, 0.95)*****	**0.58 (0.22, 0.94)****
Grip Strength, kg (n=94)	0.22 (−0.01, 0.45)	0.11 (−0.13, 0.35)

[#]Missing muscle strength data were assigned the weakest observed value for each measure. For ease of interpretation, knee extension and flexion values are scaled in units of 10 N-m. Higher SPPB scores (range 0–12) indicate better function.

[##]Model is adjusted only for baseline SPPB score.

[###]Model is adjusted for baseline SPPB score and the following covariates: age, SLAQ score, disease duration, prednisone use, LMI/FMI (LMI = lean mass index and FMI = fat mass index), physical activity level (active vs inactive), and CES-D Depression score.

*$p<0.05$,

**$p<0.01$,

***$p<0.001$

+p=0.07