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Lupus 2013 22: 972 originally published online 16 July 2013
DOI: 10.1177/0961203313496338

Lupus (2013) 22, 972–976
http://lup.sagepub.com

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Factors that determine body composition of female systemic lupus erythematosus (SLE) patients in Sri Lanka: a comparative study using dual-energy x-ray absorptiometry

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Studies on body composition and its determinants among SLE patients are limited. Estimation of body composition, analysis of determinants and associations of different body compartments are important in planning long-term care of these patients. The aim of the study was to identify the changes in body composition among SLE patients and assess the effect of corticosteroid use, patient and disease-related variables on body composition. We compared lean mass, fat mass, bone mineral density (BMD), and bone mineral content (BMC) determined by dual-energy x-ray absorptiometry technology, in a group of premenopausal women with SLE ($n = 27$) and an age-matched healthy group of women ($n = 27$). The median (IQR) duration of SLE was 3 (2-5) years while median (IQR) duration and dose of prednisolone therapy were 108 (88 – 172) weeks and 9730 (6160–15360) mg, respectively. No significant difference was observed in body mass index (BMI) or total fat mass between the two groups. SLE patients, however, had significantly lower lean mass ($p < 0.001$), BMD ($p < 0.001$) and BMC ($p < 0.005$) than healthy controls. Among cases, compared with lean mass, total body fat content showed stronger associations with total body BMD ($r = 0.49$, $p < 0.01$) and total body BMC ($r = 0.63$, $p < 0.01$). When a stepwise regression model was fitted, lean mass among controls and total fat mass among cases emerged as the best predictors of BMC/BMD. No significant correlations were found between the disease duration or cumulative glucocorticosteroid dose and total body BMD, total body BMC, lean mass or total fat content in SLE patients. *Lupus* (2013) **22,** 972–976.

Key words: Body composition; systemic lupus erythematosus; Asian; dual-energy x-ray absorptiometry

Introduction

Systemic lupus erythematosus (SLE) is an autoimmune multi-systemic disease with an unpredicted course consisting remissions and relapses. It affects females more frequently than males at a ratio of almost 9 to 1[1] and the disease prevalence has a geographical variation. It has been estimated that 1 in 3450 women in the United Kingdom, 1 in 250 Afro-Caribbean women in the United States, 1 in 1000 Chinese women and 1 in 4200 white women in New Zealand are at risk of SLE.[2–5] Asian SLE patients have a higher prevalence of systemic involvement as well as higher mortality.[6] Over the past four decades, the prevalence of SLE has nearly tripled, possibly as a result of significant improvement in survival.[7] SLE predominantly occurs between the ages of 20 and 40 years and physical disability which is multifactorial, is frequent among SLE patients, with a cumulative prevalence of 23%.[8]

SLE patients have low bone mineral density (BMD) and bone mineral content (BMC) and high incidence of fractures.[9] As low BMD and BMC are well-known risk factors of fractures, the high occurrence of fractures among SLE patients can easily be attributed to low bone mass. It is important, however, to assess the contribution made by other body compartments towards this fracture risk. While sarcopenia may increase the fracture risk further by increasing the tendency to fall, high fat mass may provide a protection from

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Received 15 July 2012; accepted 5 June 2013

10.1177/0961203313496338

fractures. The ability of fat tissue to dissipate the energy generated locally at the site of impact following a fall is well established.[10,11] Studies in this area require estimation of body composition and analysis of associations and interactions of different body compartments. Furthermore, determinants of these associations and interactions are important in planning long-term care of these patients.

Previous studies examining body composition have revealed a lower lean mass and a higher fat mass among patients with juvenile onset SLE when compared with age- and sex-matched controls.[12] The fat-free mass is a significant predictor of total body BMD among Australian female SLE patients and there is a significant association between reduced fat-free mass and SLE severity.[13] Furthermore, the role of glucocorticoids, disease activity and menstrual status on body composition of SLE patients is not clear.[12–14] Kipen et al. conclude that the disease severity and corticosteroid exposure are independently and inversely associated with both total body BMD and fat-free mass.[14] Regio et al. however, show that corticosteroid-related variables do not have harmful effects on body composition.[12] While studies examining body composition and its determinants among SLE patients are limited, studies involving patients in the Asian region are sparse. As SLE prevalence and disease activity have a geographical variation, SLE patients in the Asian region may be materially different from their European or North American counterparts. Furthermore, the geographical differences in access to health care, food pattern, physical activity and environmental factors may have an influence on their body composition and its determinants. This study was designed to identify the changes in body composition among SLE patients and the effect of corticosteroid use, patient and disease-related variables on body composition.

Methods

Female SLE patients who had been classified according to the American College of Rheumatology revised criteria[15,16] and registered in medical and rheumatology clinics at the Teaching Hospital, Galle in Sri Lanka were invited to participate in a comparative cross-sectional study. Only those aged 18 years or more were included while patients with other diseases such as primary anti-phospholipid syndrome, rheumatoid arthritis, mixed connective tissue disease, thyroid or parathyroid diseases, malabsorption and other chronic inflammatory diseases were excluded. Patients with metal implants and those who were pregnant or breast feeding were also excluded. Written informed consent was obtained from all participants and the study protocol was approved by the Ethics Review Committee of the Faculty of Medicine, University of Ruhuna. Age-matched (to the nearest 5 years) healthy females were selected from the community in the Galle district. Galle district is the service area of the Teaching Hospital, Galle and these subjects were selected in random manner using the most recent voters' registers and with the help of field health workers.

Data were collected using a pre-tested interviewer-based questionnaire and perusing medical records. All patients underwent a detailed physical examination. Data recorded included age, menstrual status and drug usage. The cumulative corticosteroid dose was calculated from medical records. The disease duration was calculated from the time of the diagnosis to the time of interview, and the disease severity was assessed clinically and categorised to mild, moderate and severe according to the systems involved during the course of the disease.[17] The activity of the disease was assesed using Systemic Lupus Disease Activity Index (SLEDAI) at the time of recruitment.[18] In the SLEDAI, serum complement levels and DNA binding were not assesed due to limited resources.

Anthropometric measurements such as body weight were measured to the nearest 0.1 kg without foot wear and height was recorded using portable stadiometer (Weight Master International, Japan) to the nearest 0.5 cm. Body mass index (BMI) was calculated by dividing weight (kg) by square value of height (m^2). Body composition was measured by dual-energy x-ray absorptiometry (DXA by Hologic Inc, Bedford, USA) and the following measurements were taken: total fat mass, truncal fat mass, lean mass, total body BMD and total body BMC. All DXA measurements and anthropometric measurements were taken by the same technician adhering to the standard protocols. The analytical software (version 12.4) provided by the Hologic manufacturer was used to estimate absolute total body BMC, total body lean and fat masses. The same software was used to estimate the regional fat content in the abdomen (truncal fat).

Statistical analysis

The descriptive data are given as either mean (SD) or median (interquartile range) depending on the data distribution. Indices of body composition were normally distributed and they were compared,

Table 1 Comparison of indices of anthropometry and body composition between cases and controls

Measurement	*Cases*[a] *(n = 27)*	*Controls*[a] *(n = 27)*	*Mean difference*	[b]p *value*
Age (years)	32.2 (8.9)	33.2 (8.2)	−1.1	0.67
Height (m)	1.53 (0.69)	1.57 (0.67)	−0.04	0.053
Weight (kg)	49.5 (10.6)	56.0 (9.9)	−6.7	0.021
BMI (kg/m^2)	21.2 (4.9)	22.9 (4.5)	−1.8	0.17
Total fat mass (kg)	17.51 (8.1)	20.0 (5.9)	−2.08	0.29
Truncal fat mass (kg)	7.09 (4.24)	7.66 (2.83)	−0.58	0.56
Lean mass (kg)	29.66 (4.93)	35.11 (6.23)	−5.45	0.001
Total body BMD (g/cm^2)	1.010 (0.099)	1.093 (0.073)	−0.083	0.001
Total body BMC (g)	1662.5 (374.7)	1893.3 (169.9)	−230.8	0.005

[a]Given values are mean (SD).
[b]*p* contracts the mean differences between cases and controls.

Table 2 Correlations between measures of body composition among SLE patients and controls

	Lean mass	*Total body BMC*	*Total body BMD*
Total fat mass	Cases = 0.15 Controls = 0.37	Cases = 0.63** Controls = 0.18	Cases = 0.49** Controls = −0.03
Lean mass	–	Cases = −0.13 Cases = −0.28	Controls = −0.28 Controls = −0.44*
Total body BMC	–	–	Cases = 0.87** Controls = 0.74**

Values are Pearson correlation (r). *$p < 0.05$; **$p < 0.01$.

between cases and controls, using the unpaired t-test.The associations between BMD, BMC, fat content and lean mass were tested using Pearson correlations and regression models. Similarly the associations between body compartments and disease or treatment-related factors among cases were examined by either a Pearson correlation or Spearman rho. $P < 0.05$ was considered statistically significant for all analyses.

Results

Among SLE patients ($n = 27$), the median (interquartile range; IQR) disease duration was 3 (2−5) years. Twenty-two of them (81.5%) were positive for anti-nuclear antibodies, while 23 (87.5%) had positive anti-ds-DNA antibodies at the time of the diagnosis. None of the patients had complement levels measured during their disease course. The median (IQR) duration of prednisolone therapy was 108 (88−172) weeks while the median (IQR) cumulative prednisolone dose was 9730 (6160−15,360) mg. The median SLEDAI (IQR) score was 4 (0−8) while the median SLICC/ACR damage index was 2 (0−3). None had fractures, vertebral collapse or avascular necrosis. As controls ($n = 27$) were age matched to SLE cases there was no significant age difference between the two groups. Compared to controls, cases were lighter but no significant difference was observed in BMI between the two groups (Table 1).

The body fat contents, both total and truncal, were not different between cases and controls. However, cases, compared with controls, had significantly low lean mass, total body BMD and BMC (Table 1). Compared with total fat mass, lean mass showed a stronger association with total body BMD (TBBMD) and total body BMC (TBBMC) among controls (Table 2). Among cases, compared with lean mass, total body fat content showed stronger associations with TBBMD and TBBMC (Table 2). When separate step-wise regression plots were fitted for the two groups with lean and fat masses as the independent variables and BMD or BMC as the dependent variable, lean mass among controls and total fat mass among cases emerged as the best predictors of BMC/BMD (data not shown). Among patients with SLE we did not find significant correlations between the disease duration or cumulative glucocorticosteroid dose and TBBMD, TBBMC, lean mass or total fat content (data not shown).

Discussion

This analysis shows that Sri Lankan women with SLE are lighter compared with age- and sex-matched controls. Furthermore, SLE patients have low lean mass, low total body BMD and BMC, compared with the matching controls. In addition, among SLE women the fat mass is the major predictor of BMD and BMC. Among healthy controls, lean mass predicts BMD/BMC better than the total fat mass.

The fact that SLE patients have lower lean mass and BMD/BMC compared with normal subjects is understandable and somewhat expected. SLE is a chronic inflammatory disease with intermittent relapses and a disease of this nature could lead to poor overall growth. In addition, among SLE patients, reduced physical activities and nutrition which are well-known determinants of muscle growth and bone accrual could partly contribute

to the findings. Drugs such as glucocorticoids have negative effects on both BMD/BMC and skeletal muscles. Hence, SLE patients can be expected to have lower lean mass as well as BMC and in turn, lower body weight and shorter stature compared with normal subjects.

We found the lean mass to be the main predictor of BMD/BMC among normal controls. Previous studies examining body composition among healthy premenopausal women in the same study area[19] and also among healthy black, white, and Hispanic premenopausal women[20] showed similar results. This association appears to have changed in SLE patients to the extent that the total fat mass emerges over the lean mass as the major predictor of BMD/BMC. This may be due to altered ratio of fat to lean mass allowing fat mass to be dominant over the lean mass. While glucocorticoids have a negative effect on lean mass[13,21] its positive influence on fat tissue is well documented.[21]

The difference of total fat mass/lean mass ratio does not appear to be the plausible explanation as we did not find this ratio to be significantly different between the two groups (cases 60.4% vs control 58.5%, $p = 0.83$). The effect may entirely be due to the difference in the lean mass. Apart from glucocorticoids, SLE by its multisystemic nature has negative effects on muscles. Although our patients had no special food habits, poor intake due to anorexia and upper gastrointestinal abnormalities may have led to a negative nitrogen balance in the body and contributed to lower lean mass. In addition, restricted physical activities among cases also may have contributed.

Several studies have described the changes in the body composition among SLE patients because of its relevance to prognosis and survival. The findings, however, have not been uniform. In a study conducted on the Chinese SLE population, Mok et al.[5] demonstrated a significant correlation between total body BMC and fat mass over lean mass. In the same analysis, body BMC did not correlate with prednisolone dosages. In contrast, Kippen et al.[14] reported fat-free mass and not the fat mass to be predictive of change in total body BMD among Australasian premenopausal SLE patients. In this analysis too, corticosteroid-related variables were not found to have deleterious effects on body composition. In a separate analysis, Kippen et al.[13] demonstrated fat-free mass to be the main predictor of total body BMD.

We were unable to find associations between disease or drug-related variables and indices of body composition. Previous studies examining the relationship between the dose of glucocorticoids and BMC/BMD have generated conflicting results. Kalla et al.[22] showed that SLE causes significant trabecular bone loss, which is not due to corticosteroid therapy. In addition, according to Li et al.[23] SLE patients had significantly low BMD compared with healthy controls but there was no relationship between dose and duration of corticosteroid treatment as well as activity and duration of the disease. However, Kipen et al.[24] demonstrated a strong inverse relationship with BMD and steroid usage. Thus our results were keeping with results of most of previous studies. But unfortunately we only assessed cumulative corticosteroid dose and not the steroid use at enrolment, indications of steroid use and calcium supplementation. A follow-up study would provide more information than our cross-sectional comparative study.

There are limitations and strengths in our study. Our study population was comparatively young (age 32+/-8.9 years) and most were premenopausal and in the reproductive age group. This allowed us to interpret BMD changes independent of the influences of reduced gonadal hormone status. Some of the previous studies included a significant proportion of postmenopausal women and their BMD/BMC could have been altered due to lack of gonadal hormones. In our study cumulative corticosteroid dose was calculated by perusal of patients' clinic notes. As these patients were on long-term therapy, some details were not easily recollected. The disease activity was assesed at the time of recruitment of the study by using SLEDAI score without assessing serum complement levels and DNA binding due to limited resources. This could have made the scoring system incomplete in assessing the disease activity. British Isles Lupus Assessment Group (BILAG) index was not used as we have not assessed disease activity comparing with prior visits.[25] Further, we collected data in a cross-sectional manner and more information could have been gathered if we followed them up with repeated scans. However, we had a control group, matched for age and sex and collected from the same study area. As the number of SLE patients we could recruit to the study was limited to 27, we did not calculate the sample size at the beginning of the study. The post-hoc power calculation, however, showed that the study had more than 85% power to detect differences in BMD, BMC, and lean and fat masses.

Our findings have a clinical relevance. The combination of low BMD and lean mass we found among our SLE patients will make them more vulnerable for fractures. Sarcopenia has been found to be a factor related to recurrent falls. Although high

body fat content can reduce the chance of fracture by reducing the impact of fall, our patients did not have a higher body fat content when compared with controls. Only the ratio between fat mass and fat free mass was altered. It is important to know the morbidity attached to the combination of low bone mass and low lean mass seen among our patients. They need to be assessed for their postural instability and incidence of falls and fractures. Further, the role of physical in intervention in mitigating the morbidity should be assessed.

Funding

This research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

Conflict of interest

The authors have no conflicts of interest to declare.

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