Self-Reported Fractures and Associated Factors in Women with Systemic Lupus Erythematosus

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ABSTRACT. ***Objective***. To determine the frequency of fractures and associated factors in women with systemic lupus erythematosus (SLE).

Methods. Women with SLE (n = 304) completed this cross-sectional study conducted from 1996 to 2002. Self-reported fractures occurring after the diagnosis of SLE were evaluated. Hip and/or lumbar spine bone mineral density (BMD) was measured using dual-energy x-ray absorptiometry, and the results were expressed as BMD Z-scores. Multiple logistic regression analyses were performed to identify factors associated with fractures.

Results. Of the 304 women with SLE, 12.5% experienced fractures. Those with fractures had significantly lower BMD Z-scores at the hip (Fracture group –0.55 vs No Fracture group –0.14, group difference 0.41; 95% CI 0.04 to 0.78), but not at the lumbar spine (Fracture group –0.25 vs No Fracture group –0.18, group difference 0.07; 95% CI –0.43 to 0.57). Among women with fractures, 60.5% and 63.2% had normal BMD Z-scores (BMD Z-score > –1.0) at the hip and lumbar spine, respectively, and 50.0% had normal BMD Z-scores at both anatomical sites. In multiple logistic regression analysis, each year of disease duration (adjusted OR 1.11; 95% CI 1.05 to 1.17) and use of osteoporosis medications (adjusted OR 4.75; 95% CI 1.62 to 13.94) were significantly associated with fractures.

Conclusion. Longer duration of SLE and use of osteoporosis medications were significantly associated with fractures. Although women with fractures had significantly lower BMD Z-scores at the hip, an unexpectedly high proportion of women with SLE having normal BMD Z-score experienced fractures following SLE diagnosis. (First Release Sept 1 2007; J Rheumatol 2007;34:2018–23)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS
OSTEOPOROSIS
FRACTURES
BONE MINERAL DENSITY

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Supported by grants from the National Institutes of Health K12-RR017707 (CL); K24-AR02213, RO1-AR4676402, RO1-HL074335, RO1-AR46588, NCRR/GCRC MO1-RR00056, AR02213; The Lupus Foundation of Pennsylvania (SM); K24-AR02318, P60-AR30692, P60-AR48098, NCRR/GCRC M01-RR00048), Arthritis Foundation Clinical Science Grant, The Lupus Foundation of Illinois, The Arthritis Foundation Greater Chicago Chapter, and unrestricted educational and research grants from Procter & Gamble Pharmaceuticals, Inc. and Merck Co., Inc. (RRG).

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Accepted for publication June 20, 2007.

Women with systemic lupus erythematosus (SLE) are at increased risk for fractures as compared to the general population. In larger studies, the prevalence of self-reported fractures in SLE ranges from 9.1%[1] to 12.3%[2], and the occurrence of radiographically identified vertebral fractures is as high as 20%[3]. Traditional osteoporosis risk factors, such as older age and postmenopausal status, are associated with reduced bone mineral density (BMD) in SLE[1] and likely contribute to fracture risk. Similarly, nontraditional SLE-related factors, such as prolonged use of corticosteroid therapy, may also elevate fracture risk.

Most prior investigations in SLE have examined factors related to reduced bone mass, including presence of osteoporosis based on BMD measurements[4-9]. By comparison, there are limited data on factors associated with fractures in patients with SLE. Given the increased incidence of SLE and longer survival among SLE patients[10], along with the growing concern over the longterm morbidities related to SLE[11], identification of risk factors associated with fracture events in SLE is needed. We examined the relationship of both traditional osteoporosis risk factors and SLE-related factors in women with and without fractures having established SLE.

MATERIALS AND METHODS

Participants. Women with SLE (n = 304) were recruited from the Chicago Lupus Database (n = 225) and Pittsburgh Lupus Registry (n = 79) from 1996 to 2002 for this cross-sectional study. All women met at least 4 American College of Rheumatology (ACR) classification criteria of SLE[12,13]. Institutional review boards at the Chicago and Pittsburgh study centers approved the protocol, and all participants provided informed written consent prior to study participation. Patients attended a single clinic visit that included an interview, physical examination, and BMD measurements of the hip and/or lumbar spine.

Fracture ascertainment. Data on self-reported fracture(s) occurring after SLE diagnosis were collected at the study visit, and fractures were verified using available medical records, which included clinic notes and radiographic reports[14]. Of the 39 women with self-reported fractures following SLE diagnosis, medical records were available for 26 (66.7%) women to ascertain the veracity of their fractures. Of the 26 women with self-reported fractures for whom sufficient medical records were available, fractures were confirmed in 24 (92.3%); there were inadequate medical records to verify the self-reported fracture for one woman, and we determined that another woman did not have a fracture based on her medical records, which included radiographic data. Therefore a total of 38 women with fractures were included in our analysis.

Traditional osteoporosis risk factors and SLE-related factors.
Study participants provided information on traditional factors related to osteoporosis, including self-designated race/ethnicity, age (age at SLE diagnosis, age at study visit, age at menopause) premenopausal or postmenopausal status, lifestyle factors (current smoking status, use of caffeine, use of alcohol), use of hormone preparations, calcium and vitamin D intake, use of medications, including use of osteoporosis medication(s) (etidronate, alendronate, calcitonin), thyroid hormones, diuretics, and anti-epileptics. Postmenopausal status was based on age of 50 years or greater with the last menses more than 1 year ago or if the participant reported a history of prior complete hysterectomy-oophorectomy. If age was less than 50 years, but there was a history of irregular menses or partial hysterectomy (i.e., hysterectomy without oophorectomy), we confirmed postmenopausal status via serum follicular-stimulating hormone measurement.

Information on potential SLE-related factors, including history and duration of SLE renal involvement defined using the 1982 revised ACR SLE classification criteria[12] or having a positive renal biopsy or duration of SLE cumulative disease damage as measured by the Systemic Lupus International Collaborating Clinics/American College of Rheumatology Cumulative Disease Damage Index (SLICC/ACR DI)[15], modified by excluding the osteoporosis/fracture item (1 point) from a possible maximum score of 46, were collected. We collected data on use of hydroxychloroquine and corticosteroids including any corticosteroid use in the past, current use of corticosteroids, current daily corticosteroid dose, and duration of corticosteroid use. For standardization, all corticosteroid preparations were converted to prednisone equivalents.

Bone mineral density measurements. BMD measurements of the hip (n = 297) and lumbar spine (n = 302) were obtained by dual-energy x-ray absorptiometry (DXA) using the Hologic QDR-4500 (Hologic, Chicago, IL, USA) or the Hologic QDR-2000 (Hologic, Pittsburgh, PA, USA). Total hip BMD measurement was performed, and the anteroposterior lumbar spine was measured from L1 to L4 to calculate the mean lumbar spine BMD. All BMD values (g/cm^2) were expressed as BMD Z-scores using the National Health and Nutrition Examination Survey age and race/ethnicity-specific female reference data applied to the BMD values from both study centers. For this study, normal BMD was defined as a BMD Z-score > –1.0.

Quality control. To assess intra- and inter-instrument variations of the 2 densitometers, we measured femur and lumbar spine phantoms on machines at both the Chicago and Pittsburgh study centers. Block phantoms of standardized densities were performed daily to test variation in system linearity[16]. The intra-instrument coefficients of variation were less than 0.56% for the lumbar spine, 0.46% for the femur, and 0.44% for the block phantoms. The lumbar spine phantom measurement was 4% higher with the Hologic QDR-2000 as compared with the Hologic QDR-4500 model. Data analyses used uncorrected lumbar spine measurements, but sensitivity analyses using a 4% correction factor applied to the lumbar spine measurement obtained in women from the Pittsburgh Lupus Registry produced similar results.

Data analysis. All statistical testing used a 2-sided nominal $\alpha = 0.05$ level. Differences between women in the "Fracture" and "No Fracture" groups and the associated 95% confidence intervals (CI) were calculated for traditional osteoporosis risk factors and SLE-related factors; 95% CI excluding zero indicated significant differences. Univariate logistic regression was used to screen traditional osteoporosis risk factors and SLE-related factors of low BMD to identify the most relevant ($p < 0.05$) factors associated with fractures for inclusion in a multiple logistic regression model. A total of 32 factors underwent univariate screening. Significant factors selected by univariate screening were evaluated for multicollinearity. We determined the strength of correlation between factors that had a significant association with low BMD in the screening. In order to avoid multicollinearity, we parsimoniously selected a single factor most strongly associated with low BMD among those factors correlating ($r \geq 0.50$) with one or more other factor(s) for inclusion in our final multiple logistic regression model, which also included study center (Chicago/Pittsburgh recruitment study centers), a design variable. Results of the multiple logistic regression model are presented as adjusted odds ratios with corresponding 95% CI. Statistical analyses were completed using SAS version 9 (SAS Institute, Cary, NC, USA).

RESULTS

Of the 304 women with SLE, 38 women (12.5%) reported fractures following the diagnosis of SLE. There were 8 ankle, 6 spine, 5 rib, 5 wrist, 3 foot, 3 leg, 3 at other unspecified sites, 2 upper arm fractures, and 1 fracture of the pelvis, lower arm, and heel. Among women with fractures, 26 had a single fracture and of the 12 women with more than one fracture, 8 women had 2 fractures, while 3 women had 3 fractures, and one woman had 4 fractures.

Traditional osteoporosis risk factors. A comparison of traditional osteoporosis risk factors between women with and without fractures is shown in Table 1. Women with and without fractures were similar in their mean ages at SLE diagnosis. However, women with fractures were older at study visit and their mean age ± SD at the time of their fracture(s) was 42.0 ± 14.9 years. Additionally, a lower proportion of women with fractures were premenopausal, but the mean age at menopause was similar to women without fractures (Fracture = 43.0 ± 9.4 vs No Fracture = 40.6 ± 8.3 yrs; group difference 2.4, 95% CI –1.4 to 6.1). In terms of racial distribution, 76.3% of all women reporting fractures were White/Caucasian, and there were no significant group differences in the proportion of women with fractures among either Whites/Caucasians (Fracture = 76.3% vs No Fracture = 71.1%; group difference 5.2%, 95% CI –9.3% to 19.8%) or Blacks/African-Americans (Fracture = 23.7% vs No Fracture = 22.9%; group difference 0.08%, 95% CI –13.7% to 15.2%). However, there was a statistically significant difference between the proportions of Hispanic women with and without fractures (Fracture = 0.0% vs No Fracture = 6.0%; group difference –6.0%, 95% CI –8.9% to –3.2%). There were no significant group differences observed for lifestyle factors, but a greater proportion of women with fractures had taken female hormones, daily calcium, thyroid hormones, osteoporosis medications, and diuretics.

Table 1. Traditional osteoporosis risk factors in 304 women with SLE with and without fractures.

Factors	Fracture Group, n = 38	No Fracture Group, n = 266	Difference (95% CI)*
Patient characteristics			
Age at SLE diagnosis, yrs	31.8 ± 15.3	32.6 ± 11.2	–0.8 (–4.8, 3.2)
Age at study visit, yrs	48.5 ± 12.7	40.7 ± 10.5	**7.8 (4.1, 11.4)**
Mean body mass index, kg/m^2 ± SD	27.4 ± 6.2†	26.8 ± 7.2‡	–0.6 (–1.8, 3.0)
Premenopausal, %	31.6	66.2	**–33.4 (–50.4, –18.8)**
Lifestyle factors			
Currently smoking, %	7.9	16.2	–8.3 (–17.9, 1.4)
Drink caffeine, %	76.3	83.3§	–7.0 (–21.3, 7.2)
Drink alcohol, %	44.7	52.1‡	–7.4 (–24.3, 9.6)
Medication and dietary supplement use			
Taken female hormones, %	37.8†	17.7	**20.1 (3.9, 36.5)**
Taken calcium, %	73.7	45.5	**28.2 (13.0, 43.4)**
Daily calcium intake, mg/day	1396.3 ± 767.7	1169.1 ± 716.9	227.2 (–19.6, 474.1)
Taken vitamin D, %	47.4	39.2‡	8.2 (–8.8, 25.1)
Daily vitamin D intake, IU/day	200.0 ± 275.1	177.4 ± 257.3	22.6 (–66.0, 111.1)
Taken thyroid hormones, %	33.3	15.3	**19.2 (3.5, 34.9)**
Taken osteoporosis medications, %	31.6	7.1	**24.5 (9.3, 39.5)**
Taken diuretics, %	47.4	24.5‡	**22.9 (6.1, 39.5)**
Taken thiazide diuretics, %	18.4	9.9§	8.5 (–4.3, 21.4)
Taken anti-epileptics, %	10.5	6.0	4.5 (–5.7, 14.7)

* Indicates the difference in proportions between SLE women with fractures and without fractures and the corresponding 95% confidence interval (CI) unless otherwise stated. 95% CI excluding zero indicate significant differences. Negative results for differences indicate lower values for SLE women with fractures. Data available on: † 37 individuals, ‡ 265 individuals, § 264 individuals. Values in bold are significant.

SLE-related factors. In terms of SLE related factors, women with fractures had longer mean disease duration, higher mean SLICC/ACR DI, and longer duration of corticosteroid use, as presented in Table 2. No significant group differences were seen with regard to the proportion of women with past use of hydroxychloroquine, current use of corticosteroids, or current dose of corticosteroid [median daily corticosteroid dose (range): Fracture = 4.0 mg/day (0 to 20 mg/day) vs No Fracture = 5.0 mg/day (0 to 60 mg/day)]. A significantly greater proportion of women with fractures had SLE renal disease and had past use of corticosteroid.

Bone mineral densitometry measurements. Based on available

Table 2. SLE-related factors in 304 women with SLE with and without fractures.

Factors	Fracture Group, n = 38	No Fracture Group, n = 266	Difference (95% CI)*
SLE-related characteristics			
Disease duration, yrs ± SD	16.2 ± 8.7	7.6 ± 7.4	**8.6 (6.0, 11.2)**
SLICC/ACR DI ± SD	2.7 ± 2.3¶	1.1 ± 1.6#	**1.6 (1.1, 2.3)**
Median SLICC/ACR DI (range)	2.0 (0 to 8)	0.0 (0 to 8)	
SLE renal disease†, %	36.8	18.1	**18.7 (2.0, 34.1)**
SLE-related medications			
Taken hydroxychloroquine, %	42.1	58.2§	–16.1 (–32.9, 0.7)
Taken corticosteroids, %	89.5	77.4	**12.1 (1.1, 23.0)**
Duration taking corticosteroids, yrs ± SD	10.8 ± 9.3	4.3 ± 6.4	**6.5 (4.1, 8.8)**
Current use of corticosteroids, %	60.5	50.0	10.5 (–6.1, 27.2)
Current dose of corticosteroids, mg/day ± SD**	4.6 ± 4.6	7.4 ± 10.1	–2.8 (–6.3, 0.6)

*Indicates the difference in proportions between SLE women with fractures and without fractures and the corresponding 95% CI unless otherwise stated. 95% CI excluding zero indicate significant differences. Negative results for differences indicate lower values for SLE women with fractures. SLICC/ACR DI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology cumulative disease damage index. † SLE renal disease: proteinuria > 0.5 g or 3+ protein; or cellular casts; or positive renal biopsy. Data available on: § 263 individuals, ¶ 37 individuals, # 260 individuals, ** 34 individuals in the Fractures and 211 No Fractures groups. Values in bold are significant

BMD measurements [Fracture group at the hip (n = 38) and lumbar spine (n = 38); No Fracture group at the hip (n = 259) and lumbar spine (n = 264)], the results of the standardized BMD Z-scores showed women with fractures to have significantly lower mean BMD Z-scores at the hip (Fracture = –0.55 vs No Fracture = –0.14; group difference 0.41, 95% CI 0.04 to 0.78), but not at the lumbar spine (Fracture = –0.25 vs No Fracture = –0.18; group difference 0.07, 95% CI –0.43 to 0.57). A significantly lower proportion of women with fractures was noted to have normal standardized BMD Z-score (BMD Z-score > –1.0) results at the hip (Fracture = 60.5% vs No Fracture = 84.6%; group difference –24.1%, 95% CI –40.2% to –7.9%), but not at the lumbar spine (Fracture = 63.2% vs No Fracture = 72.0%; group difference –8.8%, 95% CI –25.1% to 7.5%). Interestingly, more than half of all women with fractures undergoing BMD measurements had normal standardized BMD Z-scores at the hip (60.5%) or lumbar spine (63.2%). Moreover, 50.0% of women with fractures had normal standardized BMD Z-scores at both anatomical sites.

Univariate factors associated with fracture. Univariate screening of traditional osteoporosis risk factors and SLE-related factors was performed to identify the most relevant ($p < 0.05$) factors associated with fractures for inclusion in a multiple logistic regression model as shown in Table 3. Of the 32 factors screened, 13 factors were significantly associated with fractures. As might be expected, older age at study visit was significantly associated with fractures, whereas premenopausal status was inversely associated with fractures. Although none of the lifestyle factors were associated with fractures, longer disease duration, higher SLICC/ACR DI, and SLE renal disease were significantly associated with fractures. In this cross-sectional study, significant associations between fracture occurrence and use of female hormones, calcium, thyroid hormones, diuretics, and osteoporosis medications were strongly associated with fracture events. For corticosteroid use, only longer duration of taking corticosteroids was significantly associated with fractures. Not surprisingly, a higher hip BMD Z-score was inversely associated with fractures, whereas lumbar spine BMD Z-score was not significantly related to fractures. The study center, a design variable, was statistically significant in the univariate screening.

Adjusted analysis of significant univariate factors associated with fractures. The results of the multiple logistic regression model constructed after screening for collinear relationships among significant univariate factors are shown in Table 4. Of the original 13 significant univariate factors, 9 (premenopausal status, disease duration, SLICC/ACR DI, SLE renal disease, use of calcium, use of osteoporosis medications, use of thyroid hormones, use of diuretics, and hip BMD Z-score) were included in the model along with body mass index, a clinically important factor, and study center, a design variable, resulting in a total of 11 factors included in the final multiple logistic regression model. Three significant univariate factors excluded from the final model, due to their strong collinearity with other significant univariate factors, included age at study visit (correlated with premenopausal status), use of female hormones (correlated with premenopausal status), and duration of corticosteroid use (correlated with disease duration). Of the factors in the final model, only longer disease duration and use of osteoporosis medications were significantly associated with fractures.

Both disease duration and SLICC/ACR DI were included in our multiple logistic model, but their correlation coefficient ($r = 0.37$) approached, but did not exceed the predetermined multicollinearity threshold ($r \geq 0.50$). Therefore, we performed a sensitivity analysis including disease duration or SLICC/ACR DI separately in our multiple logistic regression

Table 3. Univariate screening of factors associated with fractures in 304 women with SLE.

Factors	Unadjusted OR (95% CI)*
Patient characteristics	
Age at SLE diagnosis	0.99 (0.96, 1.02)
Age at study visit	**1.06 (1.03, 1.10)**
Face	0.68 (0.34, 1.34)
White/Caucasian	1.31 (0.59, 2.90)
Black/African-American	1.04 (0.47, 2.32)
Hispanic (non-Caucasian)	0.001 (0.001, 999.99)
Premenopausal	**0.24 (0.11, 0.49)**
Body mass index, kg/m^2	1.01 (0.97, 1.06)
Study center	**2.06 (1.01, 4.18)**
Lifestyle factors	
Currently smoking	0.45 (0.13, 1.51)
Drink caffeine	0.64 (0.29, 1.46)
Drink alcohol	0.75 (0.38, 1.48)
SLE-related characteristics	
Disease duration, yrs	**1.12 (1.08, 1.17)**
SLICC/ACR DI	**1.49 (1.27, 1.75)**
SLE renal disease	**2.52 (1.22, 5.22)**
Medication and dietary supplement use	
Taken female hormones	**2.84 (1.36, 5.92)**
Taken calcium	**3.36 (1.57, 7.18)**
Daily calcium intake	1.00 (1.00, 1.01)
Taken vitamin D	1.39 (0.70, 2.76)
Daily vitamin D intake	1.00 (0.99, 1.00)
Taken osteoporosis medications	**6.00 (2.62, 13.73)**
Taken hydroxychloroquine	0.52 (0.26, 1.04)
Taken thyroid hormones	**2.94 (1.39, 6.22)**
Taken diuretics	**2.77 (1.38, 5.55)**
Taken thiazide diuretics	2.07 (0.83, 5.16)
Taken anti-epileptics	1.84 (0.58, 5.82)
Corticosteroid use	
Taken corticosteroids in the past	2.48 (0.85, 7.25)
Duration taking corticosteroids	**1.10 (1.05, 1.15)**
Current use of corticosteroids	1.53 (0.77, 3.07)
Current dose of corticosteroids	0.96 (0.90, 1.01)
BMD measurement (Z-scores)	
Hip BMD Z-score	**0.70 (0.51, 0.97)**
Lumbar spine BMD Z-score	0.97 (0.76, 1.22)

SLICC/ACR DI: modified version of the Systemic Lupus International Collaborating Clinics/ American College of Rheumatology cumulative disease damage index excluding the osteoporosis/fracture item. Bold values are significant.

Table 4. Multiple regression results of significant univariate factors associated with fractures in 304 women with SLE.

Factors	Adjusted OR (95% CI)*
Premenopausal	0.47 (0.19, 1.17)
Body mass index	1.01 (0.95, 1.07)
Disease duration, yrs	**1.11 (1.05), 1.17)**
SLICC/ACR DI*	1.24 (0.98, 1.58)
SLE renal disease	0.89 (0.31, 2.52)
Taken calcium	2.31 (0.93, 5.75)
Taken osteoporosis medications	**4.75 (1.62, 13.94)**
Taken thyroid hormones	2.50 (0.94, 6.63)
Taken diuretics	1.33 (0.50, 3.52)
Hip BMD Z-score	0.97 (0.66, 1.43)
Study center	1.51 (0.59, 3.89)

SLICC/ACR DI: modified version of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology cumulative disease damage index excluding the osteoporosis/fracture item. Bold values are significant.

model. The analysis including disease duration showed similar results to our original model, maintaining significant association with fractures (adjusted OR 1.12, 95% CI 1.06 to 1.18). In the alternative model including SLICC/ACR DI, greater disease damage was significantly associated with fractures (adjusted OR 1.40, 95% CI 1.12 to 1.74). Use of calcium and use of osteoporosis medications were also associated with fractures in both of the models in our sensitivity analysis.

DISCUSSION

Our findings indicate that for each year of having SLE there is a 10% increased association with fractures in women with SLE even after accounting for age and corticosteroid use. No prior investigation has shown a relationship between duration of SLE and fractures. Since duration of SLE and duration of corticosteroid use were both significantly associated with fractures in our univariate screening and also correlated with each other, only duration of SLE was included in our multiple logistic regression model as it demonstrated a stronger association with fractures. Therefore, the association observed between duration of SLE and fractures may indirectly reflect duration of corticosteroid use. Yet given that the other corticosteroid variables assessed in our study failed to demonstrate any significant relationship with fractures, it is unlikely that duration of corticosteroid use fully explains the association seen between disease duration and fractures. Conceivably, some women developing SLE at a younger age may have failed to reach optimal peak bone mass, in part due to longer duration of disease, thus placing them at potentially higher risk of future fractures as compared with women with shorter disease duration. Regardless of the exact role of disease duration in relation to fractures, the association between longer disease duration and fractures noted in this study has potential clinical relevance. For instance, women with longer-duration SLE may represent a group requiring greater attention toward minimizing risk factors for future fractures.

In contrast to the association seen between disease duration and fractures, age at study visit, which was indirectly represented by premenopausal status in the multiple logistic model, was not associated with fractures. In a group of 702 women with SLE as compared with women of similar age from a US population, older age was found to be a risk factor for fractures[2]. Similarly, a subsequent study of 242 patients with SLE from the UK also implicated older age as a significant predictor of fractures[1].

Although women with fractures in our study were older at study visit than women without fractures, the mean age at the time of the fractures indicates that the fracture events occurred in relatively young women. This finding suggests that factors other than older age contribute to fractures in SLE. For example, severity of disease as represented by the SLICC/ACR DI, which was significantly related to fracture in our univariate screening and sensitivity analyses, has been shown to be associated with lower BMD by our group and others[4,17]. A potentially interesting explanation is that SLE per se, particularly in cases of more severe disease, as represented by the SLICC/ACR DI, may have inherently adverse effects on bone, such as the development of osteoporosis[17], and thereby increases susceptibility for fractures. Given that SLICC/ACR DI was not significantly associated with fractures in our multiple logistic regression analysis, the SLICC/ACR DI may have a limited relationship with fractures in women with SLE.

We observed only a limited association between BMD status and fractures in women with SLE. As might be expected, women with fractures as a group had lower mean BMD Z-scores at hip and lumbar spine, albeit BMD results as compared to women without fractures were statistically lower only at the hip. Further, higher proportions of women without fractures had normal BMD findings at the hip and lumbar spine. Nevertheless, a surprisingly large proportion of women experiencing fractures had normal BMD levels at both measured anatomical sites. Lumbar spine BMD status also failed to be significantly associated with fractures in our univariate screening, and hip BMD was not significantly related to fractures when controlling for other factors. Two prior investigations have observed vertebral deformities in patients with SLE in the setting of normal BMD[3,18]. In contrast to such previous reports, our results also suggest that nonvertebral fractures may occur in the setting of normal BMD. A possible explanation for the unexpectedly high proportion of women with fractures possessing normal BMD could be a result of some women reporting non-fragility fractures rather than exclusively reporting fragility fractures.

Our findings are in contrast to those reported by Yee and colleagues, who found reduced BMD to be associated with fragility fractures[1]. One explanation for the discrepancy may be that we examined the BMD Z-score as a continuous variable, whereas in the study by Yee, BMD status was categorized as "reduced BMD" consisting of osteopenia or osteoporosis based the results of BMD T-scores. Further, the incon-

sistent relationship between BMD status and fractures in our study may be due in part to the cross-sectional study design and the relatively younger age of women in our study possessing generally higher BMD than might be seen in an older group of women. Conversely, in younger women with SLE, disease duration and the degree of disease severity may need to be considered in addition to BMD status in order to more accurately assess fracture risk.

The strong associations between fractures and use of female hormones, calcium, osteoporosis medications, and possibly the diuretics observed in our analysis likely reflect the use of these bone-protective medications and dietary supplements by a group at higher risk for fractures. With regard to corticosteroids, women experiencing fractures reported longer duration of corticosteroid use, and a greater proportion reported past use of corticosteroids, but there were limited group differences with respect to other measures of corticosteroid exposure. In addition, the mean current doses of corticosteroid in both groups of women were relatively low. The comparatively similar corticosteroid burden between women with and those without fractures may explain the absence of any significant association between some of the factors related to corticosteroid use and fracture events, a finding which is consistent with other reports[1]. In other studies, duration of corticosteroid use has been shown to be a risk factor for fractures in a large group of women with SLE[2], and use of intravenous methylprednisolone was associated with vertebral deformities[3].

The cross-sectional design of our study allowed us to identify associations between SLE-related factors with fractures in women with SLE. However, we cannot discern a causal relationship between factors assessed in our study such as between disease damage and fractures. For instance, the association between use of osteoporosis medications and fractures observed as in our cross-sectional study likely represents those women at higher fracture risk having been placed on such medications to minimize their risk for future fractures, rather than any causal relationship between use of medications and fractures. Although the number of women with self-reported fractures in our study is not trivial, insufficient power could explain the absence of any significant associations between some of the assessed variables and fractures. Longitudinal investigations are necessary to establish if such associations are actual risk factors for fractures in the SLE population.

Despite these limitations, the overall frequency of fractures in our women was consistent with the results of previous investigations that included women comparable in age and ethnic composition to those in our study[1,2]. Further, the current findings indicate that SLE-related factors are associated with fractures in women with SLE, even in the presence of normal BMD. Our study adds important information, given that a disproportionately high number of women with SLE who experienced fractures were also found to have normal BMD.

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