Ten-year Absolute Fracture Risk and Hip Bone Strength in Canadian Women with Systemic Lupus Erythematosus

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ABSTRACT. ***Objective***. Women with systemic lupus erythematosus (SLE) are at risk of osteoporosis (OP) and fractures because of SLE or its treatments. We aimed to determine in women with SLE (1) the prevalence of low bone mass (LBM) in those < 50 years of age and OP in those > 50 years of age; (2) the 10-year absolute fracture risk in those > 40 years of age using the Canadian Fracture Risk Assessment Tool (FRAX); (3) bone quality using hip structural analysis (HSA); and (4) the associations between HSA and age, SLE duration, and corticosteroid exposure.

Methods. Women without prior OP fractures were eligible. Bone mineral densities at the hip, spine, and femoral neck were determined using dual-energy x-ray absorptiometry. OP was determined using World Health Organization definitions for participants aged ≥ 50 years (32.8%), and LBM was defined as Z-scores ≤ –2.0 for those aged < 50 years. For those aged ≥ 40 years (63.5%), the 10-year probabilities of a major fracture (FRAX-Major) and hip fracture (FRAX-Hip) were calculated. FRAX-Major ≥ 20% or Hip ≥ 3% was considered high risk. HSA was done in a subgroup (n = 81) of patients.

Results. The study group was 271 women. Mean (SD) age was 43.8 (13.1) years and SLE duration was 11.6 (10.4) years. OP was diagnosed in 14.6% and LBM in 8.8%. FRAX-Major ≥ 20% was seen in 9 patients (5.3%), of whom 6 were taking OP medications. FRAX-Hip ≥ 3% occurred in 16 patients (9.4%), of whom 9 were taking OP medications. Buckling ratio at the left hip narrow neck was positively correlated with FRAX-Major, FRAX-Hip, SLE duration, and duration of corticosteroid use.

Conclusion. LBM is prevalent in women with SLE who are < 50 years of age. FRAX may identify those at higher risk of fractures while HSA can assess bone structure noninvasively. (First Release June 1 2012; J Rheumatol 2012;39:1378–84; doi:10.3899/jrheum.111589)

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Osteoporosis (OP) is a significant cause of morbidity for women with longterm complications of systemic lupus erythematosus (SLE)[1,2]. The current literature estimates an OP prevalence ranging from 4% to 23%[1,3] in patients with SLE who have significantly lower bone mineral density (BMD) values at the lumbar spine and proximal femur compared to healthy controls[4]. Ramsey-Goldman, *et al*[5] reported that women with SLE experienced 5 times more fractures than women in the US population, with nearly half the fractures occurring before menopause. Both treatment-related and disease-related factors of SLE are implicated in patients' susceptibility to osteoporotic fractures[1]. For instance, chronic use of glucocorticoids can induce bone loss and increase fracture risk[3]. Disease-dependent factors include reduced physical activity due to arthropathy, renal impairment, and endocrine dysfunction[1,4,6].

Based on World Health Organization (WHO) classifications, OP is diagnosed in postmenopausal women when a BMD measurement is ≥ 2.5 SD below normal peak bone mass when compared with normal peak values for young adult women (referred to as a T score)[7,8] or when a woman has had a fragility fracture. Fragility fractures are defined as those that occurred spontaneously or in response to minimal trauma (such as falling from standing height)[9]. They are commonly seen in the distal radius, proximal femur, vertebral body, or proximal humerus. Tools such as the WHO Fracture Risk Assessment Tool (FRAX) are used to assess 10-year absolute fracture risk for individuals older than 40 years. The FRAX incorporates clinical risk factors and femoral neck BMD to calculate a 10-year probability of a major osteoporotic event (FRAX-Major) and of a hip fracture (FRAX-Hip)[10,11]. Current National Osteoporosis Foundation recommendations suggest that probability values ≥ 20% for FRAX-Major and ≥ 3% for FRAX-Hip are high enough to warrant pharmacological intervention[10].

The applicability of the WHO classification system is questioned for premenopausal women who are younger than age 40 years with chronic conditions such as SLE, because the system was originally developed for postmenopausal and relatively healthy women[1,12]. The International Society for Clinical Densitometry recommends the use of Z-scores when assessing risk for women who are premenopausal or younger than age 50 years. A Z-score that is 2 SD from the mean when compared to sex-matched or age-matched controls could indicate low bone mass (LBM) and warrants further evaluation[1,12].

In addition, it has been reported that BMD does not entirely assess bone strength and fracture risk. Siris, *et al*[13] reported that 82% of postmenopausal white women who do not have SLE sustain fragility fractures despite having T-scores > –2.5. About 60%–80% of the bone strength is based on BMD, while 20%–40% of the strength is dependent on bone quality[1]. This includes the bone's geometric structure, microarchitecture, remodeling, turnover, and mineralization[1,8]. Among the methods used to assess bone quality is the hip structural analysis (HSA), which has been used to assess various mechanical strength measures[14,15].

The use of innovative approaches such as the FRAX, reporting Z-scores in premenopausal women, and the HSA have not been widely applied in the current care practices of patients with SLE. Therefore, the objectives of our study were (1) to estimate the prevalence of OP in women with SLE age ≥ 50 years and low bone mass in those age < 50 years; (2) to estimate the 10-year absolute risk of fracture using Canadian FRAX in women with SLE age ≥ 40 years; (3) to assess bone structure by HSA and estimate various strength measures; and (4) to determine whether there is a correlation between HSA and age, SLE duration, and corticosteroid exposure.

MATERIALS AND METHODS

Subjects were selected from those currently enrolled in the Health Improvement and Prevention Program (HIPP) study, which began in 2003. The HIPP study currently has recruited 288 women with SLE from 3 health centers in Canada [Montreal, Toronto, London (Ontario)]. Of these, 271 subjects had data available on BMD. In accord with the HIPP trial, inclusion criteria included being female ≥ 18 years of age, and meeting at least 4 of the 11 classification criteria for SLE defined by the American College of Rheumatology (ACR)[16]. The exclusion criteria included having a history of cardiovascular event or OP with a documented fracture. All patients gave their informed consent and the protocol was approved by the Research Ethics Boards of each participating center.

Demographic information collected included age, age at SLE diagnosis, SLE duration, ethnicity, body mass index (BMI), menopausal status, smoking status, and alcohol consumption. The Systemic Lupus International Collaborating Clinics/ACR (SLICC/ACR) Damage Index (SDI) scores, which estimate the degree of irreversible organ damage from SLE[17], were obtained. The collected medication profile included the use of glucocorticoids, immunosuppressants, antimalarial medications, and OP treatment (calcium, vitamin D, bisphosphonate, and other OP therapy). Duration of glucocorticoid treatment (in years) was also reported. The use and the daily dose of calcium and vitamin D supplements were self-reported. Previous history of non-OP fractures and family history of OP were also documented. All of the following information was from self-report questionnaires.

The BMD of the total spine (L1-L4), total hip, and femoral neck were determined using the dual-energy x-ray absorptiometry (DEXA) scans (densitometers from GE Lunar, Madison, WI, USA; and Hologic, Bedford, MA, USA). To estimate OP or LBM prevalence, participants were classified according to age (older or younger than 50 years). T-scores were used to assess OP according to WHO definitions for persons ≥ 50 years of age and Z-scores were used to assess the prevalence of LBM for persons < 50 years old.

The 10-year absolute risk of fracture in patients ≥ 40 years of age with SLE was calculated using the FRAX tool for the Canadian population (version 3.5). This tool is available online at http://www.shef.ac.uk/FRAX/tool.jsp?country=19. FRAX uses clinical risk factors such as age, sex, BMI, fracture history, family history, smoking, alcohol (3 or more units daily), presence of rheumatoid arthritis (RA), presence of secondary causes of OP, glucocorticoid use, and the femoral neck BMD to determine the 10-year probabilities (%) of a major osteoporotic event (FRAX-Major) and of a hip fracture (FRAX-Hip). Glucocorticoid use for FRAX purposes was defined as either currently taking glucocorticoids or exposed to glucocorticoids in the past for > 3 months at a dose of 5 mg daily. Because it is unclear whether SLE should be considered as a cause of secondary OP or whether it is interchangeable with RA, we calculated FRAX with and without substituting SLE as RA in the FRAX calculations.

Bone quality of the left hip was assessed by HSA in a subset (n = 81) of women. Patient selection was based on DEXA scan accessibility and com-

patibility with the HSA software — only the women who had their DEXA scans done with the Hologic densitometer at the Toronto General Hospital site were eligible. The HSA software analyzes the geometry of cross-sections traversing the proximal femur at 3 locations: the narrowest diameter of the femoral neck (NN), the bisector of the neck-shaft angle [the intertrochanteric (IT)], and 2 cm distal to the midpoint of the lesser trochanter (the shaft). The measurements derived from the HSA include section modulus (SM; cm^3) and buckling ratio (BR). The SM indicates bending strength for maximum bending stress in the image plane and the BR is an estimate of cortical stability in buckling (failure of a structure to react to the bending moment generated by a compressive load[18]). BR ≥ 10 is considered high fracture risk.

Statistical analyses. Statistical analyses were performed using SPSS software (version 16, SPSS, Chicago, IL, USA). Descriptive summary statistics were used to describe the demographics and prevalence of OP, LBM, and 10-year absolute fracture risks. Unpaired Student's t-test was used for 2-group comparison. Pearson correlations were used to assess associations between BMD, FRAX, and HSA and age, SLE duration, duration of glucocorticoid exposure, and other OP/SLE-related risk factors (such as calcium and vitamin D supplement intake). Logistic regression analysis was used to determine the predictors of low BMD at the 3 anatomical locations. Eleven risk factors were assessed on analysis including age at SLE diagnosis, SLE duration, BMI, alcohol use, smoking, exercise, postmenopausal status, prednisone use, calcium use, vitamin D use, bisphosphonate, and other OP medication use. All data are reported as mean ± SD or as percentages. Significant levels are defined as $p < 0.05$.

RESULTS

Subjects' demographics. Baseline data are reported in Table 1. The mean (SD) age of our cohort was 43.8 (13.0) years with SLE duration of 11.6 (10.4) years; 69.2% were taking glucocorticoids; 23.0% were taking > 7.5 mg/day prednisone for > 3 months at the time of enrollment; and 12.9% had prior non-fragility fractures (Table 1). Calcium and vitamin D supplements were used by 48% and 39%, respectively, at the time of enrollment.

Prevalence of osteoporosis and low bone mass. BMD results are reported in Table 2. Among participants, 32.8% were ≥ 50 years of age (n = 89) and 67.2% were age < 50 years (n = 182). Overall, OP was diagnosed in 14.6% of those age ≥ 50 years, according to BMD. In those age < 50 years, using Z-scores ≤ –2, LBM was diagnosed in 8.8%.

Ten-year absolute fracture risk using FRAX tool. Ten-year absolute fracture risks were calculated for women age ≥ 40 years who were not taking any OP treatments prophylactically (n = 129, 47.6%). FRAX results are reported in Table 3. Of these women, 3 (2.3%) had a FRAX-Major score ≥ 20% and 7 (5.4%) had a FRAX-Hip score ≥ 3%. Decisions on whether to prescribe OP medications were based solely on clinical judgment, BMD, and the WHO OP classification rather than on FRAX results.

When all women age ≥ 40 years who had data available for FRAX calculations (n = 171, 63.1%) regardless of OP treatment status were considered, FRAX-Major scores ≥ 20% and FRAX-Hip scores ≥ 3% were observed in 9 (5.3%) and 16 (9.4%) patients, respectively. In total, 42 women age ≥ 40 years were treated based on clinical judgment, but only 6 (3.5%) had FRAX-Major scores ≥ 20%, and 9 (5.3%) had FRAX-Hip scores ≥ 3%. Individuals with FRAX-Major scores < 10% and FRAX-Hip scores < 1% are considered to have very low 10-year absolute fracture risks. However, 27 patients with FRAX-Major < 10% and 21 patients with FRAX-Hip < 1% were receiving OP treatment. FRAX was also calculated by supplementing SLE with RA in the calculation in patients ≥ 40 years of age who were not taking OP treatments. FRAX-Major scores ≥ 20% and FRAX-Hip scores ≥ 3% were seen in 5 (2.9%) and 7 (5.4%) patients, respectively.

Associations between BMD, FRAX, and other OP and SLE-related risk factors. There were significant correlations between the BMD scores at the femoral neck ($r = –0.31$, $p = 0.001$; $r = –0.208$, $p = 0.001$) and total hip ($r = –0.41$, $p < 0.01$; $r = –0.195$, $p = 0.003$) with glucocorticoid duration and SLE duration, respectively. There were no significant correlations between BMD scores with the SLICC scores (data not

Table 1. Demographic characteristics of the 271 study subjects.

Characteristics	Mean (SD)
Age, yrs	43.8 (13.0)
Age at SLE diagnosis, yrs	32.2 (13.2)
SLE duration, yrs	11.6 (10.4)
BMI	26.3 (6.3)
SLICC score, n = 269	1.15 (1.48)
Taking calcium supplement	130 (48.0)
Taking vitamin D supplement	106 (39.1)
Vitamin D dosage[1], IU/day, n = 106	688.5 (429.4)
Calcium dosage[1], mg/day, n = 130	884.1 (416.0)
Glucocorticoid duration, yrs, n = 189	10.6 (8.70)
Risk factors, n (%)	
Smoking[2]	118 (43.5)
Alcohol use[3]	154 (56.8)
Previous fractures	35 (12.9)
Wrist	18 (6.6)
Spine	8 (3.0)
Pelvis	0 (0.0)
Hip	0 (0.0)
Leg	9 (3.3)
Parent with osteoporosis	45 (16.6)
Lack of exercise[4]	129 (47.6)
Postmenopausal[5]	102 (37.6)
OP medication use[6]	42 (16.6)
Glucocorticoid use[7]	189 (69.7)
Current dose ≥ 7.5 mg	64 (23.6)
≥ 3 months	110 (40.6)

[1] Medication dose (mg) × no. days supplement taken. Dietary intake not taken into account. [2] Defined as any individual who has ever smoked. [3] Defined as > 1 unit/day. 1 unit was defined as 12 oz. (1 bottle) of beer or 4 oz. (1 glass) of wine or 1 oz. (1 shot) of liquor. [4] Not engaging in activities that allowed a participant to break a sweat in an average week. [5] Postmenopausal status was defined as self-reported absence of menses for ≥ 1 year. [6] Bisphosphonate: 41 patients; raloxifene: 1 patient. Use defined as ever having taken these medications. [7] No. patients on glucocorticoid treatment at time of enrollment. SLE: systemic lupus erythematosus; BMI: body mass index; SLICC: Systemic Lupus International Collaborating Clinics; OP: osteoporosis.

Table 2. Bone mineral density (BMD) and the prevalence of osteoporosis or low bone mass in the study subjects.

Group	
Age ≥ 50 years, n = 89, mean (SD)	
BMD: total spine, g/cm^2	1.04 (0.16)
BMD: total hip, g/cm^2	0.90 (0.15)
BMD: femoral neck, g/cm^2	0.84 (0.15)
T-score: total spine	–0.73 (1.4)
T-score: total hip	–0.52 (1.0)
T-score: femoral neck	–0.78 (1.2)
Total spine, % of Patients	
T-score < –2.5 (osteoporosis)	11.5
–1 > T-score > –2.5 (osteopenia)	34.5
Total hip, % of Patients	
T-score < –2.5 (osteoporosis)	2.8
–1 > T-score > –2.5 (osteopenia)	33.7
Femoral neck, % of Patients	
T-score < –2.5 (osteoporosis)	5.7
–1 > T-score > –2.5 (osteopenia)	45.4
Age < 50 years, n = 182, mean (SD)	
BMD: total spine, g/cm^2	1.08 (0.14)
BMD: total hip, g/cm^2	0.97 (0.15)
BMD: femoral neck, g/cm^2	0.89 (0.16)
Z-score: total spine	–0.22 (1.1)
Z-score: total hip	0.11 (1.0)
Z-score: femoral neck	–0.19 (1.0)
Total spine, % of Patients	
Z-score ≤ –2	6.7
Total hip, % of Patients	
Z-score ≤ –2	0
Femoral neck, % of Patients	
Z-score ≤ –2	2.8

Table 3. FRAX scores in subjects age ≥ 40 years who are not taking bisphosphonate therapy (n = 129).

FRAX Scores	Mean (SD)
FRAX-Major	6.91 (5.92)
FRAX-Hip	0.62 (0.99)
Intervention thresholds, n (%)	
FRAX-Major ≥ 20%	3 (2.3)
FRAX-Hip ≥ 3%	7 (5.4)

FRAX: WHO Fracture Risk Assessment Tool; FRAX-Major: 10-year probability (%) of a major osteoporotic event; FRAX-Hip: 10-year probability (%) of hip fracture.

shown). Through logistic regression analyses, independent risk factors for a lower femoral neck BMD and total hip BMD included a longer SLE duration, lower BMI, and OP medication (bisphosphonate or raloxifene) use. Independent risk factors for a lower total spine BMD included being postmenopausal and OP medication use (data not shown).

FRAX-Major also correlated significantly with the duration of glucocorticoid use (r = 0.367, p = 0.003), age (r = 0.635, p < 0.001), and SLE duration (r = 0.230, p = 0.002). Similarly, FRAX-Hip correlated significantly with those 3 variables [duration of glucocorticoid use (r = 0.367, p = 0.003); age (r = 0.409, p < 0.001); and SLE duration (r = 0.227, p = 0.003)]. Through logistic regression analyses, SLE duration and age were independent risk factors for both greater FRAX-Hip (p < 0.0001; p < 0.0001) and FRAX-Major (p < 0.0001; p < 0.0001) scores.

In all subjects, there was no significant difference in BMD scores at any of the anatomical locations between those who were and those who were not taking calcium and/or vitamin D supplements (data not shown). There was also no significant correlation with respect to BMD scores and the dosage of calcium and/or vitamin D (data not shown).

There was a significant difference in BMD between women with SLE who were taking OP medications (bisphosphonate mainly, and 1 patient taking raloxifene) and those who were not. Scores for those taking the medications were total hip, 0.86 ± 0.17; femoral neck, 0.78 ± 0.16; and total spine, 0.98 ± 0.18. For those who did not take OP medications, scores were total hip, 0.97 ± 0.14; femoral neck, 0.90 ± 0.16; and total spine, 1.08 ± 0.14 (p < 0.01).

Hip structural analysis. HSA was performed in a subset of participants (n = 81) and results are reported in Table 4. The mean age for this subset was 42.4 (1.2) years, with an average SLE duration of 12.0 (9.9) years; 32.1% were postmenopausal. There were more women taking glucocorticoid therapy (85.2%) in this subset than in the overall study population (69.7%), and 29% were receiving doses ≥ 7.5 mg prednisone for ≥ 3 months (compared to 23% of overall study population).

At the narrow diameter of the femoral neck (NN) region, there were no significant associations between the SM values and the FRAX scores, age, glucocorticoid duration, or SLE duration. However, all BR values at the NN were positively correlated with FRAX-Major (r = 0.589, p < 0.001), FRAX-Hip (r = 0.620, p < 0.001), age (r = 0.263, p = 0.071), SLE duration (r = 0.493, p < 0.001), and duration of glucocorticoid use (r = 0.340, p = 0.046). BR values ≥ 10 were seen in 43.2% (n = 35) of participants, of which only 7 patients were taking OP treatment. Among the 35 patients with BR > 10, 11 did not have data available for FRAX, 2 had FRAX-Major ≥ 20%, and 3 had FRAX-Hip ≥ 3%. T-score < –2.5 for femoral neck only was seen in 3 patients. However, these patients were all under the age of 50 years and therefore Z-score would be more appropriate for risk assessment. Only 5 patients had Z-score ≤ –2.

At the bisector of the neck-shaft angle, the IT region, the SM values (r = –0.275, p = 0.032) were negatively correlated with glucocorticoid duration. The BR at the IT region showed significant correlation with SLE duration (r = 0.272, p = 0.014) and glucocorticoid duration (r = 0.292, p = 0.022). Among subjects, 2.5% had BR at the IT region above 10 (threshold for increased fracture risk or decreased bone strength).

At the shaft region (2 cm distal to the midpoint of the lesser trochanter), the BR values showed a nonsignificant correla-

Table 4. Hip structural analysis in a subgroup of subjects with systemic lupus erythematosus.

Variable, n = 81	Mean (SD)		
	Narrow Neck Region	Intertrochanteric Region	Femoral Shaft Region
BMD, g/cm^2	0.99 (0.18)	0.97 (0.15)	1.58 (0.20)
CSA, cm^2	2.98 (0.52)	4.64 (0.78)	4.29 (0.62)
CSMI, cm^4	2.56 (0.63)	10.58 (2.37)	3.28 (0.82)
SM, cm^3	1.47 (0.30)	3.68 (0.70)	2.22 (0.42)
Outer diameter, cm	3.18 (0.25)	5.05 (0.30)	2.84 (0.22)
Inner diameter, cm	2.80 (0.28)	4.25 (0.33)	1.60 (0.33)
CT, cm	0.19 (0.04)	0.40 (0.07)	0.62 (0.11)
BR	9.47 (2.16)	7.43 (1.41)	2.43 (0.52)

BMD: Bone mineral density; CSA: cross-sectional area; CSMI: cross-sectional moment of inertia; SM: section modulus; CT: cortical thickness; BR: buckling ratio.

tion with FRAX-Hip (r = 0.397, p = 0.055). BR values were significantly correlated with SLE duration (r = 0.351, p = 0.001) and glucocorticoid duration (r = 0.336, p = 0.008). None of the subjects had BR at the IT region above 10.

DISCUSSION

In our cohort of women with SLE and with no history of fragility fractures, OP was present in 14.6% of women age ≥ 50 years and LBM was present in 8.8% of women age < 50 years. In those over the age of 40 years, 5.3%–9.4% were found to be at risk of major OP or hip fracture in the next 10 years. In a subset of these women, low SM and high BR (suggesting poor bone strength) were associated with older age, longer SLE duration, and longer use of glucocorticoids.

The prevalence of OP observed in our study was slightly lower than in earlier reports in patients with SLE[1,3,19,20]. Pineau, *et al*[19] reported an OP prevalence of 18% and Almehed, *et al*[3] showed similar BMD values in a Swedish SLE cohort, with a prevalence of 23%. However, the prevalence we found in women age ≥ 50 years may be an underestimate of the true prevalence in the general SLE population because of the exclusion criteria of the HIPP study, the origin of these measures. A limitation of our study is therefore that individuals with a history of OP fractures were excluded.

Overall, LBM was diagnosed in 8.8% of participants < 50 years of age after excluding those with OP fractures. To our knowledge, this is the first study that reports LBM prevalence in patients with SLE by grouping according to age (older or younger than 50 years) and using the Z-score definition as set out by the International Society of Clinical Densitometry. The Z-score has been shown to provide a more conservative estimate of risk than the T-score for populations aged < 50 years[21]. While some studies report that the Z-score and T-score are interchangeable[12,22,23], more recent studies suggest that the T-score and Z-score can result in significant diagnostic disagreement, especially in women between the ages of 20 and 49 years[21,24].

In our study, in women < 50 years of age, LBM was seen more in the spine than in the hip. This was in line with findings from other studies showing a greater loss of BMD at the lumbar vertebrae in women with SLE who are premenopausal or younger than age 50 years[20,21].

LBM in patients with SLE may be due to SLE disease processes and/or its treatments[1,2,3,4,5,6]. While most studies demonstrated that patients with SLE taking glucocorticoids had lower BMD than controls[2,20,25], the evidence of an independent effect of glucocorticoids on BMD has been conflicting. We found a negative correlation between the BMD of the femoral neck and total hip and the duration of glucocorticoid use. This was in agreement with Houssiau, *et al*[2], who reported significant correlations between BMD and cumulative glucocorticoid dose. However, in a multivariate regression analysis, we did not find glucocorticoids to be an independent risk factor for BMD at the 3 anatomical sites. Kalla, *et al*[20] as well as other studies[26,27,28] found that high-dose glucocorticoids do not seem to cause nor are significantly correlated with significant trabecular bone loss in patients with SLE. The conflicting evidence of glucocorticoids and BMD may be due to differences in population characteristics of each study, SLE disease duration in particular. Further, as expected, we found significant correlations between the femoral neck and total hip BMD with SLE duration. It has been reported that the actual inflammatory component attributed to SLE itself can cause a reduction in BMD[1].

We have also looked at other associations including BMD and the use of calcium or vitamin D supplements. In our study, we did not find a significant correlation with BMD scores and the use of these supplements. However, a major limitation of this interpretation is that we did not collect data on dietary sources and intake of calcium and vitamin D. There are several metaanalyses that demonstrate fracture risk reduction with dietary calcium and vitamin D supplementation[29,30].

To our knowledge, our study is the first to use FRAX as a means of determining 10-year absolute risk of major osteoporotic or hip fracture in women with SLE age ≥ 40 years who were not taking OP medications, by taking into account the femoral BMD values and other OP-related risk factors. The FRAX tool, adapted for the Canadian population, is relatively

new but validated. The WHO FRAX tool has been constructed through the primary data of 9 population-based cohorts and has been validated in 11 independent cohorts. We did not consider SLE a secondary cause of OP. Currently, identifying a secondary cause of OP in the tool does not carry any weight in the calculations and does not change FRAX results[28]. We have also calculated FRAX scores by substituting SLE for RA. Interestingly, this did not make any difference in the number of patients who had FRAX-Hip ≥ 3%. Two more patients were identified as having FRAX-Major ≥ 20%. All clinical risk factors used for the FRAX were based on self-report questionnaires. Hence, a limitation is that we were unable to verify certain clinical risk factors (such as the absence of OP fractures based on radiograph findings).

The FRAX is mainly intended to identify patients who require treatment and is not indicated for patients who are taking concurrent treatment for OP[31]. However, we decided to calculate FRAX-Major scores in patients age ≥ 40 years who were taking OP treatments to determine whether clinical practice is in line with current FRAX recommendations. Only 66.7% and 56.2% of women who had FRAX-Major and FRAX-Hip scores meeting the intervention threshold were treated, respectively. On the other hand, a number of patients who had very low FRAX-Major (< 10%) or FRAX-Hip (< 1%) values were treated. It is worth mentioning that it is reasonable for women < 50 years of age with medical conditions to be given prophylactic OP therapy despite not meeting intervention thresholds[10]. This may be based on the complex clinical context of the patient (e.g., the clinician predicts that the patient is likely to take high-dose glucocorticoids for an extended period). It is also important to note that these threshold values are recommendations based on cost-effectiveness analyses and can vary by population[32,33].

There are many limitations of the current FRAX tool in the context of SLE. For one, it does not take SLE into account as an OP risk factor and does not include it in its algorithm. The FRAX tool may underestimate fracture risk in women with SLE because there is established evidence that SLE itself can cause bone fragility[1,4,6]. Our findings suggest that both FRAX-Hip and FRAX-Major are significantly correlated with SLE duration. The FRAX algorithm also simplifies clinical risk factors as either "Yes" or "No". This poses problems for risk factors such as glucocorticoid use because it does not consider the dose of the medication. Petri[34] demonstrated a strong association between OP fractures with cumulative prednisone dose. The tool also does not include risk factors for increased falls. Patients with SLE may be at a higher risk of musculoskeletal complications because of SLE-related symptoms including arthritis, fatigue, muscle weakness, and neuropathy[1,4].

Our study is also, to our knowledge, the first to use the hip structural analysis in patients with SLE and to report on a number of hip structural measures for the assessment of bone strength. Particular attention was given to the derived BR and SM values at the NN, IT, and shaft regions. We found positive correlations between BR values and OP and SLE risk factors, and negative correlations between SM and those risk factors. Melton, *et al*[35] found in 213 postmenopausal women that increasing SM values at different hip sites were strongly protective of moderate trauma and osteoporotic fractures, while increasing BR values were associated with significantly greater fracture risk at the NN and IT regions.

The SM and BR values that we found were in a range similar to those from previous studies[15,36]. In comparison to the 6839 postmenopausal controls in a study by Kaptoge, *et al*[15], our SM values were found to be slightly higher and our BR values lower at all 3 anatomical locations (NN, IT, and S). However, it is difficult to provide a fair comparison because the discrepancy of the values when compared to the control group in the Kaptoge study may have been due to the large difference in age. The mean age in the Kaptoge control group was 73.9 years compared with our mean age of 43.8 years. Compared with controls in the DiVasta, *et al* study[36], which had a younger group of 61 women with a mean age of 18.9 years, we had higher SM and BR values at all 3 anatomical regions.

The limitations of HSA involve attempting to analyze a 3-dimensional structure from 2-dimensional DEXA images. The BR may be highly indicative of fragility fracture, but the program makes assumptions about the shape of the cross-section, trabecular distribution, and percentage of cortical bone that may lead to inaccurate results[14]. In addition, for comparison of many of the structural measures between scans, reproduction of the same image plane is critical and even small differences in the rotation of the femur can cause large variations in the values[14,37]. Khoo, *et al*[37] reported better precision with BMD measurements than with estimates of SM and BR. Further, there is no current evidence to suggest that these structural variables are better than BMD in predicting fracture risk. Structural measures are roughly equivalent to BMD for predicting fractures, and the HSA measures themselves made only a modest independent contribution to prediction[35].

Our findings of OP and LBM prevalence in women with SLE confirms that OP is a prevalent comorbidity in our patients because of both SLE and OP-related risk factors. This is especially important for women with SLE who are age < 50 years, an age at which routine BMD monitoring is not currently part of standard care. Two additional methodologies, the FRAX and HSA, may help provide additional and unique insights to fracture risk assessment in these patients. FRAX scores may identify those at high risk who may benefit from pharmacologic treatments. HSA can assess various bone structural measures noninvasively and can assist in our understanding of bone strength and fracture risk. Use of these methods may help reduce future morbidity and mortality in patients with SLE.

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