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LOSS OF BONE MINERAL DENSITY IN CHINESE PRE-MENOPAUSAL WOMEN WITH SYSTEMIC LUPUS ERYTHEMATOSUS TREATED WITH CORTICOSTEROIDS

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SUMMARY

The adverse effect of disease and chronic corticosteroid therapy on bone mineral density (BMD) in patients with systemic lupus erythematosus (SLE) has been reported in several studies of Caucasian populations. As the factors controlling bone homeostasis may be different in Asian populations, we measured BMD in 52 pre-menopausal Chinese women (mean age 34.1 ± 8.0 yr) with SLE (mean disease duration 6.4 ± 4.5 yr) treated with prednisone (mean daily dose 11.4 ± 10.8 mg/day). Lumbar spine, hip (total and subregions) and total body BMDs were measured in the SLE patients using dual-energy X-ray absorptiometry (DEXA), and compared with those from healthy controls matched for age, sex and body mass index. Compared to controls, SLE patients were found to have lower BMD (g/cm^2) at several sites: the lumbar spine (0.98 *vs* 0.90, $P = 0.001$), Ward's triangle (0.72 *vs* 0.67, $P = 0.03$), total body (1.04 *vs* 1.01, $P = 0.04$) and total hip (0.87 *vs* 0.82, $P = 0.05$). There was no correlation between BMD at any region and duration of disease, activity of disease or prednisone therapy (mean daily dose, cumulative dose or treatment duration). When BMDs were compared between controls and SLE patients, subgrouped according to those not on calcium and those arbitrarily receiving calcium supplements (1 g/day), significantly lower BMDs were found in those not on calcium compared to both controls and SLE patients on calcium. BMDs in SLE patients on calcium were not different from those in controls. The low prevalence of osteoporosis in our SLE patients (4–6%) suggests significant loss of BMD in Chinese SLE patients on corticosteroid therapy is less than that reported in Caucasians (12–18%).

KEY WORDS: Bone mineral density, Corticosteroid, SLE, Chinese, Calcium.

THE effect of disease activity and corticosteroid therapy on bone mineral density (BMD) in patients with systemic lupus erythematosus (SLE) has been assessed by several studies over the last decade [1–5]. However, these studies have been confined to Caucasian populations and conclusions from these studies are conflicting. Most studies showed that SLE patients on corticosteroids have lower BMDs than healthy controls [2, 3, 5]; however, studies differed as to the magnitude of the corticosteroid effect and whether SLE *per se* did [5] or did not [1, 4] contribute to lower BMD. Moreover, although most studies showed that SLE patients have lower BMD at the lumbar spine (trabecular bone) compared to healthy controls, the effect on the proximal femur (cortical and trabecular bone) was less clear [1–5]. Only a few studies examined the differential effects of corticosteroids on trabecular and cortical bone by dividing the hip into subregions [2, 4, 5]. Moreover, conclusions regarding the effects of cumulative corticosteroid dose and the duration of therapy on bone loss in SLE patients have been equally conflicting. The reasons for these discrepancies most likely relate to differences in the number and type of SLE patients studied, and the difficulties in controlling for the many factors affecting BMD. However, despite these inconsistencies, it is generally accepted that bone loss in SLE patients on corticosteroid therapy is greater than that seen in controls.

There is accumulating evidence suggesting that calcium homeostasis and the effects of declining BMD are affected by ethnicity [6–10]. Studies of adolescents taking comparable doses of calcium (i.e. 1 g/day) have shown that dietary calcium absorption in Chinese is nearly 2-fold more efficient than in Caucasians (56% *vs* 36%, respectively) [6, 7]. Intakes of 500 mg/day, which are more typical for the Hong Kong Chinese population, increase absorption efficiency to 64% [6, 7]. Moreover, the decline in BMD is different in different ethnic groups [8]. Despite a lower calcium intake (about one-quarter) in Asian populations [9], the age-adjusted hip fracture incidence is only one-third that seen in Caucasian populations [10]. As the above observations suggest that there are ethnic differences in bone homeostasis, and because data in Asian populations with SLE are lacking, we undertook a cross-sectional study to examine the prevalence and severity of bone loss in a group of pre-menopausal Chinese SLE patients on chronic corticosteroid therapy.

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PATIENTS AND METHODS

Patient selection

We measured BMD in 52 Chinese pre-menopausal females with SLE attending our rheumatology outpatient clinic at the Prince of Wales Hospital, Hong Kong. All patients fulfilled the revised criteria of the American College of Rheumatology for the diagnosis of SLE [11]. All patients were ambulatory and were physically active with functional class I using the criteria of Steinbrocker [12]. All patients had been on corticosteroids for at least 5 months at the time of BMD measurement. Disease activity of the SLE patients was evaluated using the SLE Disease Activity Index (SLEDAI) [13]. Data including the age of patients, age at onset of disease, duration of disease, the mean daily dose (mean

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dose of prednisone over the whole treatment period), cumulative prednisone dose and the duration of prednisone therapy were ascertained for 42 of the 52 patients by review of patient records. Patients were excluded according to the following criteria: those with renal impairment (serum creatinine $> 107\ \mu$mol/l), those taking drugs that could affect bone metabolism (anticoagulants, anticonvulsants, barbiturates, calcitonin, thiazides, oestrogenic hormones, androgenic hormones, sodium fluoride), or those with a history of menstrual irregularities, metabolic bone disease, immobilization or hyperthyroidism. Daily dietary calcium intake, physical activity, cigarette smoking, reproductive history and drug history were assessed in the patients by a structured validated questionnaire which has been previously used in studies of osteoporosis in Chinese [14]. All patients gave informed consent and the study was approved by the Clinical Research Ethics Committee of the Chinese University of Hong Kong. Twenty of the 52 SLE patients recruited had been arbitrarily receiving a calcium supplement, prescribed on an ad hoc basis by one of the investigators (EKL), in the form of calcium carbonate 1000 mg/day (one tablet of Os-Cal 500 twice daily, Marion Merrell) prior to the commencement of this study (mean duration of 5 ± 3 months). The basis on which patients received calcium was arbitrary and due to a heightened awareness of the adverse effects of chronic low-dose corticosteroids in young Chinese. Owing to this change in management over the 2 yr preceding the study, patients on calcium tended to have a shorter duration of disease and corticosteroid treatment, generally being on higher initial daily doses. The effect of this calcium supplementation on BMD was analysed separately by subgrouping SLE patients into those receiving ($n = 18$) and not receiving ($n = 20$) calcium supplement, carefully matched with respect to disease duration and activity score together with duration and dose of corticosteroid treatment. Two SLE patients receiving calcium supplementation were excluded from the matched comparison: one who had started prednisone within 6 months of study and one who had been diagnosed as having SLE within 6 months of study. Fifty-two healthy control subjects were selected from a general Chinese population recruited among university students, healthy volunteers and staff from the Chinese University of Hong Kong. Control subjects were matched individually to patients for sex, age (within ± 2 yr) and body mass index (BMI within $\pm 5\%$). BMDs in our control population were comparable to those of another healthy group of Hong Kong Chinese women of comparable age and studied previously by the same methods [15].

Bone density measurements

Standard radiographs of the thoracic and lumbar spine were performed in all SLE subjects to detect fractures, which were defined as a reduction of $\geqslant 20\%$ in the anterior, middle or posterior height of the vertebral body on the lateral view. BMD in the lumbar spine (L1–L4), hip (total hip, neck, intertrochanter, trochanter, Ward's triangle) and total body BMD were measured by dual-energy X-ray absorptiometry (DEXA) with a Hologic QDR-2000 densitometer (Hologic, Inc., Waltham, MA 02154, USA). Standardization was performed daily by scanning of a Hologic arthropomorphic phantom of known mineral content which was accurate to 0.42%. The coefficient of variation was 0.7% for the lumbar spine, 1.2% for the femoral neck, 1.4% for the intertrochanter, 0.8% for total hip and 2.8% for Ward's triangle.

Statistical analysis

Differences between groups were compared using the independent Student's *t*-test and the Mann–Whitney *U*-test where appropriate. The effects of various parameters on BMD were assessed by linear stepwise regression analyses. Data that were not normally distributed were logarithmically transformed for analysis. All analyses were performed with the Statistical Package for the Social Sciences (SPSS) statistical software for Windows, Version 6.1 (SPSS Inc., IL, USA).

RESULTS

The demographic data of the 52 SLE patients and 52 controls are shown in Table I. The disease and corticosteroid therapy characteristics of the SLE patients are as follows [given as means ($\pm$ S.D.)]: disease duration 6.4 yr (± 4.5), daily prednisone dose 11.4 mg/day (± 10.8), cumulative prednisone dose 14.5 g (± 10.7), time on prednisone 54.0 months (± 37.4) and SLE disease activity index 4 (± 6).

Compared to healthy controls, BMDs in SLE patients were significantly lower at the lumbar spine ($P = 0.001$), Ward's triangle ($P = 0.03$), total body ($P = 0.04$) and total hip ($P = 0.05$) (Table II). Multiple stepwise linear regression analysis in the SLE patients revealed no correlation between BMD and duration of disease, corticosteroid treatment (average daily dose, cumulative dose or duration of treatment), SLE disease activity, age, height, weight, alcohol intake, cigarette smoking or amount of exercise. The only exception was BMI, which was consistently positively correlated with BMD at all sites (range for $r = 0.35$–0.67). In addition, the reduction in BMD amongst SLE patients on corticosteroid compared to controls is independent of the duration of disease, cumulative dose, mean daily dose or the duration of

TABLE I
Clinical characteristics of SLE patients ond controls

Characteristic (mean $\pm$ S.D.)	Controls ($n = 52$)	SLE patients ($n = 52$)
Age (yr)	33.7 ± 7.7	34.1 ± 8.0
Height (m)	1.58 ± 0.06	1.58 ± 0.06
Weight (kg)	52.5 ± 7.7	51.4 ± 7.9
Body mass index (kg/m^2)	20.9 ± 2.7	20.7 ± 2.9
Dietary calcium intake* (mg/day)	240 (215–269)†	228 (199–261)†

*Excludes supplementary oral calcium given to 20 SLE patients.
†Geometric mean plus 95% confidence interval.

TABLE II
Bone mineral density (BMD) in 52 SLE patients ond controls (mean ± S.D. unless stated otherwise)

BMD site	Control subjects ($n = 52$) BMD: g/cm^2	SLE patients ($n = 52$) BMD: g/cm^2	Z score† (mean ± S.E.M.)	P value *vs* controls*
Total body	1.04 ± 0.06	1.01 ± 0.08	−0.50 ± 0.01	0.04
Lumbar spine (L1–L4)	0.98 ± 0.11	0.90 ± 0.12	−0.73 ± 0.02	0.001
Neck	0.77 ± 0.10	0.74 ± 0.11	−0.30 ± 0.02	0.11
Intertrochanter	1.01 ± 0.13	0.96 ± 0.15	−0.38 ± 0.03	0.06
Trochanter	0.66 ± 0.09	0.63 ± 0.09	−0.33 ± 0.02	0.12
Ward's triangle	0.72 ± 0.13	0.67 ± 0.13	−0.38 ± 0.03	0.03
Total hip	0.87 ± 0.11	0.82 ± 0.11	−0.45 ±0.02	0.05

*t-test.
†Difference in BMD between SLE patients and controls ÷ control S.D.

corticosteroid therapy. We also subdivided patients into those who had received a mean daily dose > 10 mg/day of prednisone and those who received < 10 mg/day. When BMD was compared between these groups, a trend towards a lower BMD was seen in subjects who have been on the higher dose of prednisone, but the difference was not statistically significant (data not shown).

We then compared BMD in SLE patients subgrouped according to those not on calcium supplements and those on calcium. In an unmatched comparison, SLE patients not on calcium ($n = 32$) had significantly lower BMD than those on calcium ($n = 20$) for the hip (0.79 *vs* 0.87, $P = 0.02$), neck (0.70 *vs* 0.80, $P = 0.001$), trochanter (0.61 *vs* 0.67, $P = 0.01$), total body (0.99 *vs* 1.04, $P = 0.01$), Ward's triangle (0.64 *vs* 0.72, $P = 0.01$) and lumbar spine (0.87 *vs* 0.95, $P = 0.03$), but not the intertrochanteric region (0.93 *vs* 1.01, $P = 0.06$). Despite the smaller numbers in our matched comparison (Table III), we found that the group not on calcium ($n = 18$) had significantly lower BMD at all sites compared to those on calcium ($n = 20$): (total body $P = 0.003$, lumbar spine $P = 0.02$, femoral neck $P = 0.003$, trochanter $P = 0.008$, intertrochanteric $P = 0.02$, Ward's triangle $P = 0.04$, total hip $P = 0.006$) (Table IV). Surprisingly, we found no difference in BMD between controls and SLE patients on calcium (Table IV).

There were only two SLE patients ($n = 52$) with a lumbar spine BMD of > 2.5 S.D. below that of controls, while 18 patients had a lumbar spine BMD of 1 S.D. below the mean for controls. Thus, the frequency of osteoporosis in our SLE patients was 4% and that of osteopenia 35% according to the WHO criteria [16]. Subgrouping SLE patients according to those receiving and not receiving calcium revealed frequencies for osteoporosis of 0 and 6%, respectively, and for osteopenia of 25 and 41%, respectively, but these were not significantly different between treatment groups. No vertebral crush fractures were detected. Comparison of glucocorticoid intake between the osteopenic and the non-osteopenic patients revealed no significant differences with respect to cumulative intake, duration of therapy or mean average daily dose.

DISCUSSION

In agreement with the majority of studies in Caucasians, this study has demonstrated that BMD is significantly lower in both cortical and trabecular sites in Chinese women with SLE on chronic corticosteroids. However, our frequency of osteoporosis appears to be only one-half to one-third that reported in previous

TABLE III
Clinical characteristics of SLE patients subgrouped into those not receiving and those receiving calcium supplementation for unmatched and matched comparisons (mean ± S.D. or *geometric mean plus 95% confidence interval)

Clinical characteristics	Unmatched		Matched	
	SLE patients not on calcium ($n = 32$)	SLE patients on calcium ($n = 20$)	SLE patients not on calcium ($n = 20$)	SLE patients on calcium ($n = 18$)
Age (yr)	34.0 ± 6.7	34.2 ± 10.0	34.4 ± 5.3	34.6 ± 9.5
Height (m)	1.58 ± 0.06	1.58 ± 0.06	1.58 ± 0.07	1.58 ± 0.06
Weight (kg)	50.5 ± 6.4	53.0 ± 9.9	50.1 ± 5.4	53.2 ± 10.3
BMI	20.3 ± 2.6	21.2 ± 3.3	20.2 ± 2.5	21.2 ± 3.4
Calcium intake (mg/day)*	222.4 (188.8–262.0)	239.0 (184.3–309.9)	214.6 (168.0–274.0)	249.7 (287.6–322.5)
Disease duration (yr)*	5.8 (4.2–8.0)	3.1 (2.0–4.8)†	4.3 (2.8–6.8)	3.2 (2.1–5.0)
Daily prednisone dose (mg/day)*	8.3 (7.0–9.8)	12.2 (8.7–17.1)†	7.8 (5.9–10.2)	10.6 (8.3–13.6)
Cumulative prednisone does (g)*	13.0 (9.7–17.5)	6.4 (3.6–11.4)†	8.1 (5.8–11.3)	7.9 (4.6–13.7)
Duration on prednisone (months)	51.7 (38.3–69.6)	17.6 (8.1–38.2)‡	34.3 (22.9–51.3)	24.8 (13.7–44.9)
SLEDAI*	3.8 (3.0–4.9)	5.2 (3.4–7.9)	3.9 (2.9–5.3)	4.3 (3.1–6.0)

Unmatched comparison: †$P < 0.05$; ‡$P < 0.01$.
Matched comparison—there were no significant differences between SLE subgroups.

TABLE IV
Bone mineral density (BMD) in the controls and SLE patients subgrouped into those not receiving and those receiving calcium supplementation matched for disease and corticosteroid treatment parameters

BMD site (g/cm^2)	Control subjects ($n = 52$)	Matched SLE subgroups	
		SLE patients on calcium ($n = 18$)	SLE patients not on calcium ($n = 20$)
Total body	1.04 ± 0.06	1.04 ± 0.06	$0.97 \pm 0.07^{3,b}$
Lumbar spine	0.98 ± 0.11	0.95 ± 0.09	$0.88 \pm 0.08^{3,a}$
Neck	0.77 ± 0.10	0.80 ± 0.11	$0.69 \pm 0.08^{2,b}$
Intertrochanter	1.01 ± 0.13	1.02 ± 0.15	$0.92 \pm 0.10^{2,a}$
Trochanter	0.66 ± 0.09	0.67 ± 0.09	$0.60 \pm 0.05^{3,b}$
Ward's triangle	0.72 ± 0.13	0.72 ± 0.14	$0.62 \pm 0.09^{3,a}$
Total hip	0.87 ± 0.11	0.87 ± 0.12	$0.78 \pm 0.07^{3,b}$

Comparison between SLE patients not on calcium and controls: $1 = P \leqslant 0.05$; $2 = P \leqslant 0.01$; $3 = P \leqslant 0.001$.
Comparison between SLE patients not on calcium and those receiving calcium: $a = P \leqslant 0.05$; $b = P \leqslant 0.01$; $c = P \leqslant 0.001$.

studies of Caucasian populations. Comparable to most of the previous studies, we could find no relationship between BMD and duration of disease, or dose and duration of corticosteroid therapy. Lastly, we also found that reduced BMD in our SLE group was associated with those not on calcium supplements, while those arbitrarily receiving calcium had BMDs comparable to healthy controls. Further prospective randomized trials are, however, needed to examine this effect further.

Unfortunately, meaningful comparisons between our study and those of others are limited because of differences in the populations studied, particularly with respect to disease parameters (activity and duration of SLE) and corticosteroid therapy (indication for treatment, dose and duration). Similarly, reliable conclusions are limited because of the potential for interacting or confounding effects when comparing results in cross-sectional studies where therapies are not randomized. However, our findings in pre-menopausal SLE patients (not on calcium supplementation) support those of others showing that SLE patients on corticosteroids have decreased BMD as compared to healthy control subjects [2, 3, 5, 17–19]. In contrast, two studies failed to show a significant reduction of BMD in their SLE patients compared with controls [1, 4]. In the study by Dhillon *et al.* [1], no significant differences were observed in lumbar spine BMD between controls ($n = 10$) and SLE patients either receiving ($n = 10$) or not receiving ($n = 10$) corticosteroid therapy. Although numbers were small, there was a trend towards lower BMD in the SLE patients, but no apparent corticosteroid effect. In the study of Pons *et al.* [4], no difference could be found for BMD, at either the lumbar spine or femoral neck, between controls ($n = 43$), SLE patients who had never received corticosteroids ($n = 15$) and SLE patients on corticosteroids ($n = 28$). Although there appears to be no effect from having SLE *per se* in this study, large differences in disease duration make comparisons in BMD between those not yet on corticosteroids and those on steroids problematic. This study did, however, show that patients on higher doses of prednisone ($\geqslant 7.5$ mg/day) had lower BMD at both sites compared to SLE patients on low-dose prednisone (< 7.5 mg/day). In contrast, the study by Kalla *et al.* [2] showed that SLE patients ($n = 46$), 50% of whom were on corticosteroid, had significantly lower BMD at the lumbar spine and most sites in the femoral neck. Although a comparison of SLE patients receiving and not receiving corticosteroid showed no difference in BMD at all sites, groups were not matched for duration of disease. In the study by Formiga *et al.* [3], where all SLE patients were on corticosteroid therapy ($n = 74$), lower BMD was found at both the lumbar spine and femoral neck compared to healthy controls. BMD did not correlate with either cumulative or current prednisone dose. In the study of Houssiau *et al.* [5], BMD at all sites (lumbar spine and hip subregions) was lower in the SLE patients compared to healthy controls. When SLE patients were subgrouped according to those who never received corticosteroids ($n = 11$) and those on corticosteroids ($n = 36$), total hip BMD in the former was significantly lower than that in controls, suggesting a disease effect. Moreover, BMD at all three sites (lumbar spine, total hip and total body) was significantly lower in SLE patients on steroids compared to controls. Unlike most previous studies, those not on prednisone and those on prednisone were well matched for disease duration, and comparison of their BMD showed that lumbar spine only was significantly lower in those on prednisone. Moreover, they showed that BMD at most sites was significantly correlated with cumulative prednisone dose. This study therefore suggests both a disease and corticosteroid effect on BMD. In our study, we found no correlation between BMD and corticosteroid therapy (mean daily dose, cumulative dose or treatment duration), in agreement with the study of Formiga *et al.* [3], but not Houssiau *et al.* [5].

Therefore, when matched for disease duration, there is evidence suggesting that SLE *per se* contributes to lower BMD, at least at the hip. However, there is more consistent agreement that chronic corticosteroid use is associated with lower BMD at most, if not all, sites, although the magnitude of this effect is still not clear. Most studies, including our own, show that the lumbar spine is more consistently affected by corticosteroids than various hip subregions [2, 4, 5, 18]. This is

consistent with studies suggesting a more pronounced inhibitory effect of glucocorticoid on bone metabolism at this site [19–21], or may possibly be secondary to the effects of pro-inflammatory cytokines involved in the pathogenesis of SLE itself [22]. For this reason, the inclusion of BMD data at multiple sites (total body and subregions of the hip) in addition to the lumbar spine is important. Furthermore, two studies have shown that bone loss generally tapers or plateaus after the first 12–18 months of corticosteroid treatment [4, 23]. The relevance of this with respect to the above studies is not yet clear. Larger prospective, and where possible randomized, clinical trials are needed to clarify these findings further.

Accepting that several factors may contribute to the differential effects of corticosteroids on a bone site, using standard criteria based on lumbar spine BMD, we found a lower prevalence of osteoporosis in our Chinese population (4–6%) than that reported in Caucasians (12–18%) [3, 4]. In contrast, our frequency of osteopenia (32%) is comparable to that reported in Caucasian populations (25%) [2]. The 3-fold lower frequency of osteoporosis in Chinese compared to Caucasian SLE patients is unlikely to be due to differences in prednisone therapy as this was comparable, even before weight adjustment, with respect to both mean daily dose (11 *vs* 14 mg/day, respectively) and duration of treatment (54 *vs* 59 months, respectively). Accepting that our observation may have been a chance event, it could also reflect some important difference between Chinese and Caucasians with respect to bone homeostasis. As discussed in the Introduction, there are several studies showing that calcium homeostasis is different in Chinese compared to other ethnic groups [6–10]. It is, therefore, possible that interethnic differences in calcium homeostasis, through effects on BMD, may in part explain the lower rate of osteoporosis in our Chinese SLE patients on corticosteroids compared to those reported in Caucasians.

Perhaps of greater interest was our finding that although BMDs were significantly lower at nearly all sites in the SLE patients who had not received calcium supplement, Chinese SLE patients arbitrarily receiving calcium supplements did not have significantly different BMDs to healthy matched controls. We initially attributed this to the shorter duration of disease and prednisone treatment in the calcium-treated group, but after carefully matching for disease- and corticosteroid-related parameters, significant differences were still present. We should point out that this retrospective analysis does not rule out some other confounding effect which we have not yet identified, or even perhaps a chance finding. The average duration of calcium treatment in this study was only 5 months. Although this is shorter than most treatment periods for interventional trials on BMD, significant beneficial effects on BMD have been reported in studies with comparably short treatment periods [24]. In the calcium and non-calcium subgroups, the mean duration of disease was 3.2 and 4.3 yr, respectively, and the mean duration of prednisone treatment was 2.1 and 2.8 yr, respectively. Although not significantly different, it is still possible that the shorter duration of disease or prednisone treatment in the calcium-treated group accounts for our finding. Of note, the duration of corticosteroid treatment in both groups exceeds the 12–18 month period when corticosteroid-related bone has been found to be greatest in Caucasian populations [4, 23]. However, studies have shown that rates of bone loss may be affected by ethnicity [8] so that calcium intervention after this period may still be beneficial in non-Caucasian populations. Most importantly, as our observation stems from cross-sectional data and not a prospective placebo-controlled randomized clinical trial, we must interpret this finding with caution. In contrast to our finding in Chinese, studies in Caucasians with inflammatory joint disease have not found such a beneficial effect from calcium supplementation alone [25–27]. While suppression of bone resorption in glucocorticoid-treated patients receiving calcium has previously been shown, most reports have shown significant reductions in BMD losses in corticosteroid users taking calcitonin, biphosphonates or vitamin D analogues, but not calcium alone [25–27]. Support for a possible beneficial effect of calcium in Chinese, but not Caucasians, comes from a study showing that responsiveness to vitamin D analogues has been found to be greater in Japanese compared to Caucasians [28]. How efficacious the protective effect of calcium is as a single interventional therapy in SLE patients on corticosteroid in our population, and possibly other non-Caucasian populations, can only be ascertained in future longitudinal studies.

We propose that our observations of a lower frequency of osteoporosis in Chinese SLE patients, together with a possible protective effect from supplementary calcium, may relate, in part, to ethnic differences with respect to bone homeostasis. As outlined in the Introduction, there are several lines of evidence suggesting that factors controlling bone homeostasis are different in Chinese compared to Caucasians. Recently, a genetic polymorphism of the vitamin D receptor gene has been identified [29], and a particular variant (TT genotype defined by the *Taq*I polymorphism) has been found to be associated with higher dietary calcium absorption [30] and greater responsiveness of BMD to calcium and vitamin D supplementation [28]. The frequency of this variant is 90% in Chinese compared to 35% in Caucasian populations, and has been linked to interethnic differences in age-adjusted hip fracture rates [31]. Therefore, the difference in genotype frequencies may be related to the finding of an increased calcium absorption from the gut in Chinese compared to Caucasians, as well as the observation that Chinese populations are relatively protected from BMD loss with respect to hip fracture rates compared to Caucasians [31].

In summary, consistent with studies in Caucasians, we find significantly lower BMD in Chinese SLE on corticosteroids compared to healthy controls. Furthermore, although based on preliminary data only,

we believe our findings of a reduced frequency of corticosteroid-induced osteoporosis in Chinese, and its possible attenuation by supplementary calcium, provide further evidence suggesting an ethnic difference in the factors controlling BMD, possibly related to VDR gene effects. Assuming our hypothesis is correct, calcium supplementation as a single therapy may be a more effective means of reducing corticosteroid-related bone loss in certain ethnic groups, but not others. Further studies are clearly needed to examine this hypothesis further.

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