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Prevalence and determinants of vertebral fractures in a SLE cohort

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ABSTRACT

Objectives Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterised by multiorgan involvement. Osteoporosis and fragility fractures, particularly vertebral fractures, are significant, yet often underestimated, comorbidities in patients with SLE. This study aims to evaluate the prevalence of vertebral fractures and their associations with demographic, disease-related and therapy-related factors in patients with SLE.

Methods We conducted a monocentric, cross-sectional study to systematically evaluate bone health using dual-energy X-ray absorptiometry and vertebral fracture assessment (VFA). Associations between vertebral fractures and clinical, laboratory variables were investigated with logistic and linear regressions.

Results One hundred and six patients with SLE were included. The overall prevalence of radiographic vertebral fractures was 21.7%, whereas clinical vertebral fractures were reported in 14.2% of patients. New, previously not diagnosed, radiographic vertebral fractures were detected in 14.2% of all patients with SLE at screening with VFA. Older age, longer disease duration, cumulative glucocorticoid (GC) dose and lower bone mineral density were significantly associated with vertebral fractures. Cumulative GC dose had the strongest association with vertebral fractures. We also found a positive association between the number of vertebral fractures on VFA and cumulative GC dose (β 0.025, p=0.025).

Conclusions Our findings underscore the importance of actively screening for vertebral fractures in patients with SLE, especially those on long-term GC therapy, to prevent underdiagnosis, mitigate the risk of further skeletal damage and facilitate the timely initiation of targeted antiosteoporotic treatments when indicated.

Trial registration number NCT05590390.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Systemic lupus erythematosus (SLE) is associated with an increased risk of osteoporosis and fragility fractures. Nevertheless, both osteoporosis and vertebral fractures remain frequently underdiagnosed and undertreated in individuals with SLE.

WHAT THIS STUDY ADDS

⇒ Systematic vertebral fracture assessment revealed previously unrecognised vertebral fractures in 14.2% of patients. Cumulative glucocorticoid exposure was identified as the strongest factor associated with both the presence and the number of vertebral fractures.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ These findings underscore the importance of routine vertebral fracture screening in patients with SLE, especially those undergoing long-term glucocorticoid therapy, in order to optimise rheumatologic management and enable timely initiation of bone-protective treatment.

INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease with a complex multifactorial aetiology, characterised by multiorgan involvement.[1] The clinical spectrum of the disease is highly heterogeneous, with variable severity of symptoms. Common manifestations include skin rashes, joint pain, renal involvement and constitutional symptoms.[1]

Morbidity in patients with SLE is notably higher than in healthy individuals, partly due to the disease itself, as for chronic kidney disease or accelerated atherosclerosis and partly due to the side effects of chronic therapies, especially glucocorticoids (GCs).[2 3] The long-term adverse effects of GCs are well established, with fragility fractures being among the most common yet frequently under-recognised complications.

The risk of osteoporosis (OP) and fragility fractures in patients with SLE is significantly increased compared with healthy individuals. In SLE, the prevalence of OP ranges from 1.4% to 68%, depending on the study and on the definition of OP.[4–6] Moreover, the prevalence of radiographic vertebral fractures ranges from 20% to 50% in SLE.[7–9] A recent

large observational study on more than 47 000 individuals showed that patients with SLE had a two-fold higher risk of fracture; this risk was higher in patients with renal SLE.[10]

The mechanisms underlining bone loss and higher risk of fracture are numerous, including prevalent inflammation, metabolic alterations, early menopause, medications and SLE-related comorbidities.[11–16]

As a part of the irreversible damage related to SLE, fragility fractures are included in the Systemic Lupus International Collaborating Clinics (SLICC) Damage Index (SDI). Higher SDI scores correspond to a greater degree of damage caused by the disease, leading to a corresponding reduction in quality and life expectancy.

Despite the inclusion of fractures in the SDI, specific guidelines for the screening and management of OP and fragility fractures in patients with SLE are still lacking, particularly for populations traditionally considered at lower risk, such as premenopausal women, men and younger individuals.

Moreover, a significant proportion of vertebral fractures are asymptomatic and may occur even in individuals with normal bone mineral density (BMD); thus, detection through targeted spinal imaging is essential for accurate OP assessment, especially in patients with prolonged corticosteroid exposure.

Since radiographic vertebral fractures are frequently underdiagnosed compared with clinical ones, the present study was conducted to determine the prevalence of radiographic vertebral fractures in a well-characterised SLE cohort and to identify clinical and therapeutic factors independently associated with their presence.

MATERIALS AND METHODS

Study design

The fragility FRactures And quality of Life in SLE (FRAIL) study was a monocentric, cross-sectional observational study conducted at the Rheumatology Unit of the University of Verona Hospital Trust. Consecutive patients were enrolled from December 2022 to January 2024.

Inclusion criteria

- Diagnosis of SLE satisfying the 2019 EULAR/ACR or SLICC 2012 criteria
- Age ≥18 years
- Clinically stable SLE, defined as no new British Isles Lupus Assessment Group (BILAG) grade A or B scores within the previous 3 months
- Signed informed consent to:
  - Undergo dual-energy X-ray absorptiometry (DXA) with vertebral fracture assessment (VFA) and X-ray investigations of the spine
  - Donate blood samples for the Rheumatology Unit biobank (Reumabank, 1483CESC)

Exclusion criteria

- Bone metabolic disorders other than OP (eg, Paget's disease)
- Conditions associated with malabsorption (eg, coeliac disease, chronic inflammatory bowel disease, pancreatic exocrine insufficiency)
- Uncontrolled endocrine diseases (eg, adrenal insufficiency, Cushing syndrome, hyperparathyroidism, hypo or hyperthyroidism, hypogonadism)
- Disease flare in the previous 3 months requiring an increase/variation in therapy
- Lack of information about previous medications (both for SLE and OP)
- Any other intercurrent diseases or significant abnormal laboratory values in the investigator's opinion (eg, hypercalcemia, antihormonal therapy)
- Pregnant patients or those in the first year postpartum

A complete set of clinical, demographic and laboratoristic (including dsDNA positivity and titre, antinuclear antibodies (ANA) - pattern and titre) data were collected. Calcium intake was categorised as adequate (>1200 mg/day), moderate (700–1200 mg/day) and low (<700 mg/day), according to the previous literature.[17] BMD was assessed at the lumbar spine (L1–L4), femoral neck and total hip using DXA with a GE Lunar iDXA ME 212814 device. The coefficient of variation was 1% at the lumbar spine and 1.2% at the femoral neck. Respective T scores and Z scores were retrieved from the reference population of the instrument. VFA was performed in all patients to identify vertebral fractures using Genant's semiquantitative method,[18] and data were then confirmed with spine X-ray.

Serum samples were aliquoted and stored at −80°C for subsequent biomarker analysis. The assessed biomarkers included the bone resorption marker C-terminal telopeptide of type I collagen (CTX), the bone formation marker Procollagen I Intact N-Terminal Peptide (P1NP), the Wnt inhibitors Dickkopf-1 (Dkk1) and sclerostin, 25-hydroxyvitamin D (25OHVitD) and parathyroid hormone (PTH). CTX and P1NP levels were measured using the IDS-ISYS Multi-Discipline Automated Analyzer with chemiluminescence technology, yielding intra-assay variabilities of 3.0% for P1NP and 2.0% for CTX. Dkk1 and sclerostin were quantified using ELISA kits, with detection sensitivities of 0.89 pmol/L and 8.9 pmol/L and intra-assay coefficients of variation of 7.8% and 5.6%, respectively; interassay variabilities were 8.2% for Dkk1 and 6.9% for sclerostin. PTH levels were determined via an ELISA assay, with intra and interassay variabilities of 6% and 7%, respectively. The 25OHVitD concentration was measured using the LIAISON 25OHVitD assay, with intra and interassay variabilities of 8% and 12%, respectively. To minimise interassay variability, all measurements were conducted in a single batch.

Sample size considerations and statistical analysis

Sample size was based on feasibility criteria. Prior studies showed that the prevalence of morphometric vertebral fractures in SLE ranges from 20% to 50%. For the expected prevalence of 35%, the required sample size was

88 for the margin of error or absolute precision of ±10% in estimating the prevalence with 95% confidence.

Descriptive analyses were conducted using percentages and absolute frequencies for categorical variables, and means with SD for continuous variables with normal distributions. Group comparisons based on fracture presence were performed using Student's t-test for continuous variables. Bivariate correlations between the number of fractures and other continuous variables were assessed.

Associations with vertebral fracture presence and number were further investigated through logistic and linear regression analyses. Due to the large number of clinical variables in the dataset, we employed a Random Forest algorithm for variable selection, using the 'Rank' function in Orange V.3.37.0. This method was selected for its proven effectiveness in handling high-dimensional datasets. Random forest is a non-parametric, ensemble-based machine learning technique that is particularly well suited for high-dimensional data, as it can detect complex, non-linear relationships and interactions between variables without imposing parametric assumptions. Moreover, random forest provides robust measures of variable importance, allowing the identification of the most influential predictors while minimising the risk of overfitting and multicollinearity. The random forest model was configured with the following parameters: unlimited number of considered features, unlimited tree depth and a node splitting threshold of a maximum of five instances. Feature importance was assessed using mean decrease impurity and mean decrease accuracy. Variables with clear collinearity were excluded at this stage. To ensure stability and reduce selection bias, we applied 10-fold cross-validation during the random forest procedure. The final set of selected variables was then used to build the regression model, ensuring parsimony and interpretability while mitigating multicollinearity. The purpose was not to predict via the random forest algorithm but rather to perform a variable selection for further standard, explainable statistics.[19]

All participants provided written informed consent prior to inclusion in the study. Patient confidentiality was preserved throughout the study, and all data were anonymised prior to analysis. No animal experiments were performed. Patients and the public were not involved in the design, development or conduct of this research. The study protocol was developed by the research team without patient input.

RESULTS

One hundred and six patients with SLE satisfying inclusion and exclusion criteria were enrolled in the study. Patients' characteristics are reported in table 1.

Study population characteristics

Overall, 88.7% (n=94) were female and 56.4% were post-menopausal, with a mean age at menopause of 48.5±4.3 years (table 1).

Table 1 Cohort characteristics expressed as mean±SD or absolute percentage

Demographics and disease features	Value (mean±SD or %)
Age (years)	53.6±13.9
Weight (kg)	66.0±14.3
Height (cm)	164.2±7.9
BMI (kg/m^2)	24.4±4.7
Caucasian (%)	88.7
Female (%)	88.7
Post-menopausal (%)	56.4
Age at menopause (years)	48.5±4.3
SLE disease duration (years)	17.4±12.5
Age at SLE onset (years)	36.3±14.8
SLE involvement	
Articular (%)	76.4
Cutaneous (%)	44.3
Haematologic (%)	39.4
Renal (%)	32.1
Serositis (%)	17.0
NPSLE (%)	8.5
SLEDAI 2k	1.8±2.0
cSLEDAI 2k	0.5±1.5
SLEDAS	1.2±1.4
SDI score	1.0±1.4
Charlson Comorbidities Index	2.3±1.7
SLE therapies	**Value (mean±SD or %)**
GC assumption	
Ongoing (%)	41.5
Suspended<6 months (%)	0.9
Suspended 6–12 months (%)	5.7
Suspended>12 months (%)	45.3
Never (%)	6.6
GC cumulative dose (g)	13.6±16.3
GC therapy duration (months)	115.9±128.2
Ever received GC bolus (%)	94.3
Hydroxychloroquine	
Ongoing (%)	85.8
Previous (%)	14.2
Mean hydroxychloroquine dose (mg)	257±80
Mycophenolate ongoing (%)	28.3
Cyclosporine ongoing (%)	0.9
Methotrexate ongoing (%)	8.5
Azathioprine ongoing (%)	15.1
csDMARD (number ever)	1.5±1.2
Belimumab	
Ongoing (%)	22.9

Continued

Table 1 Continued

Demographics and disease features	Value (mean±SD or %)
Previous (%)	9.5
Rituximab ongoing (%)	0.9

BMI, body mass index; csDMARD, Conventional Synthetic Disease-Modifying Antirheumatic Drug; cSLEDAI 2k, Clinical Systemic Lupus Erythematosus Disease Activity Index 2000; GC, glucocorticoid; NPSLE, Neuropsychiatric Systemic Lupus Erythematosus; SDI, SLICC Damage Index; SLEDAI 2k, Systemic Lupus Erythematosus Disease Activity Index 2000; SLEDAS, Systemic Lupus Erythematosus Disease Activity Score; SLICC, Systemic Lupus International Collaborating Clinics.

Mean disease duration was 17.4±12.5 years, with an average of 2.4±1.1 disease domains affected over the patient's lifetime. Mean Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) was 1.8±2.0, the SDI was 1.0±1.4 on average. The mean Charlson Comorbidity Index (CCI) was 2.3±1.7.

Most patients had been exposed to GCs, with 41.5% still receiving GCs at the time of enrolment. The cumulative GC dose was 13.6±16.3 g of prednisone equivalent dose, with a mean treatment duration of 115.9±128.2 months (table 1).

OP and fractures

Overall, 15 patients (14.2%) had a documented history of at least one clinical vertebral fracture. Additionally, 34% of patients had a history of non-vertebral fractures.

Following a systematic spine assessment using VFA, the prevalence of radiographic vertebral fractures was 21.7% (n=23) and, among these, 15 patients (14.2% of 106) were diagnosed with previously unrecognised radiographic vertebral fractures. Of these 15 patients, 8 (53.3%) had no prior history of vertebral fractures, while 7 (46.7%) reported a history of previous fractures. In all patients, fractures were subsequently confirmed with standard spine X-ray.

Considering both vertebral (clinical and radiographic) and hip fractures, the total number of patients with fractures was 49 out of 106 (46.2%).

Regarding risk factors for major fragility fractures, 11.4% of patients had a positive family history for hip fracture, 29.2% had a history of smoking and 10.5% had inadequate dietary calcium intake.

Antiresorptive therapy was reported in 35.8% of patients, while 2.8% had received teriparatide in the past and 86.8% of patients received vitamin D supplements (mean dose: 1,808±1109 IU/day). All available data on bone health-related therapies and risk factors for major fractures are provided in online supplemental table 1.

Factors associated with vertebral fractures in patients with SLE

Table 2 shows the characteristics of SLE patients with and without vertebral fractures. Patients with vertebral fractures were older and shorter in stature, with a longer disease duration. They had a greater cumulative GC dose and GC therapy duration. They also showed higher CCI and SDI scores. Patients with vertebral fractures had lower T-scores at the femoral neck, total hip and lumbar spine, with no significant differences observed in Z-scores (figure 1). Among the 49 patients with fractures at any site (both vertebral and non-vertebral), only 10 (20.4%) had osteoporotic T-scores.

Mean vitamin D serum levels were 33,9±11,6 ng/mL. Approximately one-third of the population had levels lower than 30 ng/mL. Patients with fractures had higher 25OH vitamin D value and lower C reactive protein, P1NP, CTX values, with a trend for a lower bone alkaline phosphatase and C3 (table 2). The exclusion of patients with a history of antiresorptive therapy did not allow any further analysis for limited numbers.

The number of vertebral fractures per patient correlated with age (0.305, p=0.001), SDI (0.309, p=0.002), CCI (0.21, p=0.03), GC therapy duration (0.376, p<0.001) and GC cumulative dose (0.358, p<0.001). A negative correlation was observed for height (−0.305, p=0.002) and BMD values at any site as T-scores (neck −0.215, p=0.03; total −0.213, p=0.03; lumbar −0.254, p=0.009).

For the logistic regression models, the following variables were selected using the random forest algorithm (Area Under the Curve (AUC)=0.634, classification accuracy=0.799, F1 score=0.756, recall=0.750; complete metrics of the random forest model are reported in online supplemental material): sex, age, cumulative GC exposure, ongoing daily dose of GC, Z score at lumbar spine, Z score at femoral neck, Z score at total hip, SLEDAI-2K score, anti-dsDNA titre and disease duration. These variables were incorporated into the final regression model. Age (β 0.075, p=0.034) and GC cumulative dose (β −0.049, p=0.048) were independently associated with vertebral fractures in patients with SLE. Figure 2 shows the association between GC cumulative dose and the probability of having a radiological vertebral fracture in SLE.

In the linear multivariable regression analysis, we included the same set of variables as above. We found that the number of vertebral fractures was independently associated with GC cumulative dose (β 0.025, p=0.025) and age (β 0.029, p=0.017).

DISCUSSION

OP and fracture risk are often underestimated in patients with SLE, particularly compared with other rheumatologic conditions such as rheumatoid arthritis, in which bone health is more frequently studied.[5] The first key finding of this study is the discrepancy between the patient-reported history of vertebral fractures (14.2%,

Table 2 Factors associated with vertebral fractures expressed as mean±SD or absolute percentage

Cohort characteristics	Patients with vertebral fractures (n=23) Value (mean±SD or %)	Patients without vertebral fractures (n=83)	P value
Age (years)	62.6±12.1	51.2±13.4	<0.001
Age at menopause (years)	48.8±4.1	48.3±4.5	0.706
Disease duration (years)	25.2±12.7	15.2±11.6	<0.001
Height (cm)	160±9.5	165.3±7.1	0.004
Cumulative GC dose (g)	22.5±23	11.1±13.0	0.03
GC therapy duration (months)	192.3±190.9	94.7±95.9	0.03
25OH vitamin D (ng/mL)	40.6±12	32.0±10.9	0.002
P1NP (ng/mL)	38.7±18.9	62.7±34.5	0.002
CTX (ng/mL)	0.083±0.055	0.142±0.132	0.002
BAP (µg/L)	10.1±5.5	12.2±4.4	0.06
CRP (mg/L)	1.7±1.3	3.1±4.2	0.01
C3 (g/L)	0.95±0,2	1.05±0.24	0.06
CCI score	3.1±1.6	2.0±1.7	0.005
SDI score	1.7±2.3	0.8±1.1	0.009
T-score femoral neck	−1.73±1.05	−0.88±1.10	0.002
T-score total hip	−1.44±0.88	−0.59±1.32	0.001
T-score lumbar spine	−1.74±1.6	−0.57±1.32	0.001
Z-score femoral neck	−0.55±0.71	−0.34±0.85	0.294
Z-score total hip	−0.41±0.71	−0.23±0.85	0.376
Z-score lumbar spine	−0.17±1.14	0.11±1.31	0.361

BAP, bone alkaline phosphatase; CCI, Charlson Comorbidity Index; CRP, C reactive protein; CTX, C-terminal telopeptide of type 1 collagen; GC, glucocorticoid; 25OH vitamin D, 25-hydroxyvitamin D; P1NP, Procollagen Type 1 N-terminal Propeptide; SDI, SLICC Damage Index; SLICC, Systemic Lupus International Collaborating Clinics.

15/106) and the results of VFA screening, which revealed a true fracture prevalence of 21.7%. Of note, 14.2% of the population had previously unknown vertebral fractures, identified with VFA screening.

Literature data on this topic vary widely, with reported prevalences of vertebral fractures ranging from 20% to 50%.[7–9] The heterogeneity of findings stems from most studies focusing only on *symptomatic* vertebral fractures, even though a significant proportion of these fractures occur without clinical symptoms.[20] Our findings underscore the importance of actively screening for vertebral fractures when evaluating cumulative damage in SLE. Indeed, vertebral fractures are included as a component of the SDI and failure to identify them may lead to an underestimation of the extent of irreversible damage.

Previous vertebral fractures are also a well-established risk factor for subsequent fractures. Therefore, missing them may represent lost opportunities for initiating antiosteoporotic therapy or adopting more aggressive strategies to minimise GC exposure. These considerations highlight the insufficiency of relying solely on clinical history or patient-reported outcomes to assess skeletal involvement.

Notably, in our cohort, VFA identified a new vertebral fracture in 46.7% of patients with a known history of bone fragility, underscoring the need for periodic re-evaluation using spinal X-rays or VFA. Despite these observations, no specific guidelines currently exist for OP screening or treatment thresholds tailored to SLE, beyond those established for postmenopausal OP and GC-induced OP (GIOP).[21 22] However, given the strong association between GC use and fracture risk in SLE, the recommendations developed for GIOP appear to be the most applicable. They advocate for baseline assessment of fracture risk—including history of clinical and morphometric fractures, BMD measurement and VFA or spine radiography—in all adults (≥18 years) initiating or continuing GC therapy at ≥2.5 mg/day for ≥3 months.[22] Regarding the reassessment, for all individuals from low to high risk, follow-up assessment with BMD and spinal imaging is recommended every 1–2 years.[22]

Determining the optimal timing for OP screening in patients with SLE who are not on ongoing GC therapy, or in whom steroids were discontinued long ago, remains challenging. Currently, no evidence-based thresholds regarding cumulative GC dose or duration of exposure exist to guide screening in such cases.

Based on the findings reported by Garcìa-Carrasco *et al*,[23] which indicate an annual incidence of 3.5 vertebral

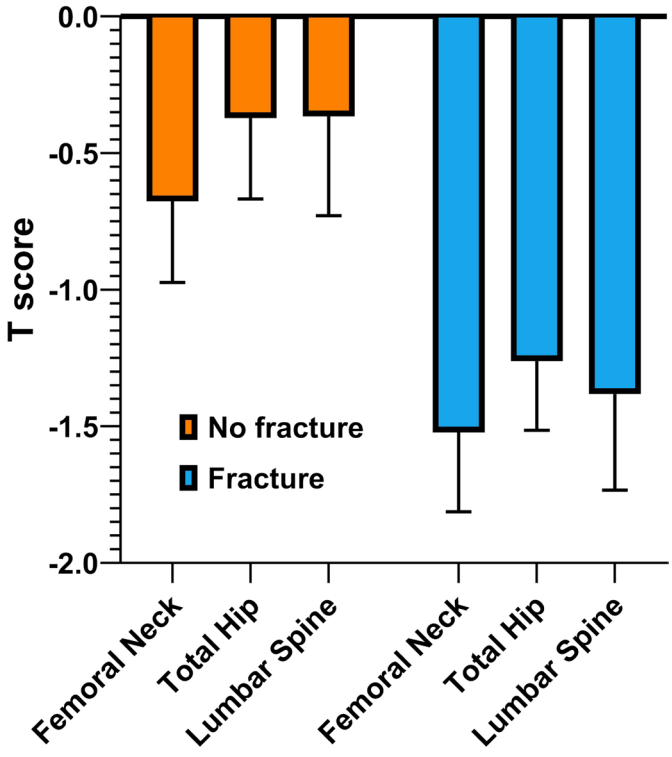

Figure 1 T-score comparison between patients with and without fractures.

fractures per 100 patients with SLE, the estimated number needed to screen to detect one fracture is 15 when performing spinal radiography every 2 years, and 10 when screening is conducted every 3 years. Therefore, we believe it is reasonable not to delay VFA or spinal X-ray screening beyond a 3-year interval.

Moreover, since DXA can be easily complemented by VFA, we might suggest to include such assessment whenever feasible.

Consistent evidence indicates that even asymptomatic radiographic vertebral fractures can contribute to pain, disability, long-term functional impairment and reduced quality of life.[24] These outcomes not only affect patient well-being but also place a substantial burden on healthcare systems. The economic impact of vertebral fractures is considerable, particularly when compounded by other GC-related adverse events, all of which contribute to significantly elevated direct and indirect healthcare costs.[25]

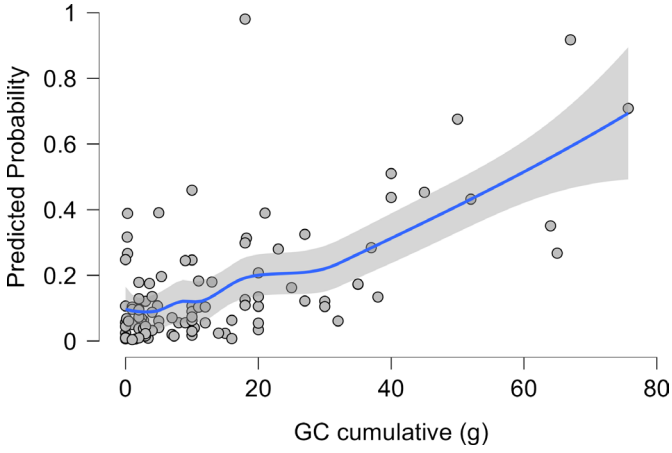

Figure 2 Correlation between GC cumulative dose and vertebral fractures. GC, glucocorticoid.

In our study, T-score values at both lumbar and femoral sites were significantly lower in patients with fractures, reinforcing the well-established association between reduced BMD and increased fracture risk.[21] Nonetheless, the mean T-score in patients with fractures remained within the mid-osteopenic range, suggesting that bone quality impairments, beyond mere reductions in bone mass, play a significant role in SLE. A strong correlation was found with GCs exposure indeed. The cumulative steroid dose clearly influenced both the presence and the number of fractures. Evidence on GIOP confirms that chronic steroid exposure significantly increases fracture risk, which cannot be fully attributed to BMD loss alone. Notably, data on pooled inflammatory rheumatic musculoskeletal diseases indicate that chronic GC at doses as low as 2.5 mg/day might increase fracture risk, which can be, however, mitigated by antiresorptive therapy.[26] Given the increasing body of evidence, recent guidelines have lowered the threshold for chronic GC therapy, recommending discontinuation whenever possible due to its strong association with damage accrual in SLE.[27–29]

We did not observe significant correlations between fractures and disease activity indexes (SLEDAI 2k/SLEDAS), but this lack of correlation was somehow anticipated, as these indices capture disease activity at a single time point rather than reflecting the cumulative burden of inflammation over time. The overall inflammatory load and chronic exposure to GCs remain key contributors to skeletal fragility in SLE, while short-term fluctuations in disease activity may not directly correlate with fracture risk. In addition, we included only patients in clinically stable disease, limiting our ability to detect an association between disease activity and fractures.

Our data on bone turnover markers, with lower formation and resorption levels in patients with fractures, likely reflect the widespread use of antiresorptive therapy in those with known fractures or high-risk factors (eg, steroid use). A similar effect may also explain the observed greater vitamin D levels in fractured patients, likely influenced by confounding by indication bias.

This study presents both strengths and limitations. A key strength is the use of VFA to determine fracture prevalence, enhancing detection sensitivity compared with reliance on medical history alone. However, the cross-sectional design and the absence of formal blinding in fracture evaluation may introduce bias and preclude causal inference. Prospective, blinded studies are therefore necessary to validate these findings and improve risk prediction.

Additionally, our results are not generalisable to patients with clinically active SLE, younger individuals or non-Caucasian ethnic groups.

Regarding methodology, the application of machine learning, specifically Random Forest, was limited to variable

selection rather than predictive modelling. While this technique effectively handles high-dimensional data, we recognise its limitations in small sample sizes, including potential instability in variable importance rankings. Our objective was to identify clinically relevant factors associated with vertebral fractures rather than to develop a prognostic tool. The study did not include internal or external validation of the proposed model; performance metrics were derived exclusively from the development sample. Future validation in larger and more diverse cohorts is needed to confirm the generalisability and robustness of these findings.

In conclusion, the high prevalence of previously undiagnosed vertebral fractures remains a significant concern in SLE, even among patients with a history of clinical vertebral fractures. Our findings further reinforce the detrimental impact of GC exposure and comorbidities on bone health. Nevertheless, key uncertainties persist regarding the most effective strategies to accurately assess fracture risk and implement targeted interventions beyond GC minimisation to reduce fracture incidence in this population.

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