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JOINT BONE SPINE

**Bone mineral density and trabecular bone score assessment
in systemic sclerosis: a cross-sectional study.**

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A higher risk of fracture has been documented in patients with Systemic sclerosis highlighting that bone assessment is important part of SSc management [1,2]. Vertebral fractures of the thoracic and lumbar spine can be diagnosed by dual-energy X-ray absorptiometry (DXA) with vertebral fracture (VF) assessment (VFA) [3]. The prevalence of VF using this technic in SSc is still unknown. Trabecular bone score (TBS) can assess bone microarchitecture through the analysis of grey levels from lumbar spine images of DXA. Therefore, TBS provides information on bone architecture that Bone Mineral Density (BMD) does not and the two methods may be complementary [4,5]. There are few studies evaluating the relevance of TBS in SSc.

The study proposed in this letter aimed to conduct a complete and non-invasive global bone evaluation (including simultaneous assessment of BMD, TBS, VFA and FRAX/TBS-FRAX) in a large population of SSc patients fulfilling the 2013 ACR/EULAR classification criteria [6,7]. FRAX® and FRAX-TBS scores were determined on a dedicated website and therapeutic thresholds were based on French recommendations [8]. This cross-sectional study was conducted in accordance with the declaration of Helsinki and was approved by the local ethics committee (approval number 16.132).

116 SSc patients were included and their clinical characteristics are presented in [Appendix A, Table S1; See the supplementary material associated with this article online]. The mean age was 61.9 years old with 78.4% of women. Key bone-associated parameters are presented in **Table 1**. 28.4% of the patients had osteoporosis defined by a T-score ≤ -2.5 and/or the history of osteoporotic fracture (**Table 2**) [9]. The prevalence of severe osteoporotic fractures was 8.6%. Their distribution is presented in **Appendix A, table S2**, 75.6% of osteoporotic fractures were VF. VFA allowed an unknown diagnosis of 5 of the 22 VF (22.7%). Patients with at least one VF had femoral neck and total hip BMD significantly lower (femoral neck BMD: $0.56 \pm 0.12 \text{g/cm}^2$ vs $0.70 \pm 0.11 \text{g/cm}^2$, $p < 0.01$ and total hip BMD: $0.63 \pm 0.13 \text{g/cm}^2$ vs $0.84 \pm 0.13 \text{g/cm}^2$, $p < 0.01$). Femoral neck, lumbar spine, and total hip BMD were correlated with TBS ($r = 0.38$, $p < 0.001$; $r = 0.59$, $p < 0.0001$; $r = 0.43$, $p < 0.0001$ respectively). Patients with longer disease duration (> 5 years) or VF had lower TBS values ($p < 0.05$ both). FRAX and FRAX-TBS scores in our population did not result in any new indication for starting anti-osteoporotic drugs considering the risk of severe fractures.

Based on the literature, BMD values in our SSc population were lower as compared to the general population whereas TBS values were similar. Mean TBS (1.296 ± 0.097) in our work was

similar to TBS in the OFELY and JPOS cohorts of post-menopausal women (1.276 and 1.310 respectively) [5,10]. The systematic coupling of VFA with BMD allowed the diagnosis of 5 previously unknown asymptomatic vertebral fractures. Considering that such fractures lead to an active anti-osteoporotic treatment regardless of BMD values, this result supports the use of VFA in daily practice in SSc. FRAX-TBS and FRAX scores had no impact on therapeutic considerations in our study suggesting that combining BMD evaluation [7], VFA and fracture history may be sufficient to select SSc patients that could benefit the most from anti-osteoporotic drugs.

DECLARATIONS :

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Conflict of interest: A Lescoat, G Coiffier, C Cazalets, N Belhomme, A Ballerie, F Robin, M Leroy, P Jégo and P Guggenbuhl report no conflicts of interest (both personal and institutional) regarding specific financial interests that are relevant to the work conducted or reported in this manuscript.

Ethics approval: This study was conducted in accordance with the declaration of Helsinki and was approved by the local ethics committee (approval number 16.132).

Consent to participate: All patients gave their informed written consent to participate.

Consent for publication: All patients gave their informed written consent for the publication of the anonymized results, and all authors approve the publication of the results in Osteoporosis international.

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Appendix A. Supplementary data

Supplementary data (Table S1-S2) associated with this article can be found in the online version at ...

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Table 1 : Bone associated-parameters in 116 SSc patients

Characteristics	N (%) or Mean (SD)
<i>Risk factors of osteoporosis</i>	
Dairy product consumption (n/day)	2.2 (1.3)
Alcohol abuse (>3 units per day)	3 (2.6)
Familial history of femoral neck fracture an a first-degree relative (n=69)	3 (2.6)
Early menopause (n=87/91 women)	5 (5.7)
Smoking (previous or current smokers)	30 (25.9)
<i>Treatments</i>	
Steroids consumption (previous or current, >7.5mg daily for more than 3 months)	30 (15.9)
Oral Vitamin D supplementation	38 (32.8)
Calcium supplementation	20 (17.2)
Hormonal supplementation (n=99)	14 (12.1)
Anti-osteoporotic drugs (current or past), including Bisphosphonate	20 (17.2)
<i>Biological characteristics</i>	
Serum calcium (mmol/L)	2.4 (0.1)
Serum phosphate (mmol/L)	1.0 (0.2)
Creatinine levels (μ mol/L) (n=114)	73.3 (28.3)
25-OH-D-vitamin (ng/mL) (n=89)	26.3 (12.68)
PTH (pg/mL)	22.9 (1.4)
<i>BMD parameters and DXA results</i>	
BMD (femoral neck) (g/cm^2) (n=115)	0.68 (0.12)
T-score (femoral neck)	-1.6 (0.99)
BMD (hip) (g/cm^2) (n=106)	0.82 (0.14)
T-score (hip)	-1.1 (1.05)
BMD (lumbar spine) (g/cm^2) (n=104)	0.92 (0.16)
T-score (lumbar spine)	-1.1 (1.45)
Osteopenia (T-score >-2.5 and \leq -1)	65 (56.0)
Osteoporosis according to BMD value only (T-score \leq -2.5)	28 (24.1)
Osteoporosis according to BMD value (T-score \leq -2.5) and fractures	33 (28.4)
TBS value (n=86)	1.29 (0.09)

SSc=Systemic sclerosis, PTH=parathyroid Hormon, BMD=Bone Mineral Density, TBS=trabecular Bone Score

Table 2 : Clinical, biological and bone characteristics associated with Osteoporosis as defined by BMD values and fracture status.

Characteristics	With Osteoporosis (n=33)	Without Osteoporosis (n=83)	OR	95%CI
Demographic				
Age (above 62 year-old)***	27	36	5.87	2.19-15.7
Male*	3	22	0.28	0.77-0.99
BMI (<25 kg/m ²)	21	47	1.30	0.56-3.00
Dairy product consumption ≥ 3 /day	13	22	2.14	0.85-5.36
Early menopause	3	2	3.98	0.63-25.0
Smoking (previous or current smokers)	6	24	0.55	0.20-1.49
Treatments				
Steroids consumption (previous or current)	11	19	1.68	0.69-4.09
Oral Vitamin D supplementation**	17	21	3.14	1.35-7.29
Calcic supplementation**	11	9	4.11	1.51-11.19
Hormonal supplementation	7	7	3.25	1.00-10.3
Anti-osteoporotic drugs ***	14	6	9.46	3.21-27.8
Disease characteristics				
Early SSc (< 5 year-old)	5	27	0.40	0.13-1.15
Diffuse cutaneous SSc	6	19	0.75	0.26-2.08
Presence of skin telangiectasia	27	55	2.29	0.85-6.2
DU history/active DU	9	26	0.82	0.34-2.01
ILD on CT scan	11	28	0.98	0.41-2.30
PAH on RHc	1	0	NA	
Calcinosis on hand X-Rays	12	22	1.70	0.69-4.20
Acro-osteolysis on hand X-Rays	6	17	0.88	0.31-2.53
Biological characteristics				
Clearance MDRD <59	4	8	1.26	0.35-4.50
25-OH-D-vitamine < 30 ng/mL	16	34	1.06	0.43-2.61
ACA	15	46	0.67	0.29-1.51
ATA	7	14	1.33	0.48-3.65
RNA pol III	0	6	NA	
Bone Characteristics and fractures				
TBS value \leq Q1=1.232***	12	8	6.11	2.08-18.0

SSc=Systemic sclerosis, BMI=Body Mass index, RP= Raynaud's phenomenon, DU= digital ulcers, ILD=interstitial lung disease, PAH=pulmonary arterial hypertension, ACA=anti-centromere antibodies, ATA=Anti-topoisomerase I antibodies, RNA pol III= anti-RNA polymerase III antibodies. TBS : trabecular bone score

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$ between patients with and without osteoporosis