LETTERS TO THE EDITOR

Bone mineral density and fracture risk in a cohort of Portuguese systemic sclerosis patients

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Dear Editor,

Patients with Systemic Sclerosis (SSc) seem to have higher prevalence of low bone mineral density (BMD) and an increased spine fracture risk[1]. Several risk factors, such as SSc subtype or low body mass index (BMI) appear to contribute to low BMD in these patients[2,3].

We aim to determine, by conventional densitometry (DXA) and using the fracture risk assessment tool (FRAX), the prevalence of low BMD and the fracture risk, respectively, in a SSc Portuguese cohort and its potential determinants.

We performed a transversal study including consecutive patients with the diagnosis of SSc. We collected data regarding demographics, BMD (lumbar spine and femoral neck) and occurrence of fracture. Ten-year risk of osteoporotic fracture was estimated using FRAX v4.1 with the Portuguese population reference[4]. Statistical analysis was performed using SPSS 23.0; $p<0.05$ was considered statistically significant.

Ninety-seven patients were included; 88.7% females (n=86) with median age of 62 years [56, 70]. Seventy-eight patients (80.4%) had limited cutaneous subtype and 5 patients (5.2%) had diffuse cutaneous subtype. Regarding clinical features: digital ulcers were present in 30 patients (30.9%), interstitial lung disease in 16 patients (6.5%), gastrointestinal involvement in 16 patients (16.5%), and pulmonary arterial hypertension in 3 patients. Regarding disease-modifying antirheumatic drugs, only 28 patients (28.9%) were under treatment: methotrexate (12.4%, n=12); mycophenolate mofetil (7.2%, n=7); hydroxychloroquine (6.2%, n=6); leflunomide (2.1%, n=2); rituximab (1%, n=1).

Nine patients (9.3%) were smokers and six patients (6.2%) reported an alcohol consumption of 3 or more units/day. Median body mass index (BMI) of 25.4 [21.4, 29.1], with 5 patients (5.2%) being underweight. Vitamin D insufficiency was reported in 19 patients (19.6%). Twenty-one patients (21.6%) have been exposed to oral glucocorticoids (GCT) for more than 3 months at a dose of prednisolone of 5mg daily or more and eight patients reported parental femoral neck fracture. Eleven patients (11.3%) had previous low impact fractures: 10 of which were vertebral and 1 wrist fracture.

Low bone mass density (BMD) was present in 45 patients (46.4%); median femoral neck bone mineral density (BMD-FN) was 0.827 (0.709, 0.893); median lumbar spine BMD was 1.026 (0.927, 1.198) and median femoral total BMD was 0.901 (0.768, 0.893). The ten-year probability of fracture (%) was calculated using FRAX: the median risk for major fracture was 5.1 [3.5, 9.7] and 3.8 [2.5, 8], with and without BMD, respectively; for hip fracture the estimated risk was 1.2 [0.6, 3.1] and 1.0 [0.4, 2.5], with and without BMD, respectively.

According to the estimated fracture risk thresholds for the Portuguese population, 25 patients (25.8%) met criteria to start treatment. Among them, 10 patients (40%) were under anti-osteoporotic treatment, whereas 7 patients (9.7%) were under treatment among the group of patients with a low risk of fracture, as the agreement between the indication to treat by FRAX and the onset of treatment was weak (k= 0.170, $p<0.001$).

BMD-FN presented a positive correlation with BMI (r=0.393, p=0.03). The risk for major fracture with and without BMD presented a positive correlation with spine fractures (Table I).

No differences were found between BMD-FN or FRAX and disease manifestations, vitamin D insufficiency, smoking or GCT use.

Our results showed that low BMD is prevalent in SSc patients and may be associated with low BMI. FRAX appears to be an useful instrument as it correlates with spine fracture risk and inversely with BMD. Estimating fracture risk using FRAX could be a useful tool for the prevention of osteoporosis in this population. Finally, we highlight the fact that this is the first study in Portugal evaluating prevalence of low BMD and fracture risk in a Portuguese SSc cohort.

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Table I. The 10-year risk of osteoporotic fracture estimated using FRAX according to different clinical characteristics.

	MOF with BMD	MOF without BMD	HF with BMD	HF without BMD
BMI	r=0.275 (p=0.07)*	r=0.296 (p=0.06)*	r=0.278 (p=0.07)*	r=0.300 (p=0.06)*
BMD-FN	r=-0.704 (p<0.01)*	r=-0.412 (p<0.01)*	r=-0.799 (p<0.01)*	r=-0.412 (p<0.01)*
Spine fractures	r=0.350 (p<0.01)*	r=0.397 (p<0.01)*	r=0.108 (p=0.22)*	r=0.178 (p=0.19)*
25-OH-vitD, ng/mL	r=0.300 (p=0.06)*	r=0.203 (p=0.10)*	r=0.298 (p=0.06)*	r=0.106 (p=0.21)*
SSc subtype	p=0.666**	p=0.085**	p=0.840**	p=0164**
Anti-topoisomerase I atb	p=0.856***	p=0.189***	p=0.369***	p=0.104***
Anti-centromere atb	p=0.547***	p=0.955***	p=0.509***	p=0.650***
Digital ulcers	p=0.493***	p=0.561***	p=0.660***	p=0.947***
Interstitial lung diseease	p=0.183***	p=0.107***	p=0.128***	p=0.233***
Gastrointestinal involvement	p=0.177***	p=0.084***	p=0.213***	p=0.152***
Myositis	p=0.775***	p=0.144***	p=0.798***	p=0.245***
Vitamin D insufficiency	p=0.097***	p=0.647***	p=0.182***	p=0.875***
Glucocorticoid usage	p=0.238***	p=0.630***	p=0.133***	p=0.844***
Smoking habits	p=0.121***	p=0.223***	p=0.100***	p=0.605***

Atb: antibody; BMD: bone mineral density; BMD-FN: femoral neck bone mineral density; BMI: body mass index; HF: hip fracture; MOF: major fracture risk; r: spearman correlation coefficient; SSc: systemic sclerosis; 25-OH-vitD: 25-hydroxyvitamin D.
Data expressed in bold presented statistically significancy. * Spearman's rank correlation; ** Kruskal- Wallis test; *** Mann-Whitney U test

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