Bone 122 (2019) 8–13

Contents lists available at ScienceDirect

Bone

journal homepage: www.elsevier.com/locate/bone

Full Length Article

Assessing bone impairment in ankylosing spondylitis (AS) using the trabecular bone score (TBS) and high-resolution peripheral quantitative computed tomography (HR-pQCT)

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ARTICLE INFO

Keywords:
Ankylosing spondylitis
Trabecular bone score
HR-pQCT
DXA
Bone density
Vertebral fractures

ABSTRACT

Objectives: To compare bone quality using the trabecular bone score (TBS) and bone microarchitecture in the distal tibia using high-resolution peripheral quantitative computed tomography (HR-pQCT) in ankylosing spondylitis (AS) patients and healthy controls (HC).

Methods: Areal bone mineral density (aBMD) and TBS (TBS iNsight software) were evaluated using DXA (Hologic, QDR 4500); while volumetric bone mineral density (vBMD) and bone microarchitecture were analyzed in the distal tibia using HR-pQCT (Scanco) in 73 male patients with AS and 52 age-matched HC.

Results: AS patients were a mean 41.6 ± 7.9 years old and had a mean disease duration of 16.4 ± 8.6 y, with a mean mSASSS 25.6 ± 16.4. No difference was observed in lumbar spine aBMD in AS patients and HC ($p = 0.112$), but total hip BMD ($p = 0.011$) and TBS ($p < 0.001$) were lower in AS patients. In the distal tibia, reduced trabecular volumetric density [Tb.vBMD ($p < 0.006$)] and structural alterations — trabecular thickness (Tb.Th), $p = 0.044$ and trabecular separation (Tb.Sp), $p = 0.039$ — were observed in AS patients relative to controls. Further analysis comparing TBS < 1.310 and TBS ≥ 1.310 in AS patients revealed a higher mean body mass index [BMI] ($p = 0.010$), lower tibia cortical vBMD [Ct.vBMD] ($p = 0.007$), lower tibia cortical thickness [Ct.Th]: ($p = 0.048$) in the former group. On logistic regression analysis, BMI (OR = 1.27; 95%IC = 1.08–1.50, $p = 0.005$), (VF 4.65; 1.13–19.1, $p = 0.033$) and tibial Ct.vBMD (0.98; 0.97–1.00, $p = 0.007$) were associated with a lower TBS (< 1.310).

Conclusions: The present study demonstrates that TBS and HR-pQCT imaging are important technologies evaluating bone impairment in AS patients. Moreover, in these patients vertebral fractures were associated with lower TBS.

1. Introduction

Ankylosing Spondylitis (AS) is a chronic inflammatory disease that primarily affects young males and is characterized by new bone growth that leads to syndesmophyte formation and subsequent vertebral ankylosis [1]. It is common for AS patients to present with low bone mineral density, including osteoporosis, which can be linked to decreased mobility and systemic inflammation [2,3]. Inflammation is associated with both trabecular bone loss, leading to osteoporosis, and new bone formation, leading to progressive ankylosis of the spine and sacroiliac joints [4]. Patients with AS have an increased risk of spinal fracture [3,5,6], and the typical hyper-kyphosis of AS is partially caused by vertebral fractures [5]. This all contributes to functional losses [6,7] and an increased risk of fractures [8].

Previously-published studies have demonstrated that AS patients have low bone mineral density in their spine [9]. In AS patients, bone mass assessments are generally based upon the results of dual-energy X-ray absorptiometry (DXA), which may be difficult to interpret due to ligamentous calcifications superimposed on the vertebrae, and because of sclerosis involving the vertebral endplates, both contributing to erroneously-increased spinal BMD readings [10–12]. Another limitation of DXA-based BMD is that DXA is a two-dimensional analysis that cannot distinguish between the trabecular and cortical compartments of bone, while inflammatory diseases generally cause quite different levels

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https://doi.org/10.1016/j.bone.2019.01.024
Received 7 December 2018; Received in revised form 19 January 2019; Accepted 28 January 2019
Available online 29 January 2019
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of deterioration in these two compartments [8,13,14].

New techniques, including the trabecular bone score (TBS), have advantages over BMD, for evaluating trabecular bone in DXA images of the lumbar spine, because interpretable even in presence of osteophytes and syndesmophytes that are characteristic of osteoarthritis and AS, respectively [15,16,17]. High-resolution peripheral quantitative computerized tomography (HR-pQCT), another novel imaging technique, can assess bone microarchitecture and biomechanical parameters at peripheral sites; this technique is also capable of analyzing the cortical and trabecular bone compartments separately [14,18].

Consequently, the over-riding objective of the current study was to compare bone mass and quality using (a) areal BMD, (b) the trabecular bone score (TBS), and (c) HR-pQCT parameters in male AS patients and healthy controls (HC).

2. Materials and methods

2.1. Patients and controls

Seventy-three male AS patients selected consecutively in the Spondyloarthritis Outpatient Clinic at the University of Sao Paulo's Clinics Hospital were invited to participate in this study. All patients fulfilled the modified New York Classification criteria for definite AS [19]. Fifty-two age-matched healthy controls (HC) who worked at the University of Sao Paulo School of Medicine, or their family members, were enrolled as healthy controls (HC). The exclusion criterion for healthy controls was any bone-associated metabolic disease, including osteoporosis. The exclusion criterion for both subject groups was the use of any medication that could potentially interfere with bone metabolism, including bisphosphonates, teriparatide, anticonvulsants, and anticoagulants. Glucocorticoids (GC) was allowed only for AS patients in doses ≤ 5 mg/day.

Prior to subject enrollment and data collection, the study had been approved by the Local Ethics Committee on Human Research at the University of Sao Paulo. All participants gave written informed consent, in accordance with the Declaration of Helsinki.

Individual subject characteristics like age, ethnicity and body mass index (BMI) were recorded. A questionnaire asking about osteoporosis risk factors was used to characterize each subject's personal history of fracture, hours per week of physical activity, current smoking status, and alcohol intake (≥ 3 U/day).

As recommended previously, duration of disease was recorded and four distinct, AS-specific clinical indexes utilized; the latter included ratings for (a) AS disease activity (*Bath Ankylosing Spondylitis Disease Activity Index*, BASDAI); (b) patient function (*Bath Ankylosing Spondylitis Function Index*, BASFI); (c) AS metrology (*Bath Ankylosing Spondylitis Metrology Index*, BASMI); and (d) patient quality of life (*Ankylosing Spondylitis Quality of Life questionnaire*, ASQoL) [20].

Human leukocyte antigen-B27 (HLA-B27) frequency was evaluated in fifty-seven AS patients. Inflammation was evaluated by measuring serum C-reactive protein (CRP) levels and erythrocyte sedimentation rate (ESR) in all patients at the time of data collection. The use of any AS-related medication was extracted from medical records, including the use of any and all nonsteroidal anti-inflammatory drugs (NSAIDs), glucocorticoids, methotrexate, and tumor necrosis factor inhibitor (TNFi).

2.2. Radiological assessments

In the AS patients, a Modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) was generated, using lateral radiographic images of the cervical and lumbar spine. The scoring system, developed by Creemers et al. [21], was applied in the anterior corners from the lower border of C2 to the upper border of Th1, and from the lower border of Th12 to the upper border of S1. The following nominal scoring system was used: 0 = no abnormality; 1 = erosion, sclerosis or squaring; 2 = at least one syndesmophyte; and 3 = complete bridging syndesmophytes. The total mSASSS was calculated by summing the scores for all the individual sites, which yielded a final summation score ranging from zero to 72.

Table 1
Clinical characteristics, laboratory parameters, Modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) and treatment in ankylosing spondylitis (AS) patients.

Parameters	
Disease duration, years	16.4 ± 8.57
Peripheral involvement, n (%)	37 (50.7)
Physical exercise, n (%)	30 (41.1)
BASDAI	2.69 ± 1.91
BASFI	3.63 ± 2.40
BASMI	3.27 ± 2.17
ASQol	5.77 ± 4.79
Positive HLA-B27[#], n (%)	44 (77.2)
ASDAS-CRP	2.15 ± 0.99
mSASSS	25.6 ± 16.4
Use of NSAID, n (%)	62 (84.9)
Use of glucocorticoid, n (%)	9 (12.3)
Use of methotrexate, n (%)	4 (5.5)
Use of sulfasalazine, n (%)	31 (42.5)
Use of TNF inhibitor, n (%)	31 (42.5)

Values for disease duration, BASDAI, BASFI, BASMI, ASQoL, ASDAS CRP and mSASSS are expressed as mean ± SD. Peripheral involvement and treatment in percentage (%). BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Function Index. BASMI: Bath Ankylosing Spondylitis Metrology Index; ASQoL: Ankylosing Spondylitis Quality of Life; HLA: human leukocyte antigen ([#]n = 57). CRP: C-reactive protein; ASDAS: Ankylosing Spondylitis Disease Activity Score. NSAID: nonsteroidal anti-inflammatory drug. TNF: tumor necrosis factor.

2.3. Areal bone mineral density (aBMD)

In all participants, areal BMD was measured for the lumbar spine (L1-L4), total hip, and forearm (distal third of the radius); while a VFA scan of the thoracolumbar spine was performed using dual-energy X-ray absorptiometry (DXA) equipment (Hologic QDR4500; Hologic, Bedfort, MA). Thoracic and lumbar (T4-L4) lateral radiographs were obtained using VFA-DXA, in accordance with a standardized protocol previously described by Genant et al. [22] and by our group [23].

2.4. Calculating lumbar spine TBS

The TBS was calculated using TBS iNsight software (Version 2.1. Med-Imaps. Bordeaux, France) as the mean measurements for vertebrae L1–L4 within the same region of interest (ROI) as the spinal aBMD. The TBS is a unitless index that characterizes bone microstructure obtained by macroscopic representation and can be applied to any X-ray image, including DXA images, by quantifying local grey-level variations [24]. In accordance with guidelines, the TBS cutoffs we used were: any TBS greater than or equal to 1.310 was considered normal; TBS values between 1.230 and 1.310 were deemed consistent with partially-degraded structure; and any TBS less than or equal to 1.230 was considered degraded structure [25]. Those AS patients with a TBS < 1.310 were ultimately compared against those AS patients with a TBS ≥ 1.310.

2.5. HR-pQCT measurements

2.5.1. Volumetric bone mineral density and microarchitecture measurements

Volumetric bone mineral density and microarchitecture were evaluated using an HR-pQCT device (Xtreme CT Scanco Medical AG, Brüttisellen, Switzerland) and the standard scanning protocol (60 kVp, 1.0 mA). The ROI was defined using a scout view. Employed

Table 2
Areal bone mineral density (aBMD) and trabecular bone score (TBS) values comparing ankylosing spondylitis (AS) patients versus healthy controls.

	AS patients (n = 73)	Healthy controls (n = 52)	AS patients vs. healthy controls p non-adjusted	AS patients vs. healthy controls p adjusted[a]
aBMD				
Lumbar spine, g/cm^2	1.080 ± 0.193	1.041 ± 0.118	0.390	0.112
Z-score	0.1 ± 1.8	−0.3 ± 1.0	0.312	0.105
Total hip, g/cm^2	0.939 ± 0.123	1.007 ± 0.112	**0.008**	**0.011**
Z-score	−0.4 ± 0.8	−0.0 ± 0.7	**0.006**	**0.201**
Distal1/3 radius, g/cm^2	0.777 ± 0.061	0.774 ± 0.060	0.739	0.385
Z-score	−0.4 ± 1.2	−0.5 ± 1.1	0.74	0.440
TBS	1.314 ± 0.121	1.396 ± 0.070	< **0.001**	< **0.001**

Values are expressed as mean ± SD (standard deviation). AS: ankylosing spondylitis. Data in bold indicate $p < 0.05$.
[a] p-Value adjusted: adjusted for age, physical exercise.

Table 3
Volumetric bone density, structure, and strength parameters in the distal tibia and radius using HR-pQCT, comparing ankylosing spondylitis (AS) patients and healthy controls.

	AS patients (n = 73)	Healthy controls (n = 52)	AS patients vs. healthy controls p value non-adjusted	AS patients vs. healthy controls p value adjusted[a]
Distal tibia				
Tb.vBMD, mg HA/cm^3	162.1 ± 39.6	186.8 ± 39.9	< **0.001**	**0.006**
Ct.vBMD, mg HA/cm^3	906.1 ± 52.7	904.9 ± 38.8	0.893	0.521
BV/TV	0.135 ± 0.033	0.155 ± 0.033	< **0.001**	**0.007**
Tb.N, 1/mm	1.81 ± 0.32	1.94 ± 0.30	**0.027**	0.083
Tb.Th, mm	0.074 ± 0.012	0.080 ± 0.013	**0.009**	**0.044**
Tb.Sp, mm	0.497 ± 0.110	0.448 ± 0.086	**0.012**	**0.039**
Ct.Th, mm	1.24 ± 0.32	1.37 ± 0.27	**0.026**	0.087
S, N/mm	254,250.8 ± 48,477.7	291,770.3 ± 52,858.4	< **0.001**	< **0.001**
F.load. N	12,098.6 ± 2240.8	13,770.2 ± 2388.1	< **0.001**	**0.001**
Distal radius				
Tb.vBMD, mg HA/cm^3	196.9 ± 44.4	194.4 ± 38.5	0.739	0.379
Ct.vBMD, mg HA/cm^3	876.7 ± 75.6	895.1 ± 64.8	0.222	0.193
BV/TV	0.164 ± 0.037	0.162 ± 0.032	0.744	0.375
Tb.N, 1/mm	2.04 ± 0.29	2.04 ± 0.29	0.920	0.678
Tb.Th, mm	0.081 ± 0.017	0.080 ± 0.015	0.818	0.600
Tb.Sp, mm	0.419 ± 0.079	0.421 ± 0.079	0.888	0.597
Ct.Th, mm	0.85 ± 0.24	0.90 ± 0.23	0.812	0.314
S, N/mm	114,104.8 ± 25,546.6	116,098.6 ± 29,915.9	0.666	0.968
F.load, N	5372.6 ± 999.6	5531.3 ± 1141.2	0.413	0.782

Values are expressed as mean ± SD. AS: Ankylosing Spondylitis. Tt.vBMD: total volumetric bone mineral density; Tb.vBMD: trabecular volumetric bone mineral density; Ct.vBMD: compact volumetric bone mineral density; BV/TV: trabecular bone volume/total volume; Tb.N: Number of trabeculae; Tb.Th: trabecular thickness; Tb.Sp: trabecular separation; Ct.Th: cortical thickness; S: stiffness; F.load: estimated failure load. Data in bold indicate $p < 0.05$.
[a] p value adjusted: adjusted for age, physical activity.

measurements included 110 slices spanning 9.02 mm in length (voxel size 82 μm) from the distal end and positioned 9.5 and 22.5 mm proximal to the reference line for the non-dominant distal radius and tibia, respectively [26]. All HR-pQCT scans were performed by a single operator. The entire volume of interest was separated automatically into cortical and trabecular regions using a threshold-based algorithm. The threshold used to discriminate cortical from trabecular bone was set to one-third of the apparent cortical bone density. Mean cortical thickness was defined as the mean cortical volume divided by the outer bone surface. Trabecular bone density (Tb.vBMD) was computed as the average mineral density within the trabecular volume of interest [27,28].

The HR-pQCT outcome variables used in analysis were (a) two volumetric bone mineral density parameters (mg HA/cm^3): trabecular volumetric bone mineral density (Tb.vBMD) and cortical volumetric bone mineral density (Ct.vBMD); and (b) four bone-structure parameters: trabecular number (Tb.N, 1/mm), trabecular thickness (Tb.Th, mm), trabecular separation (Tb.Sp, mm), and cortical thickness (Ct.Th, mm) [26,29].

In terms of precision, HR-pQCT demonstrated tibial coefficients of variation of 0.25–1.16% for density measurements and of 0.78–6.35% for morphometric measurements [30].

2.5.2. Micro-finite element analysis (μFEA)

Linear μFE models of the distal radius and tibia were created directly from the HR-pQCT images, using software-specific finite elements. This software uses the so-called *voxel conversion technique* to create finite element models (Finite Element software v. 1.13, Scanco Medical AG, Switzerland, January 2009) and thereby assess biomechanical bone strength. The two biomechanical properties analyzed using μFEA were (a) bone stiffness (S, kN/mm) and (b) estimated failure load (F.load, N) [30].

2.6. Statistical analysis

All results were expressed as a mean ± standard deviation for continuous variables or as a percentage for categorical variables. Student's *t*-test (normal distribution) or the Mann-Whitney test (non-normal distribution) were used for inter-group comparisons of continuous variables; while Pearson's chi-square analysis or Fisher's exact test for inter-group comparisons of categorical variables, comparing AS patients and healthy controls, with respect to areal BMD for the lumbar spine and total hip, the lumbar TBS, and the various HR-pQCT parameters. These parameters also were compared after adjusting for variables identified as significantly different between groups during

Table 4
Comparing clinical characteristics, mSASS, treatment, presence of vertebral fractures and bone parameters using HR-pQCT in ankylosing spondylitis (AS) patients with a TBS < 1.310 and TBS ≥ 1.310.

	TBS < 1.310 (n = 30)	TBS ≥ 1.310 (n = 43)	
Age, years	43.7 ± 8.1	40.2 ± 7.5	**0.047**
BMI, kg/m^2	28.4 ± 5.15	25.8 ± 3.22	**0.010**
Disease duration, years	12.3 ± 8.5	15.9 ± 8.7	0.49
Peripheral involvement, n (%)	13 (43.3)	24 (55.8)	0.35
Physical exercise, n (%)	12 (40)	18 (41.8)	1.00
BASDAI	2.99 ± 1.89	2.49 ± 1.92	0.28
BASFI	4.24 ± 2.48	3.2 ± 2.28	0.09
BASMI	3.84 ± 2.07	2.88 ± 2.17	**0.034**
ASQoL	6.1 ± 4.27	5.35 ± 5.15	0.37
Positive HLA-B27$^{\#}$, %	73.9	79.4	1.00
ASDAS-CRP	2.34 ± 0.96	2.01 ± 1.0	0.16
mSASSS	29.3 ± 17.9	23.1 ± 15.1	0.06
AS treatment			
Use of NSAID, n (%)	24 (80)	38 (88.4)	0.34
Use of glucocorticoid, n (%)	6 (20)	3 (7)	0.15
Use of methotrexate, n (%)	1(29)	3(40)	0.64
Use of sulfasalazine, n (%)	14(16)	17(26)	0.63
Use of TNF inhibitor, n (%)	11 (36.7)	20 (46.5)	0.47
DXA – VFA			
Vertebral fracture, grade I, n (%)	11 (36.7)	7 (16.3)	0.058
HR-pQCT - distal tibia			
Tb.vBMD, mg HA/cm^3	157.7 ± 44.1	165.2 ± 36.5	0.43
Ct.vBMD, mg HA/cm^3	882.2 ± 61.8	922.3 ± 38.3	**0.007**
BV/TV	0.131 ± 0.037	0.138 ± 0.030	0.43
Tb.N, 1/mm	1.824 ± 0.338	1.805 ± 0.311	0.80
Tb.Th, mm	0.071 ± 0.013	0.076 ± 0.011	0.08
Tb.Sp, mm	0.494 ± 0.108	0.498 ± 0.113	0.09
Ct Th, mm	1.155 ± 0.362	1.306 ± 0.279	**0.048**

Values are expressed as mean ± SD (standard deviation) or percentage (%). HLA: human leukocyte antigen ($^{\#}$n = 57). Data in bold indicate p < 0.05.

Table 5
Logistic regression fitted models for TBS < 1.310.

Model 1	OR	IC (95%)		p
		Lower	Upper	
Age	0.98	0.90	1.06	0.539
BMI	1.27	1.08	1.50	**0.005**
BASMI	1.25	0.95	1.65	0.105
Vertebral fracture - VFA	4.65	1.13	19.1	**0.033**
Tíbia Ct.vBMD	0.98	0.97	1.00	**0.007**

BMI: body mass index; BASMI: *Bath Ankylosing Spondylitis Metrology Index*. Ct.vBMD: cortical volumetric bone mineral density. Data in bold indicate p < 0.05.

baseline univariate analysis (e.g., subject age and physical activity level). In addition, anthropometric and clinical variables, the proportion with vertebral fractures, and all HR-pQCT parameters were compared in patients with a TBS < 1.310 and those with a TBS ≥ 1.310.

For multivariable analysis, logistic regression models were generated and tested to identify any variables independently associated with a TBS < 1.310. Due to collinearity between the two HR-pQCT parameters — Ct.vBMD and Ct.Th — these variables were added sequentially to the logistic regression model, resulting in two models being evaluated. The Hosmer-Lemeshow test was used to adjust the logistic regression models. Results are represented as adjusted odds ratios (ORs) with their corresponding 95% confidence intervals (CIs).

The threshold for statistical significance for all tests was set as p < 0.05. Analyses were conducted using the Statistical Package for the Social Sciences, version 20.0 (SPSS for Windows. 20.0. Chicago, IL, USA).

3. Results

3.1. Subject characteristics

All 73 AS patients and 52 healthy controls were male. Patients and controls were matched by age (41.6 ± 7.9 vs. 40.3 ± 9.6 y, p = 0.42) and BMI (26.9 ± 4.3 vs 27.4 ± 2.5 kg/m^2, p = 0.18). No significant differences were observed regarding Caucasian race (83.6% vs. 71.1%, p = 0.13), the percentage of subjects with a personal history of fracture related to fall or during physical activity (13.7% vs. 11.5%, p = 0.61) or currently smoking (16.4% vs. 7.3%, p = 0.18). Patients reported a lower level of physical exercise than controls (1.7 ± 2.5 vs. 2.8 ± 3.2 h/week, p = 0.044). No patient or controls reported excessive alcohol intake.

The clinical characteristics of the 73 AS patients are summarized in Table 1. Mean disease duration was 16.4 ± 8.6 years. Seventy-seven percent of patients were HLA-B27 positive. Means for the four AS-specific clinical indices (BASDAI, BASFI, BASMI and ASQoL), inflammatory parameters, radiographic damage scores (mSASSS) and number of medications currently being used are also shown in Table 1.

3.2. Areal bone mineral density, TBS and HR-pQCT parameters in AS patients versus controls

The mean values for aBMD in the lumbar spine and distal radius were similar in AS patients and controls (p > 0.05); however, the total hip BMD and TBS were both lower in AS patients (p = 0.011 and p < 0.001, respectively) (Table 2, p values adjusted). Forty-one percent of AS patients presented TBS below the normal values (< 1.310) compared to only 7.7% of healthy controls (p < 0.001) and 21.9% of AS patients compared to controls (0%) demonstrated TBS with degraded structure (TBS ≤ 1.230) (p = 0.002).

Ankylosing spondylitis patients exhibited lower values on HR-pQCT analysis in the distal tibia for trabecular volumetric bone density (Tb.vBMD, p = 0.006), bone structure parameters (BV/TV, p = 0.007 and Tb.Th, p = 0.044), and bone strength parameters (S, p < 0.001 and F.load, p = 0.001). Moreover, AS patients had a higher mean Tb.Sp (p = 0.039) than controls (Table 3, p values adjusted). No differences were observed in distal radius parameters by HR-pQCT (all p > 0.05).

On univariate analysis, relative to AS patients with a TBS ≥ 1.310 (n = 43), those with a TBS < 1.310 (n = 30) were older (43.7 ± 8.1 vs. 40.2 ± 7.5 y, p = 0.047), and had a higher mean BMI (28.4 ± 5.1 vs. 25.8 ± 3.2 kg/m^2, p = 0.010), lower tibial Ct.vBMD (882 ± 61 vs. 922 ± 38 mg HA cm^2, p = 0.007), lower tibial Ct.Th (1.155 ± 0.362 vs 1.306 ± 0.279 HA cm^2, p = 0.048) and a tendency to higher frequency of vertebral fracture (36.7 vs.16.3%, p = 0.058) (Table 4).

By logistic regression, after adjusting for age, BMI, BASMI, history of vertebral fracture and distal tibial Ct.vBMD, three factors were identified that were significantly associated with a TBS < 1.310. These three factors were a higher BMI (OR: 1.27 [95%IC, 1.08–1.50, p = 0.005]), higher frequency of vertebral fracture (OR: 4.65 [95%IC, 1.13–19.1, p = 0.033]) and tibial Ct.vBMD (OR: 0.98 [95%IC, 0.97–1.00, p = 0.007]) (Table 5).

4. Discussion

Our results demonstrate that the lumbar spine TBS is an accurate, noninvasive measurement that can be used, complementary to DXA imaging, to identify bone quality deterioration in AS patients. Furthermore, we demonstrated that HR-pQCT assessments of the distal tibia also can detect bone impairment in AS patients.

DXA is a widely-available technique that is considered the gold-

standard for evaluating bone mineral density; however, it is limited by only allowing two-dimensional analysis. In rheumatic diseases — like ankylosing spondylitis and osteoarthritis — the presence of either syndesmophytes or osteophytes superimposed on the vertebrae, or of sclerosis involving vertebral endplates, can render results inaccurate. In fact, with these diseases, DXA can overestimate density values, resulting in the inadequate detection of inflammation-related bone loss [11,13,17].

In our study of AS patients, the lumbar spine TBS permitted us to more accurately identify bone impairment in the lumbar spine than lumbar areal BMD, suggesting that the TBS should be used to assess vertebral bone deterioration in these patients. In fact, TBS is not influenced by the syndesmophytes from the spinal image exam and allows for more precise analysis of vertebral trabecular bone [17]. Our AS patients had a significantly-lower TBS than our healthy controls, suggesting that a heterogeneous and more-porous trabecular network was linked to reduced bone strength [25]. Trabecular bone is the compartment that is most impacted by the inflammatory process that is characteristic of AS [14,18]. One further advantage of the lumbar spine TBS is that it can be assessed using the same scan routinely acquired for lumbar spine aBMD and, as such, may already be readily adopted into routine clinical practice.

Regarding the HR-pQCT image, bone parameters assessed in the distal tibia demonstrated significant bone deterioration in our AS patients relative to healthy controls. Trabecular volumetric density, trabecular thickness, trabecular separation, and trabecular strength are affected in the distal tibia in AS patients, suggesting that HR-pQCT is another effective technique to detect bone impairment in these patients. These data may be associated with an inflammatory process and reduced mobility, also resulting in peripheral bone loss and decreased bone strength, further leading to bone fractures [31].

Interestingly, the deterioration observed in our patients' distal tibia but not radius might have been due to the decreased physical activity and increased immobility reported by our AS patients versus healthy controls. In fact, Haroon et al., demonstrated that trabecular thickness at tibia, but not at radius was the only parameter affected in AS patients compared to healthy, after adjusted by age and sex [13]. Differently, recent publication studying early nonradiographic axial spondyloarthritis (including psoriasis and inflammatory bowel disease) patients showed radius deterioration, but these authors did not evaluate tibia site [32].

Further analysis demonstrated that a lower spine TBS (< 1.310) was significantly associated with peripheral bone deterioration (lower Ct.vBMD and Ct.Th in the distal tibia). Moreover, on logistic regression analysis, TBS values below the threshold of 1.310 (reflecting at least partial bone deterioration) also were associated with the presence of vertebral fractures, reinforcing the importance of TBS analysis as a complementary DXA exam among AS patients.

The BASMI, a metric assessment of spinal mobility, also was significantly lower in AS patients with a lower TBS. However, this variable lost its significance and was dropped from the logistic model, suggesting that other factors could be more important contributors to bone impairment. Interestingly, a higher BMI was another parameter associated with a lower TBS. This finding is consistent with already-published data suggesting that obesity may impair bone metabolism, both by decreasing bone formation and by increasing bone resorption via the upregulation of proinflammatory cytokines [33]. Another explanation for this result is related to a technical problem, as TBS is negatively correlated with soft tissue thickness as it brings noise to the image [34].

In conclusion, our study is the first to simultaneously analyze the trabecular bone score and HR-pQCT parameters. Its results create a strong argument for practicing rheumatologists adopting these two methodologies to detect bone impairment in their ankylosing spondylitis patients.

Funding

This work was supported by Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP) #2011/23781-2 and Conselho Nacional de Ciência e Tecnologia (CNPQ) #305556/2017-7 (RMRP).

Disclosure statement

Didier Hans is co-owner of the TBS patent and has corresponding ownership shares and a position in the Medimaps group. All other authors declare no conflicts of interest.

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