Trabecular Bone Score: a New Simple Tool for Evaluating Osteoporosis in Patients With Axial Spondyloarthritis

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Abstract

Background: Axial spondyloarthritis (ax-SpA) increases the risk of osteoporosis and vertebral fractures (VFs). Although bone mineral density (BMD) is used to diagnose osteoporosis, it has some limitations in patients with ax-SpA. Trabecular bone score (TBS), a new tool that indirectly assesses bone microarchitecture, can be used to assess fracture risk; however, few studies have been conducted to investigate TBS in ax-SpA patients.

Objectives: To compare TBS between ax-SpA patients and 1:1 sex- and age-matched healthy controls and determine factors associated with low TBS in ax-SpA patients.

Methods: A cross-sectional study was conducted in two tertiary-care hospitals. A total of 137 ax-SpA patients and controls were enrolled. Demographics, disease characteristics, and osteoporosis-related factors were recorded. TBS and BMD at the lumbar spine and hip were measured by dual X-ray absorptiometry (DXA). Low TBS define as a TBS value <1.230. Vertebral fractures were evaluated by densitometric vertebral fracture assessment. Factors associated with low TBS were examined by logistic regression.

Results: Most ax-SpA patients were male (75.9%) and tested positive for HLA-B27 (88.3%). The mean (SD) age was 42.8 (12.0) years. The mean (SD) of TBS in the ax-SpA patients was lower than those in the controls [1.402 (0.107) vs 1.440 (0.086), respectively; $p=0.002$]. The mean (SD) of lumbar BMD in the ax-SpA patients was higher than those in controls [1.186 (0.212) vs 1.087 (0.124), $p<0.001$], whereas the mean (SD) of femoral neck BMD in the ax-SpA group was lower than that in the controls [0.867 (0.136) vs 0.904 (0.155), $p=0.038$]. High disease severity as indicated by sacroiliac joint fusion and a high ASDAS score were associated with low TBS with the odds ratios (95% confidence interval) of 11.8 (1.2-115.4) and 5.2 (1.6-16.9), respectively.

Conclusion: Ax-SpA patients had a higher prevalence of low TBS than controls. Sacroiliac joint fusion and a high ASDAS score were associated with low TBS.

Introduction

Axial spondyloarthritis (ax-SpA) is a chronic inflammatory disease that primarily affects the axial joints (spine and sacroiliac (SI) joints), as well as peripheral joints and entheses. Extraspinal manifestations such as peripheral arthritis, anterior uveitis, psoriasis, colitis, and rare manifestations such as pulmonary fibrosis and amyloidosis are also affected by Ax-SpA(1, 2). Although the pathogenesis is unknown, several hypotheses have been proposed, including the arthritogenic peptide, misfolding, molecular mimicry, and cell-surface HLA-B27 homodimer. As a result, a variety of cytokines are produced, which play a role in both the inflammatory process and the formation of new bone. During the inflammatory process, those cytokines, namely interleukin-1 (IL-1), IL-6, IL-17/23, and tumor necrosis factor α (TNF- α), stimulate the production of receptor activator of nuclear factor kappa-B ligand (RANKL), which is a potential stimulator of osteoclast differentiation, resulting in bone loss in ax-SpA patients(3, 4).

Meanwhile, bone morphogenetic protein (BMP) and Wnt signaling pathways induce osteoblast differentiation to contribute to new bone formation, leading to ankylosis and disability(4, 5).

Osteoporosis is one of the most common comorbidities in ax-SpA patients(6). Paradoxically, new bone formation occurs resulting in ankylosis of the spine and SI joints(7, 8). The prevalence of osteoporosis in ax-SpA patients ranges between 11.7 % and 34.4 %(9, 10). Several studies found that long-standing forms, spinal ankylosis, high inflammatory markers, alcohol consumption, corticosteroid use, and vitamin D deficiency were risk factors for low bone mineral density (BMD) in ax-SpA patients(8, 9). Importantly, patients with ax-SpA are at a higher risk of vertebral fractures (VFs) than the general population(11). Furthermore, elevated C-Reactive Protein (CRP), disease duration, and hyperkyphosis have also been linked to an increased risk of VFs(8).

According to the WHO criteria, osteoporosis is defined as a BMD T-score of -2.5 or less measured by dual-energy X-ray absorptiometry (DXA) at the spine, hip, or forearm (12). The 2019 update of the American College of Rheumatology (ACR)/ Spondylitis Association of America/ Spondyloarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Non-radiographic ax-SpA suggested that ax-SpA patients be screened for osteoporosis with DXA (13). However, the BMD from DXA may inadvertently increase in ax-SpA patients due to new bone formation (14).

TBS indirectly assesses bone microarchitecture, which contributes to bone strength. It assesses the pixel gray-level variations in the lumbar DXA image. Higher gray-value amplitudes and greater distance between pixels, as well as a lower slope, indicate poorer microarchitecture (11). Several studies reported that TBS was associated with fracture risk in postmenopausal women, particularly VFs. TBS, unlike DXA, is less likely to be affected by syndesmophytes. Therefore, TBS may be valuable in fracture risk assessment in ax-SpA patients (15, 16).

The objective of this study was to compare TBS in Thai ax-SpA patients with age- and sex-matched normal individuals and examine the factors associated with low TBS in ax-SpA patients.

Methods

Setting and subjects

A cross-sectional study was conducted at Phramongkutklao and Khon Kaen University Hospitals (tertiary care setting) between January 2020 and February 2021. Patients aged 18 years and older and fulfilled the ASAS classification criteria for ax-SpA were consecutively recruited(17). Patients with a history of cancer or a first-time cancer diagnosis (regardless of stage), chronic kidney disease at least stage IV(18), hyperthyroidism, hyperparathyroidism, pregnancy, and/or lactation were excluded. Each patient's healthy control participants were randomly selected from the general Thai population and matched for age and sex with a ratio of 1:1. This study complies with the Declaration of Helsinki. The written informed consent has been obtained from all participants prior to entry the study. The ethics committee and the

institutional review board at each of the participating sites approved the study (study numbers R178h/62 and HE631141, respectively).

BMD and TBS measurements

BMD was measured at the lumbar spine (LS), femoral neck (FN), and total hip (TH) using GE-Lunar iDXA (#210754) and GE-Lunar DPX Duo densitometer (GE Healthcare, Madison, WI, USA). Osteoporosis was defined as a BMD T-score of -2.5 or less in postmenopausal women and men aged ≥ 50 years. Whereas, a Z-score of -2.0 or less was defined as being below the expected range for age (low BMD) in premenopausal patients and men aged < 50 years (19). The TBS was obtained from the DXA scan (Medimaps TBS iNsight) at the lumbar spine in both settings. The TBS cut-offs were classified as normal TBS, partially degraded (or intermediate TBS), and degraded (or low TBS) if TBS > 1.310 , 1.230 - 1.310 , and < 1.230 , respectively (20).

Radiography and vertebral fracture assessment

The vertebral fracture assessment (VFA) by DXA and/or the lateral thoracolumbar X-rays were used to determine the presence of VFs. VFs were defined using Genant's semiquantitative method (21) and reviewed by a certified nuclear radiologist. In this study, the SI joints were assessed by radiograph. The modified New York criteria were used to classify sacroiliitis (22).

Measurements in ax-SpA patients

Demographic and clinical data including age, gender, body mass index (BMI), history of alcohol and smoking, duration of disease (defined as the time since ax-SpA diagnosis), family history of ax-SpA, current medications (i.e., non-steroidal anti-inflammation drugs [NSAIDs], proton pump inhibitors [PPIs], sulfasalazine, anti-TNF, anti-IL-17, and anti-osteoporotic agents [anti-OP]) were recorded.

In the present study, patient global assessment [PGA], the Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] in Thai version (23), the Ankylosing Spondylitis Disease Activity Score [ASDAS-CRP or ASDAS-ESR if high sensitivity C-reactive protein (hs-CRP) was not available], the Bath Ankylosing Spondylitis Functional Index [BASFI] in Thai version (23), and the Bath Ankylosing Spondylitis Metrology Index [BASMI] were used to assess disease activity (24).

Statistical analysis

Statistical analysis included computing the percentage frequencies for categorical variables and means (standard deviation, SD) or medians (interquartile ranges, IQR) for continuous variables. Comparisons of categorical variables were made using the chi-squared or Fisher's exact test, as appropriate. Continuous variables were tested for normality using a Shapiro–Wilk test and were compared using Student's *t*-test and one-way ANOVA or the Mann-Whitney U test and the Kruskal-Wallis test to compare two and three groups means, respectively. Medians with IQR were used for non-normally distributed variables. Univariate and multiple logistic regression analyses were used to determine the relevant risk factors for

low TBS. Only risk factors that had univariate associations of P -values <0.20 were further considered in subsequent multivariate models. Lack of collinearity was confirmed by testing variance inflation factors. P -values <0.05 were considered statistically significant. All statistical analyses were performed using SPSS software (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY: IBM Corp.).

Results

As shown in Table 1, the study population recruited 137 ax-SpA patients (115 from Phramongkutklo Hospital and 22 from Khon Kaen University Hospital) and 137 matched healthy controls. Most participants were male (75.9%), and 34.3% of women were menopause. The mean (SD) of age and mean duration of disease were 42.8 (12.0) years and 86.8 (96.9) months, respectively. HLA-B27 was found in 88.3%, whereas the family history of ax-SpA was found in only 13.1%. Patients with ax-SpA had concomitant anterior uveitis and psoriasis (5.8% and 1.5%, respectively). In ax-SpA patients, alcohol consumption who used greater than or equal to 3 units/day was found in 19.7%, whereas patients with smoking including ex-smoker were found in 35.8%.

The mean LS-BMD was significantly higher in ax-SpA patients compared with the controls. In contrast, the mean FN-BMD was significantly lower in ax-SpA patients than in the controls. There was no significant difference in TH-BMD between the two groups. The mean TBS was significantly lower in patients with ax-SpA compared with controls. The prevalence of degraded bone/low TBS in the ax-SpA patients was also significantly higher than that in the controls (7.35% vs 1.46%, $p=0.010$). The prevalence of low BMD/osteoporosis at TH was significantly higher in ax-SpA patients than that in the controls, but it was not significantly different between ax-SpA patients and the controls at LS and FN (Table 1).

As depicted in Table 2, ax-SpA patients with degraded bone/low TBS group had higher CRP level, disease activity scores (including PGA, BASDAI, BASFI, BASMI, and ASDAS), and prevalence of grade 4 sacroiliitis and current NSAIDs use than those in normal and high TBS groups. In addition, ax-SpA patients with degraded bone/low TBS group had a significantly shorter disease duration when compared with other groups. We found that patients with ax-SpA who had never received anti-TNF or anti-OP medication had lower TBS than patients who had received those medications. ($p=0.037$ and $p=0.028$, respectively). Furthermore, ax-SpA patients with degraded bone/low TBS group had significantly lower BMD at LS, FN, and TH than those with intermediate/ normal TBS groups. The radiographic VFs were found in 10 patients (7.5%, 10/134). The prevalence of VFs was significantly higher in patients with degraded bone/low TBS group as compared with patients with intermediate and normal TBS groups (30.0% vs 6.67% vs 5.5%, $p=0.019$, respectively).

Factors associated with trabecular bone score

In the univariate linear regression, ex- or current smoker, alcohol intake ≥ 3 units/day, BMI, current NSAIDs use, all parameters of disease activity, presence of syndesmophyte, and grade 4 sacroiliitis were associated with low TBS. In multivariate linear regression analysis, TBS was negatively associated with

female gender, ex- or current smoker, alcohol intake ≥ 3 units/day, ASDAS, and grade 4 sacroiliitis, whereas BMI was positively associated with TBS.

The univariate logistic regression model showed that higher disease severity measurement including PGA, ESR, hsCRP, BASDAI, BASMI, BASFI, ASDAS, grade 4 sacroiliitis and the presence of syndesmophyte, alcohol intake ≥ 3 units/day, shorter disease duration, and PPI uses were significantly associated with degraded bone/low TBS. The ASDAS and grade 4 sacroiliitis were respectively selected to represent current disease severity and damage in multivariate models. In multivariate logistic regression, ASDAS, and grade 4 sacroiliitis were independently associated with degraded bone/low TBS with the adjusted odds ratios (confidence interval: CI) of 5.228 (1.611-16.963) and 11.820 (1.211-115.412), respectively. Short disease duration was also found to be associated with degraded bone/low TBS; however, the association was modest with an adjusted odds ratio (CI) of 0.982 (0.966-0.998), (Table 3).

VFs were found in 10 patients in this study (7.5%). The prevalence of VFs was significantly higher in degraded bone/low TBS group than in intermediate and normal TBS groups (30.0% vs 6.67% vs 5.50%, $p=0.019$, respectively), (Figure 1). For identifying patients with VFs, the sensitivity (95%CI) and specificity (95%CI) of degraded bone/low TBS were 30% (6.67% to 65.25%) and 94.35% (88.71% to 97.70%), whereas the sensitivity (95%CI) and specificity (95%CI) of osteoporosis/low bone mass at LS-BMD and FN-BMD were 10.0% (0.25%-44.50%) and 94.4% (88.8%-97.72%) and 16.67% (0.42%-64.12%) and 92.56% (86.35%-96.54%), respectively.

Combining the results from TBS and BMD, ax-SpA patients who had both degraded bone/low TBS and osteoporosis/low bone mass at the femoral neck or total hip were at the highest risk of having VFs as compared to patients with normal TBS and FN-BMD group with the OR (95%CI) of 15.8 (0.88-285.48), $p=0.061$ for both femoral and total hip site. In contrast, ax-SpA patients that had normal BMD and degraded bone/low TBS at the lumbar spine had increased risk of VFs as compared with those with normal BMD and normal TBS at the same site with the OR (95%CI) of 11.3 (1.58-81.23), $p=0.016$, (Figure 2).

Discussion

In this study, patients with ax-SpA had significantly lower TBS values than sex-age matched controls. The prevalence of degraded bone/low TBS was higher in ax-SpA patients when compared with healthy controls. VFs were common in patients with degraded bone/low TBS group than in patients with intermediate and normal groups. Female gender, smoker status, alcohol intake greater than or equal to 3 units/day, shorter disease duration, elevated hs-CRP, higher disease activities, current NSAIDs use, and not receiving anti-TNF or anti-OP drugs were all significantly associated with lower TBS in patients with ax-SpA.

The findings from this study were consistent with previous studies (25-28). High disease activity related to inflammation and new bone formation, impaired function, and spinal mobility as assessed by BASFI and BASMI were found to be associated with low TBS in ax-SpA patients. These findings were supported

by an MRI study of the spine, which revealed that local inflammation, known as bone marrow edema, was detected in trabecular bone regions (29) as well as the presence of new bone formation on plain films, such as fusion of sacroiliac joints and syndesmophytes, were associated with low TBS in ax-SpA patients (30-32).

A meta-analysis of seven longitudinal studies and one randomized control trial reported that the anti-TNF treatment increased LS-BMD in AS patients by 5.1% and 8.6% after 1 and 2 years, respectively (35). Another prospective study in 12 AS patients found that, despite a significant increase in LS-BMD, there was no significant improvement in TBS after two years of anti-TNF treatment (33). Our study found that ax-SpA patients who did not receive anti-TNF treatment had lower TBS than those who did, and that low TBS was associated with high disease activity. These findings emphasized the significance of controlling disease activity with anti-TNF agents or other agents, as it could improve bone quality (TBS) and bone mass (LS-BMD) in ax-SpA patients.

In this study, alcohol and smoking were associated with degraded bone/low TBS in ax-SpA patients. Several studies in postmenopausal women found that alcohol consumption and smoking were strongly associated with low BMD (34, 35); however, these associations had not previously been reported in ax-SpA patients (27, 28). Furthermore, those risk factors have been linked to increased radiographic progression in patients with ax-SpA (36, 37). As a result, physicians should encourage ax-SpA patients to discontinue the modified risk factors.

We found that shorter disease duration was independently associated with degraded bone/low TBS; however, the association was modest. This finding supported the Danish Health Registries' findings that patients with AS had an increased risk of clinical vertebral and non-vertebral fractures, with the highest risk occurring within the first 2.5 years after diagnosis (38). In addition, previous studies demonstrated that a decrease in LS-BMD was associated with active inflammatory lesions at the lumbar spine and sacroiliac joints in early AS patients (39, 40), and the 2-year follow-up of the DESIR cohort also showed that the prevalence of low BMD at the lumbar spine was 22.4% in patients with early ax-SpA (41). As a result, appropriate bone health assessment should be performed as part of an initial treatment plan in ax-SpA patients.

Ax-SpA patients with degraded/low TBS groups had a higher prevalence of VFs and a higher risk of developing new VFs when compared to those with normal or intermediate TBS groups (27, 28, 42-44). Degraded bone/low TBS had higher sensitivity than FN-BMD and LS-BMD for detecting VFs in ax-SpA patients without losing specificity. Although the 2019 ACR recommendations suggested patients with ax-SpA should be screened for osteoporosis with DXA scan of the spine and hip (13), the results of previous studies together with findings from our study suggested TBS provided additional benefit for vertebral fracture assessment than LS-BMD and FN-BMD alone since vertebral fractures in ax-SpA patients from this study occurred at a normal BMD.

The clinical application of TBS for fracture risk assessment in patients with ax-SpA is not well established. TBS could be used in two ways to assess fracture risk in ax-SpA patients. First, degraded

bone/low TBS level could be First, degraded bone/low TBS level could be a tool for fracture risk assessment in AS patients. The cut-off for degraded bone/low TBS used in this study was derived from a meta-analysis of 14 prospective population-based cohorts from the countries around the world examining TBS in fracture risk prediction (20). However, it is unclear whether this threshold could be used in ax-SpA patients of any ethnicity since ethnicity affected the fracture predictive ability of TBS(45).

Secondly, the value of TBS could be incorporated in FRAX (fracture assessment tool) along with clinical risk factors and FN-BMD. Further research into the clinical use of FRAX and TBS is needed to determine the appropriate adjustment to assess fracture risk in ax-SpA patients.

There were some limitations in this study. First, this study did not examine some other risk factors for osteoporosis such as vitamin D level, serum calcium, and iPTH. Second, there were limited numbers of patients with low TBS and VFs and only few patients had other major osteoporotic fractures. Third, a cross-sectional study, our data might not represent overall disease activities in patients with ax-SpA, although the results showed that all parameters of disease activity were consistent with the severity of the disease. Furthermore, a few patients were menopause or had already received anti-osteoporotic treatment; however, after excluding post-menopausal status or anti-osteoporotic treatment, results were indifferent.

Conclusion

Patients with ax-SpA patients have lower TBS than controls. The proportion of ax-SpA patients with degraded bone/low TBS was higher than the proportion of controls. TBS was found to be independently associated with gender, former or current smoker, ≥ 3 units/day alcohol consumption, low BMI, high disease activity including PGA, BASDAI, BASFI, BASMI, and ASDAS, and fusion of sacroiliac joints. Therefore, TBS is a good non-invasive tool for assessing fracture risk in ax-SpA patients. TBS can be used alone or in conjunction with BMD measurement to identify ax-SpA patients at high risk for vertebral fractures.

Abbreviations

Axial spondyloarthritis (ax-SpA)

Sacroiliac (SI)

Interleukin (IL)

Tumor necrosis factor- α (TNF- α)

Receptor activator of nuclear factor kappa-B ligand (RANKL)

Bone morphogenetic protein (BMP)

Bone mineral density (BMD)

Vertebral fractures (VFs)

C-Reactive Protein (CRP)

Dual-energy X-ray absorptiometry (DXA)

The American College of Rheumatology (ACR)

Lumbar spine (LS)

Femoral neck (FN)

Total hip (TH)

Vertebral fracture assessment (VFA)

Body mass index (BMI)

Non-steroidal anti-inflammation drugs (NSAIDs)

Proton pump inhibitors (PPIs)

Patient global assessment (PGA)

The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)

The Ankylosing Spondylitis Disease Activity Score

The Bath Ankylosing Spondylitis Functional Index (BASFI)

The Bath Ankylosing Spondylitis Metrology Index (BASMI)

Confidence interval (CI)

Declarations

Ethics approval and consent to participate

The ethical approval was approved by the Institutional Review Board: Royal Thai Army Medical Department and the Human Research Ethics Committee of Khon Kaen University. The reference numbers are R178h/62 and HE631141, respectively.

Consent for publication

All authors consent for the publication and grant the publisher exclusive license of the full copyright.

Competing interests

The authors declare that they have no competing interests.

Availability of data and materials

The data that support the findings of this study are available on reasonable request from the corresponding author.

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Author contributions

PS and SC were involved in the conception of the study, performed the analyses, drafted the manuscript, and revised the manuscript. PS and AM collected data of ax-SpA patients from Phramongkutklao and Khon Kaen University hospitals, respectively. CP provided data of healthy controls and revised manuscript. The other authors assisted in interpretation of the results from the analyses and drafting the manuscript. All authors have read and approved the final manuscript and ensured that this is the case.

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Tables

Table 1 Clinical characteristics of controls and ax-SpA patients

Variable	Control (n=137)	Ax-SpA (n=137)	P-value
Age, mean (SD), years	42.80 (12.04)	42.80 (12.04)	1.000
Male, n (%)	104 (75.91)	104 (75.91)	1.000
BMI, mean (SD), kg/m ²	22.79 (3.27)	23.91 (4.95)	0.156
Bone mineral density (BMD)			
Lumbar spine: mean (SD), n=137	1.0868 (0.1238)	1.1862 (0.2123)	<0.001*
Femoral neck: mean (SD), n=128	0.9042 (0.1546)	0.8670 (0.1358)	0.038*
Total hip: mean (SD), n=128	0.9487 (0.1470)	0.9192 (0.1601)	0.119
Low BMD [§] / osteoporosis: any site, n (%)	6 (4.4)	13 (9.6)	0.093
Lumbar spine	5 (3.6)	8 (5.8)	0.394
Femoral neck	3 (2.2)	5 (3.9)	0.421
Total hip	1 (0.7)	7 (5.5)	0.024*
TBS values, n (%)			
• TBS < 1.23	2 (1.46)	10 (7.35)	0.010*
• TBS 1.23-1.31	8 (5.84)	16 (11.76)	
• TBS > 1.31	127 (92.70)	110 (80.88)	
TBS: mean (SD), n=136	1.4399 (0.0861)	1.4021 (0.1067)	0.002*

[§]Included individuals with Z score below -2.0. *p<0.05. Ax-SpA: axial spondyloarthritis.

Table 2 Characteristics of patients with ax-SpA, stratified by TBS group.

Variable	Degraded bone/ Low TBS (TBS < 1.23, n=10)	Partially degraded bone/ Intermediate TBS (TBS= 1.23-1.31, n=16)	Normal bone/ Normal TBS (TBS>1.31, n=110)	P-value
Age, mean (S.D.), years	38.4 (15.3)	48.7 (15.81)	42.4 (10.9)	0.072
Male, n (%)	6 (60.0)	12 (75.0)	85 (77.3)	0.474
BMI, mean (S.D.), kg/m ²	23.2 (1.7)	22.9 (4.1)	23.92 (4.9)	0.668
Alcohol intake ≥ 3 unit/day, n (%)	4 (40.0)	2 (12.5)	21 (19.1)	0.209
Ex- or current smoker, n (%)	4 (40.0)	10 (62.5)	35 (31.8)	0.056
Post-menopause, n (%)	1 (8.3)	1 (8.3)	10 (83.3)	0.924
Laboratory findings				
ESR, mean (S.D.), mm/h, n=126	42.6 (27.2)	30.7 (21.3)	25.8 (23.2)	0.105
CRP, mean (S.D.), mg/l, n=119	54.3 (29.2)	14.9 (21.7)	15.5 (26.1)	0.001 §, †
Disease-related data				
Duration of disease, mean (S.D.), months	28.4 (50.2)	116.4 (118.7)	86.7 (94.8)	0.008 §, †
PGA, mean (S.D.)	58.0 (23.0)	32.81 (23.8)	32.9 (25.3)	0.011 §, †
BASDAI score, mean (S.D.)	4.9 (1.1)	3.2 (2.3)	2.8 (2.2)	0.011 †
BASFI score, mean (S.D.)	3.8 (2.2)	2.8 (2.0)	2.2 (2.4)	0.024 †
BASMI score, mean (S.D.)	5.3 (1.5)	4.8 (2.1)	3.6 (2.2)	0.003 †, ¶
ASDAS, mean (S.D.)	4.1 (0.7)	2.5 (1.1)	2.4 (1.1)	<0.001 §, †
Grade 4 sacroiliitis, n (%)	9 (90.0)	9 (56.3)	35 (32.1)	0.001 †
Presence of syndesmophytes, n (%)	8 (80.0)	12 (75.0)	58 (53.7)	0.095
Medications				
Current glucocorticoid use, n (%)	1 (7.1)	0	13 (92.9)	0.348

Current NSAIDs use, n (%)	10 (100.0)	9 (56.3)	46 (41.8)	0.002 §, †
Current PPIs use, n (%)	6 (60.0)	6 (37.5)	38 (34.6)	0.278
Current sulfasalazine use, n (%)	5 (50.0)	10 (62.5)	62 (56.4)	0.816
Current anti-TNF use	0	6 (37.5)	18 (16.36)	0.037 §, ¶
Current anti-IL-17 use	0	1 (6.3)	1 (0.9)	0.233
Current anti-OP use	0	3 (18.8)	4 (3.6)	0.028 ¶
Bone mineral density (BMD)				
Lumbar spine: mean (SD), n=136	0.9417 (0.1564)	1.1282 (0.1960)	1.2114 (0.1991)	<0.001 †
Femoral neck: mean (SD), n=128	0.7640 (0.7677)	0.7381 (0.1720)	0.8967 (0.1242)	<0.001 †, ¶
Total hip: mean (SD), n=128	0.7804 (0.0966)	0.7950 (0.1801)	0.9518 (0.1523)	<0.001 †, ¶
Low BMD [§] / osteoporosis				
Lumbar spine	5 (50.0)	2 (12.5)	1 (0.9)	<0.001*
Femoral neck	2 (20.00)	2 (14.3)	2 (1.9)	0.007 †, ¶
Total hip	2 (20.00)	2 (14.3)	3 (2.9)	0.022 †, ¶
Vertebral fractures [#] , n=134	3 (30.0)	1 (6.7)	6 (5.5)	0.019 †

*Statistically significant compared within 3 groups (degraded bone group, partially degraded bone group, and normal bone group).

†Statistically significant compared degraded bone group with normal bone group.

§Included individuals with Z score below -2.0.

[#]Not included 3 cases in whom the radiologist could not interpret VFs due to artifact.

§Statistically significant compared degraded bone group with partially degraded bone group.

¶Statistically significant compared partially degraded bone group with normal bone group.

Ax-SpA: axial spondyloarthritis

TBS: trabecular bone score

Table 3 Linear regression for TBS and logistic regression for degraded bone/low TBS in patients with ax-SpA

Variable	Linear regression		Logistic regression (n=131)	
	Univariate model β (95%CI)	Multivariate model† (n=127) β (95%CI)	Univariate model OR (95% CI)	Multivariate model Adjusted OR‡ (95%CI)
Demographic				
Age, years	0 (-0.002, 0.001)		0.962 (0.905-1.024)	
Gender, female	-0.028 (-0.070, 0.014) #	-0.052 (-0.093, -0.011) *	2.23 (0.589 – 8.443)	
Ex- or current smoker	-0.042 (-0.080, -0.005) *	-0.054 (-0.090, -0.017) *	1.200 (0.322-4.477)	
Alcohol intake $\geq$ 3 units/day	-0.057 (-0.102, -0.013) *	-0.059 (-0.102, -0.016) *	2.986 (0.779-11.441) #	
BMI, kg/m ²	0.005 (0.001, 0.009) *	0.006 (0.002, 0.010) *	0.971 (0.835-1.128)	
Duration of disease	-0.000023(-0.000-0.000)		0.986 (0.971-1.002) #	0.982 (0.966-0.998)
HLA B27-positive	0.008 (-0.056, 0.072)		0.506 (0.051-4.990)	
Medication				
Current NSAIDs use	-0.058 (-0.093, -0.023) *		-.§	
Current PPIs use	-0.028 (-0.065, 0.010) #		2.795 (0.749-10.434) #	
Current SSZ use	-0.001 (-0.037, 0.036)		0.750 (0.207-2.721)	
Current IL-17 inhibitor	-0.112 (-0.262, 0.037)		-.§	
Current TNF inhibitor	0.001 (-0.047, 0.048)		-.§	
Disease severity assessment				
PGA	-0.001 (-0.002, 0.000) *		1.037 (1.010-1.064) *	
ESR, mm/h	-0.001 (-0.002, 0.000) *		1.024 (0.999-1.050) #	

CRP, mg/l	-0.001 (-0.002, 0.000) *		1.028 (1.009-1.047) *	
BASDAI	-0.012 (-0.021, -0.004) *		1.485 (1.113-1.982) *	
BASMI	-0.015 (-0.023, -0.007) *		1.326 (1.008-1.744) *	
BASFI	-0.010 (-0.018, -0.003) *		1.234 (0.981-1.552) #	
ASDAS	-0.035 (-0.050, -0.020) *	-0.025 (-0.040, -0.010) *	5.018 (2.145-11.737) *	5.228 (1.611-16.963)
Grade 4 sacroiliitis	-0.064 (-0.100, -0.029) *	-0.046 (-0.082, -0.011) *	16.568 (2.032-135.074) *	11.820 (1.211-115.412)
Syndesmophyte	-0.054 (-0.090, -0.018) *		3.086 (0.629-15.126) #	
Adjusted R ²		0.297	Nagelkerke R square	0.574

*p<0.05. #p<0.20.

†Adjusted for gender, ex- or current smoker, alcohol intake ≥ 3 units/day, BMI, current NSADIs use, current PPIs use, Hb, BASDAI, BASMI, BASFI, ASDAS, grade 4 sacroiliitis, presence of syndesmophyte.

‡Adjusted for alcohol intake ≥ 3 units/day, duration of disease, current PPIs use, BASDAI, BASMI, BASFI, ASDAS, grade 4 sacroiliitis, syndesmophyte.

§Statistical analyses cannot be performed due to zero in the one TBS group.

Figures

Figure 1

The prevalence of vertebral fractures (VFs)[§], stratified by low bone mineral density (BMD) or osteoporosis (OP) in the at lumbar spine (LS), total hip (TH) and femoral neck (FN), and TBS risks[#] in patients with ax-SpA.

[§]Not included 2 cases in whom the radiologist could not interpret vertebral fractures due to artifact.

[#]One patient whose TBS could be not analyzed data due to morbid obesity was excluded. *p<0.05, compared with normal TBS group.

Figure 2

The prevalence of vertebral fractures, stratified by trabecular bone score (TBS) and osteoporosis/low BMD by DXA

*Statistically significant compared with patients with ax-SpA with normal BMD and normal TBS

Values in the middle of each bar are odd ratios compared with normal TBS and normal BMD at the lumbar spine, total hip, and femoral neck in patients with ax-SpA.