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Utility of DXA scanning and risk factors for osteoporosis in ankylosing spondylitis—A prospective study☆

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ABSTRACT

Background: Conventional DXA imaging of spine and hip to measure bone mineral density (BMD) has limitations in patients with ankylosing spondylitis (AS). We investigated the correlation of hip and spine BMD measurements in patients with AS to determine if hip DXA will prove clinically useful while avoiding the confounding effect of spinal disease. Also, we studied risk factors for osteoporosis (OP) and osteopenia in AS.

Methods: We randomly identified patients from our validated AS registry ≥ 18 years of age who met the Modified New York Classification criteria for AS. BMD was measured and interpreted using ISCD 2007 guidelines and diagnosis of OP was based on WHO criteria. ESR, CRP, urinary N-telopeptide, and 25-hydroxy vitamin D were also measured. Correlation between the BMD (total hip and/or femoral neck) and lumbar spine was calculated. Statistical comparisons between the 2 sites, lumbar spine (AP) and hip (total hip and or femoral neck) were made using Bowker's test for symmetry and kappa statistics. Chi-square and odds ratio using logistic regression were used to assess the association of the purported risk factors for OP in these patients.

Results: Frequency of OP among AS patients ≥ 50 years of age was 23%, and that of osteopenia was 41%. Among patients < 50 years of age, the frequency of low bone mass for expected age (Z-score ≤ -2.0) was 14.7%. There was moderate correlation ($\rho = 0.59$) and a fair agreement ($\kappa = 0.26$; 95% CI: 0.10–0.42) between the lowest T-values of hip and lumbar spine (AP view). OP was significantly associated with elevated CRP level [OR = 4.2 (95% CI: 1.13–15.9), $p < 0.03$] and African American race [OR = 7.2 (95% CI: 1.18–44.99), $p < 0.03$].

Conclusion: Our results demonstrated a moderate correlation and fair agreement between the T-scores of hip and the lumbar spine (AP view) in patients with AS, suggesting that DXA of the hip and the lumbar spine (AP view) may both be useful for OP and osteopenia screening in patients with AS without fused spines. We confirm the previous reports of an association of elevated CRP level with an increased risk of OP in patients with AS, but this is the first study to demonstrate that African American patients with AS may be at a higher risk of developing OP compared to Caucasians.

Introduction

Ankylosing spondylitis (AS) is a chronic inflammatory arthritis with increased risk of vertebral compression fractures. Osteoporosis (OP) is a well-recognized complication of AS even in the early stages of the disease [1–8] and increases the fracture risk substantially [9–16]. In patients with vertebral OP and a fused spine, relatively minor physical trauma can lead to spinal fracture and any associated dislocation can result in spinal cord compression with resultant paraplegia or quadriplegia. Early recognition of OP followed by timely and effective treatment and along with prevention of physical trauma may reduce the fracture risk in patients with AS. However, this needs to be confirmed.

Dual X-ray absorptiometry (DXA) is a cost-effective, standardized, and easily available test for OP screening. It has become the gold standard for assessing bone mineral density (BMD) in clinical practice. However, this method has some limitations in patients with AS, particularly related to projection; spinal DXA measurements in anteroposterior (AP) projection are not reliable and may give falsely elevated results due to syndesmophyte formation and ligament ossification. Several studies have confirmed that BMD at the spine in patients with AS is decreased in

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early disease and falsely increased with advanced disease [17,18]. Hence, alternative imaging techniques or sites are needed for measuring BMD in patients with advanced AS.

Femoral neck BMD is also reduced in patients with AS, both with early and advanced disease and correlates with increased risk of vertebral fractures [9,19,20]. BMD has been shown to fall at 2 years at the femoral neck (but not spine) and was proportional to the degree of inflammation [21]. Hence, measurement of hip BMD (total hip or femoral neck) may be the most accurate means of detecting osteopenia or OP in patients with AS.

The aims of our study were (i) to determine the concordance of the hip (total hip or femoral neck) and AP lumbar spine BMD measurements in patients with AS, (ii) to study the risk factors of OP in patients with AS.

Methods

Subjects were randomly identified from our validated AS registry at MetroHealth Medical Center (MHMC) and recruited for the study if >18 years of age and met the Modified New York Classification Criteria of AS [22]. The registry includes 250 subjects with AS, one-third of the subjects are African Americans. About 75–100 of these patients are actively followed at MHMC.

Subjects with (i) thyroid or parathyroid disorders, chronic liver or kidney disease, or use of anti-convulsants medications as they increase the risk of OP, (ii) with bilateral total hip arthroplasties, (iii) completely fused lumbar spines were excluded from the study. The study was approved by our Institutional Review Board.

Informed consent was obtained and subjects were prospectively recruited over a period of 18 months till our sample size of 100 patients was reached.

Data collection

Patient were examined in the Clinical Research unit by either the Principal Investigator (PI) or the Co-PI. Disease activity at baseline was assessed with a validated patient-reported index, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). The following variables were collected: age, gender, duration of disease, HLA-B27 status, current smoking status, and use of non-steroidal anti-inflammatory medications and glucocorticoids ≥ 5 mg for more than 3 months. History of previous fragility fractures and family history of OP and fractures was also obtained. All this information was captured using a questionnaire and entered into RedCap database.

Radiographs and DXA scanning

BMD of the lumbar spine in the AP projection (L1–L4), the hip (femoral neck and total hip) were measured using a DXA scanner (Hologic Discovery). DXA images were reviewed by the PI who was certified by International Society of Clinical Densitometry (ISCD) in reading DXA scans. For patients aged 50 years or older the following World Health Organization (WHO) definitions of osteopenia and osteoporosis were used: osteopenia = T-score < -1 to > -2.5 SD (compared to the young normal mean), and osteoporosis = T-score ≤ -2.5 SD. The lowest value of BMD measured in the AP lumbar spine (L1–L4), or total hip or femoral neck was used [23] for detecting the frequency of OP. For patients under the age of 50 a Z-score ≤ -2.0 SD (compared to the age-matched mean) was considered to be below the expected range for age [24].

Patients had a baseline radiograph of lumbar spine in 2 planes (AP and lateral) to assess the presence of definite syndesmophytes in case radiographs were not available in existing medical records or the radiographs were more than 5 years old. The radiograph was done on the same day as the DXA scan. The radiographs were reviewed by the investigators and an independent radiologist. The modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS), a four-point scoring system for lateral radiographs of the lumbar spine was performed. A total score was obtained by multiplying the mean score of all scored sites by 12 (highest possible score of 36).

Laboratory measurements

Erythrocytic sedimentation rate (ESR) and serum concentration of C-reactive protein (CRP), alkaline phosphatase, parathyroid hormone (PTH), 25-hydroxyl vitamin D level, and urinary N-telopeptide (NTX) were measured in the hospital laboratory by established methods.

Stastistical analysis

Descriptive analysis included continuous variables (the mean $\pm$ SD) and the categorical variables percentage. Data were compared by Student's t-test and Mann–Whitney test for continuous variables. Coding for categorical variables was yes = 1, no = 2, and data missing = 3. Association between OP diagnosis and categorical variables was assessed using Chi-square test. Correlations between BMD at different sites were derived using Spearman's correlation coefficients (rs). Statistical comparisons between the 2 sites, lumbar spine (AP), and hip (total hip or femoral neck) were made using Bowker's test for symmetry and kappa statistics.

Multivariate logistic regression models were adopted to identify risk factors for OP in AS. Results of the regression models are shown as the odds ratio (OD) and 95% CI. In all the statistical tests the level of significance was set at 5% ($p < 0.05$). SAS software was used for statistical analysis.

Results

A total of, 101 patients met the inclusion criteria and completed the study with 39 patients >50 years of age. Demographics and clinical characteristics of these patients are shown in Table 1. No significant differences were found in demographic, disease duration, BASDAI scores, or health status of patients with OP,

Table 1
Demographics and baseline characteristics of the patients

	Patients with OP and osteopenia or low bone mass (T-score < -1 or Z-score < -2) ($n = 54$)	Patients with normal BMD (T-score > -1) ($n = 47$)	p
Age in years $\pm$ SD	47.8 $\pm$ 14.43	43.09 $\pm$ 13.70	0.08
% males	79.63	65.96	0.12
% African Americans	26.42	25.53	0.92
% Disease duration >5 years	85.19	80.85	0.56
% Smokers	62.96	65.96	0.75
% HLA-B27 positivity	54.55	65.00	0.33
Mean BASDAI	5.42 $\pm$ 2.43	5.57 $\pm$ 2.64	0.81
25-hydroxyl vitamin D	30.28 $\pm$ 24.49	28.85 $\pm$ 16.50	0.67
Mean ESR in mm/h	20.96 $\pm$ 25.84	16.43 $\pm$ 15.81	0.95
Mean CRP in mg/dl	1.44 $\pm$ 2.57	0.79 $\pm$ 0.72	0.02