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Original Article

Association between mean platelet volume and bone mineral density in patients with ankylosing spondylitis and diagnostic value of diffusion-weighted magnetic resonance imaging

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Abstract. [Purpose] The aim this study was to assess the relation between bone mineral density (BMD) and mean platelet volume (MPV) in ankylosing spondylitis (AS) patients, and evaluate the diagnostic role of the diffusion-weighted magnetic resonance imaging (MRI). [Subjects and Methods] Fifty patients diagnosed with AS were divided into two groups on the basis of BMD, a normal group (n=30) and an osteopenic (n=20) group. [Results] Duration of disease in the group with a normal BMD was 10.3±7.0 years, while it was 16.7±12.2 years in the osteopenia group. MPV was high in the osteopenia group, while no significant differences were observed between the groups in terms of apparent diffusion coefficient (ADC) and platelet distribution width (PDW). There was a positive correlation between MPV and duration of disease. Correlations between ADC value and the lumbar T score, femoral neck T score, and duration of disease were insignificant. A negative correlation was observed between BMD and disease duration. [Conclusion] Diffusion-weighted imaging provides valuable results in osteoporosis but is not a suitable technique for evaluating BMD in patients with AS because of the local and systemic inflammatory effects in the musculoskeletal system. The common pathophysiology of atherosclerosis and osteoporosis plays an important role in the negative correlation observed between MPV and BMD in patients with AS.
Key words: Ankylosing spondylitis, Bone mineral density, Mean platelet volume

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INTRODUCTION

Ankylosing spondylitis (AS) is an inflammatory disease of uncertain etiology that particularly affects the axial skeleton[1)]. Although new bone formation and ligament calcification are more prominent in AS, demineralization due to osteoporosis-related vertebral fractures is also important[2)]. The incidence of osteopenia or osteoporosis in these patients is reported to be 19–62%[3)]. Genetic factors, inflammatory cytokines, immobilization, drugs used, hormonal disturbances, and changes in calcium metabolism in AS constitute risk factors for osteoporosis. Deviation of mechanical stresses away from vertebral bodies due to syndesmophytes and bridges has also been implicated[4)]. Bone loss is particularly high in conditions in which inflammation cannot be prevented and the duration of disease is prolonged[5)]. The most widely used imaging technique in the evaluation of bone mineral density (BMD) is dual energy X-ray absorptiometry (DEXA). A limited number of studies have recently been performed to investigate the effectiveness of diffusion-weighted MRI (DWI) in the evaluation of BMD. Two previous studies have also assessed the relation between BMD and mean platelet volume (MPV). However, these studies have generally either been performed with postmenopausal women or else have excluded systemic and rheumatological diseases[6)]. The purpose of this study was to determine the relation between BMD and MPV and the diagnostic value of DWI in AS, which exhibits local and systemic inflammatory effects in the musculoskeletal system in addition to systemic effects.

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SUBJECTS AND METHODS

Fifty patients attending the Canakkale Onsekiz Mart University Medical Faculty Physical Medicine and Rehabilitation Department, Turkey, who had been diagnosed with AS on the basis of ASAS diagnostic criteria were included in the study. Written informed consent was obtained from each patient. Laboratory results were obtained from patients' records, and MR images (n=37) and DEXA results (n=50) were obtained from the radiology archives. Patients with vertebral fracture, spinal tumor or spondylodiscitis in their histories or at imaging were excluded. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), MPV, triglyceride, urea, creatinine, and glucose levels, Bath Ankylosing Spondylitis Functional Index (BASFI), and Bath Ankylosing Spondylitis Activity index (BASDAI), showing disease activity, were determined. Calcium, phosphorus, and vitamin D levels associated with bone metabolism were obtained from patients' records. Body mass index (BMI) was calculated as weight divided by height squared (kg/m^2). Çanakkale Onsekiz Mart University Medical Faculty ethics committee approval was obtained.

BMD was measured using regularly calibrated dual-energy X-ray absorptiometry (DEXA, GE Prodigy Advance). BMD definitions in measurements from the lumbar vertebrae (L1-4, posteroanterior position) and femoral neck were based on World Health Organization T score definitions. Subjects with T scores better than −1.0 were regarded as normal, and those scoring between −1.0 and −2.5 were regarded as osteopenic. Only two patients had T scores lower than −2.5 (osteoporotic), and they were excluded from the study.

Patients enrolled in the study were assessed with a lumbar imaging protocol on a 1.5 Tesla MRI unit (Signa Excite; GE Medical Systems, Milwaukee, WI, USA). Section thickness was determined to be 4 mm for all sequences. The imaging protocol comprised a sagittal T1 weighted fast spin-echo sequence (500/15.2 ms, repetition time/echo time, TR/TE; number of excitations [NEX], 2.0; 320 × 192 matrix; 27 × 27 cm field of view [FOV]), sagittal T2 weighted fast spin-echo sequence (3000/111 ms, TR/TE; NEX, 2.0; 320 × 224 matrix; 27 × 27 cm FOV), axial T2 weighted fast spin-echo sequence (4600/90 ms, TR/TE; NEX, 2.0; 320 × 192 matrix; 20 × 20 cm FOV), and diffusion weighted imaging (3000/90 ms TR/TE; 128 × 128 matrix; 27 × 27 cm FOV). Apparent diffusion coefficient (ADC) values were measured on a GE workstation with FuncTool software. A coefficient of b=1,000 s/mm^2 was used at imaging. ADC measurements were performed with the region of interest (ROI) localized to the vertebra body in the sagittal plane.

Analysis of the data obtained was performed using the SPSS version 19.0 software. Descriptive data were expressed as mean, standard deviation, median, minimum, maximum, frequency, and percentage values. The χ^2 test was used to compare categoric variables between groups, and the Mann-Whitney U test was used to compare constant variables. Correlations between groups were assessed using Spearman's correlation test. P values below 0.05 were regarded as significant.

RESULTS

Fifty patients (age 43.46±12.18 years, 17 female and 33 male) diagnosed with AS were enrolled in the study and divided into two groups based on BMD. On the basis of data obtained from the femoral neck, 30 patients (41.07±9.35 years) were normal, and 20 (47.05±15.05 years) were osteopenic. The gender distribution was 11 women and 19 men among the patients with normal BMD and 6 women and 14 men among the patients with osteopenia. There was no difference between the two groups in terms of mean age or sex (p=0.215 and p=0.626, respectively). There was also no difference between the groups in terms of cigarette use (p=0.265). Differences between the groups in terms of total cholesterol, triglyceride, urea, blood glucose, ESR, calcium, and vitamin D levels were insignificant. Duration of disease was 10.30±7.00 years in the normal BMD group and 16.70±12.17 years in the osteopenia group (p=0.07). The mean femoral neck T score was 0.61±1.00 in the normal group and −1.60±0.51 in the osteopenia group (p<0.001). Demographic data and laboratory results for both groups are shown in Table 1.

Analysis of the entire patient group (n=50) revealed a negative correlation between BMD and duration of disease (r= −0.434, p= 0.002). Patient age exhibited a negative correlation with femoral neck T score, but no significant correlation was determined with lumbar T score (r= −0.287, p=0.043, and r=0.041, p=0.775, respectively).

MPV values were higher in the osteopenic patients compared with the normal patients (p=0.036). ADC and platelet distribution width (PDW) values, however, did not differ significantly between the two groups (p= 0.662, p=0.943, respectively). MPV was significantly correlated with age, duration of disease, and femoral neck T score (p=0.004, p=0.041, and p=0.014, respectively). Analysis of correlation between parameters in the entire patient group revealed no significant correlation between ADC value and the lumbar T score, femoral neck T score, and duration of disease (p=0.844, p=0.528, and p=0.248, respectively).

DISCUSSION

Osteopenia and osteoporosis are the most common complication in AS, and the prevalence increases with age and duration of disease[7]. Biochemical and mechanical factors are implicated in the development of osteopenia and osteoporosis in patients with AS[8]. Cytokines such as tumor necrosis factor-α (TNF-α), IL-1, and IL-6 are powerful osteoclast activator factors. One study reported higher serum IL-6 and TNF-α concentrations in patients with AS compared with patients with mechanical back pain[9].

Maillefert et al. investigated the role of side effects in physical restriction, the inflammatory process, and drug therapy in the development of osteoporosis in AS and emphasized that the inflammatory process contributed to loss of bone mass[10]. Genetic factors, immobilization, drugs used, changes in calcium metabolism, and hormonal balances have also been implicated[11]. In addition to osteopenia and osteoporosis, new bone formation or ligament calcifications lead to loss of flexibility in the vertebral column. The risk

Table 1. Demographic characteristics and laboratory values in the normal T-score and osteopenia groups

	Normal group	Osteopenia group
Patients	30	20
Mean age ± SD (years)	41.07 ± 9.3	47.05 ± 15.05
Cholesterol ± SD (mg/dl)	179.7 ± 31.7	190.4 ± 43.5
Tryglyceride ± SD (mg/dl)	112.8 ± 54.8	94 ± 34.7
Urea ± SD (mg/dl)	28.7 ± 9.4	32.5 ± 8.01
Glucose ± SD (mg/dl)	90.8 ± 8.65	90 ± 9.79
Sedimentation ± SD (mm/h)	21.27 ± 11.51	16.85 ± 10.71
Body Mass Index ± SD *	29.07 ± 6.4	26.23 ± 5.23
BASFI ± SD	3.19 ± 1.5	3.57 ± 1.73
BASDAI ± SD	2.83 ± 1.12	3.05 ± 1.31
MPV ± SD (fl) *	8.4 ± 0.81	9.08 ± 1.05
CRP ± SD (mg/dl)	1.07 ± 0.87	1.32 ± 1.72
DVIT ± SD (ng/ml)	26.52 ± 8.1	27.65 ± 7.7
Calcium ± SD (mg/dl)	9.44 ± 0.28	9.34 ± 0.42
ADC value ± SD (mm^2/s)	$0.36 \pm 0.08 \times 10^{-3}$	$0.38 \pm 0.12 \times 10^{-3}$

*Statistically significant at $p < 0.05$

of brittleness that increases with these changes makes it essential to determine the level of demineralization.

The most widely used imaging technique in the assessment of BMD is dual energy X-ray absorptiometry. However, factors such as osteophytes, hyperostosis, aortic calcification, soft tissue calcifications, scoliosis, vertebral fractures, and facet joint fusion may cause inaccurate measurements at the lumbar level. Due to these restricting factors in patients with AS, femoral neck BMD measurements are more favored. Two studies have shown that BMD decreases in both the femoral neck and vertebrae in patients with early stage AS, and that as the duration of the disease increases, BMD remains normal in the vertebrae but continues to decrease in the femoral neck[5, 8]. In this study, the femur neck T scores were lower compared with those in the vertebrae in the osteopenic patient group, which had a greater duration of disease, and this finding is compatible with the literature. (T scores= −1.60±0.51 and −0.91±1.00, respectively). The mean disease duration in our patients with osteopenia (16.70±12.17 years) was sufficient for syndesmophytes, facet fusion, and ankylosis to occur, and this difference in BMD was therefore an expected finding. There were no compression fractures in any of our patients. We think that the absence of bone loss at the level of osteoporosis and the fact that many of the patients were young males with day-to-day living activities were influential factors in this.

DWI, which is exceedingly sensitive to changes in water molecule motion and permits the assessment of tissue microstructure, has been used in the diagnosis of osteoporosis in recent years. Hatipoglu et al. showed that ADC values decreased in association with a decline in bone mass and demineralization[12]. Similarly, Yeung et al. reported lower ADC values in osteoporotic patients compared with normal cases[13]. There was no difference in ADC values between our normal and osteopenic groups ($0.36\pm0.08 \times 10^{-3}$ mm^2/s and $0.38\pm0.12 \times 10^{-3}$ mm^2/s, respectively). The increase in fatty bone marrow in osteopenia and osteoporosis causes a decrease in extracellular diffusion and finally a decrease in ADC values. The positive correlation determined in some studies between bone marrow cellularity and ADC supports this conclusion[14, 15]. The difference between the ADC values in this study and the literature is probably the result of accompanying local and systemic inflammation in addition to osteopenia in AS. The determination of high ADC values for sacroiliac joint faces by Bozgeyik et al. in a study of patients with spondyloarthropathy supports this interpretation[16]. Another factor that can affect ADC values is the inability to interpret the effect on ADC values of the physiological decrease in perfusion occurring secondary to fat accumulation in bone marrow[12].

Another important point established in this study is the relation between MPV and BMD. The MPV in the group with a normal BMD was 8.40±0.81 fl, while the MPV was 9.08±1.05 fl in the patients with osteopenia. Analysis of the entire patient group (n=50) revealed a negative correlation between MPV and femoral neck T score. Kısacık et al. showed that MPV values decreased in patients with active AS, but increased after treatment[17]. Kapsoritakis et al. reported that MPV decreased in active inflammatory bowel disease[18]. We think that the systemic effects of AS underlie the elevated MPV values in the patients with osteopenia in this study. The inflammatory effect in the active period of the disease was prominent in both these two studies. However, changes in calcium metabolism, atherosclerosis, immobilization, drugs use, hormonal changes, syndesmophyte formation, posture disturbances, and renal-cardiac pathologies also accompany inflammation in AS[4, 19]. Moreover, AS follows a progressive course, and osteopenia increases with age and duration of disease[19]. Bessant et al. implicated cytokines such TNF-α and IL-6 in the early stage of osteopenia and osteoporosis and low mobility in the late stage[20]. We think that atherosclerosis and osteopenia/osteoporosis hav-

ing similar pathophysiological processes may be involved. For example, inflammatory cytokines cause a decrease in osteoprotegerin (OPG), and this decrease results in osteoclast activation. OPG is produced by endothelial cells in the cardiovascular system and plays a protective role for the vascular system. Research has shown that when used in concentrations inhibiting bone resorption in rats, OPG also prevents vascular calcification[21, 22]. Sumino et al. investigated the relation between OPG and AS and showed an association between brachial artery endothelial dysfunction and arterial hardening with decreased BMD[23, 24].

Duration of disease being significantly correlated with both the femoral neck T score and MPV supports the possibility of progressive loss in bone tissue. The absence of any correlation between either BASFI or BASDAI and BMD was an expected finding. This is not surprising, since progressive loss of bone tissue is a time-dependent process, and the disease activity is variable[25].

In conclusion, DWI reflects the microstructure of tissue and provides valuable results in osteopenia and osteoporosis. However, it is not suitable for assessing BMD in patients with AS due to its local and systemic inflammatory effects. In addition to systemic effects, the common pathophysiology of atherosclerosis and osteoporosis plays an important role in the negative correlation observed between MPV and BMD in patients with AS.

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