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Original Article

Relationship between bone mineral density and duration of rheumatoid arthritis

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ABSTRACT

Background: Longer disease duration is believed to be associated with more pronounced bone loss in rheumatoid arthritis (RA). This study was designed to assess bone mineral density (BMD) status in RA compared with age-matched control in relation to disease duration.

Methods: This study included 177 RA and 283 age-matched non-RA controls. BMD at the femoral neck and lumbar spine was assessed by Dual Energy X-ray Absorptiometry Osteoporosis was diagnosed according to WHO criteria. We divided patients with RA into groups based on disease duration of <2, 2–5, 5–10, and >10 years and compared them with controls. The relationship between disease duration and BMD was investigated by chi square and Spearman test.

Results: Mean age of patients and control subjects was 51.2 ± 12.5 and 52.2 ± 6.7 years, respectively and mean disease duration was 86.5 ± 73.3 months. Osteoporosis at the femoral neck and lumbar spine in patients with RA was significantly higher than in controls. Femoral neck BMD in RA was negatively correlated with disease duration and 4.5% variations of femoral neck BMD was explained by disease duration ($r^2 = 0.045$, $P = 0.005$). Odds Ratio (OR) for osteoporosis in RA patients as compared to controls was increased by prolongation of disease duration from 2.38 (0.38–14.7) in patients with disease duration <2 years to 12.56 (2.24–70.2) in patients with disease duration >10 years. For patients treated with methotrexate compared to those who had never received methotrexate the odds ratio for femoral neck osteoporosis reduced by 64% (OR = 0.36, 95% CI, 0.15–0.91).

Conclusion: There is a significant negative relationship between femoral neck BMD and disease duration in RA. The value of OR increases proportionately with lengthening of disease duration which can be reduced significantly by methotrexate therapy.

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1. Introduction

Local and systemic inflammation in rheumatoid arthritis (RA) leads to bone loss, osteoporosis (OP) and enhanced risk of bone fractures.[1,2] Inflammation alters biomechanical properties of bone by targeted action of pro-inflammatory cytokines, estrogens and other hormone-mediated pathways.[3]

Along with the traditional risk factors of osteoporosis, lack of physical exercise, inadequate disease-modifying treatment and the resultant high disease activity also contribute to the bone loss in RA.[1,4–6] Also, Rheumatoid Factor (RF), anti-cyclic citrullinated protein (anti-CCP) antibody, disease duration and steroid therapy are found to be associated with rheumatoid bone loss.[7–11]

Bone remodeling in RA has been investigated in some large, case-control cohort and longitudinal studies.[11–14] Bone mass was found to be lower in RA, compared with non-RA controls. Low bone mass at the femoral neck was particularly noted in non-treated patients with RA and in those with prolonged disease course.[9,15–18] Nonetheless, a large proportion of patients, even with active RA, presented with preserved bone mass, particularly at the lumbar spine.[1,13,15] The inconsistencies may be due to the different characteristics of the examined cohorts, particularly differing levels of inflammatory markers, disease duration and treatment modalities and variations in criteria applied for definition of low bone mass, functional disability due to the joint destruction, corticosteroid therapy can also affect the rate of rheumatoid bone loss and add to the inconsistencies of the results obtained by some studies.[5,6,8,9,19,20]

Presumably, patients with a longer disease duration present with a lower bone mass and a greater risk of fractures compared with those with a short duration. To our knowledge, the relationship between disease duration and bone mass has not been thoroughly investigated in RA. In particular, the effect of disease duration on RA bone mass, independent of a variety of confounding factors, has not been determined.

The aim of our study was to compare bone mineral density (BMD) status and frequency of osteoporosis in RA patients with different disease duration in comparison to age-matched controls.

The grouped patients were derived from a single cohort of RA with homogeneous characteristics in regard to treatment, associated factors of bone loss, lifestyle and so the results are expected to be less confounded.

2. Patients and methods

The present retrospective case-control study consisted of 177 female patients with RA diagnosed in accordance with the American College of Rheumatology (ACR) 1987 criteria[21] and 283 age-matched controls without RA who presented to the same clinic for BMD measurements.

Patients were selected consecutively according to the inclusion criteria, among RA patients presenting at the out-patients' rheumatology clinic for examination and follow-ups.

Female patients with history of established RA >3 months, who were under conventional therapy were included.

Exclusion criteria were anti-resorptive treatment, malabsorption, chronic and systemic debilitating diseases, patients with limitation of physical activities, chronic renal, hematologic, gastrointestinal and respiratory diseases and inflammatory arthritides other than RA.

Age-matched subjects were selected as controls among patients presented for bone densitometry at the same clinic. The subjects of the control group underwent BMD measurement because of menopausal state or for check up. A similar exclusion criteria was applied for the control group.

BMD at the femoral neck (FN-BMD) and lumbar spine at L2-L4 (LS-BMD) was measured by Dual Energy X-ray Absorptiometry (DEXA) using Norland densitometer. Osteoporosis was diagnosed according to the WHO criteria[22] defined as BMD values of 2.5 standard deviation or more below the mean value for young adults (T-score ≤ -2.5). The densitometer was calibrated according to manufacturer instruction and the reference value was provided from Caucasian database by the manufacturer.

Serum rheumatoid factor (RF) was assessed by latex agglutination method using RF kit purchased from Enison, Tehran, Iran, and anti-cyclic citrullinated peptide antibody (anti-CCP) was assessed by ELISA method using AESKULISA RA/CP Detect, Wendelsheim, Germany (normal >18 U/ml).

The proposal of this study was approved by the Ethics Committee of the Babol University of Medical Sciences, Babol, Iran.

2.1. *Statistical analyses*

Sample size was calculated for detection of 15% differences in the proportion of femoral neck osteoporosis between patients with RA and non-RA controls with 95% confidence interval (CI) and 80% power. Based on the prevalence of osteoporosis of 15% in the general population aged 30–70 years,[23] sample sizes of 150 subjects in each group were required. We recruited additional participants for both comparison groups to raise statistical power.

Patients with RA were grouped according to disease duration as: early RA (less than 2 years); 2–5 years; 5–10 years; and more than 10 years. The whole cohort and each group of patients with RA were compared with age-matched healthy controls.

The objective of this study was to determine the relationship between disease duration and bone mass in patients with RA, by comparison of various RA groups with age-matched control.

In statistical analysis FN-BMD and LS-BMD, and frequency of osteoporosis at the FN and LS regions in each group of RA was compared with age-matched controls. Student *t* test was used for comparison of quantitative variables with normal distribution and Mann–Whitney *U* test, Kruskall Wallis test was applied to compare quantitative variables with skewed distribution.

Chi square test and logistic regression analyses with calculation of odds ratio (OR) was also employed to determine association. In an additional analysis correlation between BMD and disease duration was determined by using Spearman's correlation coefficient and linear regression analysis.