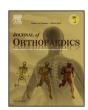
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#### Original Article

# Correlation between hand bone mineral density and joint destruction in established rheumatoid arthritis



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#### ABSTRACT

Objective: We aimed to clarify the correlation between bone mineral density (BMD) and the modified total Sharp score of the hand in Japanese patients with established rheumatoid arthritis (RA). *Methods*: We examined the hands of 57 patients who had RA for more than 20 years. BMD for the whole hand was measured using dual-energy x-ray absorptiometry. Concurrently, the hands were analyzed using radiography to estimate the van der Heijde-modified total Sharp score (vdH-S).

Results: The patients were all women with a median age of 69.7 years and RA disease duration of 29.9 years. The correlation coefficients were -0.513 (P < 0.0001) for hand BMD and vdH-S of the hand, -0.576 (P < 0.0001) for hand BMD and the erosion score of the vdH-S, and -0.339 (P < 0.0001) for hand BMD and the joint narrowing score of the vdH-S.

Conclusions: Hand BMD is correlated with the vdH-S in long-established RA. The hand BMD is important for structural assessment of the hand. Additionally, we may be able to predict the vdH-S of the hand on the basis of the hand BMD in long-established RA.

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#### 1. Introduction

Rheumatoid arthritis (RA) is associated with joint inflammation and destruction, which lead to pain, swelling, stiffness, and loss of function in joints throughout the body. The outcomes of treatment for RA have improved following recommendations and new criteria established by the European League against Rheumatism and American College of Rheumatology.<sup>1,2</sup> In the early stage of RA, involvement of the hand often causes pain and swelling. Approximately 90% of patients who experience early onset of RA demonstrate deformities of the metacarpophalangeal joint or wrist on magnetic resonance imaging.<sup>3</sup> Additionally, more than 90% of the patients with RA experience at least one hand or wrist symptom for more than 8 years.<sup>4</sup>. It is important, at all stages of the disease, to prevent destruction of the hand. A study reported that the loss of bone mineral content in the hand, as assessed using dual-energy x-ray absorptiometry (DXA), over 5

years is significantly correlated with the responses on the Health Assessment Questionnaire (HAQ).<sup>5</sup> Another previous study reported that the increase in the bone mineral density (BMD) of the femoral neck is correlated with improvements in the HAQ score. However, the BMD of the distal radius was not correlated with the HAQ score.<sup>6</sup>

Decreased hand and femoral BMD may cause functional disability. Chronic inflammation due to RA affects bone metabolism, disrupting the normal cycle of bone resorption and remodeling, thereby leading to generalized bone loss (osteoporosis) and local bone loss (joint destruction). Previous studies have suggested that generalized and local bone destruction are caused by osteoclast activation, and the mechanism of bone loss in RA is related to an imbalance in the ratio of receptor activator of nuclear factor κB ligand (RANKL) and osteoprotegerin. <sup>7-9</sup> Furthermore, the van der Heijde-modified total Sharp score (vdH-S) was found to be correlated with the bone marker urinary deoxypyridinoline in active RA.<sup>10</sup> Body mass index, disease duration, and high serum cross-linked N-telopeptidases of type I collagen level are common risk factors of osteoporosis in postmenopausal women with RA.<sup>11</sup> In RA, the changes in BMD are likely caused by accumulated inflammation.

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The goal of RA treatment is clinical, structural, and functional remission. The outcomes of joint damage due to RA have been examined on the basis of the vdH-S.<sup>12</sup> The vdH-S for the hand includes the whole hand as well as the proximal interphalangeal joint, metacarpophalangeal joint, and intercarpal joint. The joint damage is result of the combination of accumulated inflammation and changes in BMD.

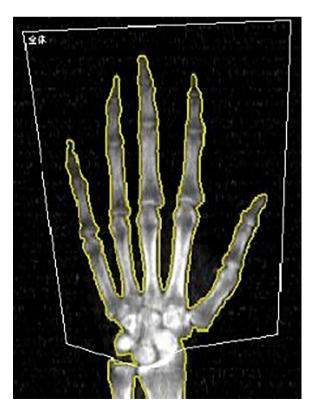
We believe that bone loss in the whole hand may be related to joint damage, particularly in long-established RA. In daily practice, we treat several RA patients with postmenopausal and chronic diseases. The aim of this study was to evaluate the frequency of osteoporosis and the relationship of the BMD and vdH-S of the hand in established RA.

#### 2. Materials and methods

This study investigated the clinical course and background variables of patients with RA that fulfilled the American College of Rheumatology classification criteria (1987). The disease duration of all patients with RA was more than 20 years. The control group comprised 50 women aged 20–39 years who were currently not receiving treatment for any diseases. A control group was necessary because there is no established baseline hand BMD for the Japanese population.

This study was approved by the ethics committee of Kamagaya General Hospital. All patients agreed to the terms of the study protocol.

Hand, lumbar spine (L2-L4 anteroposterior view), and total hip BMD were measured using DXA with the PRODIGY System (GE Healthcare, Madison, Wi, USA). In or der to measure the vdH-S, DXA and plain X-ray were performed simultaneously. The most affected hand for each patient was scanned. After excluding the hand operation history, the left hand and left hip were scanned. A flatbed scanner was used to capture radiographs as digital images.



**Fig. 1.** The measurement range of the hand BMD by DXA. BMD: bone mineral density, DXA: dual-energy x-ray absorptiometry

The hand BMD includes whole hand including the carpal bone (Fig. 1). Joint damage analysis for the hand was examined on the basis of the vdH-S. The vdH-S identifies 16 areas of erosion and 15 areas of joint space narrowing in hand.

The data analysis for the hand, lumbar spine, and total hip BMD and total sharp score, erosion score and joint narrowing score of vdH-S in hand was performed using Spearman's rank correlation. Statistical significance was established at a *P*-value <0.05.

#### 3. Results

In this study, 57 patients with RA (RA group) were enrolled. All of the enrolled patients were female and had established RA. The age and disease duration for the RA group (mean  $\pm$  standard deviation) was  $69.7\pm8.1$  years and  $29.9\pm8.7$  years, respectively. Table 1 shows the demographic characteristics of the RA group and control group.

In comparison with the control group, the hand BMD was -2.5 SD below the mean for 70.2% of patients in the RA group. Similarly the lumbar spine BMD was -2.5 SD below the mean for 43.9% of patients and the hip BMD was -2.5 SD below the mean for 22.8% of patients in the RA group.

In all patients of RA group, the correlation coefficients of hand BMD and vdH-S were -0.513 (P < 0.001) for the total score, -0.576 (P < 0.001) for the erosion score, and -0.339 (P < 0.001) for the joint narrowing score (Fig. 2). The correlation coefficients of lumbar spine BMD and vdH-S of the hand were -0.161 (P = 0.232) for the total score, -0.301 (P = 0.023) for the erosion score, and 0.046 (P = 0.736) for the joint narrowing score. The correlation coefficients of hip BMD and vdH-S of the hand were -0.281 (P = 0.034) for the total score, -0.368 (P = 0.005) for the erosion score, and -0.135 (P = 0.316) for the joint narrowing score.

In the RA group treated with biological DMARDs, the correlation coefficients of hand BMD and vdH-S were -0.565~(P<0.001) for the total score, -0.601~(P<0.001) for the erosion score, and -0.466~(P<0.001) for the joint narrowing score. The correlation coefficients of lumbar spine BMD and vdH-S of the hand were -0.156~(P=0.402) for the total score, -0.296~(P=0.106) for the erosion score, and 0.023~(P=0.902) for the joint narrowing score. The correlation coefficients of hip BMD and vdH-S of the hand were -0.375~(P=0.038) for the total score, -0.511~(P=0.003) for the erosion score, and -0.203~(P=0.273) for the joint narrowing score.

In the RA group treated with corticosteroids, the correlation coefficients of hand BMD and vdH-S of the hand were -0.368 (P=0.077) for the total score, -0.434 (P=0.039) for the erosion score, and -0.191 (P=0.371) for the joint narrowing score. The correlation coefficients of lumbar spine BMD and vdH-S of the hand were 0.224 (P=0.292) for the total score, 0.039 (P=0.856) for the erosion score, and 0.467 (P=0.021) for the joint narrowing score. The correlation coefficients of hip BMD and vdH-S of the hand were 0.102 (P=0.636) for the total score, -0.006 (P=0.979) for the erosion score, and 0.285 (P=0.176) for the joint narrowing score

The results of the correlation coefficients of the BMD and vdH-S of the hand are summarized in Table 2.

#### 4. Discussion

Joint inflammation gradually exacerbates the osteoporosis and joint destruction during RA with hand involvement. This study showed that the frequency of osteoporosis of the hand was 70.2% in patients with RA, which was comparatively higher than the frequency of osteoporosis of the lumbar spine and hip in these patients. In the general Japanese population, the frequency of osteoporosis of the lumbar spine is approximately 10% in people aged 60–69 years and approximately 30% in those aged 70–79

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