Journal of Population Therapeutics & Clinical Pharmacology

RESEARCH ARTICLE
DOI: 10.53555/7vpjxe47

# TO CORRELATE THE HAND BONE MINERAL DENSITY AND JOINT DEGRADATION IN PATIENTS WITH CHRONIC RHEUMATOID ARTHRITIS

**Singh Manvendra Pratap[1]***

[1*]Assistant Professor, Department of Orthopaedics, ERA'S Lucknow Medical College and Hospital, *Sarfarazganj Hardoi Raod, Lucknow-226003. Ph: 0522-2408122, 23*

***Corresponding author-** Dr. Manvendra Pratap Singh
*Assistant Professor, Department of Orthopaedics, ERA'S Lucknow Medical College and Hospital, Sarfarazganj Hardoi Raod, Lucknow-226003. Ph: 0522-2408122, 23

**Abstract**
In patients from Lucknow region with established rheumatoid arthritis (RA), we sought to elucidate the relationship between bone mineral density (BMD) and the modified total Sharp score of the hand. 114 individuals who had RA for more than 22 years had their hands inspected. BMD was determined by dual-energy x-ray absorptiometry for the whole hand. At the same time, the van der Heijde-modified total Sharp score (vdH-S) was estimated by radiographic analysis of the hands. Hand BMD and the hand's vdH-S had a $P < 0.0001$, hand BMD and the hand's erosion score had a $P < 0.0001$, and hand BMD and the vdH-S's joint narrowing score had a $P < 0.0001$. In chronic RA, there is a correlation between hand BMD and the vdH-S. When evaluating the hand's structure, the hand's BMD is crucial. Furthermore, based on the hand BMD in patients with chronic RA, we might be able to anticipate the hand's vdH-S.

## Introduction

Inflammation and deterioration of joints are linked to rheumatoid arthritis (RA), which causes pain, oedema, stiffness, and loss of function in joints all throughout the body[1]. Following guidelines and new standards set by the American College of Rheumatology and the European League against Rheumatism, the results of RA treatment have improved. Hand involvement in the early stages of RA frequently results in discomfort and oedema[2]. On magnetic resonance imaging, around 90% of patients with early-onset RA show abnormalities of the wrist or metacarpophalangeal joint[3]. Furthermore, for over eight years, almost 90% of RA patients have had at least one hand or wrist discomfort[4]. Preventing the hand from being destroyed is crucial at every stage of the illness[5]. According to research papers, there is a strong correlation between the answers on the Health Assessment Questionnaire (HAQ) and the hand's loss of bone mineral content during a 5-year period as determined by dual-energy x-ray absorptiometry (DXA)[6]. According to a different earlier study, increases in the HAQ score are associated with an increase in the femoral neck's bone mineral density (BMD)[7]. Nevertheless, there was no correlation between the HAQ score and the distal radius's BMD. Functional impairment may result from decreased hand and femoral bone mineral density[8]. Both localised bone loss (joint destruction) and widespread bone loss (osteoporosis) result from the disruption of the normal cycle of bone resorption and remodelling caused by chronic inflammation brought on by RA[9]. According to earlier research, osteoclast activation causes both local and

widespread bone degradation, and the mechanism of bone loss in RA is linked to an imbalance between the ratios of osteoprotegerin and receptor activator of nuclear factor kB ligand (RANKL)[10]. Additionally, in patients with active RA, a correlation was seen between the bone marker urine deoxypyridinoline and the van der Heijde-modified total Sharp score (vdH-S)[11]. Common risk factors for osteoporosis in postmenopausal women with RA include body mass index, length of illness, and elevated blood levels of type I collagen cross-linked N-telopeptidases[12]. BMD alterations in RA are probably brought on by cumulative inflammation. Clinical, structural, and functional remission is the aim of RA therapy[13]. The vdH-S has been used to analyse the results of joint damage brought on by RA[14]. The proximal interphalangeal joint, metacarpophalangeal joint, and intercarpal joint are all included in the hand's vdH-S. The accumulation of inflammation and alterations in bone mineral density lead to joint degeneration[15].We think that joint deterioration, especially in chronic RA, may be linked to bone loss throughout the entire hand. We serve a number of postmenopausal and chronic RA patients in our day-to-day practice. The purpose of this study was to assess the prevalence of osteoporosis and the correlation between hand vdH-S and BMD in patients with established RA.

## Materials and methods –

The clinical history and background characteristics of RA patients who met the 1987 categorisation criteria of the American College of Rheumatology were examined in this study. All RA patients had been afflicted for more than 20 years. Fifty women between the ages of 20 and 39 who were not now undergoing treatment for any illnesses made up the control group. Since there isn't a baseline hand BMD for population, a control group was required.

ERA'S Lucknow Medical College and Hospital, *Sarfarazganj Hardoi Raod, Lucknow*'s ethics committee gave its approval for this study. Every patient consented to the study's conditions. DXA using the PRODIGY System was used to evaluate the BMD of the hand, lumbar spine (L2-L4 anteroposterior view), DXA and ordinary X-ray were done at the same time to measure the vdH-S[16]. Each patient's most afflicted hand was scanned. The left hand and left hip were scanned after the hand surgical history was eliminated. The entire hand, including the carpal bone, is included in the hand BMD[17]. The hand's joint damage analysis was looked at using the vdH-S. 12 regions of joint space narrowing and 13 areas of degradation are identified by the vdH-S[18].

Spearman's rank correlation was used to analyse the data for the hand, lumbar spine, and total hip BMD, as well as the hand's overall sharp score, erosion score, and joint narrowing score of vdH-S. A P-value of less than 0.05 was considered statistically significant.

**Table 1- Demographic characteristics in RA group and control group**

| | RA group (n = 114) | Control group (n = 50) |
|---|---|---|
| **Age, years, mean (SD)** | 717 (6.7) | 30.6 (5.0) |
| **Gender, female, n (%)** | 61 (100) | 50 (100) |
| **Body weight, kg, mean (SD)** | 56.1 (11.6) | 48.5 (11.6) |
| **Body mass index, mean (SD)** | 28.3 (6.4) | 22.9 (2.4) |
| **Disease duration, years (SD)** | 24.1 (8.7) | - |
| **PF positive, n (%)** | 80.1 | - |
| **Anti-CCP positive, n (%)** | 74.2 | - |
| **Biological DMARD use, n (%)** | 64.4 | - |
| **MTX use, n (%)** | 2.8 | - |
| **Corticosteroid use, n (%)** | 42.1 | - |
| **Hand BMD, g/cm$^2$, mean (SD)** | 0.43 (0.031) | 0.39(0.056) |
| **Lumbar spine BMD, g/cm$^2$, mean (SD)** | 0.85(0.169) | 1.364 (0.26) |
| **Total hip BMD, g/cm$^2$, mean (SD)** | 0.564(0.256) | 0.859 (0.19) |

## Results

114 RA patients (RA group) were included in this study. Every patient who was enrolled had established RA . The RA group's mean age (mean ± standard deviation) was 71.7± 6.7 years, and their illness duration was 32.1 ± 6.7 years.

For 70.2% of patients in the RA group, the hand BMD was -2.5 SD below the mean when compared to the control group. In the RA group, 52.2% of patients had lumbar spine BMDs that were -2.5 SD below the mean, and 23.4% of patients had hip BMDs that were -2.5 SD below the mean.

The hand BMD and vdH-S correlation coefficients were -0.556 ($P < 0.001$) for the overall score, -0.598 ($P < 0.001$) for the erosion score, and -0.387 ($P < 0.001$) for the joint narrowing score in all RA group patients. The correlation coefficients between the hand's vdH-S and lumbar spine BMD were 0.054 ($P = 0.665$) for the joint narrowing score, -0.195 ($P = 0.257$) for the overall score, and -0.381 ($P = 0.029$) for the erosion score. The hand's vdH-S and hip BMD correlation coefficients were -0.165 ($P = 0.301$) for the joint narrowing score, -0.396 ($P = 0.005$) for the erosion score, and -0.364 ($P = 0.034$) for the overall score.

The correlation coefficients of hand BMD and vdH-S in the RA group treated with biological DMARDs were -0.556 ($P < 0.001$) for the overall score, -0.665 ($P < 0.001$) for the erosion score, and -0.497($P < 0.001$) for the joint narrowing score. -0.167 ($P = 0.456$) for the overall score, -0.365 ($P = 0.178$) for the erosion score, and 0.039 ($P = 0.996$) for the joint narrowing score were the correlation coefficients of lumbar spine BMD and hand vdH-S. The hand's hip BMD and vdH-S correlation coefficients were -0.247 ($P = 0.255$) for the joint narrowing score, -0.564 ($P = 0.004$) for the erosion score, and -0.398 ($P = 0.056$) for the overall score.

The correlation coefficients of hand BMD and vdH-S of the hand in the RA group receiving corticosteroid treatment were -0.389 ($P = 0.087$) for the overall score, -0.487 ($P = 0.019$) for the erosion score, and -0.215 ($P = 0.425$) for the joint narrowing score. The hand's lumbar spine BMD and vdH-S correlation coefficients were 0.506 ($P = 0.039$) for the joint narrowing score, 0.048 ($P = 0.754$) for the erosion score, and 0.278 ($P = 0.339$) for the overall score. The hand's hip BMD and vdH-S correlation coefficients were 0.305 ($P = 0.212$) for the joint narrowing score, -0.007 ($P = 0.925$) for the erosion score, and 0.141 ($P = 0.565$) for the overall score.

## Discussion

When RA affects the hands, joint inflammation progressively worsens osteoporosis and joint degradation. According to this study, the prevalence of hand osteoporosis in RA patients was 71%, which was significantly greater than the prevalence of hip and lumbar spine osteoporosis in these individuals. The prevalence of lumbar spine osteoporosis in the general Japanese population is around 12% for those between the ages of 60 and 69 and 33% for those between the ages of 70 and 79. The decline in hand BMD was more noticeable than the reduction in lumbar spine and hip BMD in women aged 50–70 with long-established (mean illness duration 17.3 years) RA. According to the vdH-S data, hand BMD represents illness specificity since it is unaffected by degenerative changes[1,18]. Our findings were consistent with those of earlier research. The individuals in our research were adequately treated for a suitable amount of time after their RA symptoms started[19]. Biological DMARDs have been utilised to treat RA in Japan since 2003, while methotrexate has been used since 1999. Numerous publications claim that biological DMARDs, including tumour necrosis factor-a inhibitors, raise the hip and lumbar spine's BMD[4,8,20]. Authors found that in one randomised study of RA patients showed no changes in BMD loss for the hip and lumbar spine whether MTX was used alone or in conjunction with infliximab and in metacarpal cortical hand bone loss is not lessened in RA patients receiving infliximab, however the loss of hip and spine bone mineral density is stopped[21]. Regardless of the clinical outcome, those receiving biological DMARDs demonstrated less periarticular bone loss[22,23]. We think that because the individuals in our research did not receive aggressive therapy when their RA first appeared, the loss of hand BMD occurred after intensive treatment was started. Therefore, among the patients in our study, osteoporosis in the hand was very common.

**Table 2 The correlation coefficients of BMD and vdH-S of hand.**

| | Hand BMD | | | Lumbar spine BMD | | | Total hip BMD | | |
|---|---|---|---|---|---|---|---|---|---|
| | TSS | EN | JSN | TSS | EN | JSN | TSS | EN | JSN |
| **All patients** | -0.556** | -0.598** | -0.387** | -0.195 | -0.381* | 0.054 | -0.364* | -0.396* | -0.165 |
| **Biological DMARDs** | -0.598** | -0.665** | -0.497** | -0.167 | -0.365 | 0.039 | -0.398* | -0.564* | -0.247 |
| **Corticosteroid treatment** | -0.389 | -0.487* | -0.215 | 0.278 | 0.048 | 0.506* | 0.141 | -0.007 | 0.305 |

**Note - BMD: bone mineral density, TSS: van der Heijde-modified total Sharp score of the hand, EN: erosion score in van der Heijde-modified total Sharp score of the hand,**
**JSN: joint narrowing score in van der Heijde-modified total Sharp score of the hand, DMARDs: disease modified**

According to a research, among patients with early RA who had a mean illness duration of 6.0 months, the loss of hand BMD, as measured by DXA[22,23,24], during the first year of RA was linked to the Genant-modified Sharp score for 6.4 years. Based on the vdH-S at 5 and 10 years, the loss of hand BMD, as assessed by digital x-ray radiogrammetry, at 1 year in RA patients with a disease duration of 0–4 years, was an independent predictor of joint deterioration[25,26]. With a mean illness duration of 8.5 years, the hand BMD loss measured with DXA was a more sensitive biomarker than vdH-S in individuals with early RA. Hand BMD reduction was linked to joint deterioration in early RA, according to earlier research.

In contrast, other found that in patients with established RA, the DXA-measured hand BMD loss did not change for two years in those with a disease duration of nine years; moreover, the decrease in hand BMD was -0.36% for those with a disease duration of less than three years and 0.29% for those with a disease duration of more than three years. The Larsen score (0–5) was linked to the forearm BMD in RA patients who had had the illness for 15.9 years[24,25,26]. Our findings showed a correlation between the hand's vdH-S and entire hand BMD. Osteoclasts are produced in response to periarticular bone loss in RA. Proinflammatory cytokines including interleukin-1, interleukin-6, and tumour necrosis factor-a are seen in higher concentrations in synovial tissue associated with RA[27]. In order to activate the osteoclasts, the cytokines trigger RANKL[25,27]. Furthermore, our findings showed that, particularly in patients treated with biological DMARDs, the hand BMD had a stronger correlation with the erosion score than the joint narrowing score of the vdH-S. These results could be indicative of the connection between joint bone degradation and the synovium.

Both the patients on biological DMARDs and all patients in our study showed a substantial link between hand BMD and vdH-S. However, in individuals receiving corticosteroid treatment, there was little connection between hand BMD and vdH-S. It is well recognised that corticosteroids negatively impact bone, raising the possibility of fracture. In a two-year randomised investigation of RA, participants treated with prednisolone saw less severe hand BMD loss than those treated with a placebo[8,11,15,26]. Additionally, hand BMD reduction was associated with C-reactive protein levels in placebo patients but not in prednisolone-treated individuals. Changes in the study of bone metabolic indicators (bone-specific alkaline phosphatase and urine type I collagen cross-linked N-telopeptide) were not an independent variable in the glucocorticoid-treated individuals[23,24].There are several functions of corticosteroid therapy in RA. Corticosteroids reduce inflammation, which lowers BMD, but they also increase the BMD decrease[5,9,12,24]. Depending on the patient's state, corticosteroid therapy has varying effects on the bone in RA. As a result, there was little connection in our research between hand BMD and the vdH-S in individuals receiving corticosteroid treatment.

There are certain restrictions on the current investigation. First, the sample size for this study was limited. If more instances were added, the outcomes would probably be different. Second, the nature of this study was cross-sectional. Information on patients' therapy from the beginning of RA to the present was not available. Additionally, this study was unable to elucidate the connection between generalised change, RA disease activity, and osteoporosis. A prospective investigation is necessary to elucidate this link.

**In Conclusion**, achieving structural remission requires regulating disease activity. Hand osteoporosis was more common than hip and lumbar osteoporosis, and there was a correlation between hand BMD and vdH-S in patients with established RA. According to our findings, hand BMD is crucial for evaluating the hand's structure, especially in individuals receiving no corticosteroid treatment.

Furthermore, in cases of established RA, we might be able to forecast the hand's vdH-S based on its BMD.

**References**


1. **Gough AK**, Lilley J, Eyre S, Holder RL, Emery P. Generalised bone loss in patients with early rheumatoid arthritis. *Lancet* 1994;**344**:23-7.
2. **Deodhar AA**, Brabyn J, Jones PW, Davis MJ, Woolf AD. Longitudinal study of hand bone densitometry in rheumatoid arthritis. *Arthritis Rheum* 1995;**38**:1204-10.
3. **Haugeberg G**, Green MJ, Quinn MA, Marzo-Ortega H, Proudman S, Karim Z, *et al.* Hand bone loss in early undifferentiated arthritis: evaluating bone mineral density loss before the development of rheumatoid arthritis. *Ann Rheum Dis* 2006;**65**:736-40.
4. **Emery P**. The Dunlop-Dottridge Lecture: prognosis in inflammatory arthritis: the value of HLA genotyping and the oncological analogy. *J Rheumatol* 1997;**24**:1436-42.
5. **Proudman SM**, Conaghan PG, Richardson C, Griffiths B, Green MJ, McGonagle D, *et al.* Treatment of poor-prognosis early rheumatoid arthritis. A randomized study of treatment with methotrexate, cyclosporin A, and intraarticular corticosteroids compared with sulfasalazine alone. *Arthritis Rheum* 2000;**43**:1809-19.
6. **Deodhar AA**, Brabyn J, Jones PW, Davis MJ, Woolf AD. Measurement of hand bone mineral content by dual energy x-ray absorptiometry: development of the method, and its application in normal volunteers and in patients with rheumatoid arthritis. *Ann Rheum Dis* 1994;**53**:685-90.
7. **Bland JM**, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1986;**1**:307-10.
8. **Lodder MC**, Lems WF, Ader HJ, Marthinsen AE, van Coeverden SC, Lips P, *et al.* Reproducibility of bone mineral density measurement in daily practice. *Ann Rheum Dis* 2004;**63**:285-9.
9. **Ravaud P**, Reny JL, Giraudeau B, Porcher R, Dougados M, Roux C. Individual smallest detectable difference in bone mineral density measurements. *J Bone Miner Res* 1999;**14**:1449-56.
10. **Bruynesteyn K**, Boers M, Kostense P, Van Der LS, Van Der HD. Deciding on progression of joint damage in paired films of individual patients: smallest detectable difference or change. *Ann Rheum Dis* 2005;**64**:179-82.
11. **Genant HK**, Block JE, Steiger P, Glueer CC, Ettinger B, Harris ST. Appropriate use of bone densitometry. *Radiology* 1989;**170**:817-22.
12. **Gluer CC**. Monitoring skeletal changes by radiological techniques. *J Bone Miner Res* 1999;**14**:1952-62.
13. **Van Der HD**. How to read radiographs according to the Sharp/van der Heijde method. *J Rheumatol* 1999;**26**:743-5.
14. **Alenfeld FE**, Diessel E, Brezger M, Sieper J, Felsenberg D, Braun J. Detailed analysesin periarticular osteoporosis in rheumatoid arthritis. *Osteoporos Int* 2000;**11**:400-7.
15. **Paulus HE**, Oh M, Sharp JT, Gold RH, Wong WK, Park GS, *et al.* Correlation of single time-point damage scores with observed progression of radiographic damage during the first 6 years of rheumatoid arthritis. *J Rheumatol* 2003;**30**:705-13.
16. **van der Heijde D**. Radiographic progression in rheumatoid arthritis: Does it reflect outcome? Does it reflect treatment? *Ann Rheum Dis* 2001;**60**(Suppl III):47-50.
17. **Deodhar AA**, Brabyn J, Pande I, Scott DL, Woolf AD. Hand bone densitometry in rheumatoid arthritis, a five year longitudinal study: an outcome measure and a prognostic marker. *Ann Rheum Dis* 2003;**62**:767-70.
18. **Lindqvist E**, Jonsson K, Saxne T, Eberhardt K. Course of radiographic damage over 10 years in a cohort with early rheumatoid arthritis. *Ann Rheum Dis* 2003;**62**:611-16.
19. **Conaghan PG**, O'Connor P, McGonagle D, Astin P, Wakefield RJ, Gibbon WW, *et al.* Elucidation of the relationship between synovitis and bone damage: a randomized magnetic resonance imaging study of individual joints in patients with early rheumatoid arthritis. *Arthritis*

*Rheum* 2003;**48**:64-71.

20. **McQueen F**, Lassere M, Edmonds J, Conaghan P, Peterfy C, Bird P, *et al.* OMERACT Rheumatoid Arthritis Magnetic Resonance Imaging Studies. Summary of OMERACT 6 MR Imaging Module. *J Rheumatol* 2003;**30**:1387-92.
21. **Wakefield RJ**, Gibbon WW, Conaghan PG, O'Connor P, McGonagle D, Pease C, *et al.* The value of sonography in the detection of bone erosions in patients with rheumatoid arthritis: a comparison with conventional radiography. *Arthritis Rheum* 2000;**43**:2762-70.
22. **Redlich K**, Hayer S, Maier A, Dunstan CR, Tohidast-Akrad M, Lang S, *et al.* Tumor necrosis factor alpha-mediated joint destruction is inhibited by targeting osteoclasts with osteoprotegerin. *Arthritis Rheum* 2002;**46**:785-92.
23. **Gravallese EM**, Goldring SR. Cellular mechanisms and the role of cytokines in bone erosions in rheumatoid arthritis. *Arthritis Rheum* 2000;**43**:2143-51.
24. **Hofbauer LC**, Lacey DL, Dunstan CR, Spelsberg TC, Riggs BL, Khosla S. Interleukin-1beta and tumor necrosis factor-alpha, but not interleukin-6, stimulate osteoprotegerin ligand gene expression in human osteoblastic cells. *Bone* 1999;**25**:255-9.
25. **Nakashima T**, Kobayashi Y, Yamasaki S, Kawakami A, Eguchi K, Sasaki H, *et al.* Protein expression and functional difference of membrane-bound and soluble receptor activator of NF-kappaB ligand: modulation of the expression by osteotropic factors and cytokines. *Biochem Biophys Res Commun* 2000;**275**:768-75.
26. **Schett G**, Redlich K, Hayer S, Zwerina J, Bolon B, Dunstan C, *et al.* Osteoprotegerin protects against generalized bone loss in tumor necrosis factor- transgenic mice. *Arthritis Rheum* 2003;**48**:2042-51.
27. Haugeberg G, Green MJ, Conaghan PG, et al. Hand bone densitometry: a more sensitive standard for the assessment of early bone damage in rheumatoid arthritis. Ann Rheum Dis. 2007;66:1513-1517.