

WJO 5th Anniversary Special Issues (10): Rheumatoid arthritis

Hand bone mass in rheumatoid arthritis: A review of the literature

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Author contributions: Kilic G and Ozgocmen S contributed to the collection and analysis of the data, and drafted the manuscript.

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Telephone: +90-352-2076666

Received: December 29, 2013

Peer-review started: December 30, 2013

First decision: March 12, 2014

Revised: July 11, 2014

Accepted: July 29, 2014

Article in press: July 29, 2014

Published online: January 18, 2015

Abstract

Rheumatoid arthritis (RA) is a common chronic inflammatory disease and periarticular osteoporosis or osteopenia of the inflamed hand joints is an early feature of RA. Quantitative measurement of hand bone loss may be an outcome measure for the detection of joint destruction and disease progression in early RA. This systematic review examines the published literature reporting hand bone mass in patients with RA, particularly those using the dual X-ray absorptiometry (DXA) methods. The majority of the studies reported that hand bone loss is associated with disease activity, functional status

and radiological progression in early RA. Quantitative measurement of hand bone mineral density by DXA may be a useful and practical outcome measure in RA and may be predictive for radiographic progression or functional status in patients with early RA.

Key words: Rheumatoid arthritis; Hand bone density; Dual X-ray absorptiometry; Periarticular; Osteoporosis

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Core tip: Periarticular osteoporosis or osteopenia affecting the hands is an early characteristic sign of bone damage in rheumatoid arthritis (RA). Dual X-ray absorptiometry (DXA) can be considered a reproducible, sensitive and non-invasive method to assess hand bone mineral density (BMD) in early RA. Quantitative measurement of hand bone loss by DXA may be a useful and practical outcome measure in RA and may have predictive value to determine radiographic progression or functional status in patients with early RA. Building up a reference population to obtain objective and accurate *T* and *Z* scores for hand BMD is needed.

Kilic G, Ozgocmen S. Hand bone mass in rheumatoid arthritis: A review of the literature. *World J Orthop* 2015; 6(1): 106-116 Available from: URL: <http://www.wjgnet.com/2218-5836/full/v6/i1/106.htm> DOI: <http://dx.doi.org/10.5312/wjo.v6.i1.106>

INTRODUCTION

Rheumatoid arthritis (RA) is a severe chronic inflammatory disease and periarticular osteoporosis or osteopenia of inflamed joints is the characteristic feature of the disease^[1]. Periarticular bone loss affecting the small joints of the hands is an early feature antedating the bone damage in RA. Hand bone loss occurs earlier than generalized

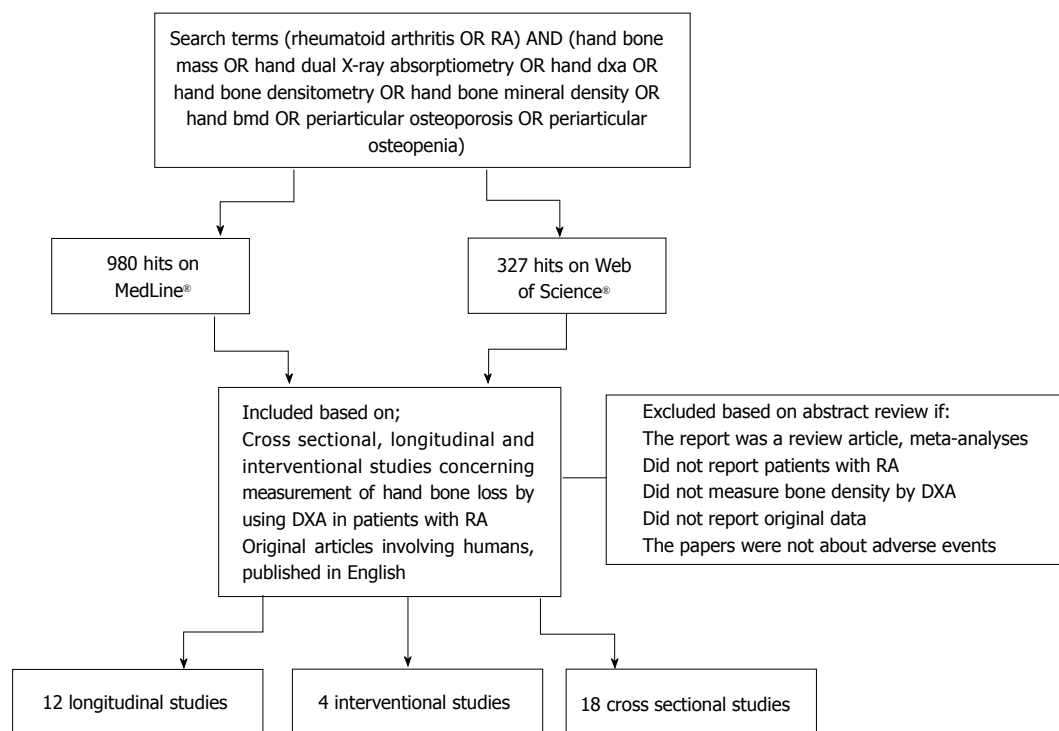


Figure 1 Flow chart. RA: Rheumatoid arthritis; DXA: Dual-X-ray absorptiometry.

osteoporosis and is associated with subsequent progressive joint destruction in patients with RA^[2-4]. Therefore, precise quantification of hand bone loss may predict the severity and progression of joint destruction.

Recently, several imaging methods have been used to assess the peripheral bone mass, including plain X-ray^[5], quantitative ultrasound (US)^[6], peripheral quantitative computed tomography (pQCT)^[7], magnetic resonance imaging^[8], digital X-ray radiogrammetry^[9] and dual X-ray absorptiometry (DXA)^[10]. Among them, DXA can be considered an accurate, repeatable and sensitive method to assess hand bone mineral density (BMD) in early RA^[11,12].

Until now, several studies have revealed the correlation of hand BMD with disease activity, functional capacity, radiographic progression or BMD at other sites in patients with RA^[3]. A review of the literature documenting the role of hand DXA in the assessment of progression and joint damage in patients with early RA is necessary. Quantitative measurement of hand bone loss may be an outcome measure for the detection of joint destruction and disease progression in early RA. Therefore, this review will examine the published literature assessing hand bone mass in patients with RA, particularly those using the DXA methods.

SEARCH

The literature was searched for articles assessing hand bone mass in patients with RA. Studies in which hand bone mass was investigated by using DXA in patients with RA were eligible. Selection criteria consisted of original articles involving humans published in English.

Articles were excluded if they were review articles or meta-analyses and did not measure bone density using DXA. In our search strategy, the following keywords were used: (rheumatoid arthritis OR RA) and (hand bone mass or hand dual X-ray absorptiometry or hand DXA or hand bone densitometry or hand bone mineral density or hand BMD or periarticular osteoporosis or periarticular osteopenia). The literature search was performed in PubMed[®] and Web of Science[®] databases between November 1993 and November 2013. Full texts of the selected articles were independently and systematically screened and data were extracted. For each trial, if applicable, information concerning sample size, study type, demographic characteristics of the patients, interventions, outcome measures and follow-up data was collected.

RESEARCH

Figure 1 shows the flow chart and the selection process. Thirty-four articles fulfilled the inclusion and exclusion criteria. 2131 patients with RA were reported within 18 cross-sectional studies, 12 longitudinal studies and 4 interventional studies. Table 1 shows the study design and characteristics of the studies.

Twelve cross-sectional studies compared patients with RA and controls. Ten studies showed that patients with RA had significantly lower hand BMD compared with matched healthy controls or patients with other rheumatic diseases^[13-22]. Similarly, five longitudinal studies reported hand bone loss was higher in patients with RA than in matched healthy controls or patients with other rheumatic diseases, including spondyloarthropathies or

Table 1 Details of the studies included in the systematic reviews

Ref.	Study type	Sample size (M/F)	Mean/Median age	Disease duration (yr)	DXA equipment	DXA site	Coefficient variation BMD	Follow-up duration (yr)	Outcome	Conclusion
Florescu <i>et al</i> ^[19]	CS	RA: 10 HC: 10	63	15.3	Norland	MC bones (II-V)	0.9%-3.0%		There was a significant correlation between hand BMD and radiographic scoring methods	Hand BMD measurement may be a useful method for the detection and monitor of disease progression
Peel <i>et al</i> ^[34]	CS	RA: 70 F	64	3-45		WH, LS, femoral neck			Increased bone loss in patients with RA <i>vs</i> controls Hands: 22.7% Lumbar spine: 10.7% Femoral neck: 16.3% Total body: 11.3%	Significant correlation between hand BMD and BMD at other sites. Hand BMD correlated with grip strength and inversely related to ESR in patients with early RA
Deodhar <i>et al</i> ^[13]	CS	RA: 56 (22/34) Controls: 95 (46/49)	M: 64 F: 64	9	Hologic	WH	1%-3%		Mean total hand BMC (grams, M/F) RA: 81.7 / 52.3 Controls: 90.9/62.2	Hand BMC correlated with disease severity but not with disease activity
Devlin <i>et al</i> ^[3]	CS	RA: 202 (61/141)	M: 59 F: 53	M: 1.6 F: 1.9	Lunar	LS Hip WH	0.6%		Hand BMD correlated with disease activity, functional capacity, lumbar and hip BMD	Hand bone loss can be used as outcome measure
Njeh <i>et al</i> ^[30]	CS	RA: 51 F Patients with osteopenia: 44 F HC: 52 F	Mean age 57.5		Lunar DPX-L	LS, Hip, WH			Mean Hand BMD (g/cm ²) in patients with RA: 0.415	Hand BMD was correlated with phalangeal ultrasound and hand functions but not CRP or ESR
Ozgocmen <i>et al</i> ^[22]	CS	RA: 30 F HC: 29 F	45.5		Lunar	WH II MC LS Hip	-		CI and C: MC ratio correlated with II. MC midshaft and hand BMD	CI may predict cortical bone mass of the hand. C: MC ratio is a useful method for evaluating progression of wrist involvement
Alenfeld <i>et al</i> ^[14]	CS	RA: 41 (18/23) HC: 103 (35/68)	54	F: 2.1 M: 2	Lunar	WH Subcondral ROI	WH: 0.9 subcondral region: 2.7%-3.2%		Hand bone loss in the subregional regions is higher than total hand BMD	In early RA periarticular osteoporosis may be better assessed using detailed hand scan analyses
Ardicoglu <i>et al</i> ^[18]	CS	RA: 49 (9/40) HC: 34 (5/29)	49.1	5	Lunar	LS Hip WH			Hand BMD correlated with disease duration, CRP and radiographic scores	Hand BMD by DXA is a useful practical and reproducible method

Harrison <i>et al</i> ^[20]	CS	RA: 17 (4/13) PsA: 15 (9/6)	RA:51 PsA:53	RA: 31 PsA: 27	Hologic	MCP, PIP, DIP joints	3.4%-6.6%	Periarticular BMD was significantly lower in patient with RA than PsA Periarticular BMD correlated with the number of swollen, tender joints in RA	Periarticular osteoporosis is associated with joint inflammation in RA but not PsA
Ozgoçmen <i>et al</i> ^[47]	CS	RA: 15 F HS: 3 F	48.5	6.8	Lunar	WH, MCP	-	Flow patterns correlated with intra-articular bone and cartilage destruction	PDUS is a useful method for monitoring disease activity and measurement of therapeutic response
Jensen <i>et al</i> ^[48]	CS	RA: 11 female	53		Hologic	MC bones, forearm	0.65%-0.83%	There was a significant association between DXA-BMD and DXR-BMD	Periarticular bone loss can be detected better and earlier with DXR than DXA in patients with RA
Castañeda <i>et al</i> ^[15]	CS	EA: 22 (2/20) HC: 16 (3/13)	EA: 48.4 HC: 49.2	0.4	Hologic	WH MCP	MCP: 1.3% -0.7% WH: 1.4 %-0.9%	Whole hand BMD: (g/cm ²) HC: 0.355 EA: 0.349 MCP BMD: (g/cm ²) HS: 0.295, EA: 0.285	Measurement of BMD at MCP joints may be a useful method to assess the diagnosis or prognosis in patients with EA
Franck <i>et al</i> ^[21]	CS	RA: 421 (64/357) HC: 98 (31/67)	M: 56.11 F: 58.4	M: 4.8 F: 4.8	Hologic	LS, hip, forearm, WH, MCP II-III	Subregional scans: 0.9%-1.4% for short term, 1.5%-2.3% for mid-term	There was a significant correlation between WH BMD and its subregions, hip and forearm. Subregional BMD was correlated with CRP, bone resorption markers and grip strength	Measurement of hand and subregional BMD by DXA is accurate and reproducible method in RA
Murphy <i>et al</i> ^[49]	CS	RA: 4 SpA: 3	36.7	1.25	Hologic	MCP/PIP	0.73%-0.78%	The precision of MCP joints was greater than PIP joints	DXA can be used as a reliable measure for periarticular BMD
Alves <i>et al</i> ^[16]	CS	Established RA: 25 EA: 25 HS: 37	Established RA: 53 Early arthritis: 52		Lunar	WH, LS, hip, MCP and/or PIP joints mid MC to mid- phalangeal	0.45%-1.07%	Mean BMD of five ROI: Established RA: 0.321 to 0.372 Early arthritis: 0.321 to 0.382 HC: 0.342 to 0.401 Mean BMD of whole hand: Established RA: 0.387 Early arthritis: 0.392 HC: 0.420	Measurement of periarticular BMD is not a useful tool to discriminate between patients with early RA from HC

Zhu <i>et al</i> ^[17]	CS	RA: 100 F	53.4	9.1	Hologic	LS, hip, ultradistal radius			BMD assessed by HR-pQCT significantly correlated with BMD at the peripheral and central skeleton	HR-pQCT is a useful method for evaluating periarticular bone loss at both cortical and trabecular bone
Moon <i>et al</i> ^[17]	CS	RA: 45 HC: 106	47.5		Lunar	Shaft and periarticular region of PIP, LS, hip			The ratio of shaft to periarticular BMD was higher in patients with RA	DXA assisted localized quantification and BMD ratio calculations are useful for assessing periarticular osteoporosis in early RA
Dogu <i>et al</i> ^[33]	CS	RA: 83	52.9	6.99	Lunar	WH	-		Hand BMD was correlated with HGS, TTP, radiological erosions but not DHI	HGS and TTP were most effective indicator of hand function
Deodhar <i>et al</i> ^[10]	LS	RA: 81 (33/48) HC: 95 (46/49)	Early RA: M: 53, F: 55 Late RA M: 65.5, F: 63	Early RA: 0.8 Late RA: 9	Hologic	WH		1	After 1 yr hand bone loss Early RA: M: 3.25%, F: 1.46% Late RA, no significant loss of hand BMD	Hand bone loss was highest in patients with early RA and correlated with disease activity
Daragon <i>et al</i> ^[25]	LS	Early RA: 15 (6/9) Other rheumatic diseases: 15 (7/8)	Early RA: 42.7 Other rheumatic diseases: 48.8	0.4	Hologic	WH		1	There was no significant correlation between hand bone loss and clinical, radiological and biological parameters except for IFN alfa	Hand BMD by DXA may be useful tool for the early classification of inflammatory disease
Deodhar <i>et al</i> ^[26]	LS	Early RA: 40	-	< 2	Hologic	WH	2.3%	5	Percent change in BMD after 1 yr: -5.5, 2 yr: -7.5, 3 yr: -9.8, 4 yr: -9.9, and 5 yr: -10	Early loss in hand BMD (in the first six months) may be a prognostic marker for disease activity, functional status or poor functional outcome
Berglin <i>et al</i> ^[31]	LS	RA: 43(13/30)	Not available	0.6	Lunar	WH		2	Hand bone loss correlated with radiographic progression	Hand bone loss and radiographic progression were retarded by early treatment
Jensen <i>et al</i> ^[24]	LS	RA: 51 (10/41) Unclassified polyarthritis: 21 (3/18)	RA: 54 Unclassified polyarthritis: 39	0.3	Norland	MCP, forearm		2	Hand BMD decreased only in patients with RA and associated with disease activity	DXR is better than DXA for detecting and monitoring periarticular osteoporosis of the MC bones

Haugeberg <i>et al</i> ^[4]	LS	Undifferentiated arthritis: 74 (9/65)	65	0.5	Lunar	LS Hip	1.07%	1	At the 1 yr follow-up, hand BMD loss; RA: -4.27 Inflammatory non-rheumatoid group: -0.49 Non-inflammatory group: -0.87	Hand DXA may be useful for determining the risk of progressive disease in RA
Haugeberg <i>et al</i> ^[36]	LS	RA: 79 (32/47)	49.7	0.7	Lunar	WH		0.9	Mean hand BMD loss 2.5% at 24 wk, 2.6% at 48 wk	Hand DXA is more sensitive than radiology can be used as outcome measure in early RA
Murphy <i>et al</i> ^[23]	LS	RA: 20 (8/12) SpA: 18 (11/7)	RA: 37, SpA: 33	RA: 0.4 SpA: 0.4	Hologic	WH LS Hip		1	Periarticular bone loss correlated with radiographic damage, disease activity and baseline TIMP-1 level	TIMP-1 may be use as a biomarker of periarticular bone loss in early RA
Hill <i>et al</i> ^[27]	LS	RA: 50 (12/38) Control: 30	57	0.75	Lunar	WH, LS, hip	1.1%	1	Hand BMD correlated with baseline CRP and radiographic score in RA	Hand BMD using DXA is a safe, reproducible procedure. It may predict radiological progression and disease activity
Bejarano <i>et al</i> ^[33]	LS	RA: 64 (27/37)	54.1	0.5		WH, lumbar spine, hip		6.4 yr	Follow-up change in hand BMD, -0.034	First year hand BMD loss was not associated with function or quality of life status but not long-term radiographic progression
Naumann <i>et al</i> ^[28]	LS	Early RA: 17 (4/13) Established RA: 35 (8/27)	Early RA: 55, Established RA with moderate disease activity: 58 Established RA with high disease activity: 53.5	Early RA: 0.2	Lunar	WH, MCP/PIP, wrist, LS hip	Wrist: 0.75 WH: 0.78	1	There was a negative correlation between hand BMD and MCP joint synovitis in patients with high disease activity. The best precision values of BMD were found for the wrist	Hand BMD measurement by DXA is highly reproducible method in patients with RA
Black <i>et al</i> ^[37]	LS	RA: 106 (29/77)	57	0.3	Lunar	WH		1	Lower hand BMD was associated with higher erosion scores	Hand BMD loss in the first 6 mo can predict early erosive change in patients with early RA
Haugeberg <i>et al</i> ^[38]	IS	RA: 20 (7/13) IFX + MITX: 10	52.2	< 1	Lunar	WH, LS, hip		1	BMD (gr/cm ²) IFX treated group: WH: 0.42, spine: 1.14, T hip: 1.04, F neck: 1.03 Placebo: WH: 0.43, spine: 1.28, T hip: 1.06, F neck: 1.01	In the IFX treated group hand bone loss arrested at the hip but not at the hand and lumbar spine

Deodhar <i>et al</i> ^[39]	IS	Placebo: 13 Denosumab 60 mg treated group: 21 (7/14) Denasumab 180 mg treated group: 22 (5/17)	Placebo: 55.2 Denosumab 60 mg treated group: 57.7 Denasumab 180 mg treated group: 58.7	Placebo: 10.3 Denosumab 60 mg treated group: 12.6 Denasumab 180 mg treated group: 15.8	Lunar	WH	1	Mean change in hand BMD at 6/12 mo (%); denosumab 60 mg: 0.8/1 Denosumab 180 mg: 2/ 2.5 placebo: -1.2/-2	Denosumab increased hand BMD and decreased progression of bone erosion in RA
Haugeberg <i>et al</i> ^[29]	IS	MTX group: 19 (10/9) MTX + IAST: 21 (8/13)	MTX group: 56.2 MTX + IAST: 53.3	MTX group: 0.5 MTX + IAST: 0.4	Lunar	WH, MCP, hip, LS	1	In the first 3 mo, hand bone loss was lower in MTX + IAST treated group than MTX treated group. Hand bone loss associated disease activity, hand function and MRI synovitis score	IAST may protect against periarticular bone loss in inflamed finger joints in RA
Szentpetery <i>et al</i> ^[32]	IS	RA: 35 (11/24) PsA: 27 (12/15)	RA: 56 PsA: 44	RA: 8 PsA: 7	Hologic	WH, PIP/ MCP, hip, LS	3	Following anti- TNF therapy hip BMD decreased but spine and hand BMD unchanged. Periarticular BMD around PIP joints increased, MCP decreased	Anti TNF therapy increased bone formation without a change in bone resorption

CS: Cross-sectional study; CI: Cortical index; MC: Carpo:metacarpal; EA: Early arthritis; DXR: Digital X ray radiogrammetry; DXA: Dual X ray absorptiometry; HR-pQCT: High-resolution peripheral quantitative computed tomography; HGS: Handgrip strength; IAST: Intra-articular corticosteroid; HC: Healthy controls; IS: Interventional study; LS: Longitudinal study; PsA: Psoriatic arthritis; ROI: Region of interest; RA: Rheumatoid arthritis; SpA: Spondylarthropathy; TIMP-1: Tissue inhibitor of metalloproteinases 1; TTP: Three-finger pinch; vBMD: Trabecular volumetric bone mineral density; WH: Whole hand; LS: Lumbar spine; BMC: Bone mineral content; BMD: Bone mineral density; EA: Early arthritis; MTX: Methotrexate.

undifferentiated arthritis^[4,10,23-25].

Hand bone mass and disease duration

Five longitudinal studies reported that hand bone loss occurred early in the disease duration in patients with RA^[4,10,23,24,26]. A 5-year longitudinal study of hand bone mineral content (BMC) in patients with early RA indicated that the rate of hand bone loss measured by DXA was more pronounced in the first years of disease and then slowed. In this study, the predictors for bone loss over five years were identified as baseline disease activity, functional status and BMC loss within the first six months^[26].

Hand bone mass and disease activity

Two cross-sectional^[3,20] and seven longitudinal studies^[4,10,23,26-29] reported that hand bone loss was significantly related to disease activity which was assessed by Disease Activity Score 28 (DAS-28), swollen joint count, CRP, Ritchie articular index or early morning stiffness in patients with early RA. However, Deodhar *et al*^[15] underscored that hand BMC correlated with disease severity but not with disease activity in their pioneering cross-sectional study. Similarly, Njeh *et al*^[30] showed that hand bone mineral density (BMD) correlated

with functional capacity but not with CRP or ESR. On the other hand, Haugeberg *et al*^[4] found that hand bone loss was associated with rheumatoid factor (RF) and mean CRP levels in their longitudinal study.

Hand bone mass and functional outcome

Five longitudinal^[26,27,29,31,32] and four cross-sectional studies^[3,18,33,34] indicated that hand bone loss correlated with functional status and health related quality of life (assessed using the outcome measures including Health Assessment Questionnaire scores, Short Form 36 (SF-36), hand function, grip strength or pinch strength) in early RA. However, 2 longitudinal studies failed to show a significant association between hand bone loss and functional status^[4,35].

Hand bone mass and radiographic joint damage

Two cross-sectional studies revealed a significant correlation between BMC of the hand and radiographic joint damage^[13,18]. Two longitudinal studies assessed the association between hand BMD and radiographic joint damage^[27,36]. Haugeberg *et al*^[36] showed that measurement of hand BMD by DXA was more sensitive than conventional radiographic scores for detecting early damage in patients

with RA. Four longitudinal studies identified the value of hand bone loss as a predictor for long term radiographic damage. A longitudinal study of 50 patients with early RA (whose hand BMD was measured at baseline, 6 and 12 mo) indicated that the baseline value of hand BMD was associated with radiographic scores at 12 mo^[27]. Another longitudinal study consisting of 64 patients with RA confirmed the predictive value of hand BMD loss in the first year for the subsequent radiographic progression (6.4 year follow up)^[35]. A longitudinal study by Black *et al*^[37] showed hand BMD loss in the first 6 mo might be a predictor for erosions at 12 mo. Similarly, Berglin *et al*^[31] found a significant correlation between hand bone loss and radiological progression over 24 mo follow up in patients with early RA. On the other hand, two studies failed to show a significant correlation between hand BMC loss and radiographic joint damage^[25,26].

The effect of therapeutic agents on hand bone mass

Two studies have reported that anti-tumor necrosis factor (anti-TNF) treatment did not have a significant effect on hand bone loss^[32,38] but reduced the bone loss at the hip^[32]. Szentpetery *et al*^[32] reported that a course of 3 years of anti-TNF treatment resulted in an increase in periarticular BMD at the proximal interphalangeal joints but not at the metacarpophalangeal (MCP) joints in patients with RA and psoriatic arthritis (PsA). A study by Haugeberg *et al*^[29] revealed that intra-articular corticosteroid injection therapy (IAST) protected the inflamed joints against bone loss which was more pronounced in the MCP periarticular regions. A study by Deodhar *et al*^[39] evaluated the effect of denosumab [a fully human monoclonal antibody against receptor activator of nuclear factor-kappa B ligand (RANKL)] on hand BMD and its correlation with erosion scores. Fifty-six patients with RA were randomly assigned to receive either placebo or one of two doses of denosumab (60 mg or 180 mg) every six months for one year. At 12 mo, mean hand BMD increased from baseline in both denosumab groups with a decreased progression of bone erosions.

Hand bone mass and bone turnover markers

Szentpetery *et al*^[32] reported that baseline hand BMD inversely associated with bone turnover markers, including bone-specific alkaline phosphatase (bone ALP), procollagen type-I N-propeptide, C-terminal cross-linking telopeptides (CTX-I) and urinary N-terminal cross-linking telopeptide of type-I collagen (NTX-I) in patients with RA. Murphy *et al*^[23] found a correlation between baseline serum levels of the tissue inhibitor of metalloproteinase 1 (TIMP-1) and periarticular bone loss after 12 mo follow-up in patients with early RA. Also the authors suggested that TIMP may be a predictive biological marker for periarticular bone loss. Daragon *et al*^[25] showed that interleukin-1 (IL-1), IL-10 and TNF- α were not correlated with hand BMD, both in patients with RA and other rheumatic diseases.

DISCUSSION

In RA, bone involvement is characterized by focal

articular bone loss (erosions), periarticular osteoporosis/osteopenia around inflamed joints and generalized osteoporosis affecting the axial and peripheral skeleton^[40]. Periarticular osteoporosis or osteopenia affecting the hands is an early characteristic sign of bone damage and precedes the development of erosions in RA. Periarticular bone loss and erosions were considered as criteria in the revised 1997 American College of Rheumatology (ACR) classification criteria for RA^[41]. Later, radiographic changes were excluded in the new 2010 ACR/European League Against Rheumatism classification criteria for RA due to the subjective evaluation of periarticular demineralization in the early stage of disease by conventional radiography^[42].

Although pathogenesis of periarticular bone loss remains less clear, studies support that the periarticular bone loss may occur as a result of imbalance in bone remodeling. In RA, subchondral bone marrow and/or synovial inflammation inhibits bone formation by inhibiting the wingless signaling pathway and increases bone resorption by stimulating production of bone-resorbing cytokines, such as iIL-1, IL-6, IL-17 and RANKL^[43,44].

Dual X-ray absorptiometry measurement of hand BMD can be considered an accurate, reproducible, sensitive, non-invasive method in early RA^[11,12]. It is also a well tolerated and fast procedure. It has a small effective radiation dose and better precision value than conventional radiography. Hand BMD measurements by DXA have been suggested as a more sensitive method than radiological scoring for detecting bone damage in early RA^[36]. DXA measurements provide quantitative results free of observer bias. On the other hand, there are many pitfalls using DXA on clinical application for measuring periarticular BMD in patients with RA. First, most elderly patients with RA have severe degenerative changes in the hands, including Heberden's and Bouchard' nodes, which may affect the result of hand BMD measurement and cause a higher result of BMC. Second, severe hand deformity in RA causes a change in hand position which results a wide variation in the hand BMD measurement but not hand BMC^[13]. Third, hand bone loss seems to be the result of generalized plus local effect of the disease. Therefore, in patients with established RA, periarticular bone osteoporosis can be difficult to distinguish from generalized osteoporosis by using hand DXA alone. Moreover, it is also important to note the influence of normal age-related bone loss, especially in postmenopausal women. Finally, standard deviation (SDs) for hand BMD measurement by DXA is unknown. All of the studies included in this review compared DXA results with small reference populations. Further studies are needed to investigate SDs from the reference population to obtain objective and accurate results in T and Z scores for the hand^[18].

Several studies support that hand bone loss occurs early in the disease process and more rapidly than at the hip and spine^[4,10,23,24,26,34]. Ten studies demonstrated that hand bone loss was higher in patients with RA than matched healthy controls and patients with other rheumatic diseases^[13-22].

Only a few studies examined the effect of several

therapeutic agents on hand bone loss assessed by DXA in RA. Several studies showed that anti-TNF drugs used in the treatment of RA reduces both disease activity and radiographic progression^[45,46]. By contrast, limited data exist on the effect of anti-TNF treatment on periarticular bone loss in patients with RA. Two studies demonstrated that anti-TNF therapy (infliximab) did not have a significant effect on hand bone loss^[32,38], whereas it reduced the bone loss in hip^[32]. The mechanism of this failure has not been extensively investigated and is still an open question. The effect of RANKL blockade with denosumab on hand BMD was examined in the three treatment arms in a study: placebo or one of two doses of denosumab (60 or 180 mg). Mean hand BMD increased from baseline and progression of bone erosions decreased in both denosumab groups compared to placebo^[39]. In RA, the effect of intra-articular corticosteroid injections into inflamed finger joints on hand bone loss was investigated in an interventional study comparing methotrexate (MTX) and IAST with MTX treatment for 1 year. The MTX and IAST treated group had a lower loss in periarticular hand BMD in the first 3 mo^[29]. These data suggest that suppressing periarticular inflammation with a potent anti-inflammatory medication such as a corticosteroid may decrease periarticular inflammation, resulting in reduced periarticular bone loss.

Several longitudinal studies suggested that early hand bone loss may have predictive value to determine which patients with early RA will develop further radiographic progression or have poor functional status^[26,27,31,35,37]. However, there are contrasting results. The discrepancy between results may be related to different radiological scoring methods, sample size, disease characteristics or therapeutic approaches used.

CONCLUSION

Quantitative measurement of hand bone loss by DXA may be a useful and practical outcome measure in RA and may be predictive for radiographic progression or functional status in patients with early RA.

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