Frequency and risk factor analyses of bone erosion of the distal interphalangeal joint in patients with rheumatoid arthritis: a cross-sectional study

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ABSTRACT

Aims: Few reports have focused on the distal interphalangeal (DIP) joint in patients with rheumatoid arthritis (RA). The purposes of this study were to evaluate the frequency of bone erosion of the DIP joint, and to determine the factors associated with its deformity.
Methods: This study reviewed 204 patients with RA in whom radiographs of hands were obtained. According to the presence/absence of bone erosion of the DIP joint, patients were divided into two groups (DIP-positive and DIP-negative groups). Additionally, wrist, metacarpal phalangeal (MP), thumb interphalangeal (IP), and proximal interphalangeal (PIP) joints were evaluated. Clinical variables such as age, sex, body mass index, disease duration, disease activity (DAS28-CRP), and drug use were investigated.
Results: Regarding the radiological findings of the DIP joint, 32 patients (15.7%) were allocated to the DIP--positive group and 172 patients (84.3%) to the DIP--negative group. The mean age, disease duration, DAS28-CRP, and the rate of corticosteroids usage were significantly higher in the DIP-positive than in the DIP-negative group ($p = 0.0031$, 0.0062, 0.0342, and 0.0011, respectively). Radiologically, concomitant bone erosions of the wrist, MP, thumb IP, and PIP joints were significantly more common in the DIP-positive than in the DIP-negative group ($p < 0.01$ for all four joints). Multivariate analysis demonstrated that advanced age, long disease duration, and the presence of radiological bone erosion of the PIP joint were independently associated with bone erosion of the DIP joint ($p = 0.0480$, 0.0307, and 0.0021, respectively). Accordingly, in patients with DIP erosions, mean DAS28-CRP was significantly higher in patients with <5 years (n = 10) than in those with ≥5 years of disease duration (n = 22, $p = 0.0088$).
Conclusions: Bone erosion can be observed at the DIP joint in patients with RA, and these cases frequently shows bone erosions of other finger joints, such as PIP joint. In addition, bone erosion can be observed soon after the onset of RA caused by uncontrolled disease activity in some patients with RA.

Keywords: Rheumatoid arthritis, Distal interphalangeal joint, Plain radiograph, Bone erosion.

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INTRODUCTION

Rheumatoid arthritis (RA) affects the small hand joints of approximately 60-80% of patients[1, 2]. Initial changes include synovial proliferation and swelling that may progress to joint destruction with severe loss of function[1]. Early manifestations of rheumatoid disease at the wrist, metacarpophalangeal (MP), thumb interphalangeal (IP), and proximal interphalangeal (PIP) joints include pain, swelling, tenderness, and limitation of motion, and subsequent joint destruction[1,3,4]. Therefore, these joints have been assessed by plain radiographs during therapy evaluation, including in prospective randomized clinical trials[5,6]. The van der Heijde-modified total Sharp score (mTSS), which is calculated from radiographs of the hands and feet, is widely used to quantify joint destruction in patients with RA. The mTSS is scored by 16 areas for bone erosion and 15 areas for joint space narrowing in both hands[7].

In contrast, few reports have focused on the distal interphalangeal (DIP) joint, since this joint is not a frequent site for observing radiological rheumatic change, such as bone erosion in patients with RA[8]. Therefore, the DIP joint is not included in the area of evaluation of the mTSS[7]. However, painful, swollen DIP joints have been reported in patients with RA[9]. The authors stated that despite the classic notion of RA affecting the more proximal finger joints, patients with RA can also

present with arthritis predominantly of the DIP joints[9]. The purposes of this study were to evaluate the frequency of bone erosion of the DIP joint, and to determine the factors associated with its deformity in RA patients.

METHODS

STUDY DESIGN, POPULATION, AND DATA COLLECTION

This study was approved by our institutional review board. We retrospectively reviewed 204 patients with RA in whom radiographs of the hands were obtained between January 2004 and December 2019. If more than one radiograph was available, the most recent was considered for evaluation. All patients fulfilled the 1987 RA classification criteria of the American Rheumatism Association (currently the American College of Rheumatology)[10]. Clinical variables such as the body mass index (BMI), presence of rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) antibody, disease activity (Disease Activity Score in 28 joints with C-reactive protein [DAS28-CRP]), and use of conventional synthetic disease-modifying antirheumatic drugs (csDMARDs), biologic agents, and oral corticosteroids at the final radiological examination of the hand were investigated.

CLASSIFICATION OF RADIOLOGICAL DEFORMITY OF THE DIP JOINT

According to the presence/absence of marginal bone erosion of the DIP joint on anteroposterior (AP) and oblique radiographs of both hands, all 204 patients were divided into three groups (DIP-positive, DIP-negative, excluded), based on the EULAR definitions (Figure 1)[11, 12]. When the radiological deformities of erosive osteoarthritis or psoriatic arthritis such as gull-wing erosion, mouse-ear type of erosion, erosion of terminal tufts, and fluffy periostitis, were observed, the patients were excluded from this study as having overlapping diseases (Figure 1)[12]. No patients met these criteria and none were therefore excluded from further analysis. The assessments were made by two observers (S.I. and S.H.). Intraobserver and interobserver variabilities were calculated with the use of kappa statistics. A kappa value of 0.21–0.4 corresponded to fair agreement; 0.41-0.6, moderate agreement; and 0.61-0.8, substantial agreement. A value of >0.81 is considered to be almost perfect[13].

In addition, the presence of bone erosion was also assessed in the wrist, MP, thumb IP, and PIP joints using AP and oblique radiographs of both hands[11]. Patients were categorized as having a positive radiological bone erosion when the deformity was observed in at least one joint of both hands on the AP or oblique radiographs.

STATISTICAL ANALYSIS

After dividing the patients into two groups (radiological bone erosion of the DIP-positive and -negative groups), clinical and radiological parameters were compared. Statistical analyses were conducted using the chi-square test to compare sex; presence of RF and anti-

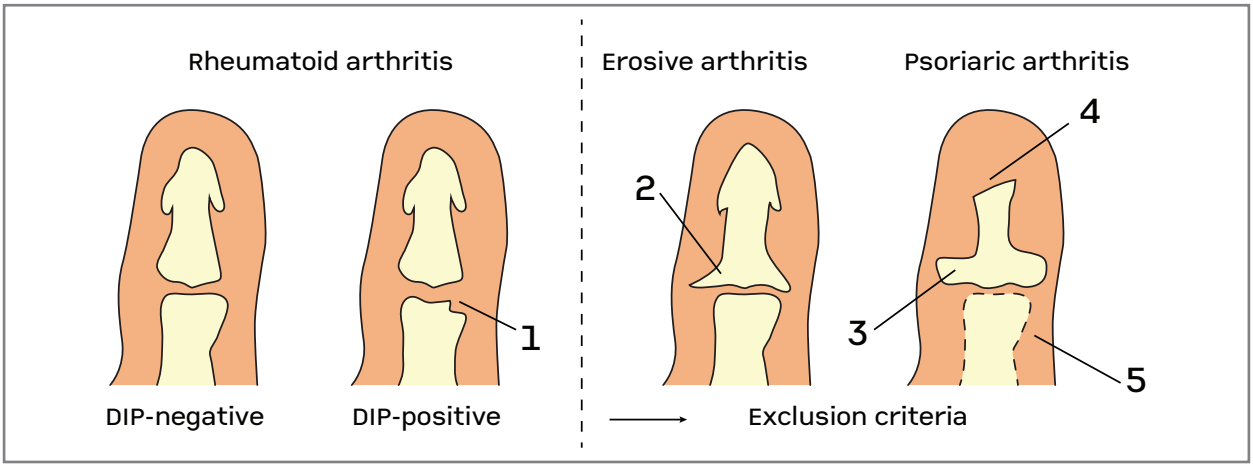

FIGURE 1. A schematic diagram showing the classification of the distal interphalangeal (DIP) joint based on radiographic findings. 1, marginal erosion; 2, gull-wing erosion; 3, "mouse-ear" type of erosion; 4, erosion of terminal tufts; 5, fluffy periostitis.

CCP antibody; the use of csDMARDs, biologic agents, and oral corticosteroids; and the presence of bone erosions of the wrist, MP, thumb IP, and PIP joints between the two groups. Age, BMI, disease duration, and DAS28-CRP were compared between the two groups using the unpaired *t*-test. A multivariate analysis was performed to identify parameters associated with bone erosion of the DIP joint by using a forward-backward stepwise logistic regression with variable selection ($p < 0.2$).

As subgroup analysis, radiological and clinical parameters were compared between patients with <5 years of disease duration and patients with ≥5 years of disease duration in DIP-positive group by using the chi-square, Fisher's exact probability, and unpaired *t*-tests[14].

The statistical analyses were performed using JMP version 9.0.1 software program (SAS Institute Inc., Cary, NC, USA). A *p* value <0.05 was considered statistically significant.

RESULTS

This study included 44 men and 160 women with a mean disease duration of 11 years. Patients' demographic data are shown in Table I. The proportions of patients using csDMARDs, biologics, and steroids were 89%, 27%, and 40%, respectively. The mean value for the DAS28-CRP was 2.6. Radiologically, rates of the presence of bone erosion of the wrist, MP, thumb IP, and PIP were 48%, 29%, 18%, and 43%, respectively. Regarding the radiological findings of the DIP joint, the bone erosions were present in 32 patients (15.7%) (Figures 2 and 3). Patients were therefore allocated to the DIP-positive (n = 32) or DIP-negative (n = 172) group. With regard to the classification of the two groups based on findings of the DIP joint, intraobserver variabilities (kappa values) of observers 1 and 2 were 0.9896 and 0.9354, respectively, which corresponded to almost perfect agreement. Interobserver variabilities (kappa values) of the first and second assessment were 0.8661 and 0.8807, respectively, which also corresponded to almost perfect agreement.

Results of univariate and multivariate analyses of 204 patients with RA in the DIP-positive and DIP-negative groups are shown in Table II. Mean age, disease duration, and DAS28-CRP were significantly greater in the DIP-positive group (65.8 years, 18.5 years, and 3.0, respectively), in comparison with the DIP-negative group (55.2 years, 9.8 years, and 2.2, respectively). There were significant differences in those variables between the two groups ($p = 0.0031$, 0.0062, and 0.0342, respectively). The proportion of patients using oral corticosteroids was also significantly higher in the DIP-positive group ($p = 0.0011$). However, dose of corticosteroid was similar between the two groups (DIP-positive group: 2.6 ± 2.6 mg/day, DIP-negative group: 1.5 ± 2.3 mg/day, $p = 0.0672$). Radiologically, rates of bone erosion of the wrist, MP, thumb IP, and PIP joints were significantly higher in the DIP-positive group than in the DIP-negative group ($p < 0.01$ for all four joints). Multivariate analysis revealed that age, disease duration and the presence of radiological bone erosion of the PIP joint were independently associated with bone erosion of the DIP joint ($p = 0.0480$, 0.0307, and 0.0021, respectively).

With regard to sub analysis of the DIP-positive, 22 patients were categorized as having ≥5 years of disease

TABLE I. PATIENTS' DEMOGRAPHIC DATA (N = 204)

Sex (male:female)	44: 160
Age (years)	57 ± 14
BMI, kg/m2	22 ± 3.7
RF positive	147 (72%)
Anti-CCP antibody positive	124 (61%)
Disease duration (years)	11 ± 12
DAS28-CRP	2.6 ± 1.1
Patients using csDMARDs	182 (89%)
Patients using biologics	55 (27%)
Patients using corticosteroids	81 (40%)
Dosage of steroids (mg/day)	1.7 ± 2.5
Bone erosion*	
Wrist	98 (48%)
MP joint	60 (29%)
Thumb IP joint	37 (18%)
PIP joint	88 (43%)
DIP joint	32 (16%)

Continuous variables represented as mean ± standard deviation. Categorical variables represented as n (%).
*Subjects were categorized as having a bone erosion when the erosion was observed in at least one joint of both hands on anteroposterior (AP) and oblique radiographs.
BMI, body mass index; RF, rheumatoid factor; CCP, cyclic citrullinated peptide; DAS28-CRP, Disease Activity Score in 28 joints with C-reactive protein; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; MP, metacarpophalangeal; IP, interphalangeal; PIP, proximal interphalangeal; DIP, distal interphalangeal.

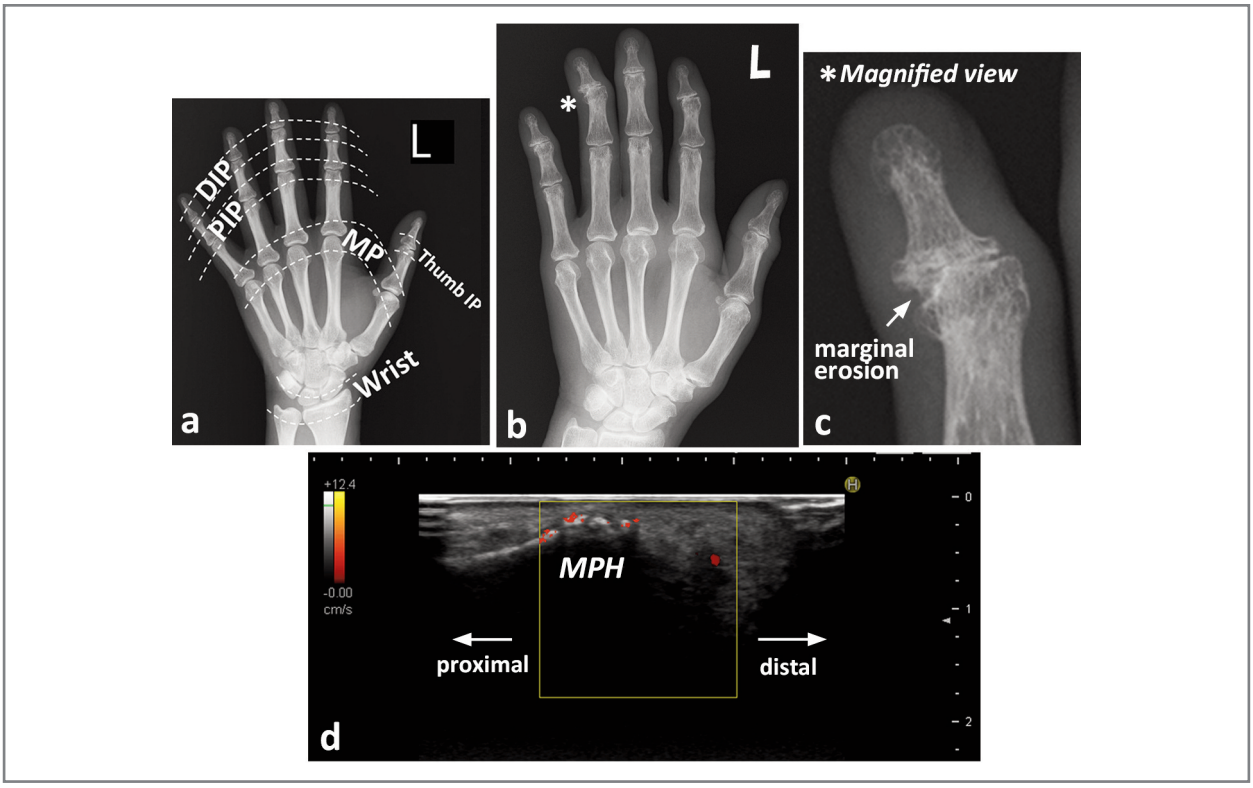

FIGURE 2. a, In this study, bone erosions are evaluated in the DIP joint, PIP joint, IP joint, MP joint, and wrist. b and c, A 62-year-old woman with a 12-year history of RA. The DAS28-CRP is 2.2, which indicates that activity of RA is well controlled. However, marginal bone erosion of the DIP joint deformity is observed at the fourth finger on the left side on the anteroposterior hand radiograph (asterisk and arrow). d, The findings of ultrasound for the DIP joint in the fourth finger on the left side. Bone erosions and slight tenosynovitis are observed at the middle phalanx head (MPH).

duration (mean 22.2 years) and 10 patients as <5 years of disease duration (mean 2.9 years) in the DIP-positive group (Table III). The mean age was similar between groups, whereas the proportion of women was significantly higher among patients with ≥5 years of disease duration (20/22 patients, 91%) in comparison to patients with <5 years of disease duration (4/10 patients, 40%; $p = 0.0049$). The mean DAS28-CRP was significantly higher in patients with <5 years of disease duration (3.6 ± 1.2 vs. 2.5 ± 1.0, respectively; $p = 0.0088$). In addition, the mean DAS28-CRP at baseline, 6, 12, and 24 months after initiation of therapy in the patients with <5 years of disease duration was 5.1, 4.1, 3.9, and 3.6, respectively. This indicates that moderate or high disease activities continued in these 10 cases until the radiological evaluation. Radiologically, the presence of erosions of the wrist (82% vs. 50%), MP (73% vs. 40%), thumb IP (59% vs. 40%), and PIP (91% vs. 80%) joints were numerically higher in patients with ≥5 years of disease duration, but did not reach statistical significance ($p = 0.096$, 0.1190, 0.4501, and 0.5717, respectively).

DISCUSSION

In RA, synovitis and subsequent joint destruction appear in the wrist, MP, thumb IP, and PIP joints[1,3,4]. Glimm *et al.* described the distribution and severity of inflammation in patients with osteoarthritis and RA by using indocyanine green-enhanced fluorescence optical imaging and ultrasonography[15]. Frequency distributions of inflammation, such as synovitis or tenosynovitis in the wrist and PIP joints, were higher than those in the DIP joints of patients with RA. However, inflammation was observed in the DIP joints with the same frequency as in the MP joints. A previous study reported that the frequency of radiological DIP erosion

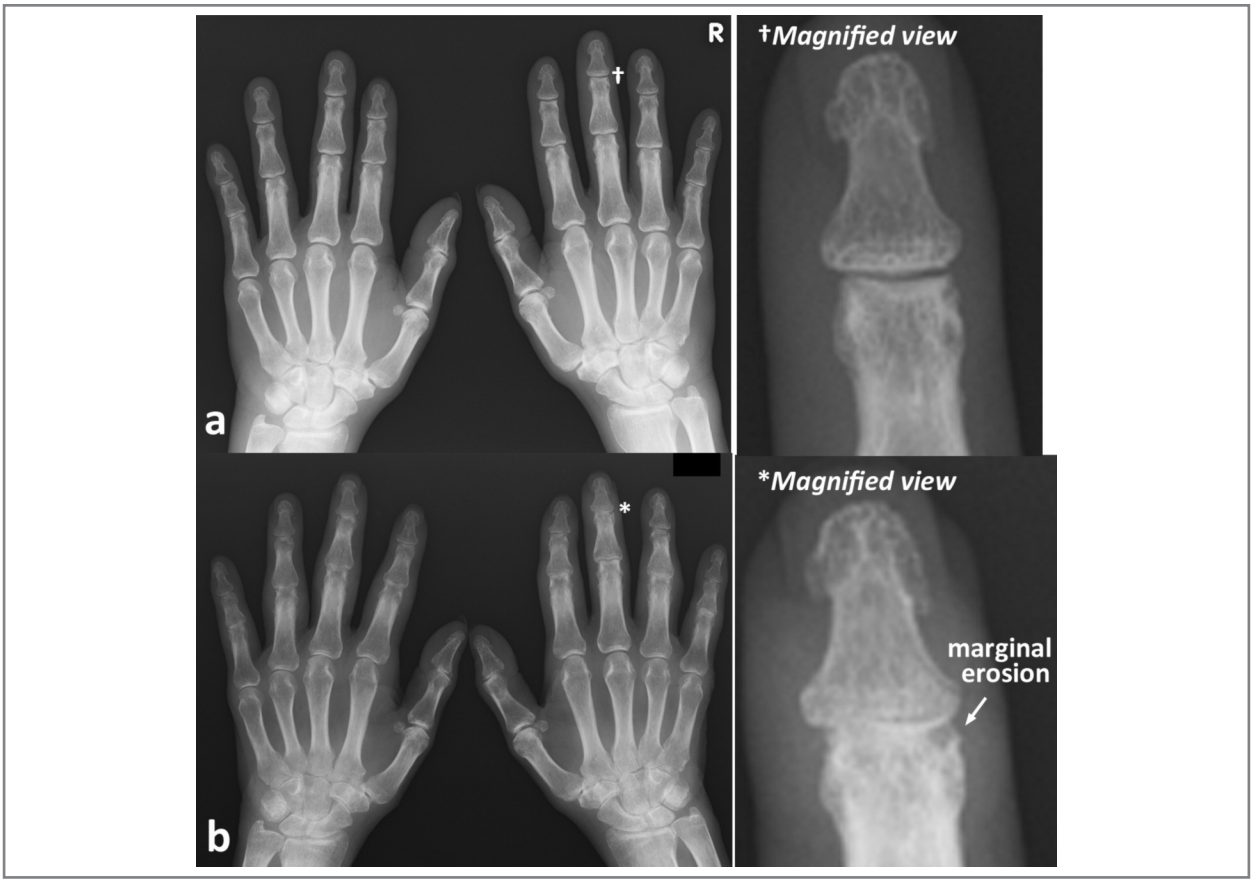

FIGURE 3. Hand radiograph of a 63-year-old man with a 2-year history of RA. a, An anteroposterior hand radiograph shows periarticular osteoporosis in the multiple interphalangeal joints. However, neither bone erosion nor joint space narrowing is observed at the initial examination. b, Two years after the onset of RA. DAS28-CRP is 4.7, which indicates that activity of RA is not controlled. Bone erosion and joint space narrowing are observed at multiple DIP joints as well as PIP joints, compared with Figure 3a.

was 37% in the seropositive RA[16]. In this study, the frequency was 15.7%, which indicates that radiological bone erosion can be observed at the DIP joint in patients with RA.

Ichikawa *et al.* evaluated DIP joints in 85 patients with psoriatic arthritis[8]. As control, those in 85 RF-positive and 50 RF-negative RA patients were assessed, and a radiographic erosive lesion was observed in 10.7% of RF-positive and 8% of RF-negative patients with RA, respectively[8]. In our study, the rate of RF-positive patients in the DIP-positive group was 72%, which was equal to that in the DIP-negative group (72%). Multivariate analyses revealed that disease duration and the presence of erosion of the PIP were independently associated with bone erosion of the DIP joint. Additionally, the rates of radiological bone erosion of the wrist, MP, thumb IP, and PIP joints were significantly higher in the DIP-positive group. Therefore, this study's results indicate that the typical patient with RA, in whom radiological bone erosion can be observed at the DIP joint, has multiple radiological bone erosions of the finger joints caused by longstanding duration even if the current activity of RA is well controlled.

In contrast, subgroup analysis revealed that bone erosion of the DIP was seen soon after the onset of RA (mean, 2.9 years) in ten of 32 patients (31%). The mean DAS28-CRP in the <5 years of disease duration group was significantly higher than that in the ≥5 years of disease duration group. In addition, moderate or high disease activity continued in these 10 cases until the radiological evaluation. These results suggest that the risk of rapid progression of the bone erosion of the DIP joint is present if RA activity is not well controlled in the early phase of RA. Proper DIP joint function is important, since pain-free stability in the DIP joint is essential for effective stable pinch[17,18]. Therefore, surgeons

TABLE II. UNIVARIATE AND MULTIVARIATE ANALYSES OF 204 PATIENTS WITH RA AND PRESENCE OR ABSENCE OF BONE EROSIONS OF THE DIP JOINT

	DIP-positive group (n = 32)	DIP-negative group (n = 172)	Univariate p values	Multivariate p values	Odds Ratio (95% Confidence Interval)
Sex (male: female)	8: 24	36: 136	0.6073		-
Age (years)	65.8 ± 6.3	55.2 ± 14.8	0.0031*	0.0480*	1.07 (1.01-1.17)
BMI (kg/m2)	21.0 ± 3.4	21.9 ± 3.6	0.3705	-	
RF positive (%)	23 (72)	124 (72)	0.9799	-	
Anti-CCP positive (%)	20 (63)	104 (60)	0.8286	-	
Disease duration (years)	18.5 ± 13.7	9.8 ± 11.2	0.0062*	0.0307*	1.07 (1.01-1.14)
DAS28-CRP	3.0 ± 1.5	2.2 ± 1.4	0.0342*	0.1208	1.74 (0.85-3.82)
Steroid use (%)	21 (66)	60 (35)	0.0011*	-	
Steroid dosage (mg/day)	2.6 ± 2.6	1.5 ± 2.3	0.0672	-	
csDMARDs use (%)	26 (81)	156 (91)	0.1136	-	
Biologics use (%)	12 (38)	43 (25)	0.1434	-	
Bone erosion					
Wrist (%)	23 (72)	75 (44)	0.0033*	-	
MP (%)	20 (63)	40 (23)	<0.0001*	-	
Thumb IP (%)	17 (53)	20 (12)	<0.0001*	-	
PIP (%)	28 (88)	60 (35)	<0.0001*	0.0021*	19.32 (2.58-475.66)

Continuous variables represented as mean ± standard deviation. Categorical variables represented as n (%). *p < 0.05 indicates significance
BMI, body mass index; RF, rheumatoid factor; CCP, cyclic citrullinated peptide; DAS28-CRP, Disease Activity Score in 28 joints with C-reactive protein; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; MP, metacarpophalangeal; IP, interphalangeal; PIP, proximal interphalangeal; DIP, distal interphalangeal.

TABLE III. COMPARISON OF PATIENTS WITH BONE EROSION OF THE DIP JOINT BASED ON DISEASE DURATION.

	< 5 years of disease duration group (n = 10)	≥ 5 years of disease duration group (n = 22)	p values
Sex (male: female)	6: 4	2: 20	0.0049*
Age (years)	63.8 ± 3.5	66.9 ± 7.3	0.2992
BMI (kg/m2)	21.0 ± 1.9	20.9 ± 4.1	0.7230
Disease duration (years)	2.9 ± 1.1	22.2 ± 10.5	<0.0001*
RF positive (%)	7 (70)	16 (73)	0.9999
Anti CCP antibody positive (%)	6 (60)	14 (64)	0.7120
DAS28-CRP	3.6 ± 1.2	2.5 ± 1.0	0.0088*
Steroid use (%)	8 (80)	13 (59)	0.4250
Steroid dosage (mg/day)	3.8 ± 2.9	1.9 ± 2.0	0.1648
csDMARDs use (%)	10 (100)	16 (73)	0.1422
Biologics use (%)	4 (40)	8 (36)	0.9999
Radiological bone erosion			
Wrist (%)	5 (50)	18 (82)	0.0960
MP (%)	4 (40)	16 (73)	0.1190
Thumb IP (%)	4 (40)	13 (59)	0.4501
PIP (%)	8 (80)	20 (91)	0.5717

Continuous variables represented as mean ± standard deviation. Categorical variables represented as n (%). *p < 0.05 indicates significance
BMI, body mass index; RF, rheumatoid factor; CCP, cyclic citrullinated peptide; DAS28-CRP, Disease Activity Score in 28 joints with C-reactive protein; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs; MP, metacarpophalangeal; IP, interphalangeal; PIP, proximal interphalangeal; DIP, distal interphalangeal.

typically choose arthrodesis for the treatment of a significant degenerative condition involving the DIP of the fingers[17,18]. We believe that it requires immediate intervention based on the treat to target (T2T) strategies to avoid DIP deformity as well as deformities of the wrist, thumb IP, and PIP joints in the early phase of RA.

The current study has several major limitations. First, synovitis of the DIP joint was not routinely confirmed using ultrasonography or contrast-enhanced magnetic resonance imaging. Second, the current study did not assess what functional disorders can be predicted by deformity of the DIP joint using patient-based scoring systems, such as the Health Assessment Questionnaire Disability Index or EuroQol-5 Dimension[19,20]. Lastly, this study was retrospective with a small number of cases. Therefore, further prospective studies with a large number of cases are necessary.

In conclusion, the frequency of bone erosion of the DIP joint in patients with RA was 15.7%. Most of these patients had a long disease duration and bone erosions of other finger joints, such as the PIP joints. However, this deformity can be observed soon after the onset of RA caused by uncontrolled disease activity in some patients with RA. Therefore, it is important to institute treatment based on the T2T strategy as soon as possible when patients are diagnosed with RA.

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