

1 **Distal interphalangeal joint involvement in patients with rheumatoid arthritis:**
2 **where we are?**

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1 Distal Interphalangeal Joint Involvement In Patients With Rheumatoid Arthritis:

2 Where We Are?

3 Abstract

4 **Background/aim:** Rheumatoid arthritis (RA) usually affects the wrist,
5 metacarpophalangeal joint, and proximal interphalangeal joint of the hands. However,
6 distal interphalangeal joint (DIP) joint involvement may be affected in RA patients. In
7 this study, we aimed to evaluate the frequency and associated factors of DIP joint
8 erosion in patients with RA.

9 **Materials and methods:** Medical records of patients with RA were reviewed
10 retrospectively. Patients with major trauma affecting DIP joints, osteoarthritis, erosive
11 osteoarthritis, psoriatic arthritis, systemic sclerosis, calcium pyrophosphate dihydrate
12 disease, and gout were excluded. Anteroposterior hand X-rays were evaluated and
13 patients were divided into groups according to auto-antibody profile.

14 **Results:** We reviewed 1213 patients with a mean age of 54.3 ± 12.5 years; 82.8% of
15 them were female and 95.4% of patients had RA-type erosive changes. The DIP erosion
16 rate was 12%. The DIP involvement was generally unilateral and asymmetric, with the
17 3rd finger was the most commonly affected joint. Patients with DIP erosions had
18 significantly higher disease duration time ($p = 0.036$). The higher age was the
19 independent predictive factor for DIP erosion ($p = 0.001$).

20 **Conclusion:** In this large-sample-sized study, we reported DIP joint involvement in
21 patients with RA. Advanced age could have affected the results because hand erosions
22 increase above 50 years in a healthy population. Our results may provide a different
23 perspective on joint involvement in RA.

1 **Keywords:** Distal interphalangeal joint, erosive arthritis, rheumatoid arthritis

2 **1. Introduction**

3 Rheumatoid arthritis (RA) is a chronic, multisystemic, and autoimmune rheumatic
4 disease affecting synovial joints, and causes joint erosions. It is one of the most
5 common inflammatory rheumatic diseases. The disease decreases work capacity and
6 quality of life during RA [1]. Joint erosion occurs in 90% of patients with RA [2]. The
7 1987 American College of Rheumatology (ACR) RA revised classification criteria
8 including clinical and radiological evaluation of hand joints such as
9 metacarpophalangeal (MCP), and proximal interphalangeal (PIP) joints [3]. The 2010
10 ACR/European League Against Rheumatism (EULAR) RA classification criteria
11 include clinical assessment of hand joints (wrist, MCP, and PIP) [4]. Distal
12 interphalangeal (DIP) joint involvement does not receive any points in the current
13 classification criteria. Disease activity score-28 (DAS-28), which is the most commonly
14 used RA disease activity scoring system, doesn't include DIP joint arthritis [5].
15 Modified Sharp Score (mSS) is one of the radiographic scoring systems evaluating joint
16 damage in patients with RA, and it includes 15 areas for joint space narrowing (JSN)
17 and 16 areas for bone erosion but neither erosion score nor JSN score includes DIP
18 joints [6]. Distal interphalangeal joint involvement with radiological changes is well-
19 defined in rheumatic diseases such as erosive osteoarthritis (EOA), hand osteoarthritis
20 (OA), and psoriatic arthritis (PsA) [7,8]. Adult-onset Still's Disease, anti-Jo-1 syndrome,
21 calcium pyrophosphate dihydrate disease (CPPD), multicentric reticulohistiocytosis,
22 and gout can also affect the DIP joints [9-13].

1 In our daily rheumatology practice, we encounter arthritis and/or arthralgia in DIP joints
2 in patients with RA. All diseases that may cause DIP involvement are evaluated. In this
3 large sample-sized study, we aimed to find the frequency and associated factors of DIP
4 joint erosions in patients with RA.

5 **2. Materials and Methods**

6 We evaluated the RA patients who were following up in our rheumatology department,
7 18 years of age or older, and who had an anterior-posterior hand x-ray within the last
8 year were included in the study. The ACR/EULAR 2010 RA classification criteria were
9 used to diagnose RA. [4]. Demographic, laboratory, clinical, and treatment
10 characteristics were noted from electronic medical records, retrospectively. Lost a large
11 portion of the finger (including at least one DIP joint), having a history of fracture in
12 hand bones, overlapping with another rheumatologic or non-rheumatologic disease
13 which can cause erosions/deformities in DIP joints such as systemic sclerosis (SSc),
14 PsA, CPPD, gout, EOA, and hand OA were the exclusion criteria. Patients having hand
15 deformities/signs on hand X-rays which were well defined for EOA or PsA such as
16 saw-tooth, gull-wing, mouse-ear, terminal tuft erosion, acro-osteolysis or fluffy
17 periostitis were also excluded [8,14].

18 Diagnosis of joint erosion in DIP joints was based on EULAR definition as ‘interruption
19 of the cortex of the bone’ [15]. ‘Rheumatoid arthritis type joint involvement (RJI)’ was
20 based on mSS [6], and defined as having any joint erosion or JSN. ‘Serious joint
21 involvement (SJI)’ was defined as having any erosion score ≥ 3 points or JSN score ≥ 4
22 points according to mSS. All of the hand X-rays were evaluated separately by the
23 rheumatologists who were blinded to the patients. If there was no agreement between

1 readers, X-rays were re-evaluated by all readers, then a final common decision was
2 made with full agreement. A nephelometric assay detected rheumatoid factor (RF);
3 serum samples with results ≥ 14 IU/ml were defined as positive. Anti-cyclic
4 citrullinated peptide antibody-2 IgG (anti-CCP) was detected by enzyme-linked
5 immunosorbent assay; serum samples with results ≥ 5 U/ml were defined as positive.
6 The study was approved by the local Ethics Committee and was conducted following
7 the principles of the 1964 Declaration of Helsinki and its later amendments (approval
8 no: 2023/03).

9 Statistical analysis was performed using the SPSS 22.0 version (IBM SPSS, Chicago,
10 IL). The results were given as a number, frequency, mean \pm standard deviation, and/or
11 median [25-75p] value. The chi-squared test and Fisher's exact test were used for the
12 analysis of categorical data and independence between variables. The Mann-Whitney U
13 test and Independent-Samples T-test were used to compare differences between groups
14 according to the distribution analyses. Logistic Regression Analysis was performed to
15 calculate the estimated values of the dependent variable as probabilities and to classify
16 according to probability rules. The results were assessed at a 95% confidence interval
17 and a p-value of less than 0.05 was accepted as significant.

18 **3. Results**

19 We reviewed 1213 patients with a mean age of 54.3 ± 12.5 years. 82.8% of them were
20 female. The median disease duration time was 5 [2-11] years. Smoking history (active
21 or ex) was 31.8%. Rheumatoid arthritis type joint involvement and SJI had a rate of
22 95.4% and 24.7%, respectively. We found the rate of DIP joint erosion as 12%. All of

1 the patients with DIP erosions had a positive history of tenderness and swelling on DIP
2 joints. None of the patients with DIP erosions had a positive family history (in first, and
3 second-degree relatives) for PsA.

4 The minimum and maximum number of eroded DIP joints in patients were one and
5 four, respectively. Only nine patients (6.1%) had bilateral-symmetrical DIP joint
6 erosions. Isolated DIP joint erosion was absent. The most commonly affected DIP joint
7 was the 3rd finger. Demographic, laboratory, clinical, and treatment characteristics are
8 given in Table 1. Table 2 shows the general characteristics of patients with and without
9 DIP involvement. Both RF and anti-CCP negative groups had the rate of DIP erosion at
10 13.1%. When evaluated according to the autoantibody profile, there were no significant
11 differences between all groups (Table 3).

12 In multivariate analysis, age was the independent predictive factor for DIP joint
13 erosions ($p = 0.001$). Disease duration time was the predictive factor for DIP erosion (p
14 $= 0.036$). And, there was no relationship between DIP joint erosion, gender, smoking,
15 RF, anti-CCP, RJI, SJI, and biological agent use ($p > 0.05$).

16 **4. Discussion**

17 In this large sample size study, we evaluated the frequency and associated factors of
18 DIP joint erosion in patients with RA. We found that erosive DIP joint involvement was
19 12.0%. The most commonly affected finger was the 3rd DIP. Distal interphalangeal
20 joint erosions were generally exhibited a unilateral-asymmetric pattern. Age emerged as
21 an independent predictive factor of DIP joint erosions ($p = 0.001$).

1 Jacob J et al. reported a higher rate of DIP joint erosion in seropositive RA patients
2 compared to the aged and sex-matched control group (37% versus 14%) [16]. In their
3 study, isolated DIP joint involvement was absent, with the most commonly affected
4 joint was 3rd DIP, and DIP joint involvement was generally unilaterally [16]. These
5 findings are consistent with our study. In another study, the rate of DIP joint erosion
6 was 16% in patients with RA. Halla JT et al. reported that the 2nd and 5th DIPs were
7 the most commonly affected joints [17]. In addition, they reported the predominance of
8 asymmetric patterns and the absence of isolated DIP involvement in RA patients [17].
9 Papisavvas GK et al. reported the rate of DIP joint erosion as 12% in patients with RA
10 and 70% of DIP joint erosion presenting an asymmetrical pattern [18]. In a prospective
11 study, erosive changes in DIP joints were 5.3% at the disease onset and 14.9% in the
12 following third years in patients with RA [19]. The exclusion of OA is a cornerstone in
13 the studies including hand articulations. Because RA patients have an increased risk of
14 developing OA than the non-RA population and OA is associated with enhanced
15 marginal erosions in DIP joints in patients with RA [20,21].

16 In one study, DIP joint erosion was present in 12% of the RA group which was nearly
17 half of the prevalence seen in the PsA group [22]. Another study reported a significantly
18 higher rate of DIP erosion in patients with PsA compared to those with RA [23]. In this
19 study, the mean age of RA patients was similar but the mean disease duration time was
20 lower compared to our study results [23]. In our study, both seropositive and
21 seronegative RA patients had a rate of DIP joint erosion of 11.5% and 12.7%,
22 respectively ($p > 0.05$). Ikemura S et al. identified an association between DIP joint
23 erosion and advanced age, long disease duration, and PIP joint erosion [24]. Mizuuchi T

1 et al. reported a clinical DIP joint involvement rate of 2.1% in RA without any
2 radiological evidence. Patients with clinical DIP involvement were significantly
3 younger and female patients were more frequently affected [25].

4 Limitations of our study included its retrospective nature, intra- and inter-observer
5 differences, lack of total modified Sharp score (mSS), and absence of imaging evidence
6 such as ultrasonography or contrast-enhanced magnetic resonance imaging to detect
7 synovitis. Distal interphalangeal joint synovitis can be documented by ultrasonography
8 and indocyanine green-enhanced fluorescence optical imaging in patients with RA [26].

9 In conclusion, we detected DIP joint erosion in %12 of RA patients and identified age
10 as an independent predictive factor for developing DIP joint erosion in RA. Advanced
11 age could have affected our results because hand erosions increase above 50 years in a
12 healthy population [27]. Our results may provide insight into the consideration of DIP
13 involvement in RA patients and its evaluation and differential diagnosis.

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1 **Table 2:** The general characteristics of patients with and without DIP involvement

Variable	DIP joint involvement (-) group	DIP joint involvement (+) group
Total patient count, n	1067	146
Male %, (n)	18.1 (193)	8.9 (13)
Female %, (n)	81.9 (874)	91.1 (130)
Smoking history %, (n)	32.1 (343)	29.4 (43)
Age (mean±standard deviation, years)	53.9±12.5	57.6±12.2
Disease duration time (median [25-75p], years)	5 [2-11]	6 [2-12]
RF positivity %, (n)	56.8 (606)	54.8 (80)
Anti-CCP positivity %, (n)	54.2 (579)	52 (76)
Biologic agent history %, (n)	30.3 (324)	33.5 (49)
Rheumatoid arthritis type joint involvement %, (n)	95 (1014)	98 (143)
Serious joint involvement %, (n)	24.2 (259)	28 (41)

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3 Abbreviations: DIP, distal interphalangeal; RF, rheumatoid factor anti-CCP, anti-cyclic
 4 citrullinated peptide

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1 **Table 3:** Classification of patients according to autoantibodies

Patient groups	Patient with DIP erosion/total patient, (%)
Group 1: RF (+) and Anti-CCP (+)	67/570 (11.8)
Group 2: RF (+) and Anti-CCP (-)	12/116 (10.3)
Group 3: RF (-) and Anti-CCP (+)	9/85 (10.6)
Group 4: RF (-) and Anti-CCP (-)	58/442 (13.1)

2

3 Abbreviations: DIP, distal interphalangeal; RF, rheumatoid factor; anti-CCP, anti-cyclic

4 citrullinated peptide