

# Comparison of Ultrasonography and X-Rays for the Diagnosis of Synovitis and Bony Erosions in Small Joints of Hands in Early Rheumatoid Arthritis: a Prospective Study

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## ABSTRACT

**Objective:** Rheumatoid arthritis (RA) is the most common inflammatory joint disease. Many studies have shown that erosions and synovitis can be picked up at an early stage on ultrasonography (US) when X-rays appear normal. Ultrasonography exams in inflammatory arthritis helps in determining objective evidence of inflammatory arthritis- synovitis, erosions, effusions and also help in monitoring therapy in established RA patients.

**Materials and methods:** Ninety patients aged over 18 years, who were diagnosed with RA (according to 2010 ACR criteria) of less than two years duration, were included in the study prospectively. Baseline data, disease activity score of 28 joints (DAS 28 score), complete clinical evaluation and laboratory investigations were registered. Conventional radiographs of both hands were taken in posteroanterior views. A power Doppler US was performed on all metacarpophalangeal (MCP) joints and proximal interphalangeal (PIP) joints of both hands.

**Results:** Out of the 90 patients, 84 had positive findings on US and only 13 subjects had positive radiographic findings. The second MCP was the most common joint involved on US. The mean cumulative

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Article received on the 4<sup>th</sup> of January 2021 and accepted for publication on the 25<sup>th</sup> of January 2021

*flow signal (CFS) score was  $4.15 \pm 5.12$ . The relation between CFS and DAS 28 scores was highly significant, with  $p$  value  $< 0.01$ .*

**Conclusion:** *Ultrasonography can detect changes in joints at an earlier stage than radiographs. Both grey scale and power Doppler US have a role in detecting synovitis and erosions.*

**Keywords:** inflammatory, sensitivity, mean CFS.

## INTRODUCTION

**R**heumatoid arthritis (RA) is the most common inflammatory joint disease. Musculoskeletal ultrasonography (US) is increasingly being used for the diagnosis and evaluation of inflammatory arthritis. Studies have shown that ultrasound can detect more erosions than X-rays and, more importantly changes can be picked up at an early stage on ultrasonography when x-rays appear normal. US is able to differentiate effusion from synovitis without contrast, unlike in MRI (1, 2). Disease modifying anti-rheumatic drugs (DMARD) therapies like anti-Tumor necrosis factor (anti-TNF) prevent irreversible damage best with early treatment (3). □

## MATERIALS AND METHODS

**N**inety patients aged over 18 years and diagnosed with RA (according to 2010 ACR criteria) of less than two years duration, who came to the medicine OPD of PGIMER Outreach Center, Sangrur, were recruited in the study prospectively for a period of six months. Patients with long standing disease ( $> 2$  years duration), those with history of trauma and pregnant patients were excluded from the study.

A pre-informed consent was obtained from all enrolled patients. The study was approved by the Institutional Review Board/Ethics committee (PGIMER, Chandigarh, functioning under the Ministry of Health and Family Welfare, Government of India).

### Methodology

Patients presenting to the medicine OPD of PGIMER Outreach Center, Sangrur, with complaints of joint pain were evaluated. Patients with RA diagnosed according to 2010ACR/EULAR criteria were selected for the study (4). Disease duration of less than two years was taken arbi-

trarily to assess the US findings of synovitis, erosions and effusion in early RA patients.

Baseline data regarding detailed disease history, demographic and clinical characteristics was collected prospectively throughout the course of study on a predesigned Performa. Patients were subjected to complete rheumatologic assessment, which included clinical, laboratory and radiologic evaluation.

### Clinical evaluation

We elicited a thorough medical history, with particular attention to joint pain, reported swelling, and the presence, location, and duration of morning stiffness.

Disease activity was assessed using the disease activity score of 28 joints (DAS28) (5), which was graded as follows:  $> 5.1$  = high disease activity;  $3.2 - 5.1$  = moderate disease activity;  $< 3.2$  = low disease activity; and  $< 2.6$  = disease remission.

### Lab evaluation

Rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies – We performed both RF and anti-CCP antibody testing when initially evaluating a patient with suspected RA. The results of both tests are informative, since a positive result for either test increases overall diagnostic sensitivity, while the specificity is increased when both tests are positive.

Erythrocyte sedimentation rate (ESR) and serum C-reactive protein (CRP) levels – Both ESR and CRP levels were evaluated since these are typically elevated in RA.

### Radiological evaluation

Radiographs of the hands, wrists, and feet – Conventional radiographs of both hands were taken in posteroanterior views and further evaluated for erosions and joint space narrowing by a single radiologist.

Ultrasonography – Ultrasound was done using Mindray DC 60 with 10-14 MHz linear probe on all patients by a single sonologist. Ultrasonography was performed on all MCP and PIP joints of both hands using a high frequency linear transducer (10-14 MHz). Power Doppler assessment was also done to assess hyperemia. While doing so, minimal pressure was used with a liberal amount of gel. Doppler gain threshold was set to increase sensitivity but to minimize artefact. While assessing the MCP joints, both longitudinal and transverse scans were done and both dorsal and palmar aspects were scanned. Also, the radial aspect of index finger and ulnar aspect of little finger were scanned. The PIP and MTP were assessed in a similar fashion.

Erosions were diagnosed using OMERACT definition, stating that in US interruption of bone surface must be seen in two planes to be categorized as erosion. One must also look at the bare areas where the capsule attaches outside the articular cartilage margin for the presence of these early erosions specifically at the dorsal and volar synovial recesses and radial aspect of the second MCP joint (6).

Semi-quantitative grading of synovitis was done using power Doppler as described by Szkudlarek M, et al (1): 0 = none; 1 = single vessel; 2 = confluent signal occupying less than half of the synovial area; and 3 = confluent signal occupying more than half of the synovial area.

Cummulative flow signal was calculated as sum of scores obtained from 20 joints (MCP and PIP joints of each hand) in each patient.

**Statistical analysis**

The data was entered into MS excel and analyzed with SPSS version 20 (IBM Corp., Armonk, NY, USA). Descriptive statistics (percentage, mean, median, mode) were calculated. Continuous variables were expressed as mean±standard deviation (SD). Unpaired Student’s t-test and Chi-square test were used to determine statistical difference between variables. The level of significance will be fixed at <0.05 at 95% confidence interval (CI). □

**RESULTS**

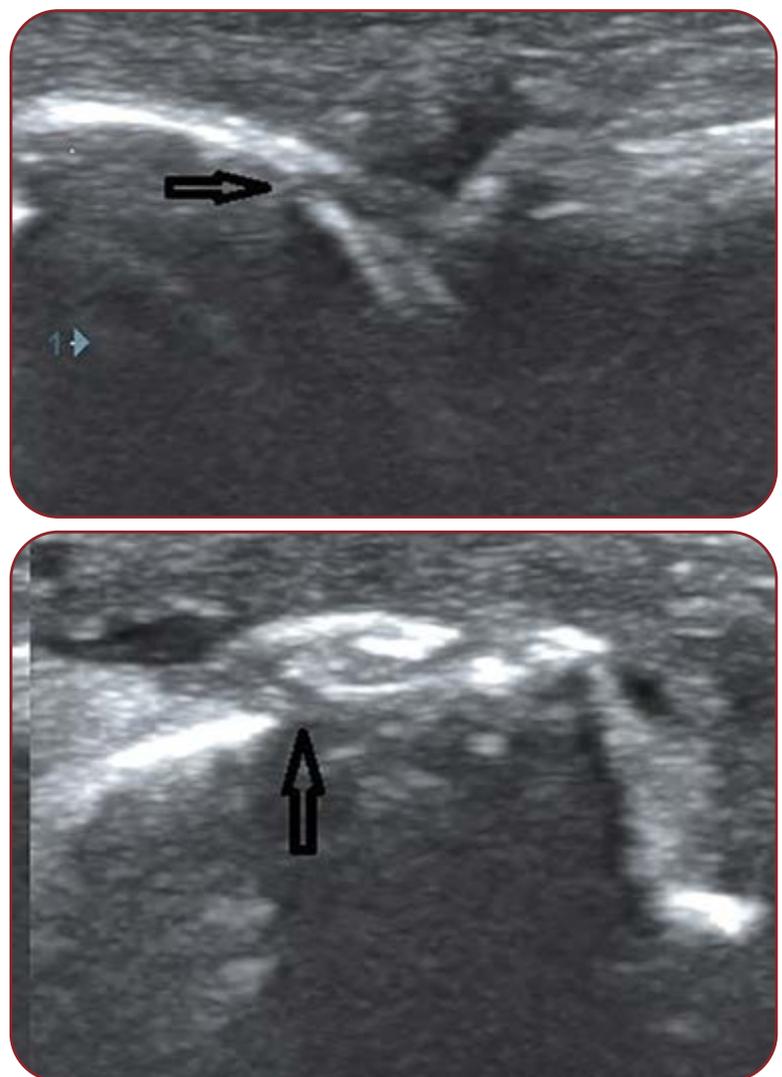
A total of 90 patients were recruited in the study, out of which 78 were females and

12 males, showing a female preponderance. Age ranged from 23 to 76 years, with a mean of 46.24±12.44. The mean ESR was 38.67±28.32 (mean±SD) mm/1st hr. The mean RA titre was 39.65±63.67 (mean±SD) IU/mL. The mean CRP was 10.45±12.43 (mean±SD) mg/dL. The mean CFS score was 4.15±5.12 (mean±SD).

DAS 28 showed low disease activity in 21 patients, moderate disease activity in 45 patients, high disease activity in 21 patients and remission in two patients.

**X-ray and ultrasonography findings**

Out of all 90 patients, 84 had positive findings on ultrasound and only 13 patients had positive



**FIGURE 1.** Images showing erosions in the second MCP joint of the right hand. Interruption of bone surface is seen in two planes (arrow)

Technique	Erosions present	Erosions absent	Total	p value
Ultrasound (%)	42 (46.67)	48 (53.33)	90 (100)	<0.00001
X-ray (%)	6 (6.67)	84 (93.33)	90 (100)	

TABLE 1. Comparison between X-rays and ultrasound in detecting erosions

Type of joint	Right hand		Left hand	
	Erosions (%)	Synovitis (%)	Erosions (%)	Synovitis (%)
1 <sup>st</sup> MCP	6 (6.67)	6 (6.67)	3 (3.33)	6 (6.67)
2 <sup>nd</sup> MCP	15 (16.67)	39 (43.33)	5 (5.55)	27 (30)
3 <sup>rd</sup> MCP	9 (10)	21 (23.33)	10 (11.11)	19 (21.11)
4 <sup>th</sup> MCP	6 (6.67)	15 (16.67)	6 (6.67)	8 (8.89)
5 <sup>th</sup> MCP	3 (3.33)	15 (16.67)	3 (3.33)	15 (16.67)
1 <sup>st</sup> PIP	3 (3.33)	3 (3.33)	6 (6.67)	4 (4.44)
2 <sup>nd</sup> PIP	7 (7.78)	4 (4.44)	8 (8.89)	3 (3.33)
3 <sup>rd</sup> PIP	8 (8.89)	9 (10)	6 (6.67)	2 (2.22)
4 <sup>th</sup> PIP	6 (6.67)	2 (2.22)	5 (5.55)	3 (3.33)
5 <sup>th</sup> PIP	6 (6.67)	6 (6.67)	2 (2.22)	4 (4.44)

TABLE 2. Percent of erosions and synovitis in MCP and PIP joints of both hands

	Low DAS 28	Moderate DAS 28	High DAS 28	Remission	p value
Number of patients (%)	21 (23.33)	45 (50)	21 (23.33)	2 (2.22)	0.004233 (significant)
CFS (mean±SD)	1±0.62	2.98±1.78	10.29±7.30	1±0.82	

TABLE 3. CFS values in patients with different DAS 28 scores

	MCP joints (n=900)	PIP joints (n=900)
Presence of synovitis	114	27
Grade 1 synovitis	84	27
Grade 2 synovitis	22	19
Grade 3 synovitis	8	3

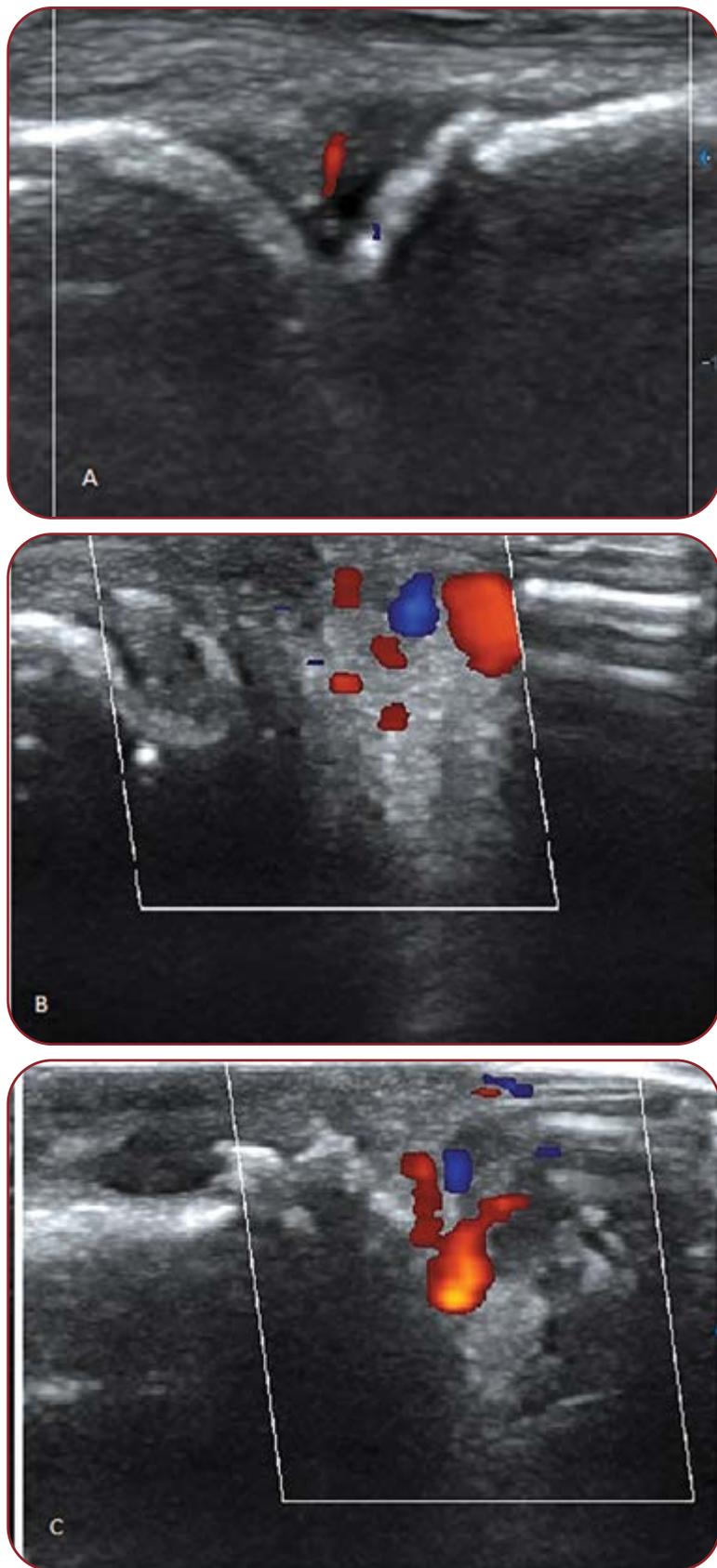
TABLE 4. Percent of erosions and synovitis in MCP and PIP joints of both hands

radiographic findings. All 13 patients with positive X-ray findings had changes on US, either synovial hypertrophy, joint effusion or bony erosions. Joint space reduction was seen in 10 patients on X-ray. Erosions were seen in six patients by X-ray and in 42 patients on US. Therefore, ultrasound has a higher sensitivity to detect erosions than X-rays in early cases of RA (Table 1, Figure 1).

The second MCP was the most common joint involved on ultrasonography, among all the MCP

and PIP joints screened in all the patients. A total of 66 second MCP joints had positive findings among 39 patients with involved second MCP joints. Total of 171 MCP joints were involved in 78 patients. (Table 2).

The most common PIP joint involved was the third PIP joint. It was involved in nine patients, in whom 15 third PIP joints had positive findings. Total of 57 PIP joints were involved in 30 patients (Table 2).



**FIGURE 2.** Images showing Grade 1 (Figure 2A), Grade 2 (Figure 2B) and Grade 3 (Figure 2C) synovitis

The mean CFS score was  $4.15 \pm 5.12$ . It was  $1 \pm 0.62$  in patients with low DAS 28;  $2.98 \pm 1.78$  in patients with moderate DAS 28;  $10.29 \pm 7.30$  in high DAS 28 patients and  $1 \pm 0.82$  in patients in remission according to DAS 28 score. The relation between CFS and DAS 28 scores was highly significant with  $p$  value  $< 0.01$  (Table 3).

Grade 1 synovitis was present in most of the joints with positive findings on ultrasonography. 84 MCP and 19 PIP joints had grade 1 synovitis; 22 MCP and five PIP joints had grade 2 synovitis and eight MCP and three PIP joints had grade 3 synovitis. (Table 4, Figure 2). □

### DISCUSSION

Ultrasound is a reliable method to diagnose early changes of rheumatoid arthritis in patients. Both gray scale and power Doppler have proved to be useful in detecting erosions and synovitis. This early detection of joint changes can significantly affect the treatment options and prognosis of the patients early in the course of the disease and thus, significantly improving the disease progression. Moreover, conventional radiographs fail to detect early synovitis and erosions (7, 8).

In our study, erosions were detected by ultrasound in 46.67% of patients, whereas X-rays could detect erosions in 6.7% of patients that is ultrasound has higher sensitivity in detecting erosions that X-rays.

A non-randomized cross-sectional clinical study done by Ying-hua Zhang in 2017 on 189 patients who had nonspecific musculoskeletal symptoms. They compared the sensitivity and specificity of US with radiography and clinical investigations in early RA patients. X-rays and US were done of second and third MCP joints, second and third PIP joints and second and fifth MTP joints. They found that grey scale US was more effective in detecting early synovitis than radiographs and clinical investigations (9). Pinar Kaplan Ozer *et al* published a study in 2017 to detect subclinical inflammation in RA patients with clinical remission by power Doppler (PD). They concluded that PD showed a crucial role in determining the subclinical synovitis. US defined remission may be considered for good functional status and real remission in patients with RA (10).

Mean CFS was higher in patients with higher DAS28 score and lower in patients with low

DAS28 score. Renu Saigal *et al* did a study in 2017 to evaluate joint involvement in RA by US including PD and gray scale imaging and its comparison with X-ray changes. They also correlated the US and X-ray changes with disease activity parameters. They included patients with early RA (< 3.5 years duration). They concluded that US detected cumulative flow signal score (CFS) which correlated significantly with DAS 28, CRP and ESR. Also, US is more sensitive than X-rays for detection of erosions (11).

A study was done by Athan Ballet in 2011 to evaluate the reproducibility of US and to compare its efficacy with that of MRI and radiography for the detection of bone erosion in RA patients. Twenty-one studies were included in this meta-analysis. US and MRI efficacies were comparable at both joint levels. US detected significantly more erosion than conventional radiography. They concluded that US is more effective for erosion detection than radiographs and has a comparable efficacy to MRI with good reproducibility (12).

Power Doppler has a very good predictive value. In a study from Arthritis and Rheumatol in 2007, initial power Doppler grade in 42 patients with early RA had the strongest correlation in one year follow up with radiographic progression vs initial clinical or laboratory parameters (13).

A study was done in 2007 to evaluate and compare power-Doppler (PD) to radiography for the detection of synovitis and erosions in patients with early RA. Ultrasound detected 15 erosions in 10 patients at baseline and 31 erosions in 12 patients on follow-up; X-rays detected one erosion at baseline and five erosions in three patients on follow-up whereas power Doppler detected synovitis in all patients at baseline and on follow-up. Therefore, they concluded that sequential US along with power Doppler can determine disease progression in patients with early RA (14).

A study was done in 2003 by C. Weidekamm *et al* and publishes in arthritis and rheumatism. They evaluated the diagnostic value of gray scale US and PD compared with that of clinical examination and X-rays. They concluded that US detects 20% more erosions than radiography. Hypervascularisation was observed in 34% of joints by PD (15).

In a study by Wakefield *et al* published in 2000 in arthritis and rheumatism, PA radiographs

and US of the dominant hands were done in 100 patients. Sonography detected more erosions as compared with x-rays. In early disease, detected rate of erosions on US was 6.5 times than by X-rays. radiography. Therefore, they concluded that sonography is a reliable technique that detects more erosions than radiography, especially in early RA (16).

Radiography is considered the gold standard and is a part of American college of Rheumatology (ACR) criteria but may not show joint damage early in the disease course because it is unable to directly visualize synovium and bone marrow. Therefore, musculoskeletal ultrasonography (US) and Magnetic Resonance imaging (MRI) is increasingly being used for the diagnosis and evaluation of inflammatory arthritis. Ultrasound has many advantages over X-ray in the assessment of synovitis. Ultrasound exams in inflammatory arthritis helps in determining objective evidence of inflammatory arthritis- synovitis, erosions, effusions and also help in monitoring therapy in established RA patients. Complications of local inflammation like tendon tear, nerve compression and infection can also be picked up by US. US is easily available, radiation free, reliable technique US has high sensitivity than clinical investigations and X-rays in identifying early synovitis. US can rapidly assess many widely spaced joints, coupled with clinical correlation. With US we can dynamically move and compress the synovial spaces and tendons and also, US can be used to guide therapy. The use of colour flow Doppler studies enables us to directly visualize the blood flow and vascular supply within the synovium of joints and tendons, and within tendons themselves without the use of contrast, unlike MRI in which contrast is necessary. Therefore, in patients where MRI contrast is contraindicated, US is much safer option. Advantages of MRI include a larger field of view, better image presentation, and MRI can demonstrate cartilage and deep joints in their entirety. Contrast enhanced MRI provides a better measure of capillary permeability and extracellular fluid than does ultrasound (17). Therefore, early diagnosis and treatment of rheumatoid synovitis can reduce the progression of RA and new Disease modifying anti-rheumatic drugs (DMARD) therapies like anti-Tumor necrosis factor (anti-TNF) prevent irreversible damage best with early treatment.[3] □

## CONCLUSIONS

We conclude that ultrasonography can detect changes in joints at an earlier stage than radiographs. Both grey scale and power Doppler ultrasonography have a role in detecting synovitis and erosions. Ultrasound also has

higher sensitivity in detecting erosion than conventional radiographs. This can have a great impact on the diagnosis, treatment and prognosis of patients with RA. □

*Conflicts of interest: none declared.*

*Financial support: none declared.*

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