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Diagnostic Value of Musculoskeletal Ultrasound in Newly Diagnosed Rheumatoid Arthritis Patients

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Abstract

Objective: This study aimed to assess the efficacy of musculoskeletal ultrasound (US) in the detection of inflammatory and destructive changes in finger and wrist joints and tendons in patients with rheumatoid arthritis (RA) and compared US with contrast-enhanced magnetic resonance imaging (MRI).

Material and Methods: We included a cohort of patients with newly diagnosed RA. The wrist and finger joints of the same hand; 2., 3., 4. metacarpophalangeal (MCP); and 2., 3., 4. proximal interphalangeal (PIP) joints were evaluated using both US and MRI. US evaluated active synovitis, the power Doppler (PD) signal, bone erosion, and tenosynovitis in joints. Clinical examination and the erythrocyte sedimentation rate and C-reactive protein level were simultaneously evaluated.

Results: We enrolled 31 patients with newly diagnosed RA and included 279 joints in the study. Radiocarpal synovitis was detected more frequently than midcarpal and ulnocarpal joint synovitis in the wrist joints. The sensitivity, specificity, and accuracy of US in detecting PD synovitis in wrist joints were 0.73, 0.76, and 0.74, respectively, compared with MRI. Both PDUS and gray-scale US had lower sensitivity, specificity, and accuracy in detecting synovitis and erosions in finger joints compared with MRI. PD synovitis total scores were highly correlated with disease duration, morning stiffness, and hand grip strength ($r=0.448$, $p=0.032$; $r=0.500$, $p<0.001$; $r=0.843$, $p<0.001$).

Conclusion: We demonstrated that the efficacy of US is comparable with that of contrast-enhanced MRI in detecting arthritis. However, clinicians must be careful so as to not obtain misleading information regarding MCP and PIP joints using US in patients with synovitis and erosions.

Keywords: Rheumatoid arthritis, ultrasonography, magnetic resonance imaging, inflammation

Introduction

The synovial membrane is the primary site of rheumatoid inflammation. In early rheumatoid arthritis (RA), synovitis appears to be the primary abnormality responsible for structural joint damage (1). Early diagnosis of arthritis and early administration of immunosuppressive medications are now recommended to prevent disability (2). Therefore, the usefulness of clinical examination in the diagnosis of early RA may be limited.

The higher resolution of musculoskeletal structures offered by high-frequency transducers has increased the use of ultrasonography (US) in rheumatology (3). US has been found to be better than clinical examination in detecting synovitis, with some authors suggesting that it should be used in place of clinical assessment for patient evaluation (3,4). Despite some studies

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that evaluated US for assessing RA, the validity, sensitivity, and specificity of US in detecting RA remain unclear.

Several previous studies have highlighted the ability of US to detect tenosynovitis (5). Despite good results in detecting synovitis and tenosynovitis, visualizing bone erosions by US can be problematic.

In recent years, MRI usefulness in patients with RA has been widely investigated, and its value has been confirmed in studies of both large joints and finger joints in comparison with histological evaluation (6,7). The ability of magnetic resonance imaging (MRI) to demonstrate bone erosion and bone edema in RA is the greatest strength of this method over US.

We evaluated joints and tendons using gray-scale US and power Doppler US (PDUS) and compared the findings with those using MRI T2- and T1-weighted scans and scans with contrast. This study aimed to assess US for the detection of inflammatory and destructive changes in finger and wrist joints and tendons in patients with RA.

Material and Methods

The study included 31 patients with newly diagnosed RA who were defined according to the 2010 RA American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria (8). In all patients, radiocarpal, midcarpal, and ulnocarpal joints; finger joints of the same hand 2., 3., 4. metacarpophalangeal (MCP); and 2., 3., 4. proximal interphalangeal (PIP) joints were examined in the more-affected hand using contrast-enhanced MRI, gray-scale US, and PDUS. A total of 279 joints were examined: 31 radiocarpal, 31 midcarpal, 31 ulnocarpal, 93 MCP, and 93 PIP joints. All findings were retrospectively obtained from the patients' charts. The study was approved by the Local Ethics Committee of Sakarya University. Informed consent was obtained from each patient.

All joints were clinically assessed by the same investigator who was an experienced rheumatology clinician. The presence of tenderness and swelling (1) or the absence thereof (0) was scored for each of the seven joints (wrist, 2., 3., 4. MCP joints, and 2.3.4. PIP joints). Each patient was asked regarding the duration of disease (in years) and duration of morning stiffness (in minutes). Hand-grip strength was evaluated in three degrees on the Likert scale. Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) levels, anti-cyclic citrullinated peptide (CCP), and rheumatoid factor (RF) were assessed in each patient on the same day as the US and MRI examinations.

Ultrasonography

The hand joints were examined using a 5–13-MHz linear array probe (General Electric, New York, United States of America). All patients were examined by a trained ultrasonographer with 2 years of experience (US1), after which the examinations were repeated by another trained ultrasonographer with 6 months of experience (US2); both clinicians had a rheumatology background. The more clinically affected hand was assessed. The dorsal aspect of the wrist was scanned from side to side in the longitudinal plane and from superior to inferior in the transverse plane. The finger joints were scanned in the longitudinal and transverse planes from the palmar and dorsal aspects.

Synovitis was classified on gray-scale images using a semi-quantitative scoring method. The approach features use of a 0–3 scale, in which 0 corresponds to no synovitis, 1 to mild synovitis, 2 to moderate synovitis, and 3 to severe synovitis (9). Grade 1 synovitis may occur in normal populations; therefore, patients of grades 2 and 3 (only) were considered to have abnormal synovitis (9). The presence of synovitis (1) or the absence thereof (0) was scored for each of the nine joints, and total synovial scores were calculated.

The maximal area of augmentation on PDUS was recorded using a previously described semi-quantitative technique featuring the use of a 0–3 scale, in which 0 corresponds to normal/minimal vascularity, 1 to mild hyperemia, 2 to moderate hyperemia, and 3 to marked hyperemia (10). The presence of PD synovitis (1) or the absence thereof (0) was scored for each of the 26 joints, and total PD synovitis scores were calculated.

Tenosynovitis was recorded in the extensor digitorum carpi, extensor carpi ulnaris, extensor carpi radialis, and in each of the three flexor digitorum tendons of each region. A four-grade semi-quantitative scoring system (i.e., grade 0, normal; grade 1, minimal; grade 2, moderate; grade 3, severe) was used to score tenosynovitis that was revealed on gray-scale US. The presence of tenosynovitis (1) or the absence thereof (0) was scored for each of the six tendon regions, and total tenosynovitis scores were calculated (11).

Bone erosion was defined as irregularities of the bone surface of the area adjacent to the joint and was observed in longitudinal and transverse planes. The presence of bone erosion (1) and the absence thereof (0) were scored for each of the nine joints, and total bone erosion scores was calculated (12). US examinations were completed in 20 min, and all images were stored.

Magnetic Resonance Imaging

On the following day, MRI was performed by a radiologist who was experienced in musculoskeletal MRI (1.0 T Siemens Impact MR unit (Siemens, Erlangen, Germany). Continuous axial and coronal pre-gadolinium–diethylenetriamine penta-acetic acid (pre-Gd-DTPA) and post-Gd-DTPA T1-weighted spin-echo sequences of the second to fourth MCP, PIP, and wrist joints and preselected tendons of the dominant hand were scanned. The Gd-DTPA (0.1 mmoL/kg body weight) was intravenously injected between repeated T1-weighted spin-echo MRI sequences. The definitions of the applied MRI RA pathologies were in accordance with the Outcome Measures in Rheumatology Clinical Trials (OMERACT) recommendations (13).

The scans were assessed in quadrants for bone erosion (Figure 1) and signs of inflammation (synovitis and tenosynovitis) (Figure 2,3). Synovitis was scored according to the semi-quantitative system (grades 0–4) that was introduced by the EULAR–OMERACT RA MRI reference image atlas for the wrist, MCP, and PIP joints.

Statistical Analysis

The SPSS statistical software was used for statistical analysis (IBM SPSS statistics version 20.0, Chicago, IL, USA). The agree-

ment between imaging methods compared with the clinical examination is reported as the overall agreement, which is defined as the proportion of exact agreements to the overall number of trials (expressed as a percentage). Furthermore, the agreement was expressed as mean sensitivity and specificity. The correlation between US and MRI synovitis scores was estimated using a Pearson's correlation test. Intraclass correlation coefficients (two-way mixed effects model, consistency definition) and unweighted kappa statistics were used to calculate the interobserver agreement.

Results

We included 31 patients with newly diagnosed RA and 279 joints in the study. The main demographic and clinical features are summarized in Table 1. Of the cases, 38.7% were RF positive and 29% were anti-CCP positive. US demonstrated synovitis, tenosynovitis, and bone erosions (Figure 4-6).

Of a total of 217 examined joint regions, 25% (n=54) of patients had tender joints and 18% had swollen joints. On clinical examination, wrist swelling was detected in 64% (n=20) of wrist joints. MCP and PIP joint swellings were detected in 18% and 9%, respectively, of finger joints (n=17 and n=9, respectively). Compared with US and clinical examination, clinical examinations identified fewer cases of joint synovitis (Table 2).

Of a total of 279 examined joint regions, 37% (n=106) had synovitis detected by US. Radiocarpal synovitis was detected more frequently than midcarpal and ulnocarpal joint synovitis in wrist joints (Table 2). The second MCP and 2.PIP were more likely to exhibit synovitis than the other finger joints (12% and 7%, respectively).

An increased PD signal was demonstrated in 33.6% of (n=94) these joints. Radiocarpal PD synovitis was detected more frequently than in the midcarpal and ulnocarpal joint regions in the wrist joints. The second MCP and PIP joints were the most likely sites of synovitis in the finger joints [7/93 (7%), 4/93 (4%)].

Thirty-two percent of patients showed evidence of tenosynovitis in at least one wrist tendon on gray-scale US, and 11% showed evidence of tenosynovitis in at least one finger tendon.

Bone erosions were detected in 8% (n=23) of the 279 total joint regions using US. Ulnocarpal joint erosions, midcarpal, and MCP joint erosions were the most frequent (Table 2).

Table 1. Clinical and laboratory features of the patients

	Mean±SD [IQR]
Age (year)	56.31±13.62 [57.75]
Disease duration (month)	5.69±5.64 [7.00]
Morning stiffness (hour)	1.41±0.58 [1.50]
ESR (mm/hour)	43.49±26.58 [38.50]
CRP (mg/L)	23.91±22.09 [21.35]
Total synovitis scores	2.35±1.08 [2.50]
Total PD synovitis scores	2.16±1.03 [2.50]
Total bone erosion scores	0.26 ±0.81 [0.00]

ESR: erythrocyte sedimentation rate; CRP: C-reactive protein;, PD: power doppler, IQR: interquartile range; SD: standard deviation

This study found a whole concurrence of 87%, 89%, and 73% for the presence/absence of US synovitis, PD synovitis, and bone erosions, respectively, in the inter-observer reliability evaluation, with κ=0.69, 0.70, and 0.59 for the presence/absence of US synovitis, PD synovitis, and bone erosions, respectively.

The sensitivities, specificities, and test accuracies of the US parameters compared with MRI are shown in Table 3.

Synovitis total scores were highly correlated with morning stiffness and hand-grip strength (r=0.591, p=0.001; r=0.833, p=0.000). PD synovitis scores were highly correlated with the disease duration, morning stiffness, hand-grip strength (r=0.448, p=0.032; r=0.500, p<0.001; r=0.843, p<0.001). Tenosynovitis was correlated with morning stiffness and hand-grip strength (r=0.506, p<0.001; r=0.335, p=0.05). However, bone erosions were correlated with only the disease duration (r=0.642, p=0.001).

Among the laboratory parameters, ESR and CRP levels were correlated with PD synovitis total scores (r=0.378, p=0.043; r=0.412, p=0.02). Tenosynovitis was weakly correlated with CRP

Table 2. Ultrasonographic and clinical examination of wrist and finger joints in patients with RA

	US examination (patients %)	Clinical examination (patients %)
Synovitis		
Radiocarpal Joint	87% (27/31)	N/A
Midcarpal joint	80% (25/31)	N/A
Ulnocarpal joint	67% (21/31)	N/A
Wrist joint tenderness	N/A	70% (22/31)
Wrist joint swelling	N/A	64% (20/31)
MCP joint	23% (22/93)	N/A
MCP joint tenderness	N/A	23% (22/93)
MCP joint swelling	N/A	18% (17/93)
PIP joint	12% (11/93)	N/A
PIP joint tenderness	N/A	12% (11/93)
PIP joint swelling	N/A	9% (9/93)
PD Synovitis		
Radiocarpal Joint	87% (27/31)	N/A
Midcarpal joint	77% (24/31)	N/A
Ulnocarpal joint	51% (16/31)	N/A
MCP joint	17% (16/93)	N/A
PIP joint	11% (11/93)	N/A
Bone erosion		
Radiocarpal Joint	6% (2/31)	N/A
Midcarpal joint	9% (3/31)	N/A
Ulnocarpal joint	12% (4/31)	N/A
MCP joint	9% (9/93)	N/A
PIP joint	5% (5/93)	N/A

MCP: metacarpophalangeal; PIP: proximal interphalangeal; Power Doppler: power doppler; US: ultrasound; N/A: not available

Table 3. Sensitivity, specificity, and test accuracy of US parameters with MRI as the standard reference method

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Test accuracy
Synovitis					
Radiocarpal Joint	92	100	100	66	87
Midcarpal joint	84	100	84	60	87
Ulnocarpal joint	90	60	76	40	74
Wrist joint	89	80	94	66	87
MCP joint	64	64	68	60	64
PIP joint	50	49	21	78	51
PD synovitis					
Radiocarpal Joint	74	100	100	36	77
Midcarpal joint	75	100	100	53	80
Ulnocarpal joint	68	60	64	64	64
Wrist joint	73	76	89	52	74
MCP joint	66	61	48	77	64
PIP joint	64	64	68	60	64
Bone erosion					
Radiocarpal Joint	100	65	16	100	67
Midcarpal joint	66	75	28	95	74
Ulnocarpal joint	66	67	18	95	67
Wrist joint	75	69	18	96	69
MCP joint	43	46	40	50	45
PIP joint	27	65	34	57	51

MCP: metacarpophalangeal; PIP: proximal interphalangeal

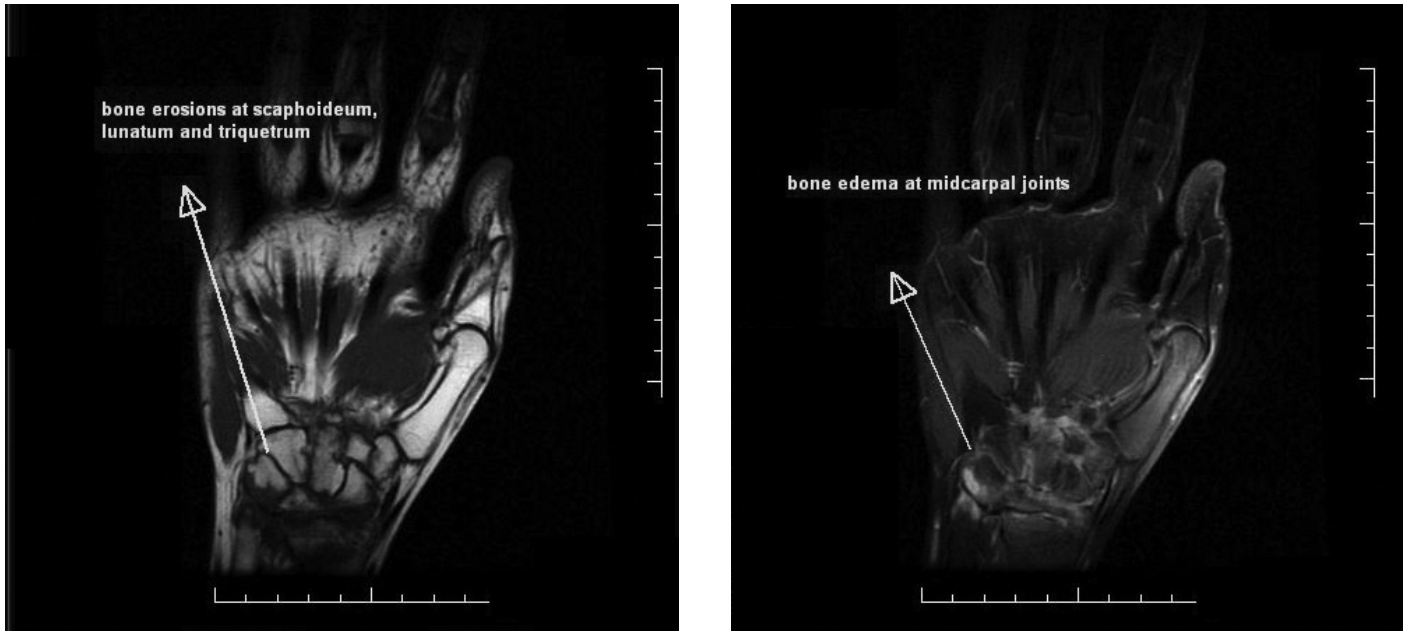


Figure 1. Coronal T1-weighted magnetic resonance image with contrast administration reveals multiple erosions at the wrist joint

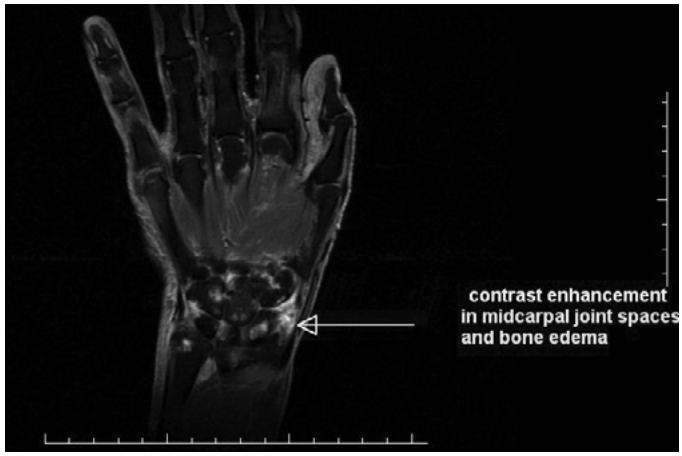
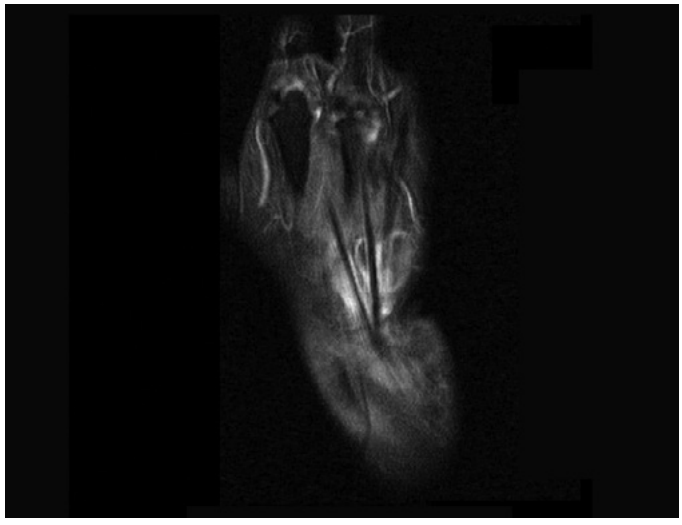


Figure 2. Coronal T1-weighted magnetic resonance image with contrast administration reveals synovitis at the wrist joint



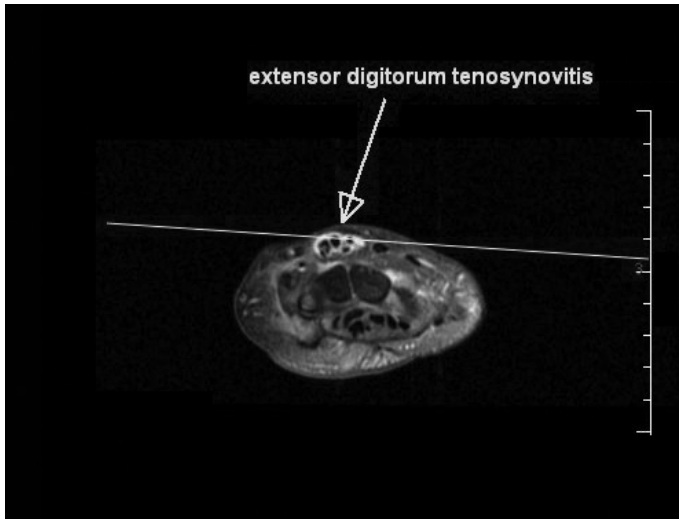


Figure 3. Coronal and axial magnetic resonance image with contrast administration detects tenosynovitis at the wrist joint

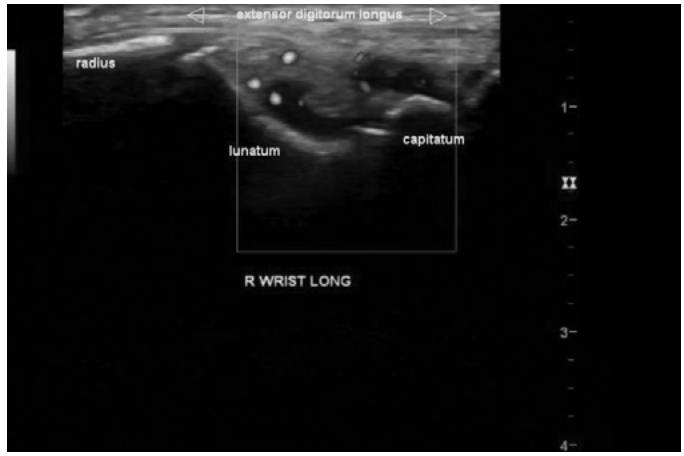


Figure 4. Power Doppler signals show active synovitis at the wrist joint

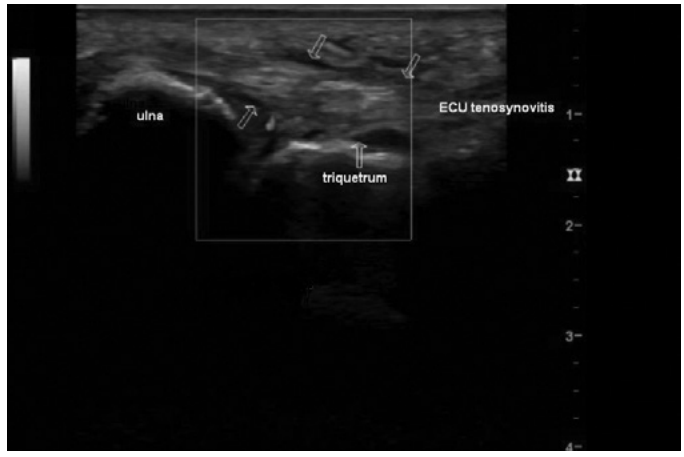


Figure 5. Ultrasonography of extensor tenosynovitis in the wrist joints

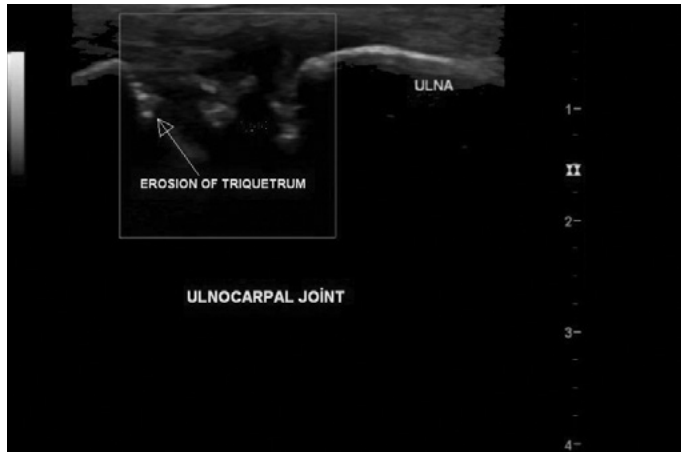


Figure 6. Ultrasonography of bone erosion at the ulnocarpal joint

levels (r=0.446, p=0.012); however, there was no correlation between synovitis scores and ESR or CRP levels.

Discussion

We evaluated the inflammatory and destructive changes in finger and wrist joints and tendons affected by RA using US and MRI. Radiocarpal synovitis was detected more frequently than midcarpal and ulnocarpal joint synovitis in wrist joints. The sensitivity, specificity, and accuracy of US in detecting PD synovitis in the wrist joints were 0.73, 0.76, 0.74, respectively, compared with MRI. The sensitivity, specificity, and accuracy of US in detecting PD synovitis in finger joints were low.

Although many studies have compared US and MRI of finger joints, studies on wrist joints are scarce. Terslev et al. (13) reported 75% accuracy between US and MRI in the determination of synovial inflammation of wrist and finger joints. Horikoshi et al. (14) suggested that PD synovitis yields more specific results compared with MRI. Szkudlarek et al. (15) found that the sensitivity of US for synovitis in the MCP and PIP joints was 76%. For assessing synovitis in the wrist joints, we demonstrated high test accuracy between US and MR for the radiocarpal, midcarpal, and ulnocarpal joints. However, the MCP and PIP joints revealed moderate test accuracy.

The hyperemia, neoangiogenesis, and hypervascularized pannus-accompanying inflammatory synovitis appear to lead to the damage of the cartilage and bone (16). Hypervascularized pannus is observed as a PD signal on US and contrast-enhanced MRI of synovial tissue. Ogishima et al. (17) showed that low-field MRI was more sensitive than PDUS for detecting subclinical synovitis and recommended both modalities for reliable detection. Fukuba et al. (18) evaluated 220 finger joints with active RA and found a 95% accuracy of PDUS for active synovitis compared with MRI. Horikoshi et al. (14) showed that PDUS specificity was higher than its sensitivity, and the overall agreement between PDUS and MRI was 0.76 for the MCP and PIP joints in established RA. They suggested that PDUS was more valuable than gray-scale US.

From a different point of view, the main strength of our study was the assessment of both wrist and finger joints. Furthermore, we compared contrast-enhanced MRI to gray-scale US and PDUS. Using MRI as a reference, the accuracies of PDUS were 0.74, 0.64, and 0.64 for assessing wrist, MCP, and PIP joints, respectively. This was because of the ability of MRI to more clearly visualize the inflamed synovial membrane.

Data on wrist joint erosions in patients with newly diagnosed RA are limited. Most US studies have been focused on finger joints as they are most easily accessible in patients with RA. Hammer et al. (19) compared US and MRI for only distal ulnar erosions and reported that the presence of erosions at the distal ulna on US was correlated with the MRI findings in hand joints. Rahmani et al. (20) suggested that the test agreement of US was acceptable for detecting MCP and PIP joint bone erosions compared with MRI in early RA. According to the review by Baillet et al. (21), US is more reliable for detection of erosions in finger joints than radiography and has an efficacy comparable with that of MRI.

In the current study, we found US to be moderately sensitive and specific for wrist erosions compared with MRI, and the test accuracy was 0.69. Test accuracy increased when midcarpal and radiocarpal joints were separately evaluated. The MCP and PIP joint erosions were difficult to assess because of technical challenges. Nevertheless, the test accuracy of US was 0.50 for finger joint erosions.

Although tenosynovitis is the main feature of spondyloarthropathies, it is not uncommon in patients with RA. Tenosynovitis was detected in 32% and 11% of wrist and finger regions, respectively, in this study. Although extensor tenosynovitis is clinically diagnosed less frequently, its diagnosis by US examination is increasing.

We wish to point out that US was more effective in evaluating wrist joints than finger joints. It should be noted that MRI detected bone marrow edema, thus providing additional information regarding disease activity compared to US.

One other important finding of this study was the relationships among clinical, laboratory, and US findings in newly diagnosed RA. Morning stiffness and hand-grip strength were the main indicators of synovitis and tenosynovitis (r=0.591, p=0.001; r=0.833, p<0.001, r=0.506, p=0.005; r=0.335, p=0.05). As expected, ultrasonographic bone erosions were correlated with only the disease duration. Visser et al. (22) showed that long-standing morning stiffness may be useful in distinguishing between permanent and self-limiting diseases in patients with RA. Yazici et al. (23) reported that the duration of morning stiffness is weakly correlated with the number of tender joints. Therefore, morning stiffness should be assessed in the first physical evaluation if RA is a differential diagnosis.

Moreover, we would like to draw attention to the correlation between inflammatory markers and PD synovitis. On the basis of the results of our study, PD synovitis was correlated with all clinical parameters and levels of inflammatory markers, such as ESR and CRP. However, US synovitis without a PD signal was not correlated with inflammatory marker levels. A longitudinal study of the effect of PDUS on radiographic damage in RA revealed that PD synovitis was associated with rapidly progressive disease (24). We would like to emphasize once again on the importance of the PD signal in detecting synovitis in patients with RA.

This study had several limitations. Inter-observer reliability was good to excellent using this approach; however, patients were not evaluated by the same operator at different times, so the intra-reader reliability for PD synovitis and US synovitis scores could not be calculated.

Conclusion

Our data should encourage clinicians to use US for assessing arthritis in patients with RA. Moreover, clinicians must be aware of the possible misleading findings on US examination in the MCP and PIP joints and erosions. Morning stiffness and hand-grip strength should not be ignored in patients with RA.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Sakarya University Faculty of Medicine.

Informed Consent: Verbal informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - H.H.; Design - H.H., İ.T.; Supervision - İ.T.; Resources - H.H., H.S.H.; Materials H.H., M.S., S.H.; Data Collection and/or Processing - H.H., M.S., S.H.; Analysis and/or Interpretation - H.H.; Literature Search - H.H.; Writing Manuscript - H.H., M.S., İ.T.; Critical Review - İ.T., S.H.; Other - M.S., S.H.

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