



RESEARCH ARTICLE

ULTRASOUND VERSUS MAGNETIC RESONANCE IMAGING IN RHEUMATOID
ARTHRITIS IN WRIST JOINTS AND HAND

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ABSTRACT

Purpose: to evaluate and compare role of grey scale and power Doppler ultrasonography and MRI in the assessment of the extent of damage of hand and wrist joints in rheumatoid arthritis.

Material and methods: this prospective study included 25 patients, 20 females and 5 males, mean age 43.48 years±13.64SD. Initial clinical assessment was carried out and Disease Activity Score (DAS28) was used for grading the disease activity; followed by ultrasound and MRI evaluation.

Results: Accuracy and validity of US as confirmed by MRI revealed most optimum results in the assessment of tenosynovitis with 100% sensitivity and specificity as well as synovial effusion (100 % sensitivity, 90% specificity). The least sensitivity was encountered in the detection of bony erosions (sensitivity 21.05%, specificity 100%).

Significant correlations were found between US parameters for synovial thickening & bone erosions by MRI and DAS28 score. Yet, no significant correlation was found between synovial thickening by MRI and DAS28 score.

Conclusion: GS and PDUS are powerful tools for early detection and grading of inflammatory changes and disease follow up. MRI is superior in the estimation of the severity of structural bony changes and recommended as the baseline study for proper treatment and evaluation of treatment outcome.

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INTRODUCTION

Rheumatoid arthritis (RA) is a systemic autoimmune disease, with an estimated prevalence rate approximately 0.5 - 1 % of the adults in the developed populations. RA is two to three times more common in women than in men (Doran *et al.*, 2002). In most patients, the disease exhibits a chronic fluctuating course, which if left untreated, can result in progressive destruction of the joint and irreversible long-term disability (Van der linden, 2011).

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The joints of the hands are the first to be affected; therefore, they are of primary interest in the assessment of patients with early RA (Taouli *et al.*, 2002). The wrist is included in the assessment as hand and wrist joints, together, form a functional unit (Harris, 2005). Bone erosions represent the most sensitive and specific diagnostic hallmark of joint damage in RA. The detection as well as the increase in number or size of bone erosions indicate poor disease prognosis (Wolfe, 1998). Consequently, in daily clinical practice, conventional radiography is still regarded as the standard imaging technique for the detection and scoring of joint damage (Gutierrez *et al.*, 2010). However, it is now recognized that that RA starts with an early stage of disease presentation termed "undifferentiated arthritis" in which radiographic results are normal.

Early disease recognition during this stage markedly benefits response to treatment with favorable outcomes. That is why revised criteria were introduced in 2010 by American College of Rheumatology/European League Against Rheumatism collaborative initiative; and radiographic erosions were notably not included in the proposed scoring system (Aletaha *et al.*, 2010). The major abnormalities in early RA appear in the synovial joints in the form of synovial hypertrophy, synovial effusion, bursal and tendon sheath swelling (Gibbon, 1999). Direct visualization of the important joint structures coupled with high diagnostic sensitivity in detecting early abnormalities associated with RA are the reasons why US and MRI are essentially integrated in joint evaluation (Tan *et al.*, 2012). Thus, the purpose of the study was the examination of hand and wrist joints using both grey scale ultrasound (GSUS) and power Doppler ultrasound (PDUS) as well as MRI in patients with rheumatoid arthritis. The results were compared and correlated with the clinical score; aiming to evaluate the role of both modalities in the assessment of the extent of damage of hand and wrist joints in rheumatoid arthritis.

MATERIAL AND METHODS

Patients

This prospective research study was carried out in the period between April 2015 and May 2017 after the approval from the university Research Institutional Board was granted. *Inclusion criteria:* Patients with rheumatoid arthritis of the hand and wrist joints as defined by the American College of Rheumatology / European League Against Rheumatism (Aletaha *et al.*, 2010); who agree to join the study according to the ethical considerations. *Exclusion criteria:* patients with history of fracture or surgical operation in the hand or wrist joint; patients with contraindication to perform MRI study e.g., cardiac pacemaker, presence of metallic foreign body in the eye or aneurysm clips in the body; severe claustrophobia.

Clinical assessment

The initial assessment was carried out by specialized Rheumatology clinicians in Rheumatology and Immunology departments (3rd and 4th authors), and the following data was recorded: disease duration, patient complaint of pain, morning stiffness; presence of joint swelling and joint tenderness. Laboratory test results were collected for C-reactive protein (CRP) level (normal level ≤ 5 mg/liter) and erythrocyte sedimentation rate (ESR; normal level ≤ 20 mm/hour) and rheumatoid factor (RF; normal ≤ 15 IU/mL). The Disease Activity Score (DAS28) was used for grading the disease activity according to the classification criteria offered by Backhaus *et al.*, 2009 (10): $DAS28 \leq 2.6$ = clinical remission, ≤ 3.2 = mild disease activity, ≤ 5.2 = moderate disease activity, and > 5.2 = severe disease activity.

Ultrasonography

All the Ultrasound examinations were conducted by the second and fifth authors. The ultrasound machine utilized was LOGIQ P5 premium (GE Healthcare; United States of America); using transducer with frequency of 7.5-12 MHz. The examination was applied to the wrist, metacarpophalangeal (MCP), proximal interphalangeal (PIP) joints in the transverse and longitudinal planes.

B-mode grey-scale ultrasonography (GS-US) was used to evaluate inflammatory changes (synovitis, tenosynovitis, effusion) and joint erosion. Power Doppler (PD-US) was used for the detection and grading of the hyperemia associated with synovitis.

Magnetic Resonance Imaging

The dominant hand was scanned using 1.5-T, whole body scanner (Achieva; Philips medical systems, Best, Netherlands). The following pulse sequences were implemented: Axial and coronal T1 Turbo-spin echo (TSE): TR, 450-600 msec; TE, 15-25 msec). Axial and coronal T2 TSE & fat saturated (T2FS): TR, 2000-4000 msec; TE, 90-130 msec. Coronal Turbo STIR images (TR, 3000-4000 ms; TE, 30-60 ms; TI, 140 ms). The scan duration was approximately 30 minutes. MR Imaging interpretation was performed by the first and second authors.

Interpretation and grading

Inflammatory changes

Synovitis: Semi-quantitative scale for grading (Fernandes *et al.*, 2008) indicates: 0: normal, imperceptible synovium; 1: mild, perceptible synovial thickening; 2: moderate, proximal capsule distension; 3: marked synovial proliferation, distension extends distally. Semi-quantitative scaling of synovial inflammation by power Doppler ultrasound (PD-US) (Lopez, 2007) as follows: 0: hypoechoic synovial tissue is seen without any appreciable power Doppler signal. 1: single vessel is seen; 2: multiple vessels in less than 50% of the thickened synovium; 3: multiple vessels, more than 50%. MRI scoring of synovial hypertrophy (S-score) (Taouli *et al.*, 2004): 0: none; 1: mild, $<$ third maximum capsule distension; 2: moderate, two-thirds maximum capsule distension; 3: marked, $>$ two-thirds maximum capsule distension.

Tenosynovitis: a semi-quantitative 4-grade scoring system was adopted for grading by both GS-US and MRI (14) as follows: 0: normal; 1: mild amount of fluid around the tendon; 2: moderate amount; 3: marked amount.

Effusion: grading of the amount of synovial effusion by both GS-US and MRI as follows: 0, no effusion; 1: minimal effusion; 2: moderate amount of effusion, not associated with joint capsule distension; 3: marked, associated with capsule distension (Szkudlarek *et al.*, 2003).

Structural changes

Erosions: by GS-US: grading: 0: normal; 1: unifocal, not more than one erosion per quadrant; 2: multifocal, 1-3 erosions per quadrant; 3: massive: more than 3 erosions per quadrant (Narváez *et al.*, 2010).

Erosions score (E-score) by MRI: 8-point scale was adopted as follows (Taouli *et al.*, 2004): 0: normal, 0.5: subtle loss of continuity; 1: mild, small erosions, typically in the bare area, comprising $<$ 25% of the articular surface area); 1.5: mild to moderate, small to medium sized erosions, involving $<$ 25% of the articular surface of one or both of the articular bones; 2: moderate, erosions occupy 50% of the articular surface area; 2.5: erosions occupy 50-75% of the articular surface area; 3: more than 75%; 3.5: entire articular surface is involved.

Bone marrow edema: is defined by MR imaging as ill-defined signal intensity perceptible by STIR sequence (Bhasin, 2015). Scoring is based on the volume of edema: 0: normal; 1: 1%-33% of bone is involved; 2: 34%-66%; 3: 67%-100%.

Statistical analysis: Statistical analysis was done using statistical package (SPSS, Version 20 for Windows, SPSS Inc., Chicago, IL, USA). Variables were medians and ranges for non-normally distributed continuous variables and frequencies for categorical variables. Spearman’s correlation coefficient was used for correlation between MRI grading of edema and disease severity on clinical assessment.

RESULTS

Twenty-five adult patients clinically diagnosed as having RA were included in the study. They were 20 females (80%) and 5 males (20%), their ages ranging from 20 to 72 years with the mean age 43.48 years ± 13.64 SD. The disease duration ranged from 6 months to 25 years, median 3 years. Results of clinical assessment of the wrist and hand joints & Disease Activity Score (DAS28) are summarized in Tables (1,2), charts 1,2 (Fig. 1,2); respectively. Sonographic findings, most affected joints and tendons, GS-US and PD-US scores, are illustrated in Table (3), Chart (3) (Fig.3).

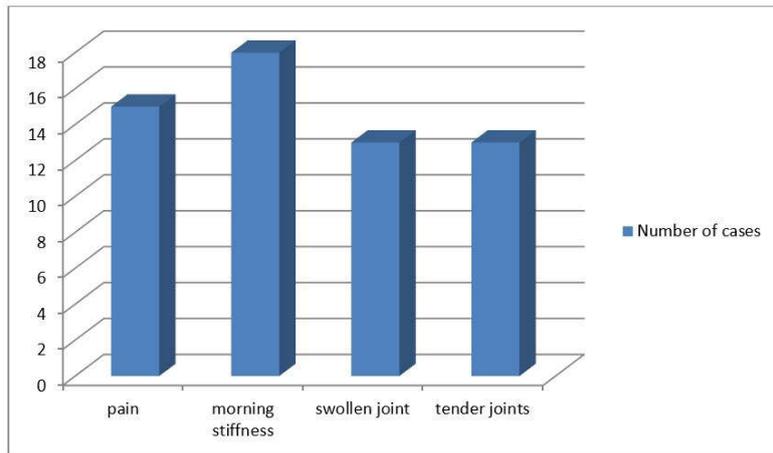


Fig. 1. Chart. 1. Results of clinical assessment of the wrist and hand joints in rheumatoid arthritis patients

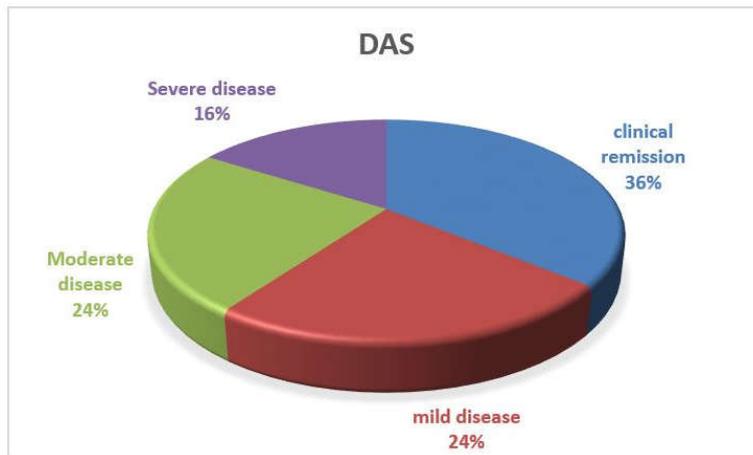


Fig. 2. Chart. 2. Disease activity assessment by DAS28 score

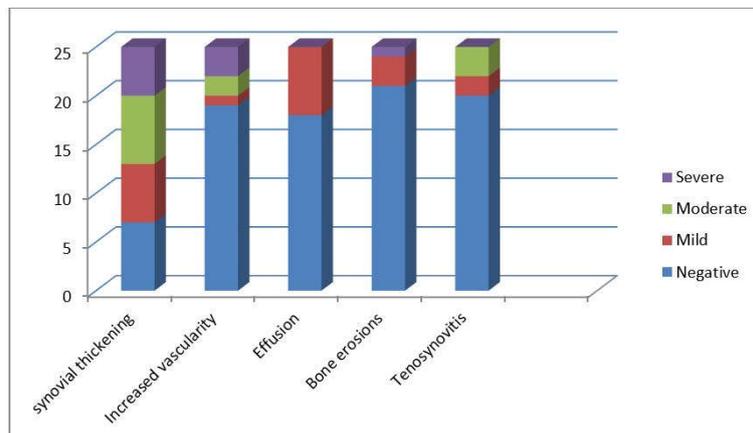


Fig. 3. Chart. 3. Ultrasound findings in rheumatoid arthritis patients

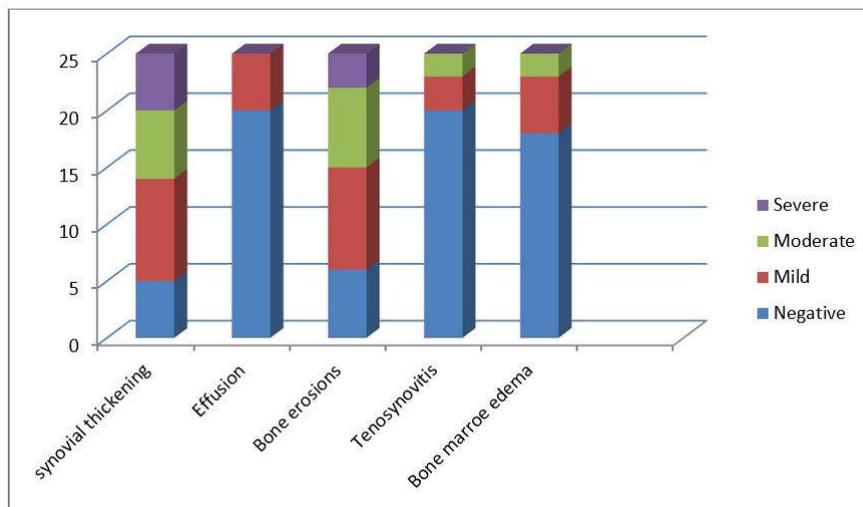


Fig. 4. Chart. 4. MRI findings in rheumatoid arthritis patients

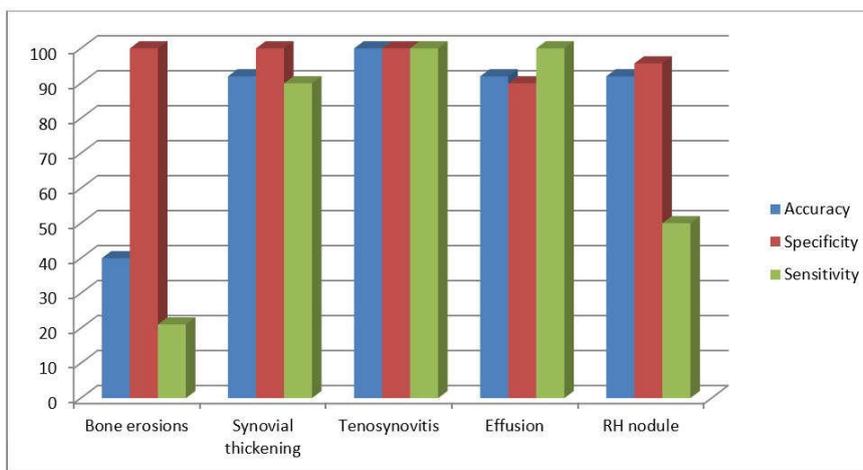


Fig. 5. Chart. 5. Accuracy and validity of US as confirmed by MRI

Table 1. Clinical assessment of the wrist and hand joints in RA patients

Complaint	No. of patients	Percentage
Pain	15	60%
Morning stiffness	18	72%
Swollen joints	13	52%
Tender joints	13	52%

N.B. Multiple patients have more than one finding

Table 2. Disease activity assessment by DAS28

DAS 28 (median-range)		3.08	1.68-6.01
DAS	clinical remission	9	36.0%
	mild disease activity	6	24.0%
	Moderate disease activity	6	24.0%
	Severe disease activity	4	16.0%

DAS: Disease Activity Score

detection of Synovial thickening by GS-US was 90% with specificity 90%.

Table 3. Ultrasound findings of RA patients

Ultrasound	Score	No	Percentage
Erosions	CB	-ve	21 84.0%
		Mild	3 12.0%
		moderate	0 0.0%
		Severe	1 4.0%
Grey scale (synovial thickening)	MCPJ	-ve	7 28.0%
		Mild	6 24.0%
		moderate	7 28.0%
		Severe	5 20.0%
Power Doppler (synovial hyperemia)	MCPJ	-ve	19 76.0%
		Mild	1 4.0%
		moderate	2 8.0%
		Severe	3 12.0%
Tenosynovitis	ECUT	-ve	20 80.0%
		Mild	3 8.0%
		moderate	2 12.0%
		Severe	0 0.0%
Effusion	Wr J	-ve	18 72.0%
		Mild	7 28.0%
		moderate	0 0.0%
		Severe	0 0.0%
Nodule	MCP	Negative	23 92.0%
		Positive	2 8.0%

*Abbreviations for most affected joints and tendons: CB: carpal bones, MCPJ: Metacarpophalangeal joint, ECUT: Extensor carpi ulnaris tendon, Wr J: Wrist joint

MRI evaluation results and scores for inflammatory and structural bony changes are illustrated in Table (4), chart (4) (Fig. 4). Accuracy and validity of US as confirmed by MRI were estimated (Table. 5, Fig. 5) and revealed most optimum results in sonographic assessment of tenosynovitis with 100% sensitivity and specificity in five tendons; the most commonly affected tendon was Extensor carpi ulnaris tendon (ECUT). Ultrasound sensitivity for the detection of synovial effusion was 100 %, with specificity 90%. While sensitivity for the

Table 4. MRI findings of RA patients

MRI	Score	No	%
Erosions	CB	-ve	6 24.0%
		mild	9 36.0%
		moderate	7 28.0%
		severe	3 12.0%
Synovial thickening	MCPJ	-ve	5 20.0%
		Mild	9 36.0%
		Moderate	6 24.0%
Tenosynovitis	ECUT	Severe	5 20.0%
		-ve	20 80.0%
		Mild	3 12.0%
Joint effusion	WRIST J	Moderate	2 8.0%
		Severe	0 0.0%
		-ve	20 80.0%
Bone marrow edema	CMJ	Mild	5 20.0%
		Moderate	2 8.0%
		Severe	0 0.0%
		-ve	18 72.0%
Nodule	MCP	Negative	22 88.0%
		Positive	3 12.0%

*Abbreviations for most affected joints and tendons: CB: carpal bones, MCPJ: Metacarpophalangeal joint, ECUT: Extensor carpi ulnaris tendon, Wr J: Wrist joint, CMJ: Carpometacarpal joint

Table 5. Accuracy and validity of US as confirmed by MRI

	True+ve	False -ve	True-ve	False+ve	Sensitivity	Specificity	PPV	NPV	Accuracy
Bone erosions	4	15	6	0	21.05%	100.00%	100.00	28.57	40.00
Synovial thickening	18	2	5	0	90.0%	100.0%	100.00	71.43	92
Tenosynovitis	5	0	0	0	100%	100%	100	100	100
Effusion	5	0	18	2	100.0%	90%	71.43	100.00	92.00
Nodules	1	1	22	1	50.0%	95.7%	50.00	95.65	92.00

+ve = positive, -ve = negative

PPV: positive predictive value; NPV: Negative predictive value

Table 6. Correlation between ultrasound, MRI and DAS28

	GS Ultrasound (synovial thickening)	PD Ultrasound	Bone erosions MRI	Synovial thickening MRI
DAS28	r .575**	.455*	.715**	.326
P	.003	.022	.000	.111

r: Spearman correlation coefficient; P: Probability

*: significance <0.05 **: High significance

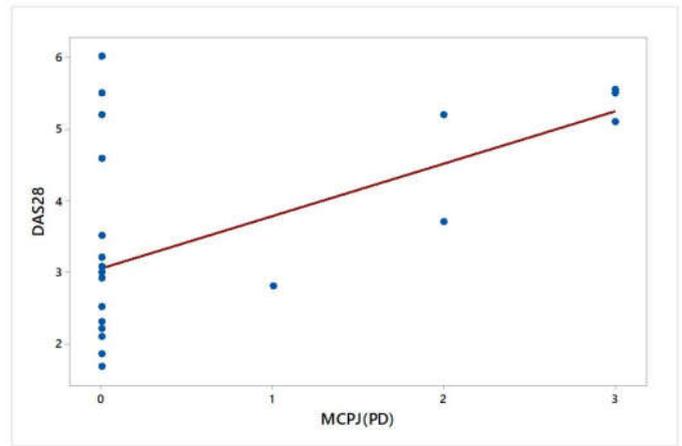
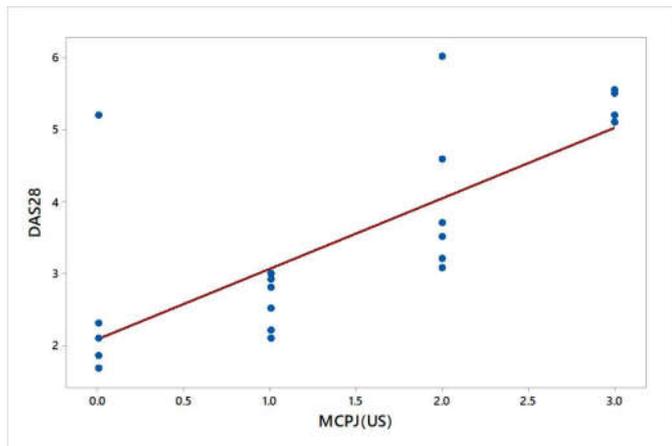


Fig. 6. Correlation between ultrasound synovial thickening and DAS28

Fig. 7. Correlation between PD ultrasound and DAS28

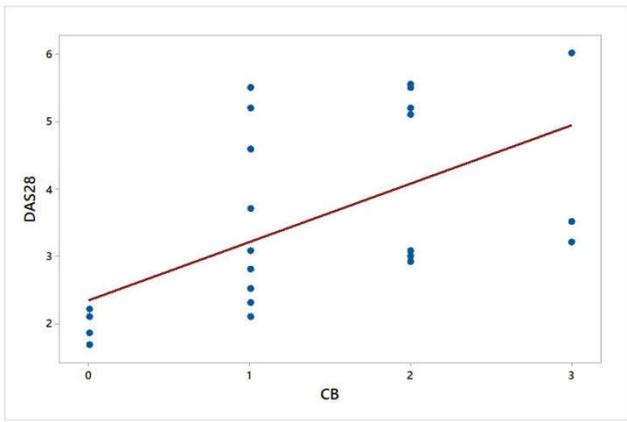


Fig. 8. Correlation between MRI bone erosions and DAS28

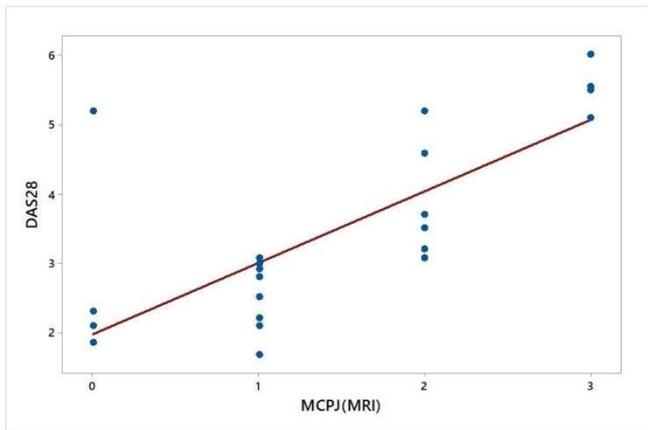
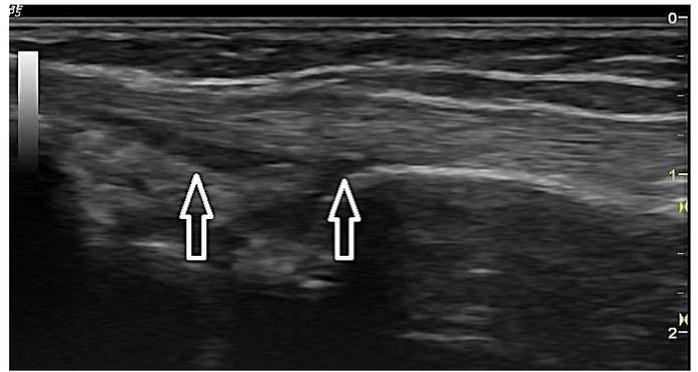
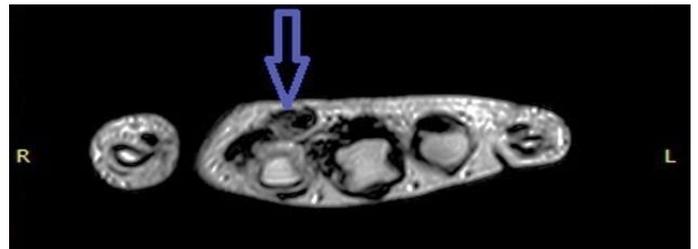


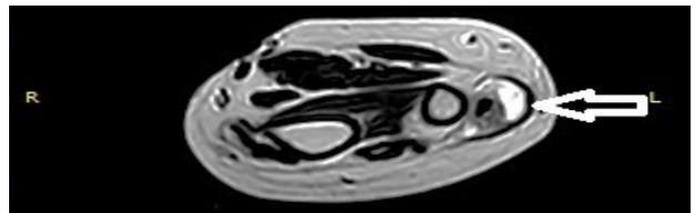
Fig. 9. Correlation between MRI synovial thickening and DAS28



10c



10d



10e



10 a



10b

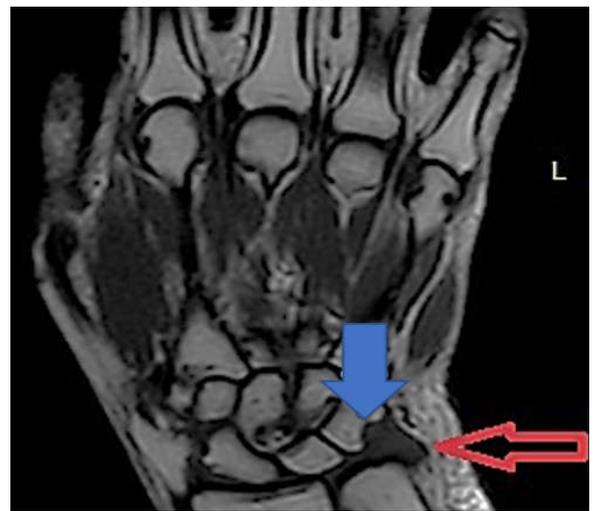


10f

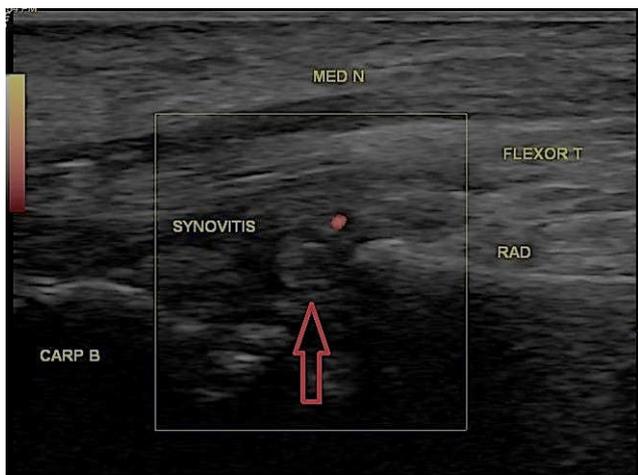
Fig. 10. Case (1): Seventy-two years old male patient with RA for 20 years, presented with pain and swelling of the wrist and palm. (A,B) GS-US shows marked tenosynovitis of the flexor digitorum tendons associated with marginal synovial proliferation as well as globular soft tissue thickenings surrounding the tendon. (C) PD-US shows no vascularity, denoting chronic tenosynovitis. (D, E) Coronal T1 and STIR images: showing extensive tenosynovitis, the marginal synovial thickening is clearly seen on T1 and displays intermediate signal intensity. While the globular proliferations are depicted on STIR as signal void foci against the background of high fluid signal intensity



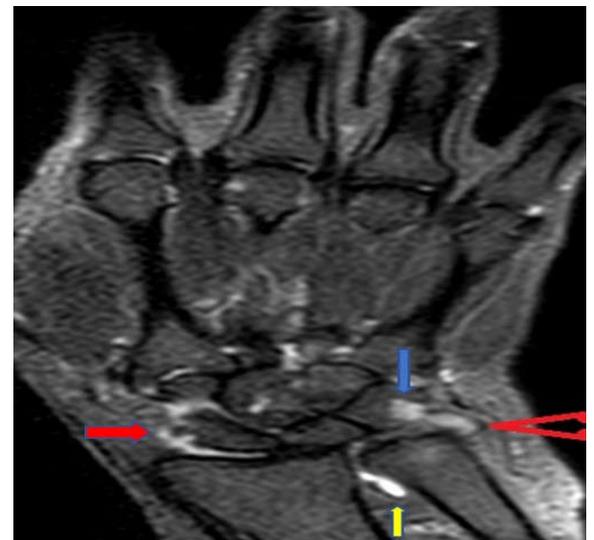
11a



11e



11b



11f



11c



11g

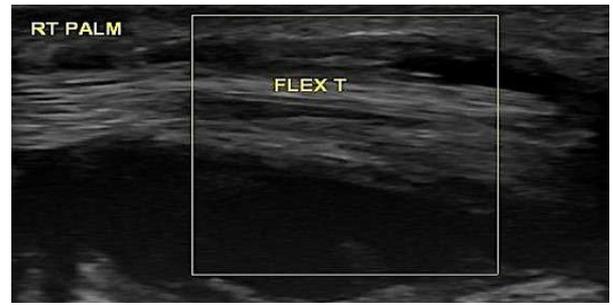


11d



11h

Fig. 11. Case 2: Fifty years old female patient, suffering from RA for 4 years. She presented with tenderness and swelling of the wrist joint. Ultrasound: GSUS shows synovial thickening of the MCP and radiocarpal joints (red arrow) in A&B, respectively. Moderate tenosynovitis is seen in extensor digitorum tendon as well as flexor pollicis longus tendons (white arrows) in C&D, respectively. PDUS shows mild increased vascularity of thickened synovium at radiocarpal joint and extensor digitorum tendon (B,C). MRI: Coronal images of the wrist joint and hand showing: (E) T1: synovial proliferation opposite the superior border of ulna (red arrow) (F) T2FS: synovial proliferation opposite the superior border of ulna as well as early proliferation around the lateral border of radius (red arrows). Bony erosion in scaphoid (blue arrow) and mild effusion in distal radio-ulnar joint (yellow arrow) are clearly depicted. (G, H) Coronal STIR images display: tenosynovitis of the extensor digitorum tendon and flexor pollicis longus tendon, respectively (white arrows)



12c



12d



12a



12b



12e

Fig. 12. case 3: Thirty-two years old female patient, suffering from RA for 2 years. She presented with tenderness and swelling at the index finger. GSUS shows: (A) synovial thickening of the 3rd MCP joint (red arrows) associated with subcutaneous rheumatoid nodule opposite the 2nd MCP joint (blue arrow) in (B) and mild tenosynovitis of the extensor carpi ulnaris tendon (white arrows) in (C). PDUS shows no increased vascularity of thickened synovium at the MCP joint (B). (D) Axial T2 image of the hand at the level of the metacarpal heads shows: subcutaneous rheumatoid nodule opposite the 2nd MCP joint (blue arrow). (E, F) Axial T2 and Coronal STIR images of the wrist joint and hand show: moderate tenosynovitis of the extensor carpi ulnaris tendon (white arrow). In axial T2 weighted image (E) the intermediate signal of synovial proliferation within the tendon is clearly discriminated from the surrounding reactive tenosynovitis. Bone marrow edema in the base of the second metacarpal bone (yellow arrow) and erosions in triquetrum (red arrow) are clearly seen in the coronal STIR image (F)

The least sensitivity was encountered in the detection of bony erosions (sensitivity 21.05%, specificity 100%). Rheumatoid nodules were detected in two cases by ultrasound opposite the 2nd and 4th MCP joints showing diagnostic sensitivity and specificity 50% and 95.7% as compared with MRI. Correlation analysis was attempted between radiologic findings and clinical evaluation by DAS28 score (Table. 6, fig. 6-9). Significant statistical correlation was found between changes in US parameters for synovial thickening by GS-US & increased vascularity of the thickened synovium by PD-UD and the DAS28 changes (GSUS/DAS28: $r = 0.575$, $P < 0.003$; PDUS/DAS28: $r = 0.455$, $P < 0.022$). There was also a high significant correlation for bone erosions by MRI and DAS28 changes ($r = 0.715$; $P < 0.001$). However, no significant statistical correlation was found between synovial thickening by MRI and DAS28 changes ($r = 0.326$, $P < 0.111$).

DISCUSSION

Early diagnosis of Rheumatoid arthritis (RA) is an important determinant factor for early treatment and improvement of the long-term disease outcome (Sommer *et al.*, 2005). Moreover, rapid development of powerful and expensive therapeutic agents in the last decade can achieve favorable clinical outcome if early intervention has occurred. Thus, the aim of our study was to evaluate the effectiveness of ultrasonography (US) and magnetic resonance imaging (MRI) in the early detection and grading of the extent of severity of rheumatoid arthritis. As many previous studies MRI was considered the gold standard diagnostic modality, as there is much evidence in the literature documenting that inflammatory changes found on MRI can mirror the pathologic findings (Tan *et al.*, 2012; McQueen, 2006; Szkudlarek *et al.*, 2004,19,20). Our study showed synovial thickening in 78% of RA patients by MRI with similarity in 72% of patients by US (case 1, Fig.10). The accuracy, sensitivity, and specificity of US as confirmed with MRI were 92%, 90% and 100% respectively. This matched with the results described by Szkudlarek *et al.*, 2004 (20) who compared US with MRI as the reference modality. They suggested that the visualized inflammatory changes are similar using both modalities. Furthermore, later, Szkudlarek *et al.*, 2006 (21) reported the sensitivity, specificity and accuracy of US as compared with signs of inflammation at T1 weighted MRI sequence as a reference were 70%, 78% and 76%, respectively. We strongly confirm this observation. The intermediate signal intensity of synovial proliferation can be easily depicted against the background of bright marrow signal on T1 (case2; Fig.11, E) and correlated with its appearance on GSUS (case 2, Fig.11, A) with no need for contrast material. Our results revealed that 28% (7 cases) of patients showed joint effusion by US which outnumbered those seen by MRI (20%, 5 cases). Similarly, Szkudlarek *et al.*, 2006 (Szkudlarek, 2006) and Scheel *et al.*, 2006 reported that US was sensitive for the detection of very small amounts of fluid accumulation and proved to be better than MRI. They explained that in contrast to MRI, US is a real-time modality, which permits the evaluation of target joints during motion and under probe compression. Additionally, better resolution and higher magnification of joints with US can efficiently increase its diagnostic sensitivity.

The number of cases diagnosed as tenosynovitis by ultrasound was equivalent to that diagnosed by MRI (5 cases, 20%); with 100% diagnostic sensitivity and specificity of US as confirmed with MRI. Tenosynovitis is considered the hallmark of early

tendon affection (Grassi *et al.*, 2000) and in some cases with early rheumatoid arthritis, tenosynovitis predominates over joint synovitis. It is of critical importance, as tendon sheath synovitis and synovial proliferation may progress to tendon rupture due to fraying of the tendon sheath against the eroded bone margins (17). In our study, extensor carpi ulnaris (ECUT) tendon was most commonly affected (Tables 3,4) (Fig.12, case 3, C, E,F); which is concordant with the study by Lillegraven *et al.*, 2011 (Lillegraven *et al.*, 2011).

Structural bone changes are far better detected by MRI than ultrasound. Bone marrow edema was found in 28% of cases (7 patients) by MRI (case 3, Fig., 12, F) and none was seen on sonographic evaluation. MR imaging using water sensitive sequences (STIR and T2 fat saturated sequences) provides a useful diagnostic tool for the detection of bone marrow edema while ultrasound has no role (18, 25). Early detection of bone marrow edema is important for proper management as studies have shown that subsequent bone marrow edema can develop within 12 months after the onset of marrow edema (McQueen, 2006). Carpal and metacarpal bone erosion was reported in 4 cases only by ultrasound (case 4; Fig. 13 B) as compared with 19 cases by MRI (Fig.12, F; Fig. 13, F), showing diagnostic sensitivity 21.05%, yet specificity and positive predictive value were 100%. McQueen and Østergaard, 2007 considered MRI the reference method for the assessment of bone erosions as ultrasound results in their study yielded sensitivity 59%, specificity 96% and accuracy 86%. Thus, a strong significant correlation was found in our study between bone erosions graded by MRI and the clinical DAS28 score for the disease activity. On the other hand, no significant correlation was found between synovial thickening graded by MRI and DAS28 score. This could be attributed to the dependence on conventional MRI without contrast. Meanwhile, inflammatory changes in the form of synovial thickening & increased vascularity of the synovial membrane reported by GSUS and PDUS significantly correlated with the clinical score according to our results as well as others (Backhaus *et al.*, 2009; Filippucci *et al.*, 2006). Consequently, we can conclude that GS and PDUS are powerful diagnostic tools for the early detection and grading of the inflammatory changes in Rheumatoid arthritis and for disease follow up. MRI is superior in the estimation of the severity of structural bony changes and recommended as the baseline study for the decision of proper treatment and evaluation of treatment outcome.

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