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Study of Role of Shear- Wave Elastography and Musculoskeletal Ultrasound in Assessment of Hand and Wrist in Rheumatoid Arthritis Patients

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ABSTRACT
Background: Joint damage, disease activity, and prognosis in rheumatoid arthritis can now be evaluated by shear-wave elastographic ultrasonography (SW-EUS). **Objective:** Evaluate of the role of musculoskeletal ultrasound in early diagnosis of rheumatoid arthritis and monitoring treatment, as well as evaluating the added value of using Elastography. **Patients and methods:** A case-control study that included 30 rheumatoid arthritis patients and 30 controls have same age and sex of chronic cases; we did shear wave elastography ultrasound (SW-EUS) image obtained for all subjects. **Results:** Statistically significant differences were found in SWE parameters, as well as between recently diagnosed RA patients and after 2 months follow up between RA patients and healthy control where the mean of Elastic Modulus (KPa) that was statistically lower among RA patient than among healthy control. Also, the mean of Elastic Modulus (KPa) increased from 15.67 ± 10.56 to 42.07 ± 17.8. Additionally, mean of Mean Velocity (m/sec) increased from 2.19 ± 0.63 to 3.47 ± 0.91 that was statistically higher after 2 months. An Elastic Modulus (KPa) Cut-off level of Elastic Modulus (KPa) < 44.35 had sensitivity of 100 %, and specificity of 94 % in detecting RA changes. Also, Cutoff level of Mean Velocity (m/sec) < 3.76 had sensitivity of 100 %, and specificity of 93.3 % in detecting RA changes of high statistical significance.
Conclusion: Diagnosing and assessment of disease activity in RA can be evaluated with SW-EUS.
Keyword: Shear-wave elastography, Musculoskeletal ultrasound, Rheumatoid arthritis.

INTRODUCTION

In rheumatoid arthritis (RA), musculoskeletal ultrasonography (MSKUS) is routinely used for diagnosis, illness monitoring, and joint damage assessment. Both grey scale ultrasonography (GSUS) and power Doppler ultrasound (PDUS) are commonly used to evaluate tissue shape and blood flow, respectively [(1)].

Significant limitations exist despite the fact that GSUS and PDUS can detect synovitis and joint degeneration and may aid in predicting future erosions in rheumatoid arthritis (RA) [(2)]. Up to 8.5% of patients with osteoarthritis (OA) may exhibit synovial thickness and power Doppler flow, both of which add to diagnostic ambiguity. Furthermore, the Pearson's correlation between PDUS and erosions is only 0.6, and the sensitivity for erosions is as low as 45% [(3)].

Currently employed in liver, thyroid, and breast imaging, shear-wave elastographic ultrasonography (SW-EUS) shows promise in evaluating the synovium [(4)]. Patients with RA may have softer synovium compared to age- and sex-matched individuals without inflammatory arthritis, according to recent research. In addition, a number of disease activity markers were found to have a negative Pearson association with SWV, suggesting that a softer synovium may be indicative of increased disease activity [(5)].

This study objective was evaluation of role of musculoskeletal ultrasound in early diagnosis of rheumatoid arthritis and monitoring treatment, as well as evaluating the added value of using Elastography.

SUBJECTS AND METHODS

Our case-control study that was conducted at Radiodiagnosis Department, Zagazig University Hospitals on a sample of 30 rheumatoid arthritis patients who complained of wrist and hand pain, swollen or limited movement. 30 chronic cases of same age and sex were involved as control group.

Inclusion criteria: Symptomatizing patients with positive Rh antibodies, however no clinical signs for RH arthritis. Patients recently diagnosed as RA willing treatment and evaluated over two consecutive study visits. Chronic cases suffering from rheumatoid arthritis. Control cases of the same numbers of chronic cases: asymptomatic chronic cases individuals with matched age and sex.

Exclusion criteria: Missed patients during follow up. Patient with known other causes of arthritis (negative Rh factor). Patients (suffering from disease/taking drugs) can change bone density as hyperparathyroidism, thyroxin or steroid therapy. Other autoimmune inflammatory diseases and patients with chronic renal failure or chronic liver diseases. Bone disease, fracture, or previous surgery on the hand or wrist.

Methods:

All patients were subjected to: Taking complete history and complete clinical examination.

Laboratory investigations: ESR, CBC and rheumatoid factor.

Imaging including: Plain radiography: AP & lateral views to exclude any osseous lesions. Synovial thickening, effusion, erosion, and tenosynovitis were evaluated using grey scale ultrasonography and power Doppler ultrasound of the wrist and hand joints in all

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instances using linear probes of 12MHZ. Synovial thickening and PDUS flow in GSUS will be scored on a zero to three point scale. With shear wave elastographic ultrasonography, a picture of the joint is taken at multiple points, with the highest SWV (measured in kilopascals) recorded at the moment of scanning. Every picture was saved for a later characterization.

Technique:

Gray scale ultrasonography and power Doppler ultrasound examination: An expert musculoskeletal (MSK) radiologist performed the ultrasound (USG) analysis. The dorsal aspect of the wrist and hand is evaluated first, and then the palmar aspect is evaluated using USG pictures acquired in various wrist positions (flexion, extension, pronation, and supination) with the patient seated in front of the examiner.

Shear wave elastographic ultrasound SWE:

The research was conducted with a linear array probe attached to an Ultrasound (USG) device (CANON APLIO 500) (12 MHz). The GS USG images were shown with the elastography photos to guarantee that the evaluation was performed in the correct location. To minimise bias, patients first underwent ultrasonography, and then underwent shear wave elastography (SWE), both of which were performed by two separate radiologists who were unaware of the results from the other modality. Statistical analysis was then used to compare the results of the two types of imaging.

Ethical approval: The Faculty of Medicine, Zagazig University ethical Committee gave its ethical approval for this investigation. After receiving all the facts, every patients gave their signed approval. The Helsinki Declaration was upheld throughout the course of the investigation.

Statistical analysis:

For this study, we used IBM SPSS Version 27.0. Numerical data were summarized using minimum and maximum values, as well as means, standard deviations, medians, and interquartile ranges. The results were considered significant if they fell within a 95% confidence interval. There was a Chi-square test performed. Mann-Whitney U (MW test) was used for assessing statistical differences between pairs of categories. When comparing quantitative variables across more than two groups, the Kruskall-Wallis test (KW test) was employed. Numbers were compared between pairs of data using the Wilcoxon signed-rank test (before and after assessment)

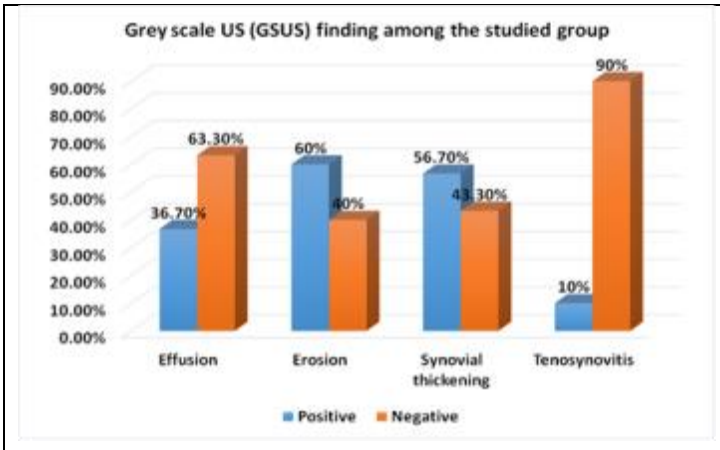
RESULTS

Table (1) showed that the studied patients mean age was 45.23 ± 12.79 years old, with a range from 19 to 65 years old and more than half (53.3%) of the studied patients were female.

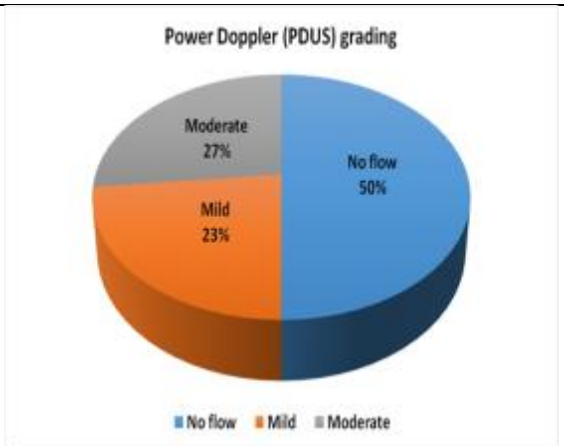
Table (1): Demographic data of the studied patients

Demographic data	Studied patients (N=30)	
	No.	%
Sex		
Male	14	46.7
Female	16	53.3
Age (years)		
Mean ± SD	45.23 ± 12.79	
Median (Range)	46.5 (19-65)	

Figure (2) showed that the most considerable U/S finding was joint erosion in 60 % of patients, followed by synovial thickening and effusion in 56.7% and 36.7 % of cases respectively. Tenosynovitis was found in only 10 % of cases. There was no flow in half of cases according to power Doppler (PDUS) grading, while it was mild and moderate in 23.3% and 26.7% respectively.



(A)



(B)

Figure (1): (A) Bar chart representing Grey scale US (GSUS) finding among the studied group, (B): Power Doppler (PDUS) grading among the studied group

Table (2) showed that the most considerable U/S finding was joint erosion in 60 % of patients, followed by Synovial thickening and effusion in 56.7% and 36.7 % of cases respectively. Tenosynovitis was found in only 10 % of cases. Also we found that about ¼ of the studied RA patients were group 1 (26.7%), group 2 and group 3 patients were in 30% and 43.3% respectively.

Table (2): Grey scale US (GSUS) finding among the studied group

Item	Studied gr (N=30)	
	No.	%
Effusion		
• Negative	19	63.3
• Minimal	9	30.0
• Mild	2	6.7
Erosion		
• Positive	18	60.0
• Negative	12	40.0
Synovial thickening		
• Positive	17	56.7
• Negative	13	43.3
Tenosynovitis		
• Positive	3	10.0
• Negative	27	90.0

Table (3) showed that joint effusion was mild in 15.4% of chronic patients with RA vs zero% in recently diagnosed and symptomatic cases with no clinical signs of arthritis. Positive synovial thickness increased among 69.2% of chronic patients with RA vs 62.6% among recently diagnosed patients with no statistically significant difference. Erosion was statistically higher among chronic patients with RA vs symptomatic cases with no clinical signs of arthritis and recently diagnosed (84.6 %, 77.8 % & zero %)**.**

Table (3): Grey scale US (GSUS) finding among RA patients in relation to symptoms

Item	Recently diagnosed (N=8)		symptomatic patients but no clinical sign for arthritis (N=9)		Chronic patients with RA (N=13)		p-value
	No.	%	No.	%	No.	%	
Effusion							
• Negative	3	37.5	7	77.8	9	69.2	0.101
• Minimal	5	62.5	2	22.2	2	15.4	
• Mild	0	0.0	0	0.0	2	15.4	
Erosion							
• Positive	0	0.0	7	77.8	11	84.6	0.000*
• Negative	8	100.0	2	22.2	2	15.4	
Synovial thickening							
• Positive	5	62.5	3	33.3	9	69.2	0.230
• Negative	3	37.5	6	66.7	4	30.8	
Tenosynovitis							
• Positive	1	12.5	1	11.1	1	7.7	0.930
• Negative	7	87.5	8	88.9	12	92.3	

Chi-square test ($\chi 2$).

Table (4) showed that joint effusion improved from mild effusion to negative after 2 months follow-up (62.5% vs 12.5 % of cases respectively). Synovial thickness decreased among 25% of cases.

Power Doppler grading decreased from 25% of moderate grade at start to be 0% of patients after follow-up with no statistically significant difference.

Table (4): Grey scale US (GSUS) finding and power Doppler among recently diagnosed RA patients after 2 months follow up among the studied group

Item	At start (N=8)		After 2 months follow up (N=8)		p-value
	No.	%	No.	%	
Effusion					
• Negative	3	37.5	7	87.5	0.219[a]
• Minimal	5	62.5	1	12.5	
Erosion					
• Positive	0	0.0	0	0.0	1.000
• Negative	8	100.0	8	100.0	
Synovial thickening					
• Positive	5	62.5	5	62.5	0.516
• Negative	3	37.5	1	12.5	
• Decreased thickening	0	0.0	2	25.0	
Tenosynovitis					
• Positive	1	12.5	1	12.5	1.000[a]
• Negative	7	87.5	7	87.5	
Power Doppler (PDUS) grading					
• No flow	3	37.5	7	87.5	0.157
• Mild	3	37.5	1	12.5	
• Moderate	2	25.0	0	00.0	

Wilcoxon Signed Ranks Test, Mc Nemar test [a]

Table (5) showed that there was highly statistically significant difference in SWE parameters between RA patients and healthy control where the mean of Elastic Modulus (KPa) was statistically lower (16.77 ± 15.0) among RA patient than (101.2 ± 27.9) among healthy control. Also, mean of mean velocity (m/sec) was statistically lower among RA patients (2.16 ± 0.94 (m/sec) vs 5.53 ± 1.14 (m/sec) respectively).

Table (5): Shear wave (SWE) among the studied RA patients and control group

Shear wave (SWE)	Studied RA patients (N=30)	Healthy control (N=30)	p-value
Elastic Modulus (KPa)			
Mean ± SD	16.77 ± 15.0	101.2 ± 27.9	0.000* (HS)
Median (Range)	11.3 (3.9 -57.5)	100.3 (46.6 -140)	
Mean Velocity (m/sec)			
Mean ± SD	2.16 ± 0.94	5.53 ± 1.14	0.000* (HS)
Median (Range)	1.98 (0.74 – 4.35)	5.7 (3.7 – 7.59)	

Table (6) showed that there was statistically significant difference in SWE parameters among recently diagnosed RA patients and after 2 months follow up where the mean of Elastic Modulus (KPa) increased from 15.67 ± 10.56 to 42.07 ± 17.8. Also, mean of mean velocity (m/sec) increased from 2.19 ± 0.63 to (3.47 ± 0.91 that was statistically higher after 2 months.

Table (6): Shear wave (SWE) among the studied recently diagnosed RA patients in after 2 months follow up

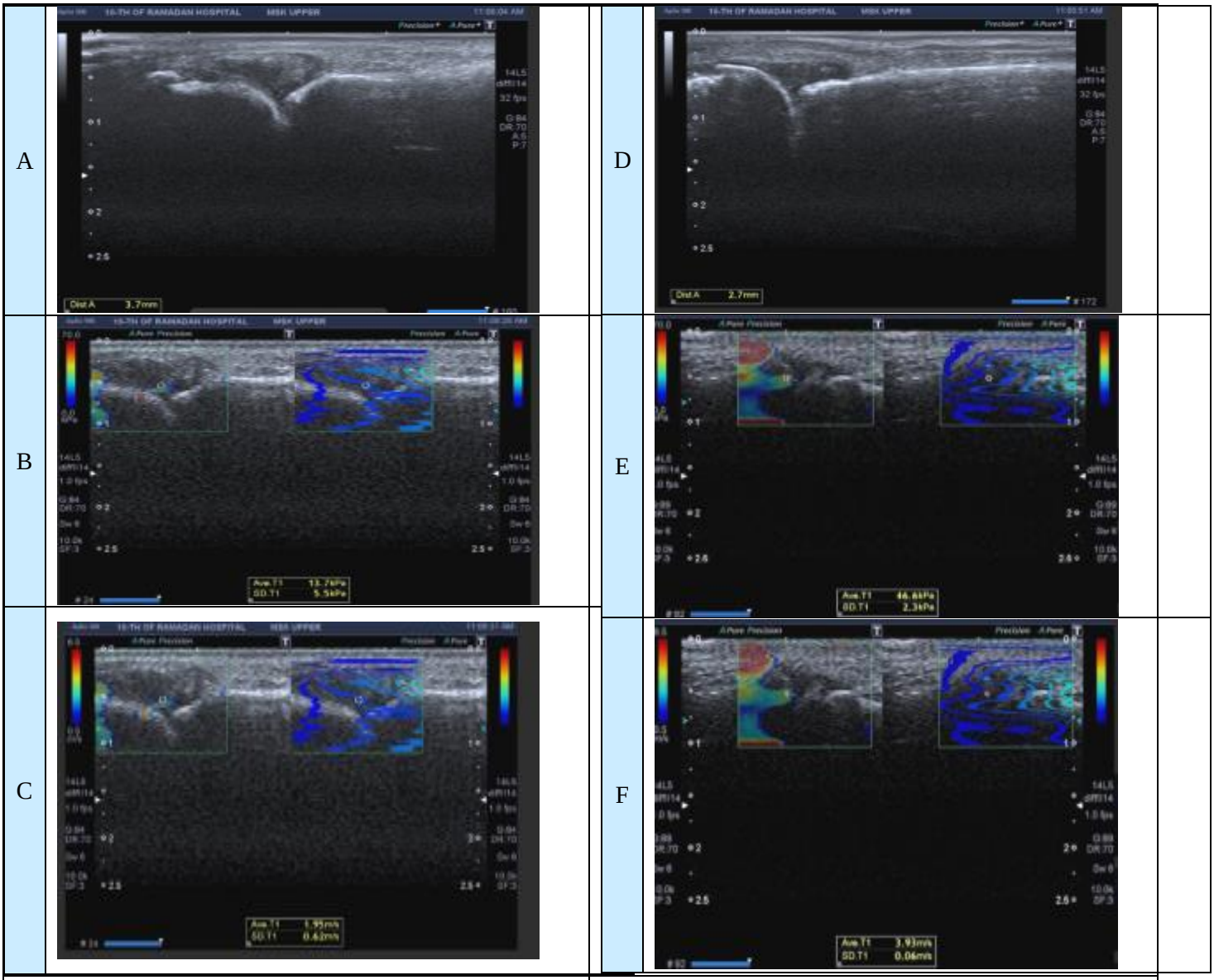
Shear wave (SWE)	Recently diagnosed (N=8)	After 2 months follow up	p-value
Elastic Modulus (KPa)			
Mean ± SD	15.67 ± 10.56	42.07 ± 17.8	[a]0.017* (S)
Median (Range)	11.3 (7.9 - 40.9)	40.4 (11.5-72.3)	
Mean Velocity (m/sec)			
Mean ± SD	2.19 ± 0.63	3.47 ± 0.91	[a]0.017* (S)
Median (Range)	1.98 (1.65 – 3.68)	3.5(1.74-4.52)	

[a]Wilcoxon Signed Ranks Test

Diagnostic potential of shear wave (SWE) in rheumatoid arthritis: Concerning ROC curve for Level of **Elastic Modulus (KPa)**, area under the curve = 0.99, cutoff level of **Elastic Modulus (KPa)** < 44.35 had sensitivity of 100 %, and specificity of 94 % in detecting RA changes. Also, as regards ROC curve for Level of **Elastic Modulus (KPa)**, area under the curve = 0.99, cutoff level of **Mean Velocity (m/sec)** < 3.76 had sensitivity of 100 %, and specificity of 93.3 % in detecting RA changes with high statistical significant difference (Table 7).

Table (7): Diagnostic potential of Shear wave (SWE) parameters relation to presence of RA changes among the studied groups with ROC curve

Test Result Variable (s)	Cut Off point	AUC	95% Confidence Interval		Sensitivity	Specificity	p-value
			Lower Bound	Upper Bound			
Elastic Modulus (KPa)	< 44.35	0.996	0.98	1.000	100%	94%	0.000*
Mean Velocity (m/sec)	< 3.76	0.987	0.96	1.000	100%	93.3%	0.000*



Grey Scale US (GSUS) & Power Doppler study revealed :Image (A) : Longitudinal image of dorsal aspect of right little finger MCPJ show hypoechoic synovial hypertrophy (3.7 mm)s (white arrow), with normal bright underlying metacarpal and phalangeal bones and extensor tendon with no vascularity on Power Doppler, Shear Wave Elastography (SWE) :
Image (B): colour elastogram illustrating synovium as a zone ranging from yellow to blue. The elastic modulus of the hypertrophied synovium (circle in the following figure) is 13.7kPa. Image (C): Synovium is represented on a colour elastogram as a zone ranging from yellow to blue. Below, a circle represents a region of interest (ROI), and its mean velocity of 1.95 m/s can be seen in the hypertrophied synovium.

Follow up after 2 months of treatment
Grey Scale US (GSUS) & Power Doppler study revealed - Image (D): Longitudinal image of dorsal aspect of right little finger MCPJ show normal synovial thickening (white arrow), with normal bright underlying metacarpal and phalangeal bones and extensor tendon, Shear Wave Elastography (SWE)
Image (F): colour elastogram illustrating synovium as a yellow-to-red zone. The elastic modulus of the synovium is depicted as 46.6 kPa within the circled area of interest (ROI) in the image below.
Image (F): colour elastogram illustrating synovium as a yellow-to-red zone. Synovium ROI (circle) averaged 3.93 metres per second in the below image.

Figure (2): Female patient 50 years old with history of being recently diagnosed as rheumatoid arthritis (rheumatoid factor positive). Complain of bilateral hand and wrist pain, limitation of movement, morning stiffness and swollen joints since 1 month.

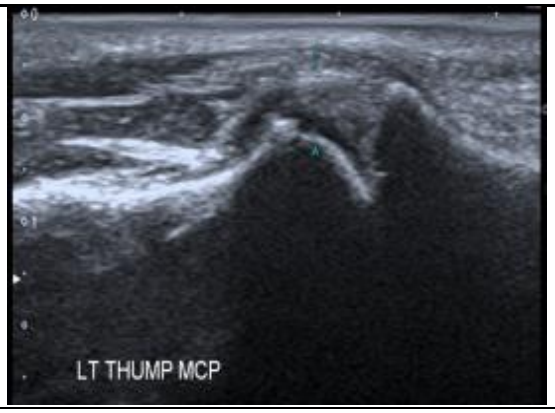
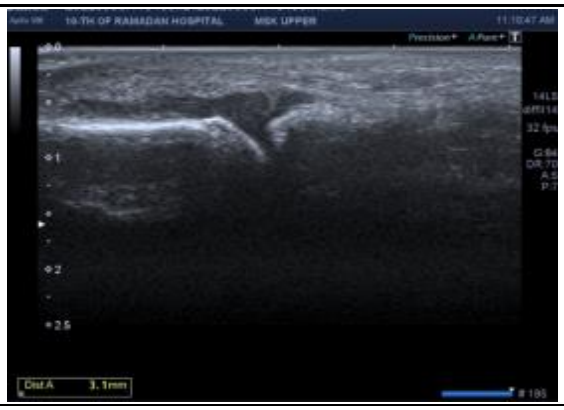
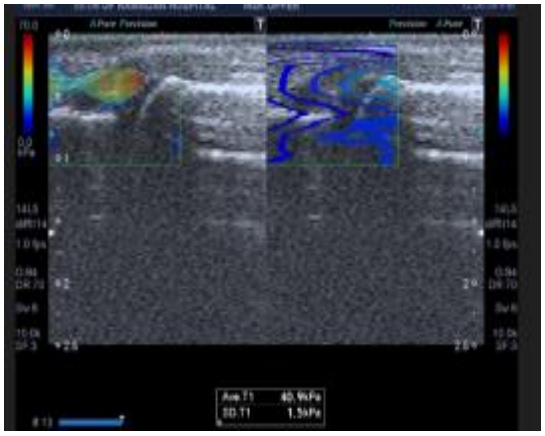
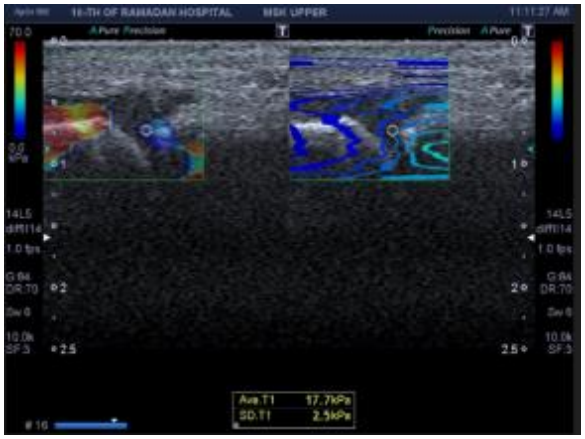
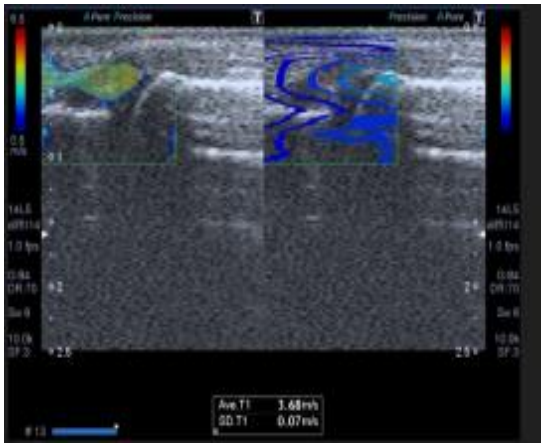
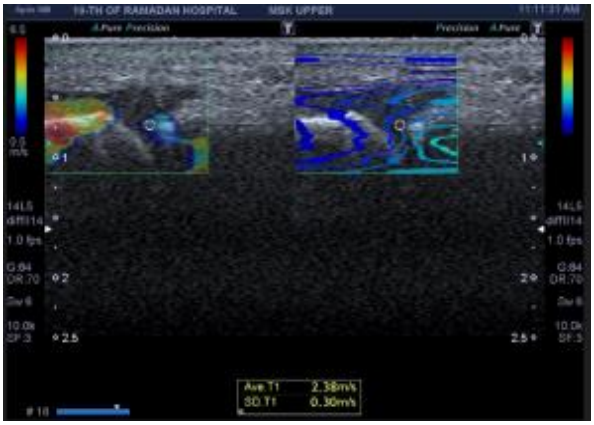
A		D	
B		E	
C		F	
Female patient 43 years old with history of being diagnosed as rheumatoid arthritis 10 years ago with (rheumatoid factor positive), on medical treatment. Complain of hand and wrist pain with limitation of . Scale US (GSUS) & Power Doppler study revealed Image (A): Longitudinal image of dorsal aspect of left thumb MCPJ show hypoechoic synovial hypertrophy (3.3 mm) (white arrow), with normal bright underlying metacarpal and phalangeal bones(white arrow head) and normal extensor tendons(black arrow), with no increase in vascularity on Power Doppler study. Shear Wave Elastography (SWE) Image (B): showing synovium on a colour Elastogram as a gradient from yellow to blue. Below is a picture of hypertrophied synovium with a ROI (circle) exhibiting an elastic modulus of 40.9 kPa.. Image (CColor Elastogram showing synovium (yellow to blue area). The average speed of the hypertrophied synovium in the circled area in the next image is 3.68 metres per second.		-Male patient 65 years old with history of being diagnosed as rheumatoid arthritis (rheumatoid factor positive) but no clinical signs., Complain of bilateral hand pain, limitation of movement since 2 weeks. Grey Scale US (GSUS) & Power Doppler study revealed : Image (D): Longitudinal image of dorsal aspect of right thumb finger MCPJ show hypoechoic synovial hypertrophy (3.1 mm) (white arrow) with normal bright underlying metacarpal and phalangeal bones and extensor tendon. Shear Wave Elastography (SWE) Image (E): colour elastogram with the synovial membrane shown in blue. The elastic modulus of the hypertrophied synovium in the circled area of the following image is 17.7kPa. Image (F): The synovium is represented on the colour elastogram by the blue area. The average speed of the hypertrophied synovium in the circled area of interest (ROI) below is 2.38 metres per second.	

Figure (3): 2 Cases study of group 2 symptomatic patients with positive Rh factor, however no clinical signs and group 3 chronic RA patients

DISCUSSION

Currently employed in liver, thyroid, and breast imaging, shear-wave elastographic ultrasonography (SW-EUS) shows promise in evaluating the synovium [4]. In our study we found that group 1 (recently diagnosed patients) had synovial thickening in 62.5%. This coincides with result of **Okasha *et al.*** [7] who performed a study on thirty patients with rheumatoid arthritis to evaluate the value of ultrasonography and power Doppler in detecting early inflammatory changes in these patients and distinguishing between active and inactive synovitis. They found synovial thickening in active synovitis but not in non-active synovitis (73%). Also, this agrees with **Mendonca and colleagues** [8] who found that 66.6% of individuals had synovial thickening by GSUS.

In our study joint effusion was detected in 62.5% that agrees with **Okasha *et al.*** [7] who found joint effusion in 50%. These results disagree with the work of **Botar and colleagues** [9] who detected effusion in only 14.7 % of their patients. This may be due to the difference in inclusion criteria.

In our study tenosynovitis detected in only one case (12.5%), which disagree with **Okasha *et al.*** [7] who found 43% of cases had tenosynovitis, this difference may be due to small sample size of our study in comparison with **Okasha *et al.*** [7]**.** While, **Wakefield *et al.*** [6] evaluated 100 RA patients and found that US is a reliable technique for detecting erosions, especially in the early stages of RA. Our findings suggest otherwise, although we found no evidence of bone degradation in newly diagnosed RA patients.

Our study found that power Doppler US was able to detect hypervascularity in 62.5% of patients, which is consistent with the findings of **Scirè *et al.*** [10]**,** whose research looked at the utility of a systematic approach to musculoskeletal ultrasound imaging using grey scale (GS) and power Doppler (PD) to evaluate early-stage rheumatoid arthritis in 106 patients. Hypervascularity was detected with the use of power Doppler ultrasonography (PDUS) in only 28.7% of the small joints. These findings do not agree with the work of **Szkudlarek *et al.*** [11]**.** Differences in inclusion criteria may account for the observed hypervascularity variances.

After two months of follow-up we found that there was improvement in synovitis and effusion by 25% & 12.5% respectively that agree with the study of **Filippucci *et al.*** [12] that after 12 weeks of treatment, both clinical and US results revealed considerable improvement and with study of **D'Agostino *et al.*** [13] that showed early improvement was observed in power Doppler signal, synovial hyperplasia and joint effusion.

In group 2 (symptomatic patients with positive Rh factor with no clinical sign for arthritis),

joint effusion was mild in 15.4% of examined patients that is in agreement with study of **De Stadt *et al.*** [14] who detected joint effusion in 15% of examined patients.

Synovial thickening was 69.2% of examined patients that disagrees with study of **Van Beers-Tas *et al.*** [15] who detected synovial thickening in only 30% of examined patients. Also, **Van De Stadt *et al.*** [14] who detected synovial thickening in only 18%. This difference may be due to small sample size.

In group 3 (chronic patients with RA), we found that 33.3 % of examined patients had synovial thickening that broadly is in line with study of **Naredo *et al.*** [16] who found synovial thickening in more than 30% of examined patients and with study of **Brown *et al.*** [17] who found that 36% had synovial thickening and disagree with **Vreju *et al.*** [18] who found that 54.7% of examined patients had synovial thickening. This difference is due to small sample size of our study.

We found bone erosion in 77.8% of examined patients that disagrees with **Vreju *et al.*** [18], who found it in only 21.7% of their examined patients. This difference may be due to bias in inclusion criteria.

We found tenosynovitis in 11.1% of examined patients that disagrees with **Brown *et al.*** [17] who found 37.7% of examined patients had tenosynovitis. This difference may be due to that some tenosynovitis might have been missed and small sample size of our study in comparison with study of **Brown *et al.*** [17] who performed a study on 107 patients with rheumatoid arthritis.

In our study, we found that there was highly statistically significant difference in SWE parameters between RA patients and healthy control where the mean of Elastic Modulus (KPa) was statistically lower (16.77 ± 15.0) among RA patient than (101.2 ± 27.9) among healthy control. Also, mean of mean velocity was statistically lower among RA patients 2.16 ± 0.94 (m/sec) vs 5.53 ± 1.14 (m/sec) respectively. It's possible that this means that RA patients' synovium is softer than that of age- and sex-matched individuals without inflammatory arthritis. We agree with **Sammel *et al.*** [5] in assessment of RA patients by shear wave velocity measurement that our average was 2.16 ± 0.94 (m/sec) in comparison with 2.62 ± 5 (m/sec). We disagree with **Prakash *et al.*** [19] whose study was about role of shear wave elastography of synovium to differentiate rheumatoid and tubercular arthritis. When compared to our data, which were 16.77 ± 15.0 kPa & 2.62 5 m/sec, they observed that the average elastic modulus (kPa) of the synovium for the RA group was 54.81 ± 10.61 kPa & 4.20 ± 0.42 m/s. This discrepancy could be because of the relatively limited sample size of RA patients used by **Prakash *et al.*** [19]**.**

This is the first study to use SWE-US to follow-up patient with RA after treatment study, where the mean of Elastic Modulus (KPa) increased from 15.67 ± 10.56 to 42.07 ± 17.8. Also, mean of mean velocity (m/sec) increased from 2.19 ± 0.63 to 3.47 ± 0.91 that indicate that there was decrease in disease activity after

follow-up and there was improvement after treatment & SWE had a role in the diagnosis and assessment of disease activity in RA.

In our study, we found that cut off level of Elastic Modulus (kPa) > 44.35 had sensitivity of 100 %, and specificity of 94 % in detecting RA changes. Also, cut off level of mean velocity (m/sec) > 3.76 had sensitivity of 100 %, and specificity of 93.3 % in detecting RA. This is in agreement with study of **Prakash *et al.*** [19] that a value of 43.60 kPa was determined to be the elasticity threshold, which was shown to have a sensitivity of 86.7% and a specificity of 80%. The resulting velocity cutoff value was 3.76 m/s, which was shown to have 86.7% sensitivity and 80% specificity.

CONCLUSION

Synovial hypertrophy and effusion, as well as soft tissue and bone damage, can be evaluated in the early stages of rheumatoid arthritis with the help of HRUS and PD. Patients with rheumatoid arthritis with SW-EUS had considerably lower mean maximal SWV and Elastic Modulus than controls. Increasing softness may be an indicator of disease activity, the authors argue. Further research into the role of SW-EUS in the diagnosis and evaluation of disease activity in RA is warranted.

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Competing interests: Nil.

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