

VALUE OF METACARPOPHALANGEAL AND PROXIMAL INTERPHALANGEAL JOINTS ULTRASOUND IN EARLY RHEUMATOID ARTHRITIS, COMPARISON WITH MAGNETIC RESONANCE IMAGING, A CROSS SECTIONAL STUDY.

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ABSTRACT

Background: The metacarpophalangeal and interphalangeal joints are very early sites of affection by Rheumatoid arthritis and are suitable for ultrasound evaluation; the purpose of the study is to evaluate the diagnostic value of ultrasound in detecting radiological signs of early Rheumatoid arthritis as compared to magnetic resonance imaging. Results: The most frequent radiological finding was synovial thickening in both US and MRI (84.3% versus 89.3%), followed by erosion (34.3% versus 32.1%) and effusion (11.4% versus 10%), while the least was tenosynovitis (4.3% in both US and MRI). US showed high sensitivity (94.4%, 100% and 100%), specificity (100%, 98.4% and 100%) and accuracy (95%, 98.5% and 100%) for synovial thickening, effusion and tenosynovitis respectively and a lower sensitivity (84.4%), specificity (89.5%) and accuracy (87.8%) in detecting bone erosions in the finger joints compared to MRI. Conclusion: US is a reliable method in diagnosing most features of early Rheumatoid arthritis compared to MRI. Therefore, the US can be implemented as a primary diagnostic tool in evaluating early Rheumatoid arthritis.

Keywords: Ultrasonography, magnetic resonance imaging, rheumatoid arthritis metacarpophalangeal joints, proximal interphalangeal joints, erosions, synovial effusion, synovial thickening, tenosynovitis

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INTRODUCTION

Background: Rheumatoid arthritis is a chronic autoimmune disease affecting approximately 1% of the world population. The disease primarily involves the synovial joints, leading to pain, deformity, disability and life-threatening complications. The essential pathological process of the condition is attributed to synovitis with synovial hypertrophy, i.e. soft tissue process to start with, that subsequently impacts the articular cartilage and the articular bone causing destructive inflammatory changes (1, 2). With the new advances in treatment, namely the wide availability and use of biological agents, and consequently improved survival and prognosis, there comes a need for early disease detection for rapid employment of effective treatment. (5). The disease is classically, and still nowadays, primarily investigated by plain radiography, which, despite its shortcomings, remains the fundamental diagnostic modality. (2, 6).

But conventional radiographs have little sensitivity to most soft tissue inflammation forms, which characterize an early disease; thus, it plays only a little part in this area. (2, 4, 6). Moreover, even in established bone damage, x rays may have a limited diagnostic utility; a large cohort study indicated that radiographically detected erosions were present in only 30% of patients at

the time of disease diagnosis and in 70% three years later (7). Given their superior soft tissue detail, both MRI and ultrasound are more sensitive indicators of the disease's early stages, namely within the first 12 months of the disease onset (2, 6, 8, 9, 10, 11).

Ultrasound gains trust and competence in clinical studies to detect synovitis (8, and 12). Not only both MRI and ultrasound are imaging techniques that enable superior soft tissue evaluation, being sensitive for detection of synovitis and tenosynovitis, but also both are also of superior value to radiography in the detection of early articular cortical erosions that may be occult radiographically (13, 14, 15, 16, 17). Several studies already addressed the use of MRI in evaluating early rheumatoid arthritis and found a very high accuracy for detecting early disease in the evaluation of soft tissue changes and detection of erosions, 19, 20, 21, and 22).

Ultrasound off Coase has many obvious benefits, including but not limited to its low cost, wide availability, relative ease of the procedure, lack of radiation and no harmful contrast media. Still, the current role of ultrasound and the precise accuracy for overall diagnosis and specifically for the presence of erosions is a matter of current research and ongoing investigative work, especially as ultrasound gives the imager a limited imaging window into the underlying bone and cartilage, a major limitation in comparison to MRI images. (8). In this study, we tried to evaluate various ultrasound features of rheumatoid arthritis, both soft tissue and bone changes using MRI as a reference to understand what this modality may offer in early and accurate disease diagnosis.

Aim of the study, the study aims to evaluate the diagnostic value of ultrasound in detecting radiological signs of early Rheumatoid arthritis affecting the metacarpophalangeal and proximal interphalangeal joints as compared to magnetic resonance imaging.

METHODS

2.1. Data collection and study design

This cross-sectional hospital-based diagnostic study was conducted on 35 patient in the radiology department at Imamain Al-Kadhymain medical city (formerly AL-Kadhymia Teaching Hospital) during the period from December 2018 to December 2019. A total of 35 patients (1 male and 34 females), with a mean age of 43.8 years (ranged 23to 58), with a diagnosis of rheumatoid arthritis, were included in the study

2.1.1. Inclusion criteria

All patients included in the study were referred from the rheumatology unit with a proven diagnosis of rheumatoid arthritis within the last 12 months. Diagnosis of rheumatoid arthritis (RA) was based on ACR/EULAR criteria assessed by the rheumatologist.

2.1.2 Exclusion criteria:

1. Patients younger than 18 years old.
2. Patients who had a history of trauma, previous surgery or congenital anomaly in the hands.
3. Patients with an equivocal diagnosis of RA.
4. Patients with any contraindication to MRI.
5. Presence of any mass lesion or significant deformity that preclude proper US or MRI examination to interfere with interpretation of findings.

2.2 Data acquisition and imaging analysis:

2.2.1 US examination:

2.2.1.1 Equipment:

Ultrasound examination was carried out using GE Voluson (E6- USA) version 2010 ultrasound unit, equipped with a high-frequency probe (7—12 MHZ).

2.2.1.2 Technique:

All patients were examined in a sitting position, opposite to the examiner, with their hands resting on the side of the bed, in both pronation and supination positions, to properly assess the palmer(flexure) and dorsal(extensor) aspects of the fingers.



Figure (1) Evaluation of the flexor aspect of the second MCPJ.

Avoiding excessive probe pressure that can obliterate small quantities of fluid and reduce the sensitivity for detecting blood flow may obscure synovitis. Sagittal images are the mainstay for diagnosis, with axial (MCPJ) and coronal (PIPJ) images used in support. The superficial structures, including skin, subcutaneous tissue tendon and tendon sheath, were assessed before the joints themselves.

The examination was done on MCP, proximal and distal IP joints of the 2nd and 3rd fingers as they are the early RA site, using a grayscale, looking for effusion, synovial thickening, bone erosion, and tenosynovitis. Simple effusion should be completely transonic, compressible, and with no increase in Doppler signal. Synovial thickening was considered when the synovium measures more than 3 mm thickness (23). Bony erosion was assessed by detecting an intra-articular discontinuity of the bone surface visible in two perpendicular planes. Acute erosions tend to show rather fluffy irregular margins and have poorly defined bases, which allows through the transmission of sound, associated active synovitis is also frequently appreciated. A common source of confusion is the normal depression present on the dorsal aspect of the head of the metacarpals. Unlike erosions, this is usually smooth, with a clearly defined floor that does not allow through sound transmission and is unassociated with overlying synovitis (23).

2.2.2. MRI equipment and technique:

MRI images were obtained using 1.5-tesla imagers (MAGNETOM Aera2016-Siemens). Bilateral imaging of the hands was done. The areas of interest were the MCP, the proximal and distal IP joints, using a flexible surface coil with a small FOV (80—120 mm). The scanning sequences were as follows; 1) T1-weighted images in axial and sagittal planes, 2) T2-weighted images in sagittal, axial and coronal planes, 3) T1WI with fat suppression in axial and coronal planes. 4) In cases in which tenosynovitis was suspected, the small joints were examined with intravenous contrast media using gadolinium-diethylene triamine pentetic acid (Gd-DTPA-0.2ml/kg body weight); T1 fat-saturated imaging is preferable after administration.

The imaging findings to look for were synovitis, effusion, bone marrow oedema, erosion and tenosynovitis. 2.3. Statistical analysis was done by using SPSS (statistical package for social sciences) version 20. Frequency, percentage, mean and standard deviation as descriptive statistics. Sensitivity, specificity, PPV, NPV and accuracy were measured for US compared with MRI for each finding. Kappa test was used to measure agreement between right and left side. P-value ≤ 0.05 was considered statistically significant.

3. RESULTS:

3.1: patient demographics:

A total of 35 patients had been included in this Table (1) Showing the overall frequency and percentage of the findings by US and MRI.

Finding	US		MRI	
	Number	Percentage	Number	Percentage
Synovial thickening	118	-84.30%	125	-89.30%
Erosion	48	-34.40%	45	-32.10%
Effusion	16	-11.40%	14	-10%
Tenosynovitis	6	-4.30%	6	-4.30%

3.2.1: Synovial thickening: There were high sensitivity and specificity of ultrasound in diagnosing synovial thickening. Table (2) Validity of ultrasound in diagnosing synovial thickening compared to MRI.

	Middle finger		Index finger	
	Right	Left	Right	Left
Sensitivity	92.80%	96.50%	94.10%	96.90%
Specificity	100%	100%	100%	100%
PPV	100%	100%	100%	100%
NPV	66.70%	85.70%	33.30%	66.70%
Accuracy	91.40%	97.10%	91.40%	97.10%

3.2.2: Erosions:

Table (3) Validity of ultrasound in diagnosing erosion compared to MRI.

	Middle finger		Index finger	
	Right	Left	Right	Left
Sensitivity	70%	62.5%	93.3%	100%
Specificity	92%	92.6%	80%	91.3%
PPV	77.8%	71.4%	76.4%	85.7%
NPV	88.4%	89.3%	94.1%	100%
Accuracy	85.7%	85.7%	85.7%	94.3%

3.2.3: Effusion:

Using ultrasound, any case with effusion will be diagnosed correctly with no false-negative, but there are false-positive cases that make the specificity 96.9%. Table (4) Validity of Ultrasound in diagnosing effusion compared to MRI.

3.2.4: Tenosynovitis:

Table (5) Validity of ultrasound in diagnosing tenosynovitis compared to MRI

	Middle finger		Index finger	
	Right	Left	Right	Left
Sensitivity	100%	100%	100%	100%
Specificity	100%	100%	100%	100%
PPV	100%	100%	100%	100%
NPV	100%	100%	100%	100%
Accuracy	100%	100%	100%	100%

3.2.5: Overall validity of ultrasound in diagnosing different findings Compared to MRI, the ultrasound was highly accurate for tenosynovitis (100%) and the least accurate for erosion (87.8%). Table (6) Overall validity of ultrasound in diagnosing different findings

	Sensitivity	Specificity	PPV	NPV	Accuracy
Tenosynovitis	100%	100%	100%	100%	100%
Effusion	100%	98.4%	87.5%	100%	98.5%
Synovial thickening	94.4%	100%	100%	68.2%	95%
Erosion	84.4%	89.5%	79.1%	92.4%	87.8%

3.2.6: Right versus left sided findings:

We noticed some occasional differences in the validity of US between the right and left sides. So, we performed a statistical analysis using the McNemar test to compare the right and left side findings. It was statistically insignificant; the P-value for tenosynovitis was (0.652), for effusion was (0.718), for synovial thickening (0.892) and bony erosion was (0.371).

4. DISCUSSION

4.1. Overall evaluation:

The (MCP) and (PIP) joints of the hand are among the primary areas to be affected in RA (1, 2, 4, and 5). Within the current study, 280 joints of 35 RA patients were examined (right and left MCP and PIP joints of both index and middle fingers, in both flexure and extensor sides). The foremost frequent radiological finding was synovial thickening in both US and MRI (84.3% versus 89.3%), followed by erosion (34.3% versus 32.1%) and effusion (11.4% versus 10%), while the smallest amount was tenosynovitis (4.3% in both US and MRI). The current study showed an awfully high US sensitivity (94.4%, 100%, and 100%), specificity (100%, 98.4%, and 100%) and accuracy (95%, 98.5%, and 100%) for synovial thickening, effusion and tenosynovitis respectively compared to MRI. In contrast, Szkudlarek et al. reported a lower value for sensitivity, specificity and accuracy (70%, 78%, and 76% respectively) people, with signs of inflammation on MRI sequences because of the reference method (24), while the corresponding sensitivity/specificity values for detecting soft-tissue abnormalities within the study reported by Rahmani et al. (25) was higher (83%) and 94% respectively).

During this current study, US had a lower sensitivity (84.4%), specificity (89.5%), and accuracy (87.8% in detecting bone erosions within the finger joints compared to MRI in correlation to other above findings (i.e. synovial thickening, effusion, and tenosynovitis). Compared to Szkudlarek et al. study (24), sensitivity within the current study was higher (84.4% vs 59%) while the specificity (89.5% vs 98%) and accuracy (87.8% vs 96%) were lower in detecting bone erosions. Similarly, our study was beyond Rahmani et al. (25) regarding the sensitivity (84.4% vs 63%) and lower regarding specificity (89.5% vs 98%). US showed 100% sensitivity, specificity, and accuracy in detecting tenosynovitis within the current study, while a study was

done by Wakefield et al. showed lower sensitivity and a comparable specificity people versus MRI within the detection of flexor tenosynovitis (0.44and0.99), respectively.

4.2. US versus MRI in evaluating radiological findings in early RA

4.2.1. Synovial thickening:

Proliferative synovitis is the earliest pathologic change seen in atrophic arthritis and is sometimes but not exclusively bilateral and symmetric. Both US and MRI can detect progressive synovitis, and both are superior to clinical assessment in detecting synovitis (27). The OMERACT definition of synovitis using ultrasound is abnormal hypoechoic (relative to subdermal fat but sometimes isoechoic or hyperechoic) intraarticular tissue that's not displaceable and poorly compressible, which may exhibit Doppler signal (28). On MRI, the OMERACT definition of synovitis could be a thickened area of the synovial compartment that shows greater than normal enhancement on gadolinium-enhanced T1- weighted images (29). Several published studies document the high level of agreement between MRI-reported synovitis and pathologic findings (27). For this reason, MRI was considered because the reference standard within the current study assessing the accuracy folks detection of synovitis using grayscale ultrasonography (GSUS) and colour Doppler (CD). In our study showed very high specificity(100%) in detecting synovial thickening and synovitis, with no false-positive cases and also high sensitivity and accuracy (94.4% and 95%, respectively) with some false-negative cases(7 joints) giving relatively low NPP.

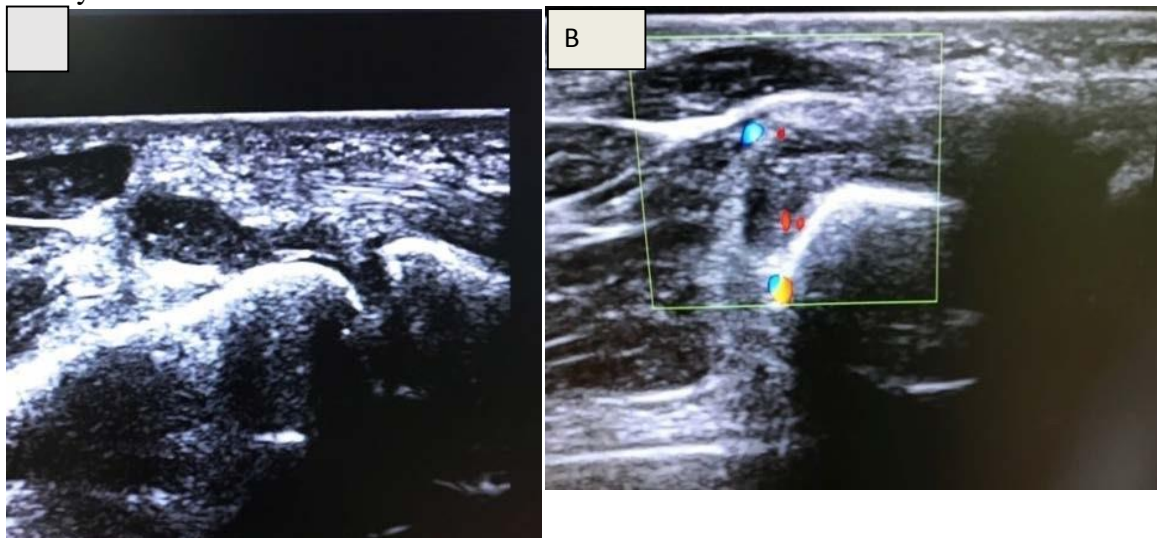


Figure (3): US of the 2nd MCPJ shows, a) nodular synovial thickening, b) Color Doppler shows hyperemia (synovitis).

A recent study during which examination of the IP joints with both US and MRI further like conventional radiography and clinical examination done by Wittoek et al. showed good agreement between US and MRI within the detection of synovitis (86.5%) and concluded that US was a reliable and valid method of assessment of synovitis (27,30).

4.2.2. Erosions:

Erosions are a typical finding in RA and are present in up to 97% of patients with the condition. The presence of bone erosions at the time of diagnosis is expounded to a poor long-term clinical outcome (27). The OMERACT definition of abrasion on MRI may be a sharply margined bone lesion with correct juxta-particular location and typical signal characteristics visible in 3 a minimum of two planes with a cortical break seen in a minimum of one plane (29). In addition to the cortex's breach, the erosion itself generally contains inflammatory tissue or fluid, showing a high signal on T2-weighted images. The inflammatory tissue or synovium within the erosion will usually enhance with IV gadolinium (27). The OMERACT definition of an erosion seen on

US imaging is an intraarticular discontinuity of the bone surface visible in two perpendicular planes (28). Bone erosion was the second most frequent finding in early RA during this present study,

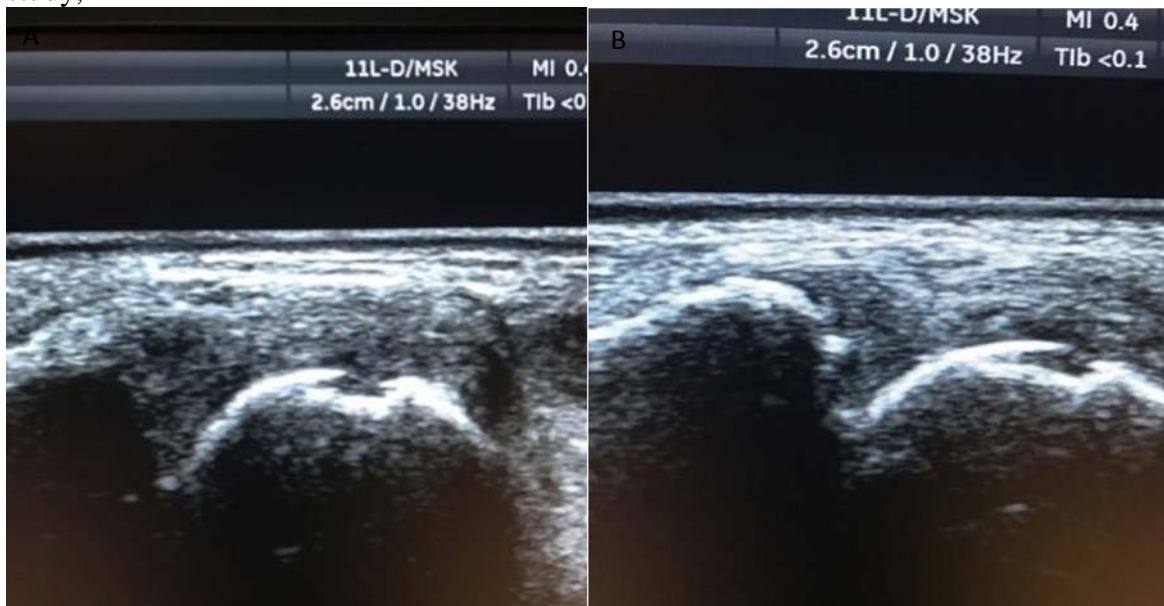


Figure (2) US of 2nd MC Head. Erosion (arrows) of dorsal aspect in two planes (a) transverse scan, (b) longitudinal scan.

The US sensitivity, specificity, and curacy were 84.4%, 89.5%, and 87.8%, respectively, compared to MRI because of several false-negative and, to a lesser extent, false-positive cases.31 Dohn et al. (31) reported sensitivities of only 68% and 42% for MRI and ultrasound, respectively, although only 17 patients with RA were included in their study. One problem seen with US, not with MRI is that some parts of the joint 40 could also be relatively inaccessible, for instance, examining the radial and ulnar aspects of the MCP joints. Another potential pitfall folks detection of erosions is that the misinterpretation of normal anatomic variants as erosions. Depressions seen on the dorsal aspects of the metacarpal heads that will be interpreted as erosions to the unwary operator are described in healthy volunteers. However, metacarpal head depressions will have regular margins and no discontinuity of the cortex (27). Studies have reported a better sensitivity of MRI (19) and US (32)in detecting bone erosion compared to traditional radiography. However, the precise position of folks relative to MRI remains undetermined (27). Although Hoving et al. (33) reported that MRI has significantly increased sensitivity compared with US for detection of erosions within the hand and wrist, Magnani et al. suggested that US is a minimum of pretty much as good as MRI in detecting wrist and MCP joint erosions and should even be better for the MCP joint(34).

4.2.4. Tenosynovitis

Tenosynovitis most commonly affects the hands and wrists and is seen on both US and MRI as fluid or synovitis within a tendon sheath (27). The extensor carpi ulnaris tendon appears to be most commonly affected (36). Thickened tenosynovium will show enhancement with IV contrast administration on MRI (33). The current study showed that tenosynovitis was the least frequent (4.3% in both MRI and US) radiological finding in a period up to 12 months after onset of symptoms with very high sensitivity, specificity and accuracy (100% for all) of US using GSUS and CD.



Figure (4). GSUS of the extensor tendon sheath of 2nd MCPJ. There is nodular hypoechoic thickening, indicating extensor tendon sheath inflammation (tenosynovitis).

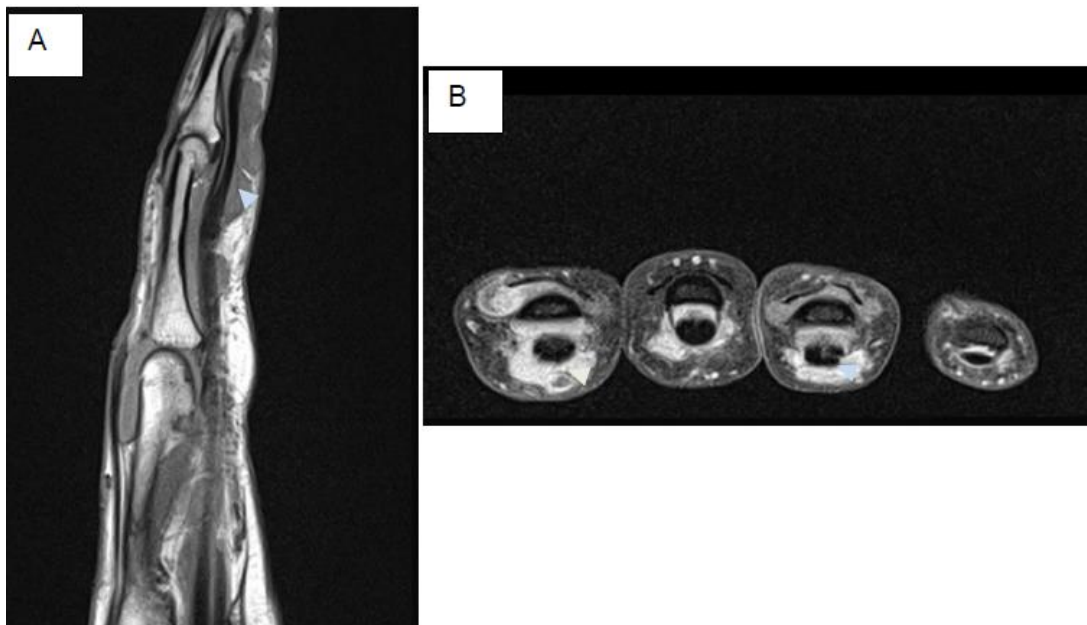


Figure (5) T1 MRI (2nd MCPJ), [a] sagittal and [b] axial contrast-enhanced T1 (level of MCPJs). Thickened synovium and tenosynovium (arrows) will show enhancement with IV contrast administration.

(figure 4,5). Using MRI as a reference method, Wakefield et al. reported the sensitivity, specificity, positive predictive value and negative predictive value for US (utilizing GSUS) - detected flexor tenosynovitis were 0.44, 0.99, 0.98 and 0.49, respectively, showing very high specificity, least false positive case and many false-negative cases. The study also showed the corresponding values for US detected peri extensor tendon disease as 0.15, 0.98, 0.86 and 0.63, respectively.

4.3. Limitation of the study:

4.2.3 Effusion

A small amount of fluid may be associated with synovitis. The fluid appears anechoic on US (figure 3), with no evidence of flow on CD, and is compressible, i.e. can be expelled from the region by compression with the transducer. On MRI, the fluid shows high signal intensity on T2-

weighted images and low signal intensity on fat-suppressed gadolinium-enhanced T1-weighted images (34). Effusion was the second least frequent finding in the current study both by US and MRI (11.4% versus 10 %). This disagreed with a study performed by Saran et al. (41), who found joint effusion to be a frequent finding on both US and MRI (50.7 % versus 59.5%). In the current study, the sensitivity, specificity and accuracy of US in detecting joint effusion compared to MRI were 100%, 98.4%, 98.5%, respectively, with few false-positive cases. On the contrary, Saran et al. reported a lower sensitivity (77%) and relatively comparable specificity (96.4%) for joint effusion. Szkudlarek et al. mentioned that MRI did not detect joint effusion in any of the examined finger joints, whereas US revealed joint effusion in 22 out of the 433 examined finger joints (24). Using a large footprint linear transducer that is not readily accessible for the small hand joints. Doppler evaluation was, unfortunately, not performed due to technical limitations.

CONCLUSION

US is a reliable method in diagnosing most features of early RA compared to MRI. Therefore, US can be implemented as a primary diagnostic tool in the evaluation of early RA. The current study showed an awfully high US sensitivity, specificity, and accuracy for synovial thickening, effusion and tenosynovitis, respectively, compared to MRI, but lower sensitivity, specificity, and accuracy in detecting bone erosions within the finger joints again as compared to MRI.

List of abbreviations

ACR: American College of Rheumatology CD: Color Doppler EULAR: European League against Rheumatism GSUS: greyscale ultrasound IP: interphalangeal joint MCPJ: Metacarpophalangeal joint MRI: magnetic resonance imaging NPV: negative predictive value OMERACT: Outcome Measures in Rheumatology Clinical Trials PIPJ: proximal interphalangeal joint PPV: positive predictive value RA: Rheumatoid arthritis US: Ultrasound.

7. Declarations:

7.1 Ethics approval and consent to participate in the Iraqi board of health specializations institutional board approval was obtained. Committee's reference number: not applicable, the data obtained were part of the diagnostic workup of patients done for diagnostic purposes, no additional test was done to justify additional written procedures, as it is the standard work of the Iraqi Board of Health Specializations in dealing with standard diagnostic procedures done for the sake of the patients, without extra-intervention for research; nonetheless, all the procedures followed were with accordance with the ethical standards of the responsible committee on human experimentation and with the Helsinki declaration of 1975, revised in 2008, Patient's informed verbal consent was obtained from all the subjects in the study, despite being part from their own diagnostic workup.

7.2. Consent for publication: not applicable.

7.3. Availability of data and material: All data generated or analyzed during this study are included in this published article [and its supplementary information files].

7.4. Competing interests: The authors declare that they have no competing interests.

7.5. Funding: no funding received, no financial disclosures.

7.6. Authors' contributions:

H.F Salman: Contributed to the acquisition, analysis, and interpretation of data; he has approved the submitted version (and any substantially modified version that involves his contribution to the study); He has agreed both be personally accountable for his own contributions and to ensure that questions related to the accuracy or integrity of any part of the work, even ones in which he was not personally involved, are appropriately investigated, resolved.

N.A. Fayadh: Has made substantial contributions to the conception and design of the work; the acquisition, analysis, and interpretation of data; AND she approved the submitted version (and any substantially modified version that involves her contribution to the study); She has agreed

both be personally accountable for her own contributions and to ensure that questions related to the accuracy or integrity of any part of the work.

Haider Najim Al-Tameemi : Has made substantial contributions to the conception, design of the work, approved the submitted version, agreed to be personally accountable for his own contributions, and ensured that questions related to the accuracy or integrity of any part of the work.

N.K. Al Waely: Has made substantial contributions by drafting the work and substantively revising it, she has approved the submitted version (and any substantially modified version that involves the author's contribution to the study); she agreed both to be personally accountable for her own contributions and to ensure that questions related to the accuracy or integrity of any part of the work.

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