

Reliability of Ultrasound for the Detection of Rheumatoid Arthritis

Rabia Hassan*, Sobia Hussain, Raham Bacha, Syed Amir Gillani, Sajid Shaheen Malik

Faculty of Allied Health Sciences Department, University Institution of Radiological Sciences and Medical Imaging Technology, The University of Lahore, Lahore, Pakistan

Abstract

The aim of this review article was to investigate the pooled sensitivity and specificity of musculoskeletal ultrasound (MSUS) for the detection of synovitis and early bone erosion in the small joint in rheumatoid arthritis (RA). In addition, investigate the pooled sensitivity and specificity of Power Doppler ultrasonography (PDUS) for the detection of synovial hypervascularity in small joints in RA. A systematic literature search of PubMed, Wiley online library, Google Scholar, Research gate, E-book, BioMed Central, the Journal of Rheumatology and Springer Link were investigated from 2001 to 2017. Original researches related to the article written in English including RA, synovitis, bone erosion, grayscale, and PDUS were included in this study. The sample size, study design, sensitivity, and specificity were analyzed. The review summarizes the value of MSUS for the detection of RA as it is the first choice of modality. Results show the acceptable reliability of US for the diagnosis of early bone erosions, synovitis, and synovial hypervascularity.

Keywords: Bone erosion, rheumatoid arthritis, sensitivity, synovitis

INTRODUCTION

Rheumatoid arthritis (RA) is a long-term autoimmune disease and inflammatory disorder. It affects the synovial membrane resulting in synovitis that is a primary abnormality and leads to structural destruction such as bone erosions, cartilage damage.^[1-3] Small joints are frequently involved in RA such as metacarpophalangeal (MCP) joints, proximal interphalangeal (PIP) joints and metatarsophalangeal (MTP) joints.^[4] Early and accurate diagnosis of structural damage is necessary for early treatment.

Musculoskeletal ultrasound (MSUS) is, nowadays, widely used worldwide for the diagnosis of RA.^[5,6] Magnetic resonance imaging (MRI) is considered a sensitive imaging modality for the detection of synovitis, joint effusion, and early bone erosions.^[7] However, MRI has some limitations and disadvantages as it is expensive and not easily accessible.^[8] In contrast, US is readily available, relatively cheap, easy to tolerate by the patient, free of bioeffects and portable. It is, therefore, the modality of choice due to its numerous benefits.^[9] Several studies have reported that US is more sensitive and specific technique for the detection of RA as compared to clinical assessment and laboratory examination.^[10-13]

On gray-scale US (GSUS), the inflammatory and destructive activity of small joints in RA can be visualized with the help of high-frequency linear array transducer.^[10,12] Power Doppler ultrasonography (PDUS) is a good tool for the evaluation of inflammatory activity of joints in RA. Blood flow to the Synovial membrane can be detected by PDUS.^[14-16]

Bone erosion is another sign of RA; however, it also is seen in other rheumatoid diseases.^[17] Early bone erosions changes in RA cannot be detected by conventional radiography (CR); however, the US and other imaging modalities can detect the earliest bone erosive changes.^[18] Hence, the review is aimed to justify the “use of US in the diagnosis of RA by evaluating its reliability.

METHODOLOGY

Articles were collected related to our topic from 2001 to 2017. Thirty-six articles were studied in which twenty-nine

Address for correspondence: Dr. Rabia Hassan,
Ibrahim street Awan Town Multan Road Lahore,
The University of Lahore, Lahore, Pakistan.
E-mail: rabiahassan464@gmail.com

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articles were included and summarized. Seven articles were excluded in which two articles reported large joints such as shoulder and knee.^[19,20] The remaining five articles were not provided sufficient information regarding RA as they mention the keywords of RA^[21-25] These articles were provided by the university library and online source of PubMed, Google Scholar, AJR, and Wiley online library, BMJ Journal, Researchgate, E-book, BioMed Central, The Journal of Rheumatology and Springer Link. Seventeen articles reported the sensitivity and specificity of US for the detection of synovitis, synovial hypervascularity and bone erosion in which 934 patients were examined that have RA.^[7,10,11,13,14,17,26-35] Different types of studies such as cohort study, case-control study, and case study were included in this study.

SYNOVITIS

MSUS (including GS and PDUS imaging) is a reliable and useful tool for the detection of synovitis. GSUS often detects the signs of synovitis such as synovial hypertrophy and synovial fluid or effusion.^[16] Previous five studies discussed the sensitivity and specificity of US for the detection of synovitis by comparing with different modalities such as MRI, CR, laboratory, and clinical assessments that are summarized in Table 1.^[10,13,18,27,33] PDUS has increased the sensitivity of US and able to detect the synovial hypervascularity in small joints. Previous four studies have discussed the sensitivity and specificity of PDUS for the detection of hypervascularity in RA and compare with different modalities such as MRI, CR, laboratory, and clinical examination that is summarized in Table 2.^[14,27-29]

Previous five studies reported the sensitivity and specificity of GSUS for the detection of synovitis.^[10,13,18,27,33] The sensitivity of GSUS for the detection of synovitis ranged from 47.4% to 92% as shown in Table 1. However, we have excluded the 47.4% sensitivity as it decreased the mean sensitivity.^[27] The specificity of GSUS ranged from 74% to 90.9% as shown in Table 1. However, we were excluded Freeston *et al.*, study as this study reported low sensitivity.^[27] A study conducted by authors; Szkudlarek *et al.*, in 2004 with the objective to compare the US with MRI, CR and clinical examination in the evaluation of bone destruction and signs of inflammation in the MTP joints of patients with RA. They have assessed one hundred MTP joints of twenty healthy control and two hundred MTP joints of forty patients with RA. They were assessed synovitis in 36 patients, 31 patients, and 21 patients with the help of US, MRI, and clinical examination, respectively. They were considered the MRI as a reference method and reported the US sensitivity 87% and specificity 74% for MTP joints, while for clinical examination, the corresponding values 43% and 89%. They evaluated that by comparing with MRI, US was found to be more sensitive and accurate than CR and clinical examination.^[18] Another study conducted by authors; Scheel *et al.*, in 2005 with the objective to evaluate the synovitis with help of US of finger

joints in patients with active RA. They were performed MRI in 10 patients and compared the results with the US and found a good correlation between MRI and US for the detection of synovitis. They were reported US sensitivity 94% and specificity 89% for MCP and sensitivity 90% and specificity 88% for PIP joints for the detection of synovitis. Hence, the sensitivity and specificity for MTP joints were high.^[13] Another study conducted by authors; Szkudlarek *et al.*, in 2006 with the objective of to investigate whether US can provide information synovitis that is not available with CR and clinical examination and also compare with MRI. T1-weighted MRI sequences as the reference method, they were reported the US sensitivity 70% and specificity 78% for MCP and PIP joints with synovitis and reported 40% sensitivity and 85% specificity for the clinical examination. Their results indicated that with MRI as a reference method the US had higher sensitivity and accuracy.^[10] Another study conducted by authors; Wakefield *et al.*, in 2008 with the objective of compare clinical examination and the US with high-field MRI as the reference method for the detection of synovitis in RA. They have compared MRI as the gold standard with clinical examination and with the US reported the sensitivity 76% and specificity 70% for hind foot. They were reported clinical examination sensitivity 69% and specificity 34.5% for the detection of synovitis. They evaluated that US is more sensitive and specific than clinical examination when compared with MRI as Gold standard.^[33] According to four studies, the pooled sensitivity and specificity of GSUS for the detection of synovitis of small joints is 83.5% and 79.8%, respectively, as shown in Table 3 and Graph 1. All these above studies agreed with pooled sensitivity and specificity of US for the detection of synovitis.

Previous four studies reported the sensitivity and specificity of PDUS ranged from 71.1% to 92% and 40% to 97.9%, respectively mentioned in Table 2. A study conducted by authors; Szkudlarek *et al.*, in 2001, with the objective of to diagnose the effectiveness of PDUS for the evaluation of inflammatory activity in the MCP joints of patients with RA, using T1-weighted MRI sequences as a reference method. They have assessed 54 MCP joints of 15 patients with active RA and 12 MCP joints of three healthy controls. They were detected flow signal on PDUS in 17 of 54 MCP joints in RA patients. They were reported a good sensitivity of 88.8% and specificity 97.9% for MCP joints.^[14] Another study conducted by authors, Kiris *et al.*, in 2006 with the objective of to evaluate synovial vascularity and flow pattern in MCP joints and ulnar styloid regions of hand and wrist of patients with RA. They have examined 240 MCP joints and 48 ulnar styloid regions in 24 patients with RA. They were reported good sensitivity 92% but not good specificity 40% MCP and USLT regions. Hence, we have not included Kiris *et al.*, study as it too much decreased the overall mean specificity.^[29] Another study conducted by Freeston *et al.*, in 2010 with the objective of assesses the value of PDUS in patients with early RA. They have examined 50 patients

Table 1: Sensitivity and specificity of grayscale ultrasonography for the diagnosis of small joints synovitis

Articles name	Authors	Year	Sample size	Study design	Type of joints	Sensitivity (%)	Specificity (%)	Disease duration	Machine brand and model	Frequency	Comparison
Ultrasonography of the Metatarsophalangeal Joints in RA Comparison With MRI, CR, and clinical examination	Szkudlarek <i>et al.</i> ^[18]	2004	60	Case-control	MTP9	879	74	Early disease duration <2 years Established disease duration >2 years	General electric LOGIQ-500 unit	7-13 MHZ	MRI, CR and clinical assessment
A novel ultrasonographic synovitis scoring system suitable for analyzing finger joint inflammation in RA	Scheel <i>et al.</i> ^[13]	2005	56	Cohort	MCP PIP	94 90	89 88	Early disease duration <1 year Mean SD duration 8.5 years	HDI 3500 high-end system	10-5 MHZ	MRI
Ultrasonography of the metacarpophalangeal and proximal interphalangeal joints in RA: A comparison with MRI, CR and clinical examination	Szkudlarek <i>et al.</i> ^[10]	2006	60	Case-control	MCP and PIP	70	78	Early disease duration <2 years. (0-1 years Established disease duration 8 years [0-20 years] years)	General electric LOGIQ 500 unit	7-13 MHZ	MRI, CR and clinical examination
The optimal assessment of the RA hindfoot: A comparative study of clinical examination, ultrasound, and high field MRI	Wakefield <i>et al.</i> ^[33]	2008	22	Comparative	Hind, foot	76.5	70	Mean duration 6.8 years	ATL HDI 3000 high definition imaging	10-5 MHZ	MRI and clinical assessment
A diagnostic algorithm for persistence of very early inflammatory arthritis: The utility of power Doppler ultrasound when added to conventional assessment tools	Freeston <i>et al.</i> ^[27]	2010	50	Cross-sectional	Hand and wrist	47.4	90.9	Early arthritis <12 weeks	Philips HDI 5000	None	PDUS, CR and laboratory examination

RA: Rheumatoid arthritis, MRI: Magnetic resonance imaging, CR: Conventional radiography, MTP: Metatarsophalangeal, PIP: Proximal interphalangeal, PDUS: Power Doppler ultrasonography, MCP: Metacarpophalangeal

Table 2: Sensitivity and specificity of power Doppler ultrasonography for the detection of synovial hypervascularity of small joints

Articles names	Authors	Year	Sample size	Study design	Types of joints	Sensitivity (%)	Specificity (%)	Disease duration	Machine brand and model	Frequency	Comparison
Power Doppler ultrasonography for assessment of synovitis in the metacarpophalangeal joints of patients with RA: A comparison with dynamic MRI	Szkudlarek <i>et al.</i> [14]	2001	18	Case-control	MCP	88.8	97.9	8 years (0-20 years)	LOGIQ 500 unit	7-13 MHZ	MRI
Power Doppler assessment of overall disease activity in patients with RA	Kiris <i>et al.</i> [29]	2006	24	Cross section	MCP and USLT regions	92	40	8 years (2-20 years)	Aplio SSA770A and LOGIQ7	7-14 MHZ	None
A diagnostic algorithm for persistence of very early inflammatory arthritis: the utility of power Doppler ultrasound when adding to conventional assessment tools	Freeston <i>et al.</i> [27]	2010	50	Cross-sectional	Hand and wrist	71.1	81.8	Early arthritis <12 weeks	Philips HDI 5000	None	PDUS, CR and laboratory examination
Diagnostic value of MSUS in newly diagnosed RA patients	Harman <i>et al.</i> [28]	2015	31	Case-control	Finger and wrist	73	76	Mean disease duration 5.69 month	General electrical	5-13 MHZ	MRI

RA: Rheumatoid arthritis, MRI: Magnetic resonance imaging, CR: Conventional radiography, MTP: Metatarsophalangeal, PIP: Proximal interphalangeal, PDUS: Power Doppler ultrasonography, MSUS: Musculoskeletal ultrasound

with or without a sign of early RA with the help of clinical, laboratory, and imaging assessments. They were reported sensitivity 71.1% and specificity 81.1% for hand and wrist joints.^[27] Another study conducted by authors; Harman *et al.*, in 2015 with the objective to evaluate the efficacy of PDUS for the detection of RA and compare the PDUS findings with contrast-enhanced MRI. They were examined the wrist and hand joint including MCP and PIP joints using MRI and US. They have enrolled 31 patients with early RA and included 279 joints in the study reported the sensitivity of 73% and specificity 76% for finger joints.^[28] According to three studies, the pooled sensitivity and specificity of PDUS for the detection

of synovial hypervascularity of small joints is 77.633% and 85.233% as shown in Table 3 and Graph 2. All these above studies agreed with pooled sensitivity and specificity of US for the detection of synovial hypervascularity.

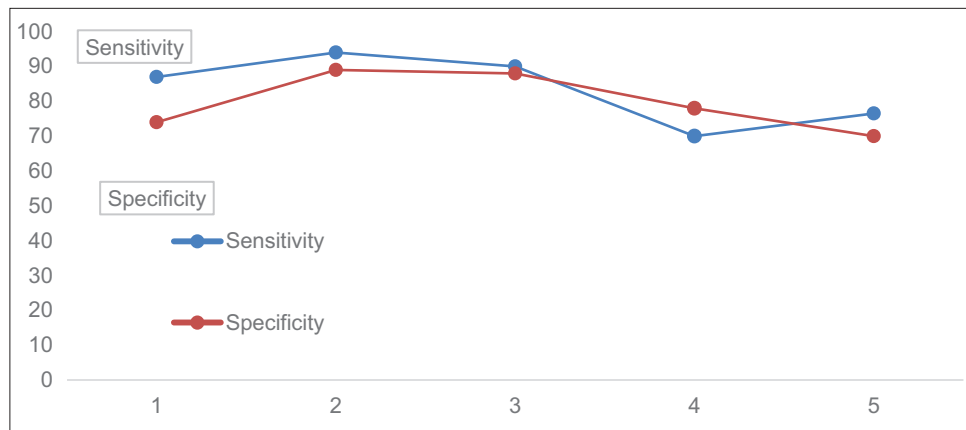
BONY EROSION

US is increasingly being used for the detection of early destructive changes in RA.^[36] Previous eleven studies have described the sensitivity and specificity of US for the diagnosis of early bone erosions and these studies also discussed the US comparison with MRI, CR, CT, and clinical

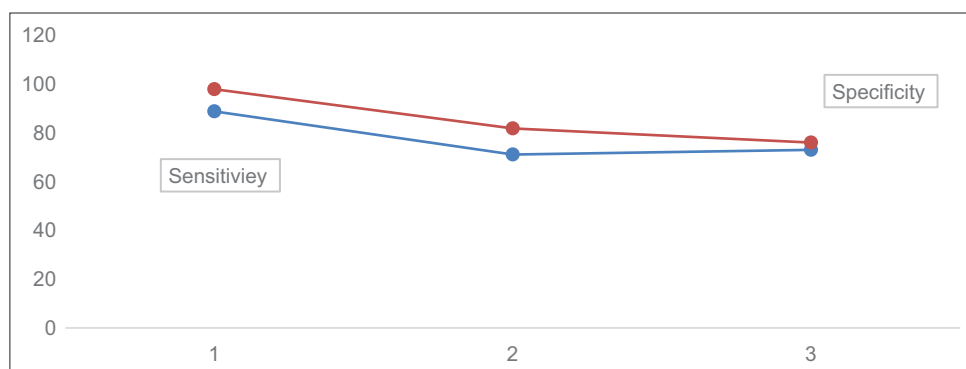
Table 3: Pooled sensitivity and specificity of musculoskeletal ultrasound

	Number of studies	Minimum	Maximum	Mean	SD
GSUS in small joints synovitis					
Sensitivity	5	70.00	94.00	83.5000	9.94987
Specificity	5	70.00	89.00	79.8000	8.43801
PDUS for the detection of synovial hypervascularity					
Sensitivity	3	71.10	88.80	77.6333	9.71717
Specificity	3	76.00	97.90	85.2333	11.34651
GSUS of the bone erosion in RA					
Specificity	11	85.19.00	98.00	93.859	11.72635
Sensitivity	11	32.90	100.00	58.385	22.86399

RA: Rheumatoid arthritis, GSUS: Grayscale ultrasonography, PDUS: Power Doppler ultrasonography, SD: Standard deviation



Graph 1: Sensitivity and specificity of grayscale ultrasound for the diagnosis of small joints synovitis



Graph 2: Sensitivity and specificity of Power Doppler ultrasonography for the detection of synovial hypervascularity

assessment.^[7,10,11,17,18,26,30-32,34,35] A number of articles have shown the sensitivity and specificity of US for the detection of RA that is mentioned in Table 4.

These studies described the sensitivity and specificity ranged from 32.9%–100% to 85.19%–98% respectively as shown in Table 4. Some studies described the US sensitivity and specificity for the detection of bone erosions with MRI as a reference method.^[7,18,26,31,32,35] Moreover, some studies described the US sensitivity and specificity for the detection of bone erosions with CT as the reference method. These studies described the lower sensitivity of US for bone erosion.^[17,26,30,32] According to Rashad *et al.*, in 2014, reported (100%) sensitive and 85.19% specificity for foot joints bone erosions and 58.33% sensitivity and 91.67% specificity for hand joints bone erosions.^[31] Remaining nine studies reported sensitivity ranged from 32.9% to 83% and specificity ranged from 85.19% to 98% for the small joint as summarized in Table 4.^[7,10,11,17,18,26,32,34,35] In 2015 Peluso *et al.*, reported very low sensitivity only 9% that was not included as it decreased the mean.^[30]

A study conducted by authors; Szkudlarek *et al.*, in 2004 with the objective to compare the US with MRI, CR and clinical examination in the evaluation of bone destruction and signs of inflammation in the MTP joints of patients with RA. They have assessed one hundred MTP joints of twenty healthy control and two hundred MTP joints of forty patients with RA. They have diagnosed bone erosions in 26 patients with the help of US, compared with MRI and radiography as these modalities diagnosed 20 patients and 11 patients, respectively. They were reported the sensitivity of US and radiography as 79% and 32%, respectively, by compared with MRI as the standard method. They were reported the specificity of US and radiography as 97% and 98% respectively with MRI as a reference method.^[18]

Another study conducted by authors; Døhn *et al.*, in 2006 with the objective of to evaluate whether bone erosions in RA in MCP joints diagnosed with MRI and US, but not with radiography, represent with true bone erosive changes. They

have examined 17 patients with RA and four healthy controls. With CT as the reference method, they have detected the sensitivity, specificity, and accuracy for bone erosions as 19%, 100%, and 81%, respectively, for radiography; 68%, 96%, and 89%, for MRI; and 42%, 91%, and 80% for the US. Hence, they were reported MRI and US had high specificity for the detection of bone erosions.^[32]

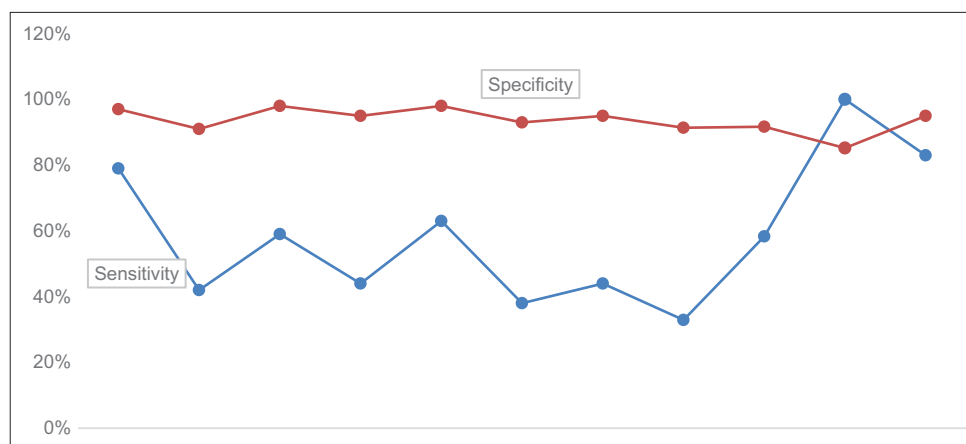
Another study conducted by authors; Szkudlarek *et al.*, in 2006 with the objective of to investigate whether US can provide information bone destruction in RA fingers joint that are not available with CR and clinical examination and also compare with MRI. T1-weighted MRI sequences as the reference method, they were reported the sensitivity, specificity, and accuracy as 59%, 98%, and 96%, respectively, for the US; 40%, 99%, and 95% for the radiography.^[10]

Another study conducted by authors; Døhn *et al.*, in 2011 with the objective to evaluate the bone erosions in patients with RA using MRI, US, radiography, and CT. They have examined 52 patients with RA. The sensitivities and specificities for bone erosion in MCP joint were 68% and 92% for MRI; 44% and 95% for the US; and 26% and 98% for radiography, with CT as the reference method.^[26]

According to eight studies, the pooled sensitivity is 58.385% and pooled specificity is 93.85% as shown in Table 3 and Graph 3. All the above studies agreed with pooled sensitivity and specificity of US for the detection of bone erosions.

REVIEW RESULTS

The pooled sensitivity and specificity of GSUS for the detection of synovitis of small joints were 83.5% and 79.8%, respectively. The pooled sensitivity and specificity of PDUS for the detection of synovial hypervascularity were 77.633% and 85.23%, respectively. The pooled sensitivity and specificity of US for the detection of early bone erosion were 58.385% and 93.859%, respectively.



Graph 3: Sensitivity and specificity of ultrasound for the detection of bone erosion in rheumatoid arthritis

Table 4: Sensitivity and specificity of ultrasonography for the detection of bone erosion in rheumatoid arthritis in small joints

Articles name	Authors	Year	Sample size	Study design	Types of joints	Sensitivity (%)	Specificity (%)	Disease duration	Brand and model of machine	Frequency	Comparison
Ultrasonography of the Metatarsophalangeal Joints in RA Comparison With MRI, CR, and clinical examination	Szkudlarek <i>et al.</i> ^[18]	2004	60	Case-control	MTP	79	97	Early disease duration <2 years Established disease duration >2 years	General Electric LOGIQ-500 unit	7-13 MHZ	MRI, CR, and clinical assessment
Are bone erosions detected by MRI and Ultrasonography true erosions? A comparison with CT in RA metacarpophalangeal joints	Döhn <i>et al.</i> ^[32]	2006	21	Case-control	MCP	42	91	8 (4-22) years	Philips 5000 HDI Unit	15-7 MHZ	MRI AND CT
Ultrasonography of the metacarpophalangeal and proximal interphalangeal joints in RA: A comparison with MRI, CR, and clinical examination	Szkudlarek <i>et al.</i> ^[10]	2006	60	Case-control	Finger joint	59	98	1. Early rheumatoid arthritis disease 2. Established rheumatoid arthritis disease	General electric LOGIQ 500 unit	7-13 MHZ	MRI, CR, and clinical assessment
No overall progression and occasional repair of erosions despite persistent inflammation in adalimumab-treated RA patients: results from a longitudinal comparative MRI, ultrasonography, CT and radiography study FREE	Döhn <i>et al.</i> ^[26]	2011	52	Cohort	MCP	44	95	None	General Electric LOGIQ9 unit	14-9 MHZ	CR, CT, MRI
Detection of bone erosion in early RA: Ultrasonography and CR versus noncontrast MRI	Rahmani <i>et al.</i> ^[35]	2010	12	Correlational	MCP and PIP	63	98	<6 months, mean duration 3.42	Anthares (Siemens, Germany) Scanner	11.8 MHZ	CR AND MRI
The utility of ultrasound joint counts in the prediction of RA in patients with very early synovitis	Filer <i>et al.</i> ^[11]	2011	80	Cohort	Hand and foot	38	93	<3 months	Siemens acuson antares scanner	5-13 MHZ	NONE

Contd...

Table 4: Contd...

Articles name	Authors	Year	Sample size	Study design	Types of joints	Sensitivity (%)	Specificity (%)	Disease duration	Brand and model of machine	Frequency	Comparison
Detection, scoring and volume assessment of bone erosions by ultrasonography in RA: Comparison with CT	Döhn <i>et al.</i> ^[17]	2013	49	Correlational	MCP	44	95	7 (0-36) years	General electric LOGIQ unit	14-9 MHZ	CT
The specificity of ultrasound-detected bone erosions for RA	Zayat <i>et al.</i> ^[34]	2015	130	Case control	MCP, PIP and MTP	32.9	91.4	Early disease mean duration 24 months Establishes disease mean duration 130 months	General electric LOGIQ E9	6-15 MHZ	None
The diagnosis of early RA using musculoskeletal ultrasonography	Rashad <i>et al.</i> ^[31]	2014	40	Cross-sectional	Hand Foot	58.33 100	91.67 85.19	Mean 6.65 months (2-12) months	General Electric LOGIQ 3 digital US Scanner	7.5-10 MHZ	MRI
Detection of bone erosions in early RA: 3D ultrasonography versus CT	Peluso <i>et al.</i> ^[30]	2015	20	Cross sectional	MCP and PIP	9	55	Early disease duration <12 months	General Electric LOGIQ 9	8-15 MHZ	CT
Diagnostic value of high-frequency ultrasound and magnetic Resonance imaging in early RA	Wang <i>et al.</i> ^[7]	2016	39	Cohort	MCP and PIP	83	95	Early disease duration 8.8 months	LOGIQ-10 General Electric Company	12 MHZ	MRI

?: According to false findings of erosions the researcher give the name true bone erosion. RA: Rheumatoid arthritis, MRI: Magnetic resonance imaging, CR: Conventional radiography, MTP: Metatarsophalangeal, PIP: Proximal interphalangeal, PDU: Power Doppler ultrasonography, CT: Computed tomography, MCP: Metacarpophalangeal

CONCLUSION

The US has good pooled sensitivity and specificity for the detection of synovitis and synovial hypervascularity. The specificity of US for the detection of bone erosions is high, but sensitivity is low so examiner should be familiar with the use of US for the evaluation of bone erosions in small joints in early RA.

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Conflicts of interest

There are no conflicts of interest.

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