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# Which joints and why do rheumatologists scan in rheumatoid arthritis by ultrasonography? A real life experience

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## ABSTRACT

**Objective.** Ultrasonography (US) has been demonstrated to improve assessment of synovitis and disease activity in rheumatoid arthritis (RA). However, the utility and feasibility of US in RA in clinical practice in real life is not known. We aimed to investigate: i) the indications for performing US in RA in daily practice; and ii) whether the number of scanned joints varies according to the purpose.

**Methods.** Consecutive patients who had a US scan either for diagnosis or follow-up for RA from 5 centres were recruited. The sonographers were asked to mark the joints that had a US scan and grade their findings. Descriptive analysis was applied to find out the sites and the number of joints scanned and compared according to the indications of US.

Results. Two hundred consecutive patients were recruited. The most common indication was assessing disease activity (48.5%) followed by diagnosis (45.5 %). Wrists (66%) and MCPs (63.5) were the most frequently scanned joints followed by knees (26%), PIPs (20%). The number of joints scanned by US was significantly higher when performed for diagnostic purposes as compared to assessing disease activity and guidance for injections (p=0.001). Conclusion. The current data highlight differences between the numbers of joints for which that the clinician feels necessary to perform US in real life. This observation may be a guide when providing recommendations regarding which joints need to be scanned according to the indication.

### Introduction

In recent years, there have been major changes in management of patients with rheumatoid arthritis (RA). According to the recommendations by the experts, the ultimate target of treatment has been set as a state of remission (1). It has also been recommended that the follow-up of patients should be done using a composite index and treatment should be modified until remission is achieved. However there are limitations with composite indices. Tender joint counts are subjective and depend-

ent on patients' threshold of pain and may also be increased in patients with concomitant fibromyalgia. In addition, in patients with longstanding disease swollen joint counts can be difficult to assess, as chronic synovitis may not necessarily suggest an active disease. It has been demonstrated that musculoskeletal ultrasound (US) improves the accuracy of physical examination (2-4). Longitudinal studies showed that around 50% of RA patients, who are considered to be in clinical remission according to the physician, have subclinical disease activity detected by power Doppler signal and that those joints with power Doppler signal have a 12-times higher risk of developing erosions at follow-up (5).

In addition to its use in assessing disease activity, US is also commonly used for diagnostic purposes. It has been shown that US changes the initial clinical diagnosis of 60% of the anatomical sites and therapy were modified in 25% of patients according to the US assessment (6). Another use of US is to improve the success of intra-articular injections. A meta-analysis showed that US guided injections to the wrist resulted in greater reductions in pain at follow-up compared to unguided (7). In another randomised controlled trial, it has been demonstrated that US-guided injections performed by a trainee rheumatologist were more accurate than the blind injections performed by more senior rheumatologists (8).

In view of all these advantages, US has an increasing use in the field of rheumatology. The OMERACT (Outcome Measures in Rheumatoid Arthritis in Clinical Trials) US group have been working on the definitions of abnormalities as well as scoring methods (9-12). Also training programmes have been developed by the EULAR US group in order to increase the quality of US education worldwide (13-15).

In addition to these working groups, Targeted Ultrasound Initiative (TUI) is an educational international group of US experts providing guidance and tools to rheumatologists for making US a standard outcome in RA clinical practice (16). This initiative federates several international countries, and aims to



Fig. 1. TUI synovitis evaluation form: ultrasound form introduced by the TUI group to assess synovitis in patients with a suspicion or diagnosis of rheumatoid arthritis.

evaluate and improve the clinical use of US. Despite all these advantages and efforts, there is no data about real life practice on why and how rheumatologists perform US.

In this study we aimed to understand, in clinical practice, the reasons why rheumatologists are performing US in real life and whether there are any differences in the site and number of joints scanned according to the indication.

#### Methods

A multicentre audit was conducted in-

volving 5 rheumatologists from different centres who have had experience in musculoskeletal US for at least 8 years. The audit was approved by the local ethics committee. Two-hundred consecutive patients with established or suspected RA who underwent a US scan for either diagnosis or follow-up were recruited in two months. The US scans were made by the same rheumatologist who thought US was indicated for the patient. A standardised evaluation form (i.e. TUI Form) was used (Fig. 1). The sites which are scanned

by US, number of joints and their grading of severity (both in grey-scale (GS) and Doppler) were recorded. The percentage of each indication as well as the percentage of sites having a US assessment was calculated. The number of joints according to the indications of US was compared by Kruskal Wallis test, followed by a Mann-Whitney Utest to make a pair comparison.

#### Results

The mean  $\pm$  SD age was 48.5 $\pm$ 15 and the symptom duration was  $7.1\pm9$  years. RF and/or ACPA data were available in 104 patients and were found positive in 61%.

The most common indication was the evaluation of disease activity (48.5%), closely followed by diagnosis (45.5 %) (Table I). Wrists (66%) and MCPs (63.5%) were the most frequently scanned joints followed by knees (26%), PIPs (20 %), ankles (18%) and MTPs (12%). Elbows (5.5%), shoulders (2.5%) and hips (0.5%) were the least frequently scanned sites. The number of joints scanned was significantly higher for diagnostic purposes (mean± SD: 9.7±9.5) as compared to monitoring  $(7\pm5.8)$  (p=0.02) or guidance for injections (1.4±0.9) (p<0.001) (Table I).

There were differences in positive US findings among groups, being higher for injections (p < 0.0001 for all of the US findings: finding at least one joint with GS 1, PD 1, GS >1 and PD >1) (Table I). When analysed according to subgroups, patients who had US for diagnostic purposes had fewer US positive joints when compared with patients who had US for follow-up (p=0.002 for any GS (+); p < 0.0001 for GS >1, any PD (+) and PD >1). Within patients who had US for diagnostic purposes, patients presenting with arthralgia had less US positivity compared to others (p=0.006 for any GS (+), p<0.0001 for GS >1, any PD (+) and PD >1). If the patient had a US for follow-up, then the US positivity was higher if the US assessment was made for monitoring as opposed to assessing true remission (p=0.002 for any GS (+), p=0.001 for, any PD (+) and PD >1; p=0.04 for GS >1). Since patients in clinical remission had less US findings, this was also com**Table I.** Number of patients and joints according to the indication of the ultrasound scan and the number (n) and percentage (%) of finding any grey-scale (GS) synovitis. power Doppler (PD) and any joint with grade 2 or 3 GS and PD.

Indication		Number of	Number of joints (mean±SD)	Any GS (+)		GS score>1		Any PD (+)		PD score >1	
		patients (70)		n	%	n	%	n	%	n	%
Diagnosis		91 (45.5)	9.7 ± 9.5	64	70.3	40	44	41	45.1	27	29.7
	arthralgia	48 (24)	$10.5 \pm 9.2$	27	56.2	13	27.1	12	25	5	10.4
	early arthritis	28 (14)	$10.2 \pm 11.3$	23	82.1	14	51.9	15	53.6	10	35.7
	rheumatoid arthritis	15 (7.5)	$6 \pm 6$	14	93.3	13	86.7	14	93.3	12	80
Disease activity		97 (48.5)	$7 \pm 5.8$	86	88.7	72	74.2	76	78.4	60	61.9
	remission	29 (14.5)	$7.1 \pm 3.1$	21	72.4	17	58.6	16	55.2	10	34.5
	active disease	68 (34)	$6.9 \pm 6.4$	65	95.6	55	80.9	60	88.2	50	73.5
Guidance for injection		12 (6)	$1.4\pm0.9$	12	100	10	83.3	10	83.3	4	33.3

pared with US positivity for patients who had a diagnostic US and it was observed that the frequency of a US abnormality was similar within these 2 groups.

The likelihood of having any synovitis (GS alone or with Doppler) was highest for large joints when compared to small joints (*e.g.* shoulders GS positivity 6/10 (60%) vs. 80/639 (12.5%) in MCPs, and any Doppler signal in knees: 34/78 (43.5%) vs. 59/639 (9.2%) in MCPs).

#### Discussion

The current study shows that clinicians have different requirements when scanning patients by US depending on the indication. It was observed that in real life, US is more frequently performed for assessing RA disease activity, providing objective information alongside a more subjective clinical assessment. We also observed a difference in the number of joints scanned, with a higher number scanned for diagnostic purposes. This is probably due to the need of maximising the detection of inflammation when there is widespread pain, whereas for detecting ongoing synovial activity, the choice is probably guided by the presence of symptomatic joints or choosing the more frequently affected sites. This approach can also explain the difference observed in the presence of GS and Doppler findings according to the size of the joints: a higher number of asymptomatic small joints are scanned for screening purposes whereas large joints are almost always scanned when they are symptomatic. Since US is an objective, non-invasive tool with acceptable costs, it has a significant potential to improve RA management. Time, however seems to be the major limitation for performing US on a regular basis in centres equipped with a US machine (17). The current audit shows that rheumatologists working in 5 different university settings usually scan fewer than 10 joints in real life, which probably is limited by the time the clinician can spent on US. Whether these numbers are sufficient for the purpose of the assessment is another research question.

When used for diagnostic purposes, not only the number of joints but also the likelihood of positivity of the US assessment varied by indication. If the patient had arthralgia and early arthritis, then the clinicians were found to scan more joints, however positive scans were also lower in patients with arthralgia (any GS: 56.2%, any PD: 10.4%), compared to early arthritis (any GS: 82.1%, any PD: 35.7%) and RA (any GS: 93.3%, any PD: 80%). This may be due to the characteristic of patients: Patients with clinical RA are already expected to have a higher degree of inflammation by US compared to arthralgia. However a further reason for the differences among subgroups can be in case of finding a Doppler positivity which is in compliant with the clinical findings, scanning more joints and other sites may not be necessary for diagnostic purposes.

This audit also showed that there are discrepancies between the rheumatologists' clinical assessment and US. This is best seen in the PD positivity of patients that are scanned for monitoring. Patients who had a US for the objective assessment of remission had any PD signal in 55% cases and a PD >1 in 35% cases, even by scanning 7 joints on a mean. Similarly 12% of patients who had a US scan for better understanding the disease activity had no PD signals and 27% did not have a PD signal >1. This supports the contention that sonographic evaluation may aid the clinical diagnosis to varying degrees and which has been especially important in verifying clinical remission and in differentiating patients who have arthralgia from the ones with arthritis.

Regulations are variable among different countries and the scanning protocol may also be dependent on the rules outlined by the regulatory policy. In the current audit, there were no such restrictions, therefore exactly represents the practice of the rheumatologist guided by their own judgment.

In conclusion, this audit shows that physicians are in need of scanning different number of joints depending on the purpose of the scan. This information is important in highlighting what clinicians need and how they modify their behaviour depends on the needs and circumstances. Recommendations may guide the clinicians in routine practice, but besides aiming to provide the best patient care, they also need to be feasible increasing the applicability of the recommendations. The present audit may assist when providing recommendations about which joints need to be scanned in particular indications.

#### References

 SMOLEN JS, ALETAHA D, BIJLSMA JW et al.: Treating rheumatoid arthritis to target: recommendations of an international task force. *Ann Rheum Dis* 2010; 69: 631-7.

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- WAKEFIELD RJ, GREEN MJ, MARZO-ORTE-GA H et al.: Should oligoarthritis be reclassified? Ultrasound reveals a high prevalence of subclinical disease. Ann Rheum Dis 2004; 63: 382-5.
- 3. SALEEM B, BROWN AK, KEEN H et al.: Should imaging be a component of rheumatoid arthritis remission criteria? A comparison between traditional and modified composite remission scores and imaging assessments. Ann Rheum Dis 2011; 70: 792-8.
- 4. BROWN AK, QUINN MA, KARIM Z et al.: Presence of significant synovitis in rheumatoid arthritis patients with disease-modifying antirheumatic drug-induced clinical remission: evidence from an imaging study may explain structural progression. *Arthritis Rheum* 2006; 54: 3761-73.
- BROWN AK, CONAGHAN PG, KARIM Z et al.: An explanation for the apparent dissociation between clinical remission and continued structural deterioration in rheumatoid arthritis. Arthritis Rheum 2008; 58: 2958-67.
- MICU MC, ALCALDE M, SAENZ JI et al.: Impact of musculoskeletal ultrasound in an outpatient rheumatology clinic. Arthritis Care Res (Hoboken) 2013; 65: 615-21.
- 7. DUBREUIL M, GREGER S, LAVALLEY M,

CUNNINGTON J, SIBBITT WL, JR., KISSIN EY: Improvement in wrist pain with ultrasoundguided glucocorticoid injections: a metaanalysis of individual patient data. *Semin Arthritis Rheum* 2013; 42: 492-7.

- CUNNINGTON J, MARSHALL N, HIDE G et al.: A randomized, double-blind, controlled study of ultrasound-guided corticosteroid injection into the joint of patients with inflammatory arthritis. Arthritis Rheum 2010; 62: 1862-9.
- IAGNOCCO A, NAREDO E, WAKEFIELD R et al.: Responsiveness in rheumatoid arthritis. a report from the OMERACT 11 ultrasound workshop. J Rheumatol 2014; 41: 379-82.
- 10. CHAVEZ-LOPEZ MA, HERNANDEZ-DIAZ C, MOYA C *et al.*: Inter- and intra-observer agreement of high-resolution ultrasonography and power Doppler in assessment of joint inflammation and bone erosions in patients with rheumatoid arthritis. *Rheumatol Int* 2013; 33: 173-7.
- MANDL P, NAREDO E, WAKEFIELD RJ, CON-AGHAN PG, D'AGOSTINO MA: A systematic literature review analysis of ultrasound joint count and scoring systems to assess synovitis in rheumatoid arthritis according to the OMERACT filter. J Rheumatol 2011; 38: 2055-62.

- NAREDO E, WAKEFIELD RJ, IAGNOCCO A et al.: The OMERACT ultrasound task forcestatus and perspectives. J Rheumatol 2011; 38: 2063-7.
- NAREDO E, BIJLSMA JW, CONAGHAN PG et al.: Recommendations for the content and conduct of European League Against Rheumatism (EULAR) musculoskeletal ultrasound courses. Ann Rheum Dis 2008; 67: 1017-22.
- 14. NAREDO E, MOLLER I, MORAGUES C *et al.*: Interobserver reliability in musculoskeletal ultrasonography: results from a "Teach the Teachers" rheumatologist course. *Ann Rheum Dis* 2006; 65: 14-9.
- 15. SCHEEL AK, SCHMIDT WA, HERMANN KG et al.: Interobserver reliability of rheumatologists performing musculoskeletal ultrasonography: results from a EULAR "Train the trainers" course. Ann Rheum Dis 2005; 64: 1043-9.
- WAKEFIELD RJ, D'AGOSTINO MA, NAREDO E et al.: After treat-to-target: can a targeted ultrasound initiative improve RA outcomes? *Postgrad Med J* 2012; 88: 482-6.
- 17. CAKILLI OT, PAY S, INANC N et al.: Use of musculoskeletal ultrasound in Rheumatoid arthritis in Turkey among rheumatologists: A national targeted ultrasound initiative survey *Eur J Rheumatol* 2015; 2: 43-4.