Ultrasonographic assessment of inflammatory activity in rheumatoid arthritis: Comparison of extended versus reduced joint evaluation

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ABSTRACT

Objective. *To investigate the validity of reduced joint counts for ultrasonographic (US) assessment of joint inflammatory activity in patients with rheumatoid arthritis (RA).*

Methods. *Ninety-four patients with RA were included. C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) levels were recorded for each patient. The presence of tenderness, swelling and a subjective swelling score from 0 to 3 were assessed by two rheumatologists who reached consensus in 60 joints examined in each patient. All patients underwent an US examination by a third blinded rheumatologist, using power Doppler (PD). US joint effusion, synovitis and PD signal were graded from 0 to 3 in the 60 joints. A 60-joint count and index for effusion, synovitis and PD signal were recorded. A 6-, 10-, 16-, 18-, and two 12-joint counts and indices for US parameters that included the most frequently US involved joints were calculated for each patient.*

Results. *A 12-joint assessment for effusion, synovitis and PD signal, including bilateral wrist, second and third MCP, second and third PIP of hands and knee joints highly correlated with corresponding 60-joint US counts and indices. This reduced-joint US evaluation showed a similar correlation with clinical and laboratory parameters of disease activity to corresponding 60-joint assessment.*

Conclusion. *We propose that a 12-joint evaluation may be a useful tool for US assessment of overall joint inflammatory activity in RA.*

Introduction

Grey-scale ultrasonography (US) and color Doppler (CD) or power Doppler (PD) have been used in the evaluation of synovial inflammatory activity in patients with rheumatoid arthritis (RA) and other chronic inflammatory arthropathies (1-8). Recently, we demonstrated a correlation between US findings and clinical joint swelling in 60 joints as well as the biological parameters of disease activity in 94 RA patients (8). Reduced joint US assessment including the most frequently involved joints can be easier and faster to perform in daily management and clinical trials.

The aim of this study was to compare the 60-joint US findings with reduced joint US assessment in the 94 RA patients included in our previous study (8).

Patients and methods

Ninety-four consecutive patients who fulfilled the 1987 American Rheumatism Association criteria for RA (9) were included. Twenty patients were male and 74 female. Mean age was 57.6 ± 14.3 years (23-88) and median disease duration was 69.3 ± 58.2 months (5-280). Therapeutic regimens included non-steroidal anti-inflammatory drugs (64% of the patients), corticosteroids (60%), methotrexate (65%), leflunomide (19%), sulfasalazine (11%), antimalarial drugs (11%), gold salts (10%), infliximab (9%), etanercept (4%), cyclosporin (2%), and azathioprine (2%). Patients who had suffered traumatic, septic or microcrystalline arthritis, previous joint surgery or isotopic synovectomy within the past 12 months before the study were excluded.

C- reactive protein (CRP) level (nephelometry) and erythrocyte sedimentation rate (ESR) (Westergren method, VESMATIC 60, version 2.05, Menarini Laboratory, Barcelona, Spain) were recorded from each patient within 1 week of the study. The institutional ethics committee approved the study and informed consent was obtained from all patients before the clinical and US evaluation.

Clinical assessment

Clinical evaluation was performed by two rheumatologists (FG and GB) who reached consensus. The following bilateral joints were assessed for tenderness and swelling: glenohumeral, acromioclavicular, sternoclavicular, elbow, wrist, metacarpophalangeal (MCP), and proximal interphalangeal (PIP) of hands, hips, knees, tibiotalar, subtalar, midtarsal, metatarsophalangeal (MTP), and PIP of feet (total in 94 patients: 5,640 joints). Hip swelling was indirectly considered if pain on passive motion was detected by physical examination. A subjective swelling score from 0 to 3 was assigned for all joints except for the hip

(0 = absence; 1 = mild; 2 = moderate; 3 = marked). Tender joint count (TJC), swollen joint count (SJC) and a 60 swollen joint index (SJI) (sum of the swelling score from each joint) were recorded for each patient.

US examination

All patients underwent a US examination within 30 minutes of the clinical evaluation, by a single rheumatologist, experienced in US (EN) and blinded to the clinical findings. Grey scale and PD US examination was performed using multifrequency linear array transducers [Logiq 400CL, General Electric Medical Systems, Korea (scanner 1) and Logiq 700, General Electric Medical Systems, Waukesha, WI, USA (scanner 2)]. The first 69 patients were examined with scanner 1 and the last 25 patients with scanner 2. The presence of joint effusion and synovitis was systematically evaluated by US in each of the 60 joints clinically examined. US scanning method and diagnostic criteria for effusion and synovitis in each joint were described in a earlier report (8). Joint effusion and synovitis were subjectively graded from 0 to 3 (0 = absence; 1 = mild; 2 = moderate; 3 = marked).

Synovial vascularization was assessed by PD US in each of the 60 joints. The intraarticular PD signal was subjectively graded on a semiquantitative scale from 0 to 3 (0 = absence, no intraarticular flow; 1 = mild: single vessel signal; 2 = moderate: confluent vessels; 3 = marked: vessel signals in more than half of the intraarticular area). In each patient, the joint count for US effusion (USJCE), the joint count for synovitis (USJCS), the joint count for PD signal (USJCPD) and a 60-joint index for effusion (USJIE), synovitis (USJIS) and PD signal (USJIPD) (sum of the effusion, synovitis and PD signal scores, respectively, obtained from each joint) were recorded.

We considered reduced joint counts and indices for effusion, synovitis and PD signal that included the most frequently US involved joints. Reduced joint US finding were compared with extended US assessment, clinical and laboratory parameters of overall inflammatory activity.

Statistical analysis

Pearson and Spearman's correlation were applied for comparing continuous variables. Any p value under 0.05 was considered statistically significant.

Results

Ultrasonographic joint involvement and reduced joint assessment

Effusion, synovitis and PD signal were most frequently found in wrists (effusion and synovitis in > 70% of patients, PD signal in > 60% of patients), knees (effusion and synovitis in > 40% of patients, PD signal in > 20% of patients), second and third MCP (effusion and synovitis in > 30% of patients, PD signal in > 25% of patients) and first, second and third MTP joints (effusion and synovitis in > 30% of patients, PD signal in > 15% of patients). Among PIP joints, second and third PIP joint of hands were the most commonly involved (effusion and synovitis in > 25% of patients, PD signal in > 15% of paients). All of these joints were also the most frequently tender and swollen except for the MTP joints that were commonly tender (> 30% of patients) but infrequently swollen (< 5% of patients). The remaining joints showed effusion and synvoitis in < 20% of patients and/or PD signal in < 15% of patients. The acromioclavicular joint frequently showed capsular distension with internal echogenic material. However, this latter joint was not included because these pathological findings may also be associated with degenerative shoulder disorders and aging (10).

Six-joint, 10-joint, 16-joint, 18-joint and two 12-joint counts and indices were calculated in each patient. The 6-joint US assessment included bilateral wrist, second and third MCP joints. The 10-joint US evaluation included bilateral wrist, second and third MCP and second and third PIP joints of hands. First 12-joint (12A) US assessment included bilateral wrist, second and third MCP, second and third PIP of hands and knee joints. Second 12-joint (12B) US evaluation included bilateral wrist, second and third MCP and first, second and third MTP joints. The 16-joint US assessment included bilateral wrist, second and third MCP, second and third PIP of hands and first, second and third MTP joints. Lastly, the 18-joint US evaluation included bilateral wrist, second and third MCP, second and third PIP of hands, first, second and third MTP and knee joints.

Correlation between 60-joint US assessment and reduced joint US findings

Correlations between the 60-joint count

Table I. Correlation between 60-joint and reduced-joint ultrasonographic parameters.

	USJCE-6	USJCE-10	USJCE-12A	USJCE-12B	USJCE-16	USJCE-18
USJCE-60	0.77*	0.82*	0.83*	0.88*	0.90*	0.92*
	USJCS-6	USJCS-10	USJCS-12A	USJCS-12B	USJCS-16	USJCS-18
USJCS-60	0.76*	0.82*	0.83*	0.88*	0.88*	0.92*
	USJCPD-6	USJCPD-10	USJCPD-12A	USJCPD-12B	USJCPD-16	USJCPD-18
USJCPD-60	0.80*	0.81*	0.84*	0.89*	0.90*	0.93*
	USJIE-6	USJIE-10	USJIE-12A	USJIE-12B	USJIE-16	USJIE-18
USJIE-60	0.84*	0.87*	0.87*	0.89*	0.91*	0.93*
	USJIS-6	USJIS-10	USJIS-12A	USJIS-12B	USJIS-16	USJIS-18
USJIS-60	0.84*	0.86*	0.87*	0.92*	0.92*	0.94*
	USJIPD-6	USJIPD-10	USJIPD-12A	USJIPD-12B	USJIPD-16	USJIPD-18
USJIPD-60	0.83*	0.84*	0.86*	0.90*	0.92*	0.94*

*$p < 0.001$.

USJCE: ultrasonographic joint count for effusion; USJCS: ultrasonographic joint count for synovitis; USJCPD: ultrasonographic joint count for power Doppler signal; USJIE: ultrasonographic joint index for effusion; USJIS: ultrasonographic joint index for synovitis; USJIPD: ultrasonographic joint index for power Doppler signal.

and index for US effusion, synovitis and PD signal and corresponding reduced joint counts and indices are shown in Table I. The 10, 12A, 12B, 16 and 18-joint US assessment correlated highly with the 60-joint US evaluation ($r > 0.8$, $p < 0.001$).

Correlation between reduced joint US assessment, clinial and laboratory parameters

The best correlations were found between the 12A-joint and 18-joint US findings and biological and overall clinical swelling (Table II). Both reduced joint US assessments for effusion, synovitis and PD signal showed a similar correlation with clinical and laboratory parameters to the 60-joint counts and indices.

Discussion

Grey-scale US and CD or PD have been proposed as sensitive and reliable non-invasive methods complementary to standard clinical assessment for evaluating rheumatoid inflammatory activity in daily management and clinical trials (1-8). Previous studies have shown a high correlation between US findings and local clinical evaluation of inflammatory activity in a small number of joints such as the knee (1), and MCP and PIP joints of the hands (2, 6, 7) of patients with RA and other inflammatory arthritis. However, no correlation between US findings and global parameters of disease activity has been reported (6,7). This fact could be due to the selection of a small number of joints which were not representative of overall joint inflammation.

We previously compared grey-scale US effusion, synovitis and PD signal with clinical and biological assessment of overall inflammatory activity in 94 RA patients (8). We found that US was more sensitive than the physical examination in detecting joint swelling. US parameters correlated with overall clinical joint swelling, CRP and ESR. However, US findings correlated better with CRP and ESR than clinical swelling. In addition, the 28-joint count proposed by Smolen *et al*. (11) for US effusion, synovitis and PD signal highly correlated with the corresponding 60-

Table II. Correlation between extended and reduced ultrasonographic, laboratory and clinical parameters.

	CRP	ESR	SJC	SJI	Overall
60-joint US assessment (overall)	0.63	0.49	0.53	0.60	0.56
USJCE-60	0.62	0.50	0.53		
USJIE-60	0.64	0.51		0.61	
USJCS-60	0.63	0.50	0.52		
USJIS-60	0.64	0.51		0.58	
USJCPD-60	0.62	0.45	0.55		
USJIPD-60	0.63	0.44		0.60	
6-joint US assessment (overall)	0.50	0.43	0.48	0.51	0.48
USJCE-6	0.42	0.36	0.47		
USJIE-6	0.51	0.42		0.54	
USJCS-6	0.42	0.36	0.47		
USJIS-6	0.48	0.40		0.49	
USJCPD-6	0.60	0.50	0.49		
USJIPD-6	0.59	0.51		0.50	
10-joint US assessment (overall)	0.51	0.44	0.47	0.52	0.49
USJCE-10	0.45	0.40	0.44		
USJIE-10	0.55	0.43		0.53	
USJCS-10	0.45	0.40	0.45		
USJIS-10	0.49	0.42		0.49	
USJCPD-10	0.56	0.50	0.51		
USJIPD-10	0.57	0.51		0.54	
12A-joint US assessment (overall)	0.57	0.49	0.49	0.54	0.52
USJCE-12A	0.51	0.45	0.47		
USJIE-12A	0.60	0.49		0.55	
USJCS-12A	0.51	0.44	0.47		
USJIS-12A	0.54	0.46		0.51	
USJCPD-12A	0.63	0.56	0.54		
USJIPD-12A	0.62	0.53		0.57	
12B-joint US assessment (overall)	0.54	0.41	0.43	0.53	0.48
USJCE-12B	0.48	0.36	0.41		
USJIE-12B	0.55	0.41		0.55	
USJCS-12B	0.47	0.37	0.41		
USJIS-12B	0.54	0.42		0.55	
USJCPD-12B	0.60	0.44	0.46		
USJIPD-12B	0.62	0.45		0.50	
16-joint US assessment (overall)	0.55	0.43	0.45	0.56	0.50
USJCE-16	0.50	0.40	0.44		
USJIE-16	0.57	0.42		0.59	
USJCS-16	0.49	0.38	0.41		
USJIS-16	0.56	0.44		0.56	
USJCPD-16	0.59	0.47	0.49		
USJIPD-16	0.61	0.48		0.53	
18-joint US assessment (overall)	0.59	0.48	0.48	0.59	0.54
USJCE-18	0.54	0.44	0.46		
USJIE-18	0.59	0.48		0.61	
USJCS-18	0.53	0.44	0.45		
USJIS-18	0.58	0.48		0.59	
USJCPD-18	0.65	0.52	0.52		
USJIPD-18	0.65	0.51		0.56	

*$p < 0.001$

US: ultrasonographic; USJCE: ultrasonographic joint count for effusion; USJCS: ultrasonographic joint count for synovitis; USJCPD: ultrasonographic joint count for power Doppler signal; USJIE: ultrasonographic joint index for effusion; USJIS: ultrasonographic joint index for synovitis; USJIPD: ultrasonographic joint index for power Doppler signal; CRP: C reactive protein; ESR: erythrocyte sedimentation rate; SJC: swollen joint count; SJI: swollen joint index.

joint counts (8). Furthermore, analysis of the results from scanner 1, a cheaper and more affordable machine than scanner 2, showed that they were comparable with the overall results.

Reduced joint US evaluation that included the most frequently involved joints by US, such as the 12A-joint and the 18-joint hereby proposed, correlated highly with the extended US assessment, as well as showing a similar correlation with the clinical and laboratory parameters of inflammatory activity to the corresponding 60-joint US evaluation. They are easier to perform and have a shorter scanning duration. The 60-joint US examination took 30 minutes for each patient (8) , not including documentation, while the US evaluation of 12 joints can be performed in less than 10 minutes.

Although MTP joints were not included in the 12A-joint US assessment, we did not find significant differences between the 12A-joint and the 18-joint US evaluation with regard to the correlation with the 60-joint US parameters and clinical and laboratory findings.

Therefore, we suggest that US assessment of bilateral wrist, second and third MCP, second and third PIP of hands and knee joints could be enough for evaluating overall inflammatory activity by US. We propose that this 12-joint assessment may be a useful tool for US evaluation of joint inflammatory activity in RA. A longitudinal study that demostrates sensitivity to change of the reduced joint US evaluation is highly warranted.

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