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Wrist ultrasound analysis of patients with early rheumatoid arthritis

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Abstract

In the present study, we evaluated 42 wrists using the semi-quantitative scales power Doppler ultrasound (PDUS) and gray scale ultrasound (GSUS) with scores ranging from 0 to 3 and correlated the results with clinical, laboratory and radiographic data. Twenty-one patients (17 women and 4 men) with rheumatoid arthritis according to criteria of the American College of Rheumatology were enrolled in the study from September 2008 to July 2009 at Universidade Estadual de Campinas (UNICAMP). The average disease duration was 14 months. The patients were 66.6% Caucasians and 33.3% non-Caucasians, with a mean age of 42 and 41 years, respectively. A dorsal longitudinal scan was performed by ultrasound on the radiocarpal and midcarpal joints using GE LOGIQ XP-linear ultrasound and a high frequency (8-10 MHz) transducer. All patients were X-rayed, and the Larsen score was determined for the joints, with grades ranging from 0 to V. This study showed significant correlations between clinical, sonographic and laboratory data: GSUS and swollen right wrist (r = 0.546), GSUS of right wrist and swelling of left wrist (r = 0.511), PDUS of right wrist and pain in left wrist (r = 0.436), PDUS of right wrist and C-reactive protein (r = 0.466). Ultrasound can be considered a useful tool in the diagnosis of synovitis in early rheumatoid arthritis mainly when the anti-cyclic citrullinated peptide and rheumatoid factor are negative, and can lead to an early change in the therapeutic decision.

Key words: Power Doppler ultrasound; Gray scale ultrasound; Rheumatoid arthritis; Wrist; Synovitis

Introduction

Joint ultrasound has proved to be an important tool to evaluate synovitis, which could be considered the first abnormality in early rheumatoid arthritis (RA) (1-4). X-ray has been the method most frequently used to assess bone and joints, but an important drawback is that it does not show lesions in soft tissues in the early stage of disease (5-7).

Ultrasound is a sensitive technique for the detection of synovitis, effusion and bone erosion in RA, often difficult to determine by clinical assessment and traditional radiography (6,7). Subclinical synovitis can be diagnosed early in inflammatory diseases by ultrasound and its evolution may even be monitored, thus being a precursor of oligoarthritis and polyarthritis (8). Ultrasound facilitates the early detection of arthritis and allows an earlier establishment of therapy (9-12).

Material and Methods

Twenty-one patients were enrolled from September 2008 to July 2009 at Universidade Estadual de Campinas (UNICAMP), Campinas, Brazil. Seventeen women and 4 men were included: 66.6% Caucasians and 33.3% non-Caucasians, with a mean age of 42 and 41 years, respectively, with RA according to criteria of the American College of Rheumatology. Gray scale (GS) and power Doppler (PD) ultrasound were applied to patients with early RA and correlated with clinical, laboratory and radiological data. The average disease duration was 14 months since presenting the first sign of arthritis. The medications used by the patients are listed in Table 1.

Clinical evaluation consisted of Disease Activity Score based on 28 joints (DAS28), calculated using the concentration of the C-reactive protein (CRP) or erythrocyte sedimentation rate (ESR). The DAS28 can range from 0 to 10, and studies have shown that the lower rate of disease activity is 3.2 (13). This study used DAS28 equal to or greater than 3.2 as inclusion criteria.

The study was approved by the Universidade Estadual de Campinas (UNICAMP) Ethics Committee and all patients

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gave written informed consent after completing the specific quality of life instrument - Health Assessment Questionnaire (HAQ), which evaluates disability, discomfort and pain at the time of the exam (14,15).

The ultrasound was performed with the patient seated and with hands flat on the top of the table**.** The radiocarpal and midcarpal regions were examined by a dorsal longitudinal scan, when evaluating the cross-scan of the wrist joint. The equipment used was a linear GE LOGIQ XP Ultrasound apparatus (USA) with a high-frequency (8-10 MHz) transducer, which accurately shows surface structures such as tendons, synovia, and other structures. All structures were documented to ensure high reproducibility of the results (16,17).

The ultrasound analysis using a GS ultrasound reflects an increase of the synovium as a hypoechoic image and PD ultrasound demonstrates the microcirculation in the phase of synovial hypertrophy, identifying inflammatory activity. Using a semi-quantitative scale, a joint capsule was classified as having a degree of 0 to 3 of synovial proliferation, and a degree of intense or important signal by PD (18-21).

Synovitis was scored by GS ultrasound (GSUS) as 0 = absence, 1 = mild (describes a small hypoechoic/anechoic line beneath the joint capsule), 2 = moderate (the joint capsule is elevated parallel to the joint area), and 3 = severe or marked (characterizes a strong distension of the joint capsule).

Synovitis was scored by PD ultrasound (PDUS) as: 0 = absence (no intra-articular color signal), 1 = mild (up to 3 color signals or 2 single and 1 confluent signal in the intra-articular area, 2 = moderate (greater than grade 1 to <50% of the intra-articular area filled with color signals), and 3 = marked (≥50% of the intra-articular area filled with color signals).

The Doppler settings were optimized to 'low flow', with a medium wall filter (to minimize flash artifact) and a pulse repetition frequency of 800 Hz.

Wrist radiography was performed in all patients and the Larsen score was used to evaluate the aspects in the X-ray. Joints received grades of 0 to V, as follows: grade 0 = normal; grade I = mild abnormality (presence of one or more of the following lesions: edema of soft tissues, osteopenia around the joint and a slight decrease in joint space); grade II = definite abnormality (presence of small erosions, decreased joint space is not obligatory); grade III = marked abnormality (presence of erosions and decreased joint space); grade IV = severe abnormality (the original joint surface remains partially preserved), and grade V = mutilating abnormality (the original joint surface disappeared; huge deformity is present) (22-25).

Results

Clinical, laboratory and imaging results

Fourteen (66.6%) patients had pain in the right wrist and 13 (61.9%) had pain in the left wrist; 16 (76%) patients had swelling of the right wrist and 14 (66.6%) had swelling of the left wrist. The mean (± SD) DAS28 for this sample was 4.0 ± 1.1 (data variation: 0 to 10), the mean HAQ was 1.2 ± 0.5 (0 = without disability to 3 = severe disability), with 145.7 IU/dL (normal <22 IU/dL) anti-cyclic citrullinated peptide (anti-CCP) and the average rheumatoid factor was 231.63 IU/dL (normal <20 IU/dL). Mean CRP was 6.97 ± 11.13 mg/dL (normal >6 mg/dL) and mean ESR was 4.7 ± 1.0 mm (normal >10 mm). Synovitis was detected by GSUS in 66.6% (N = 14) and 61.9% (N = 13) of right and left wrists, respectively. In the right wrist, the synovitis determined by GSUS was 28.5% (N = 6) grade 1, 19% (N = 4) grade 2 and 19% (N = 4) grade 3. In the left wrist, synovitis was 33.3% (N = 7) grade 1, 14.2% (N = 3) grade 2, and 14.2% (N = 3) grade 3. PDUS was seen in 23.8% (N = 5) of the right and left wrists. In the right wrist, 9.5% (N = 1) were grade 2 and 19% (N = 4) were grade 3. In the left wrist, 16% (N = 4) were grade 2 and 4.76% (N = 1) were grade 3 (Figures 1 and 2).

The Spearman correlation coefficient at the $P < 0.05$ level of significance revealed the following significant correlations: GSUS and swollen right wrist ($r = 0.546$), GSUS of right wrist and swelling of left wrist ($r = 0.511$), PDUS of right wrist and pain in left wrist ($r = 0.436$), PDUS of right wrist and CRP ($r = 0.466$). At the $P < 0.001$ level of significance, the following correlations were obtained: GSUS and PDUS of right wrist ($r = 0.730$), GSUS and PDUS of left wrist ($r = 0.758$), PDUS of right and left wrist ($r = 0.732$), GSUS of right and left wrist ($r = 0.552$), PDUS of left wrist and GSUS of right wrist ($r = 0.574$), PDUS of right wrist and GSUS of left wrist ($r = 0.687$), as presented in Table 2.

The detection of synovitis by GSUS was higher than by PDUS. This may have occurred because a unit of frequency for low power Doppler was used. This may have caused the

Table 1. Drugs used by the patients at the time of examination.

	Prednisone	Methotrexate	Leflunomide	Chloroquine diphosphate	Hydroxychloroquine
Percent of patients (N)	52% (11)	57% (12)	14% (3)	14% (3)	9.5% (2)
Dose (mg)	10	12.5	20	250	400
Time of use (months)	4	3	2	8	1

underestimation of the capture of active microcirculation, which is always important in the evaluation of synovitis by GSUS.

There was no significant correlation between wrist GSUS and PDUS and DAS28, HAQ score or radiography. The assessment of intra-observational (same reader) Larsen score for the X-ray had a mean kappa value of 0.185 and there was no agreement with a semi-quantitative ultrasound scale, since only radiographic osteopenia of the carpal bones and soft tissue edema of both wrists was detected.

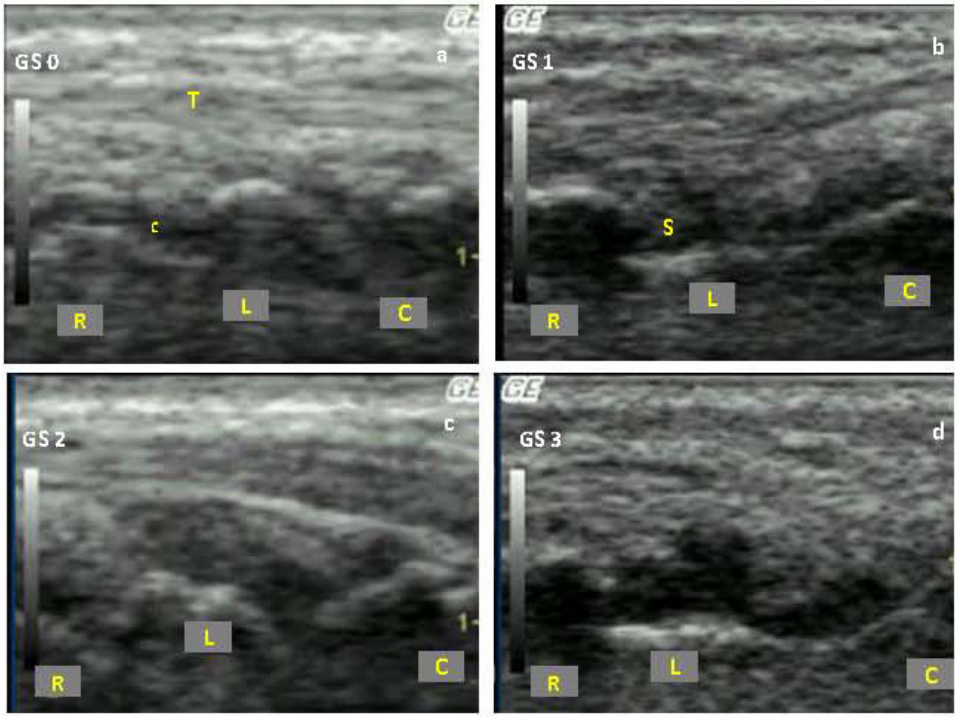

Figure 1. Synovitis identified by gray scale (GS) ultrasound in a dorsal longitudinal wrist scan. a = grade 0; b = grade 1; c = grade 2; d = grade 3. T = tendon; S = synovitis; R = radius; L = lunate; C = capitate bone; c = cartilage.

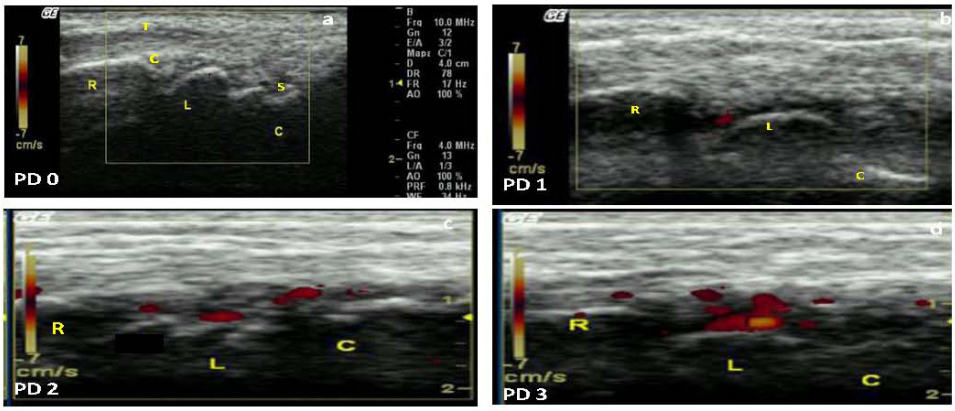

Figure 2. Synovitis identified by power Doppler (PD) ultrasound in a dorsal longitudinal wrist scan. a = grade 0; b = grade 1; c = grade 2; d = grade 3. T = tendon; S = synovitis; R = radius; L = lunate; C = capitate bone; c = cartilage.

This study showed an important correlation between the clinical and laboratory data, such as the correlation of the CRP and ultrasound data.

Table 2. Correlation between clinical and ultrasound examination.

	Clinical and ultrasound data			
	Pain	Swelling	GSUS synovitis	PDUS synovitis
Right wrist	14 (66.6%)	16 (76%)	14 (66.6%)	5 (23.8%)
Left wrist	13 (61.9%)	14 (66.6%)	13 (61.9%)	5 (23.8%)

Data are reported as number with percent in parentheses. GSUS = gray scale ultrasound; PDUS = power Doppler ultrasound.

Discussion

In the present study, 42 wrist joints were evaluated by ultrasound in a population with very early RA characterized by 14 months of disease. PDUS showed significant synovitis changes indicated by the existence of active microcirculation in the joint capsule, as demonstrated by a semi-quantitative scale. PDUS and GSUS are important tools for confirmation of synovitis, which can be dissociated from the clinical findings, as reported in the literature (7). A positive and significant correlation between GSUS and PDUS of both wrists may characterize the symmetry of clinical involvement of the joints in RA. Thus, these variables detected by ultrasound could enhance the clinical diagnosis of early RA, even when CCP and the rheumatoid factor are negative. When we evaluated the level of intra-observational agreement (kappa) between the results of ultrasound and the X-ray data a discrepancy was identified, e.g., the number of changes seen by ultrasound in patients with early RA was higher than that seen by the X-ray, and the changes found in the X-ray of the wrists were edema of soft tissues or osteopenia. The treatment of the RA has greatly progressed and currently intends to induce clinical remission based on the hypothesis that the inflammatory process leads to structural damage. Thus, there is a need to change the focus of evaluation, using a method that characterizes structural changes in the joint rather than only edema or osteopenia (26).

The ultrasound is important in the practice of the rheumatologist to prevent future structural damage, providing more comfort to the patient by fast, unlimited and safer scanning without irradiation. It can be considered a useful tool in the diagnosis of synovitis in early RA and can lead to an early change in the therapeutic decision.

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