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● *Original Contribution*

SONOGRAPHIC CUTOFF VALUES FOR DETECTION OF ABNORMALITIES IN SMALL, MEDIUM AND LARGE JOINTS: A COMPARATIVE STUDY BETWEEN PATIENTS WITH RHEUMATOID ARTHRITIS AND HEALTHY VOLUNTEERS

Flávia Soares Machado,* Rita Nely Vilar Furtado,* Rogerio Diniz Takahashi,†
Ana Leticia Pirosi de Buosi,* and Jamil Natour*

*Rheumatology Division, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo, Brazil; and †Radiology Department, Universidade Federal de São Paulo/Escola Paulista de Medicina (UNIFESP/EPM), São Paulo, Brazil

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Abstract—To determine ultrasound measurements indicative of abnormalities in small, medium and large joints, we conducted a cross-sectional study comparing 60 patients with rheumatoid arthritis (RA) and 78 healthy volunteers. A MyLab 60 ultrasound machine (Esaote) and a linear multifrequency probe were used. Quantitative measurements of synovial recesses and semiquantitative measurements of synovial hyperplasia, power Doppler and bone erosion (scores = 0–3) were performed. The cutoff values for synovial recesses indicating RA (receiver operating characteristic curve, area under the curve >0.800) were found to be (radiocarpal) 3.78 mm and (ulnocarpal) 3.07 mm. Those measurements with the greatest chance of indicating RA (logistic regression analysis expressed as odds ratios [ORs]) were ($p < 0.001$) measurements of synovial hyperplasia (ulnocarpal, OR = 100, and radiocarpal, OR = 70); synovial power Doppler (radiocarpal, OR = 66); synovial bone erosion (radiocarpal, OR = 324); fifth metatarsophalangeal joint (OR = 100); and second metacarpophalangeal joint (OR = 92). We concluded that for both quantitative and semiquantitative ultrasound measurements, radiocarpal abnormalities increase the chance of detecting RA. (E-mail: jnatour@unifesp.br)

Key Words: **Arthritis, Rheumatoid, Ultrasonography, Synovitis, Bone erosion.**

INTRODUCTION

In rheumatoid arthritis (RA), the inflammatory process begins at the synovial membrane (Firestein 2003). Deformities caused by the chemical and mechanical aggressiveness of the hypertrophic and hyperplasic synovial tissue occur at variable intervals (Jacoby et al. 1973); however, joint destruction can take place prematurely and rapidly (Lee and Weinblatt 2001). Thus, current recommendations confirm the need for early and aggressive treatment aimed at remission (Mottonen et al. 2002; Nell et al. 2004; Raza et al. 2006; Resman-Targoff and Cicero 2010; Smolen et al. 2010), resulting in a demonstrably improved articular prognosis and quality of life (Davis and Matteson 2012). Accordingly, recent studies have reiterated the need for the early diagnosis of this potentially destructive disease (Bartok and Firestein 2010), and several attempts have been made to find potential predictors of its development.

Some serologic, genetic and synovial pathology aspects have already been mentioned in the literature as potential predictors of RA (Raza and Filer 2009); recently, imaging has also gained importance for this objective (Raza and Filer 2009).

In recent years, ultrasound has been used in rheumatologic clinical practice as a supplemental physical examination (Grassi 2003), because of its unquestionable diagnostic potential (Grassi et al. 2004). Ultrasound also has advantages over magnetic resonance imaging (Wakefield et al. 2004b) and proven superiority over physical examination for the evaluation of effusions and synovial proliferation (Kane et al. 2003; Karim et al. 2004; Szkudlarek et al. 2006; Wakefield et al. 2004a, Wakefield et al. 2004b) and over X-rays for the demonstration of bone erosions (Lopez-Ben et al. 2004; Szkudlarek et al. 2006; Wakefield et al. 2000;

Address correspondence to: Jamil Natour, Rheumatology Division, Universidade Federal de São Paulo. Rua Botucatu, 740. CEP 04023-900, São Paulo, SP, Brazil. E-mail: jnatour@unifesp.br

Weidekamm et al. 2003). In addition, ultrasound has been used to visualize changes in the articular cartilage, to guide intra- and peri-articular aspirations and infiltrations (Kane et al. 2004) and to monitor therapeutic responses (Iagnocco et al. 2008; Naredo et al. 2008).

Studies on the use of articular ultrasound as an indicator of abnormality, however, are few and not comprehensive (Filer et al. 2011; Millot et al. 2011; Salaffi et al. 2010; Scheel et al. 2005; Terslev et al. 2008). With the exception of the study of Filer et al. (2011), the data published are only for the small joints of the hands and feet (Millot et al. 2011; Salaffi et al. 2010; Scheel et al. 2005; Terslev et al. 2008), but none of the investigations have concomitantly evaluated quantitative and semiquantitative sonographic measurements of joints of different sizes in the aim of estimating sonographic ultrasound cutoff values able to differentiate healthy persons from RA patients, which was the main purpose of our study.

METHODS

The present work was a cross-sectional study involving 78 healthy volunteers (HVs) (control group) recruited from the community and 60 patients classified as having established RA (Arnett et al. 1988) (RA group) from the Rheumatology Clinic of the Universidade Federal de São Paulo. The collection period was between March 2010 and June 2011. This study was reviewed and approved by the Research Ethics Committee of the Universidade Federal de São Paulo.

The control group included volunteers without pain or known joint disease (based only on information from the participant). The RA group included patients with RA that had progressed longer than 1 y, matched to the control group for gender and age. Both groups included only individuals aged between 30 and 60 y who had read, agreed to participate and signed the consent form approved by the ethics committee of the institution.

Individuals with diabetes mellitus, hypothyroidism, hemophilia, history of trauma, septic arthritis, joint surgery, symptomatic primary osteoarthritis of the joints or severe deformities resulting from primary osteoarthritis or who were suspected of being pregnant, currently pregnant, less than 6 mo postpartum or breastfeeding were excluded from both groups. The RA group did not include patients with overlap syndrome, the presence of irreducible deformities in the joints to be studied or a history of intra-articular injection in the preceding 6 mo in any joint.

A physical examination was performed by a "blinded" rheumatologist to exclude any joint disease or the presence of deformities in the control group. In the RA group, a specific examination targeting disease activity score based on 28 joints (Disease Activity Score Calculator for Rheumatoid Arthritis) was performed, and the Brazilian version of the subscale for functional disability of the Stanford Health Assessment Questionnaire was completed. In the RA patients, blood samples were collected for erythrocyte sedimentation rate (ESR) measurement and analysis of rheumatoid factor and anti-cyclic citrullinated peptide (anti-CCP). Weight, height and body mass index were recorded for both groups, as were answers to questions regarding race (white or non-white) and data on medications for RA patients. Each patient's disease status was classified as active or in remission based on American College of Rheumatology criteria (Pinals et al. 1981).

The ultrasound evaluation was performed by a radiologist with 10 y of experience in musculoskeletal ultrasound and "blinded" with respect to the groups and to each patient's physical examination. All of the examinations were performed during the morning with a MyLab 60 machine (Esaote, Biomedica, Genoa, Italy), using a linear transducer at 6- to 18-MHz frequency and a room temperature of 23°C. For the examination, the patient should have been at rest for the preceding hour and comfortably positioned to maintain the joint to be studied at rest. A gel was used as a sound transmission medium, in sufficient amount for viewing the skin on top of the image. The pressure applied to the transducer was below that required to cause visible deformities of the anatomic structures. Ultrasound measurements were performed after joint positioning and transducer placement, according to the methods of Backhaus (2001) and Schmidt et al. (2004). Table 1 lists the recesses under study and the transducer placement in each recess for performance of the measurements.

Ultrasound parameters evaluated

Synovial hypertrophy was defined based on the Outcome Measures in Rheumatology consensus (Wakefield et al. 2005). Quantitative measurements were taken (distance from the bone to the joint capsule) of the largest synovial recess, and semiquantitative measurements of the proximal interphalangeal (PIP), metacarpophalangeal (MCP) and metatarsophalangeal (MTP) joints were scored from 0 to 3 (Szkudlarek et al. 2003). For the medium and large joint recesses, semiquantitative scores were created on the basis of the small joint scoring system, also ranging from 0 to 3, as illustrated in Figure 1. For B-mode evaluation, the frequency and gain varied according to the joint under study. In Figure 2 are sonographic images representing synovial hypertrophy scores 0 and 3 for small, medium and large joints.

Synovial blood flow was assessed by the presence of signal to power Doppler (PD) (Wakefield et al. 2005), using a semiquantitative score ranging from 0 to 3 (Szkudlarek et al. 2001, 2003). The ultrasound velocity