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● *Original Contribution*

ADVANCED POWER DOPPLER TECHNIQUE INCREASES SYNOVIAL VASCULARITY DETECTION IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Abstract—We compared the diagnostic performance of an advanced power Doppler technique (superb microvascular imaging [SMI]) with that of power Doppler Imaging (PDI) and B-mode ultrasound (US) in patients with early rheumatoid arthritis (RA) and RA under treatment with rituximab. Thirty patients (21 women aged 45 ± 11 y) affected by RA with remission to moderate disease activity were examined. Both hand joints were evaluated using US, PDI and SMI. Two radiologists reviewed all video clips and evaluated synovial vascularity intensity using a semi-quantitative scoring system. SMI revealed the presence of synovial vascularity in a significantly larger number of patients than PDI ($p = 0.02$). Inter-observer agreement for US, PDI and SMI was moderate ($\kappa = 0.59$), very good ($\kappa = 0.87$) and very good ($\kappa = 0.82$), respectively. We conclude that SMI detects more vessels than PDI in RA patients. This may allow increased sensitivity for early diagnosis of synovial inflammation, monitoring of its dynamic changes under therapy and evaluation of true imaging remission. (E-mail: io@lucasconfienza.it) © **2017 World Federation for Ultrasound in Medicine & Biology.**

Key Words: **Ultrasound, Power Doppler, Superb microvascular imaging, Rheumatoid arthritis, Synovitis.**

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic inflammatory disease affecting 0.3% to 1% of the general population (Suresh 2004). The synovial membrane represents the main site of inflammation as the inflammatory process enhances capillary perfusion and permeability. Long-term active synovitis results in structural articular and peri-articular damage, which is responsible for significant functional impairment and disability (FitzGerald and Bresnihan 1995; Sconfienza et al. 2012). Thus, to prevent joint damage and optimize long-term outcomes, RA management requires early initiation of a tailored treatment, which includes mainly synthetic or biological disease-modifying anti-rheumatic drugs and glucocorticoids (Smolen and Aletaha 2015).

Proximal interphalangeal and metacarpophalangeal finger joints are among the first to be affected in RA patients, and findings in such joints are regarded as markers of overall joint damage (Cyteval 2009). Several studies have focused on imaging modalities, mostly magnetic resonance imaging (MRI) and ultrasound (US), enabling early detection and monitoring of finger joint inflammation (Cyteval 2009; Klauser et al. 2002; Szkudlarek et al. 2001). A correlation between imaging-delivered information and laboratory inflammation data has also been proven (Mandl et al. 2012). As a cost-effective, quick and non-invasive imaging technique that also provides dynamic assessment and high-resolution depiction of small joints (Gitto and Draghi 2016; Gitto et al. 2017; Lacelli et al. 2008; Orlandi et al. 2012), ultrasound (US) represents a valuable diagnostic modality widely diffused in rheumatology departments and recommended for clinical practice (Colebatch et al. 2013). US can detect a wide range of inflammatory and structural alterations, such as joint effusion, synovial

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membrane thickening and bone erosion (Ben Abdelghani et al. 2015; Colebatch et al. 2013; Kawashiri et al. 2013; Mandl et al. 2014; Micu and Fodor 2015; Nakagomi et al. 2013; Nguyen et al. 2014). Its integration with Doppler techniques helps to promptly detect modifications in synovial vascularity resulting from either the natural history of RA or the response to therapy (Bhasin and Cheung 2015; Fukae et al. 2014; Toprak et al. 2014). Power Doppler imaging (PDI) applies a wall filter to remove clutter and motion artifacts, resulting in a loss of small blood vessels whose flow is low and almost equals the tissue motion velocity (Boote 2003). Advanced flow detection modalities have overcome these limitations. Among these is superb microvascular imaging (SMI; Toshiba Medical Imaging, Japan), an innovative, powerful and effective technique that can separate flow signals from overlying tissue motion artifacts, preserving subtle low-flow components with high detail and definition. SMI analyzes clutter motion and uses a new adaptive algorithm to identify and remove tissue motion and reveal true blood flow (Jiro 2014). PDI was developed with the primary goal of visualizing blood flow at higher resolution. Moving beyond this goal, SMI allows for visualization of minute vessels with low-velocity blood flow as well (Jiro 2014). To our knowledge, there is a single article describing a study that investigated the role of SMI in the assessment of synovial vascularity in RA patients (Wenxue et al. 2016).

The objectives of this study were (i) to evaluate the use of SMI in patients affected with early RA and patients with RA under treatment with rituximab, and (ii) to compare the diagnostic performance of SMI with that of PDI and B-mode US in the assessment of inflammatory changes in the synovial membrane.

METHODS

Study design and population

The local ethics committee approved this work, and written informed consent was obtained from all patients. This prospective study was conducted over a 24-mo period and included patients referred for US examination with a clinical diagnosis of early RA diagnosed within 3 mo before inclusion (subset 1) or established RA under treatment with rituximab (subset 2). All patients fulfilled the 2010 American College of Rheumatology/European League Against Rheumatism classification criteria for RA (Aletaha et al. 2010a, 2010b). Exclusion criteria were: (i) disease activity score in 28 joints (DAS28) >5.1, indicating high disease activity (Prevoo et al. 1995); (ii) a history of direct trauma in the wrist and hand; and (iii) an inability to comply with the requirements of the study protocol.

Clinical (disease duration and disease activity measured with DAS28) and laboratory (IgM rheumatoid factor and serum C-reactive protein [CRP]) data were collected. Disease activity was classified as remission (DAS28 <2.6), low activity (2.6 ≤ DAS28 ≤ 3.2) and moderate activity (3.2 < DAS28 ≤ 5.1) (Prevoo et al. 1995).

To determine what to expect in a healthy population, we also used PDI and SMI on five volunteers. Inclusion criteria were: (i) no history of current or previous disease potentially affecting the joints and (ii) a history of direct trauma in the wrist and hand.

US examination

All US examinations were performed with the patient sitting opposite the operator and the hands resting on a flat surface. The ulnar recess, metacarpophalangeal I to V and proximal interphalangeal I to V joints of both hands were evaluated in axial and longitudinal planes by a musculoskeletal radiologist with more than 10 y of experience using a high-end US system (Aplio 400 US system, Toshiba Medical Imaging, Japan) equipped with a 7- to 18-MHz broadband linear-array transducer (18 L7) and SMI module. Dorsal B-mode scans were used to select the region of interest for subsequent combination of PDI and SMI, which had to include the cortical bones, joint space and a variable amount of adjacent soft tissues. During PDI and SMI examinations, the transducer was placed lightly on the skin surface to apply as little pressure as possible and prevent the collapse of vascular structures. The color velocity scales, gain, filter and frequency settings were automatically adjusted by the US system using a specific tool installed on the machine and designed to obtain the maximum color signal from vessels. From each US examination, short video clips of B-mode US of articular and peri-articular structures, as well as PDI and SMI of synovial vascularity, were registered and exported for image analysis.

Image analysis

Two radiologists with 5 and 10 y of experience in musculoskeletal radiology, blinded to the patients' clinical and laboratory data, randomly and independently reviewed video clips registered for all patients. Synovial vascularity intensity was evaluated by means of both PDI and SMI and reported with a semi-quantitative scoring system (Szkudlarek et al. 2003) as follows: 0 = no synovial flow, that is, normality; 1 = single-vessel signals; 2 = confluent vessel signals in less than half of the area of the synovial membrane; 3 = vessel signals in more than half of the area of the synovial membrane. The joint with the highest score was considered for statistical analysis (Szkudlarek et al. 2003). Synovial thickening was assessed on B-mode US scans with a