

Systematic Review of Treatment Effectiveness and Outcome Measures for Enthesitis in Psoriatic Arthritis

Ana-Maria Orbai, Joshua Weitz, Evan L. Siegel, Stefan Siebert, Laura J. Savage, Sibel Z. Aydin, Jolanda J. Luime, Ori Elkayam, Barbara Neerinx, Slavo Urbancek, Kurt de Vlam, Christopher T. Ritchlin, and the GRAPPA Enthesitis Working Group

ABSTRACT. Enthesitis is a characteristic feature of psoriatic arthritis (PsA) and is important in disease pathogenesis and classification. Use of clinical outcome measures for enthesitis is heterogeneous, and only 1 measure has been specifically developed and validated in PsA. Ultrasound and magnetic resonance imaging assessments of enthesitis may have advantages over clinical examination but are insufficiently studied. As part of an update of treatment recommendations by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA), we performed a systematic literature review and identified randomized controlled trials with enthesitis outcomes in PsA. For each treatment agent we calculated treatment effect sizes (where applicable) and graded the level of evidence. (J Rheumatol 2014;41:2290–4; doi:10.3899/jrheum.140878)

Key Indexing Terms:

ENTHESITIS

ENTHESOPATHY

PSORIATIC ARTHRITIS

OUTCOME MEASURES

TREATMENT

Enthesitis or inflammation at sites where ligaments, tendons, and joint capsules attach to bone (1) is prevalent (25%–78%) in psoriatic arthritis (PsA); (2) may be the initial inflammatory manifestation¹; and (3) may be centrally involved in disease pathogenesis in PsA^{2,3}. While the entheses have become a key outcome in clinical trials⁴, a number of enthesitis instruments are available, and 5 different enthesitis outcome measures were used across

12 clinical trials (Table 1). The Leeds Enthesitis Index (LEI)⁵ is the only enthesitis measure developed and validated for PsA.

Both power Doppler ultrasound (PDUS) and magnetic resonance imaging (MRI) can identify both inflammatory and chronic changes, with PDUS providing additional information on vascularity, and MRI on osteitis; thus enthesitis can be detected at earlier stages and with greater sensitivity. Sensitivity to change of both imaging modalities for enthesitis has been shown in various studies, supporting their use in clinical trials.

MATERIALS AND METHODS

In a centralized systematic literature search performed by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) to support evidence-based updated treatment recommendations for PsA manifestations⁶, 32 full-text articles were identified for enthesitis in PsA. Eligibility for inclusion in the enthesitis review was defined as interventional randomized controlled trials (RCT) with enthesitis outcomes performed in PsA. Of these 32 full-text articles, 15 did not correspond regarding study design (open-label, case-control, case report, comment, review); 1 study reported additional results of a trial already included⁷; 7 did not report on PsA; and 2 did not report enthesitis outcomes; therefore, 7 of those initially identified full-text articles remained and are included here^{8,9,10,11,12,13,14}.

The GRAPPA Enthesitis Working Group also included the first double-blind RCT in PsA with enthesitis outcomes¹⁵, and several additional RCT that were searched by hand after consulting experts in the field. Thus, 5 articles, representing the initial sulfasalazine trial in PsA¹⁵ and trials completed after the date of the initial literature search^{16,17,18,19}, were added to the initial 7 articles^{8,9,10,11,12,13,14}, for a total of 12 articles included in this review.

A standardized data collection form was used to extract study information (year, author, journal); study type; participant diagnosis; treatment and comparator drug; dose; number of participants; enthesitis measure(s)

From Johns Hopkins Arthritis Center, Baltimore, Maryland; Dermatology Associates of Rochester, Rochester, New York; Arthritis and Rheumatism Associates, Rockville, Maryland, USA; Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow; Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, UK; Department of Rheumatology, Koc University, Faculty of Medicine, Istanbul, Turkey; Department of Rheumatology, Erasmus Medical Center, Rotterdam, The Netherlands; Department of Rheumatology, Tel Aviv Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel; University Hospital Leuven, Leuven, Belgium; Department of Dermatology, F.D. Roosevelt Hospital, Banska Bystrica, Slovakia; and Allergy, Immunology, and Rheumatology Division, University of Rochester Medical Center, Rochester, New York, USA.

A.M. Orbai, MD, MHS, Johns Hopkins Arthritis Center; J. Weitz, MD, Dermatology Associates of Rochester; E.L. Siegel, MD, Arthritis and Rheumatism Associates; S. Siebert, MD, Institute of Infection, Immunity and Inflammation, University of Glasgow; L.J. Savage, MD, Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds; S.Z. Aydin, Department of Rheumatology, Koc University Faculty of Medicine; J.J. Luime, PhD, Department of Rheumatology, Erasmus Medical Center; O. Elkayam, MD, MPH, Department of Rheumatology, Tel Aviv Medical Center and Sackler Faculty of Medicine; B. Neerinx, MD, University Hospital Leuven; S. Urbancek, MD, PhD, Department of Dermatology, F.D. Roosevelt Hospital; K. de Vlam, MD, PhD, University Hospital Leuven; C.T. Ritchlin, MD, MPH, Allergy, Immunology, and Rheumatology Division, University of Rochester Medical Center.

Address correspondence to Dr. A.M. Orbai, Johns Hopkins Arthritis Center, 5501 Hopkins Bayview Circle, Room 1B.19, Baltimore, MD 21224, USA. E-mail: aorbai1@jhmi.edu