Development of Simple Clinical Criteria for the Definition of Inflammatory Arthritis, Enthesitis, Dactylitis, and Spondylitis: A Report from the GRAPPA 2012 Annual Meeting

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ABSTRACT. Dermatologist and primary care clinicians are in an ideal position to identify the emergence of psoriatic arthritis (PsA) in patients with psoriasis. Yet these clinicians are not well trained to distinguish inflammatory musculoskeletal disease from other more common problems such as osteoarthritis, traumatic or degenerative tendonitis and back pain, or fibromyalgia. A simple set of clinical criteria to identify inflammatory disease would aid recognition of PsA. At its 2012 annual meeting, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) discussed development of evidence-based, practical, and reliable definitions of inflammatory arthritis, enthesitis, dactylitis, and spondylitis. This project will be a sequential process of expert clinician nominal-group technique, patient surveys and focus groups, and Delphi exercises to identify core features of inflammatory disease, testing these in a small group of patients with and without inflammatory disease, and finally validating these criteria in larger groups of patients. (J Rheumatol 2013;40:1442–5; doi:10.3899/jrheum.130459)

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ARTHRITIS ENTHESITIS DACTYLITIS SPONDYLITIS PSORIATIC ARTHRITIS

Psoriatic arthritis (PsA) may occur in up to 30% of patients with psoriasis, but often goes unrecognized[1]. If unrecognized and inadequately treated, patients may have joint damage, functional disability, and increased mortality compared to the general population[2,3]. PsA can present in an unpredictable, heterogeneous, and insidious manner, variably involving joints, tendon and ligament attachments, and the spine, making it difficult to distinguish from other musculoskeletal (MSK) conditions. Additionally, there is no single diagnostic measure, leaving it up to the clinical acumen of the examiner to render an accurate diagnosis. Just as PsA may be underrecognized, patients with psoriasis who have osteoarthritis (OA), gout, fibromyalgia, or other MSK conditions may be inappropriately diagnosed with PsA and potentially exposed to inappropriate treatments that would not otherwise be indicated for their actual condition. Indeed, in one series of patients with psoriasis presenting with MSK symptoms, 43% did not have PsA[4].

Most well trained rheumatologists recognize the clinical features of inflammatory arthritis, enthesitis, dactylitis, and spondylitis. On the other hand, while primary care clinicians and dermatologists are ideally positioned to detect PsA in their patients, many are unable to recognize clinical features of PsA. Several patient-completed screening questionnaires have been developed to help these clinicians make a tentative diagnosis of PsA and refer the patient for rheumatologic evaluation; however, these are not widely used[5]. It would be very practical for clinicians to have a simple set of questions and physical examination elements, with high sensitivity and reasonable specificity, to identify the presence of inflammatory MSK disease. Although such criteria could include laboratory and imaging [especially ultrasound or magnetic resonance imaging (MRI)] procedures to improve sensitivity and specificity, requirement of these additional measures would render the criteria less practical for the busy clinician who may not habitually order laboratory or imaging tests or be as capable of interpreting the results as a rheumatologist. Further, a recent study found that laboratory and imaging did not meaningfully increase the likelihood, beyond history and physical examination, of a rheumatologist correctly diagnosing PsA[1]. Thus, a criteria set limited to history and physical elements (without

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laboratory or imaging) would be the simplest and most practical unless it was unacceptably insensitive. An acute-phase reactant marker such as C-reactive protein or erythrocyte sedimentation rate can be obtained easily and inexpensively, and its inclusion might also be considered.

The CASPAR (ClASsification of Psoriatic ARthritis) criteria (Table 1), the current most widely applied criteria for classifying PsA, were developed to specifically and sensitively identify PsA for clinical trials and registry studies[6]. The "stem" of these criteria requires the patient to have evidence of inflammatory arthritis, enthesitis, or spondylitis before determining if enough additional elements are present to fulfill the criteria. One additional element is an inflammatory MSK component, dactylitis. The CASPAR criteria were developed by rheumatologists, who can understand and accurately distinguish between inflammatory and noninflammatory MSK disease through evaluation of patient history, physical examination, and as needed, laboratory and imaging procedures. Complete confidence in the diagnosis would require biopsy of inflamed tissue, but this step is invasive and impractical in the clinic and therefore rarely performed. Advanced imaging techniques such as ultrasound or MRI can also increase specificity of diagnosis, but are unlikely to be ordered by nonrheumatologists, and have yet to be fully researched even by rheumatologists. Since patients with psoriasis suspected of having PsA are typically referred to rheumatologists, and there are not enough rheumatologists to see all patients, it is important for referring clinicians (e.g., dermatologists, primary care providers, physiatrists, orthopedists) to be able to recognize the presence of inflammatory MSK disease and distinguish it from degenerative or traumatic MSK disease. This would facilitate appropriate referral to rheumatologists, leading to proper diagnosis and prompt institution of therapy, and thereby prevent longterm MSK damage and the morbidity and mortality due to comorbidities associated with inadequately treated inflammatory disease.

Members of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recognize the need to define for nonrheumatologists the key signs and symptoms that distinguish inflammatory arthritis, enthesitis, dactylitis, and spondylitis from degenerative, traumatic, mechanical, or infectious forms of these conditions. The development of these criteria was discussed at the GRAPPA 2012 annual meeting.

Inflammatory arthritis. Of the variables that could define inflammatory arthritis, some features can distinguish the overall set of inflammatory arthritides from noninflammatory ones, and others can help distinguish between the inflammatory arthritides, e.g., rheumatoid arthritis (RA) versus PsA. Features common to all inflammatory arthritides [RA, PsA, and spondyloarthritis (SpA)] when inflammation involves the synovial joint include the presence of joint tenderness, synovial tissue swelling, and prolonged stiffness after rest. Other clues may include patient age, distribution and pattern of joint involvement, and possibly improvement with activity. Whereas noninflammatory arthritis such as osteoarthritis may be characterized by joint tenderness, joint enlargement is usually hard and bony, not soft; stiffness in noninflammatory arthritis is minimal, and symptoms typically worsen with activity.

Inflammatory enthesitis. Enthesitis in PsA and other spondyloarthritides includes inflammation at the attachment

Table 1. Classification criteria for psoriatic arthritis (CASPAR*)[6].

Established inflammatory musculoskeletal disease (joint, spine, or entheseal) with 3 or more of the following:	
1. Psoriasis	
(a) Current†	Psoriatic skin or scalp disease present today as judged by a qualified health professional
(b) History	History of psoriasis that may be obtained from patient or qualified health professional
(c) Family history	History of psoriasis in a first or second-degree relative according to patient report
2. Nail changes	Typical psoriatic nail dystrophy including onycholysis, pitting, and hyperkeratosis observed on current examination
3. Negative test for RF	By any method except latex but preferably by ELISA or nephelometry, according to the local laboratory reference range
4. Dactylitis	
(a) Current	Swelling of an entire digit
(b) History	History of dactylitis recorded by a qualified health professional
5. Radiological evidence of juxtaarticular new bone formation	Ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of hand and foot

* The CASPAR criteria have specificity of 98.7% and sensitivity of 91.4%. † Current psoriasis is assigned a score of 2; all other features are assigned a score of 1. CASPAR: ClASsification of Psoriatic ARthritis; RF: rheumatoid factor.

of tendons, ligaments, fascia, and joint capsule fibers into bone[7]. Clinically, enthesitis is reported in 35%–50% of patients with PsA; however, the true prevalence may be underestimated, and more entheseal sites should be assessed, preferably using advanced imaging techniques such as ultrasound[2,8]. Common sites of enthesitis in PsA include the attachment of the plantar fascia and Achilles tendon, patellar tendons, and ligament insertion sites around the pelvis, ribs, and elbow. Enthesitis often occurs in the spine at ligament insertion sites on the vertebra. Patients may experience pain at entheseal sites (e.g., persistent pain at the Achilles tendon insertion), often without a clear traumatic onset, but typically attributed to overuse. Often, the patient cannot distinguish the difference between arthritis and enthesitis (e.g., patellar tendon pain vs knee joint pain). Diffuse chest pain may not be recognized as inflammation arising from ligament insertion at the costochondral joints or ribs. The patient also may not recognize the presence of enthesitis until palpation elicits tenderness. Other features indicating inflammatory enthesitis may include absence of precipitating trauma, redness at the insertion of tendons into bone, persistent pain associated with stiffness that improves with activity and is worsened by rest, chronic entheseal site pain in the context of other features of SpA, and lack of response to measures such as physical therapy. Some features have not been formally studied, e.g., whether inflammatory entheseal pain more typically improves with nonsteroidal antiinflammatory therapy.

Dactylitis. Dactylitis is swelling with tenderness of a whole finger or toe, representing a combination of tenosynovitis, enthesitis, and synovitis of the whole digit. It is commonly seen in the spondyloarthritides, especially PsA (30%–50% of patients)[2,9]. Dactylitis can also be caused by a number of other diseases[9], such as infections (e.g., tuberculosis, syphilis) and other inflammatory diseases (e.g., sarcoid arthritis, gout). Dactylitis is a secondary element of the CASPAR criteria for PsA[6], and appears to be reliably assessed by rheumatologists but not by dermatologists[10]. Key features that distinguish dactylitis upon clinical examination include swelling of the whole digit that is discernibly different than adjacent digits (wherein asymmetry from the contralateral digit can be helpful) and tenderness. The use of a measurement tool like the Leeds Dactylometer facilitates the identification of dactylitis in borderline cases[11].

Inflammatory spondylitis. Spondylitis, which encompasses sacroiliitis, facet arthritis, enthesitis of intervertebral ligaments, and osteitis, is frequently observed in patients with PsA. Depending on the criteria used to define axial disease in PsA, its frequency varies between 25% and 75%. The higher values are based on radiographic sacroiliitis regardless of symptoms[12]. Spondylitis can be especially difficult to distinguish from mechanical or degenerative back pain. A working group of the Assessments in SpondyloArthritis (ASAS) international society developed a practical definition of inflammatory back pain (IBP) that can be used by clinicians to distinguish IBP from mechanical or degenerative back pain[13]. Utilizing a list of features characteristic of IBP, 13 expert clinicians examined 20 patients with chronic back pain and suspected axial SpA. The highest sensitivity and specificity for the presence of IBP was met in 4 of the following 5 characteristics: (1) age at onset < 40 yrs, (2) insidious onset, (3) improvement with exercise, (4) no improvement with rest, and (5) pain at night (with improvement upon getting up; sensitivity 77.0%, specificity 91.7%). This definition of IBP was validated in an ASAS multicenter study of 686 patients with chronic low back pain, to establish criteria for axial SpA. In this study, presence of 4/5 characteristics yielded a sensitivity of 79.6% and specificity of 72.4%[13].

GRAPPA members proposed the following steps to distinguish inflammatory from noninflammatory MSK disease.

1. Ascertain from expert clinicians and patients the key identifiers of a clinical condition. Patient history and physical examinations will be the focus because of their practicality and feasibility for initial screening purposes; laboratory and imaging results will increase specificity but are not as practical for screening purposes in nonrheumatology clinics. Methods used to elicit initial expert clinician and patient opinion will include group discussions (e.g., the 2013 GRAPPA annual meeting), focus groups of patients (with inflammatory arthritis, enthesitis, dactylitis, and spondylitis and noninflammatory arthritis, tendonitis, and spine disease) conducted at select clinical centers; and Delphi exercises. Key elements will be identified to define inflammatory versus noninflammatory arthritis, enthesitis, dactylitis, and spondylitis. Harmonizing these inputs will be necessary because patients and clinicians may identify clinical features with differing methods and weights. Patients with research expertise will participate on a research steering committee during all phases of design and data analysis.
2. A group of expert clinicians, both rheumatologists and dermatologists, will be gathered to examine individual patients with PsA and noninflammatory arthritis, tendonitis, and back pain, and determine which elements from the agreed list of history and physical examination features yield the highest sensitivity and specificity. Available laboratory and imaging data will be analyzed in relationship to history and examination determinations.
3. A final validating step will apply the key features identified in Steps 1 and 2 to a large group of patients with inflammatory MSK disease compared with control groups of patients with noninflammatory diseases and identify which features are most discriminative and practical to use in a screening algorithm. Validation will then be performed in prospectively evaluated patients in clinics where inflam-

matory arthritis patients are seen, including rheumatology, dermatology, and primary care clinics. As in Step 2, laboratory and imaging data will be analyzed in relationship to history and examination determinations.

Conclusion

It is hoped that development of simple and practical definitions for inflammatory arthritis, enthesitis, dactylitis, and spondylitis will help clinicians, especially nonrheumatologists, to more accurately identify the presence of inflammatory MSK disease for timely referral to rheumatologists, to determine if PsA is present and facilitate proper application of the CASPAR criteria. It is possible that this project in criteria development will stimulate similar work in other forms of inflammatory arthritis and aid nonrheumatologists in the evaluation of patients with chronic MSK symptoms.

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