Assessment Tools in Psoriatic Arthritis

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ABSTRACT. A key objective of the assessment working group of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) was to identify, develop, evaluate, and validate outcome measures for use in clinical trials of psoriatic arthritis (PsA) and in clinical practice. In plenary and breakout sessions at the GRAPPA annual meeting (Boston, September 2007), the current status of measures used in clinical trials was reviewed, and development of simplified measures for use in various types of clinical practice (rheumatology, dermatology, and general practice) was discussed. We present a review of those discussions. (J Rheumatol 2008;35:1426–30)

Key Indexing Terms:

PSORIATIC ARTHRITIS	PSORIASIS	OUTCOME MEASURES
ASSESSMENT	ENTHESITIS	SPONDYLOARTHRITIS

A key objective of the assessment working group of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) has been to identify, develop, evaluate, and validate outcome measures for use in clinical trials of psoriatic arthritis (PsA) and in clinical practice, recognizing the overlap and the significant divergence in these 2 applications. Measures used in clinical trials must have a high degree of reliability, validity, and discrimination to be effectively used and trusted by pharmaceutical companies and regulatory agencies. Trial measures also tend to be longer, more complex, and numerous in order to accurately identify the multidomain experience of PsA, and typically they require training and skilled application. In a busy practice setting, however, simpler and fewer measures that can be rapidly applied and interpreted are needed so that practitioners of various disciplines can use them with little or no training. Yet these should be accurate enough to reflect the true influence of disease, monitor the effects of therapy, maintain tight disease control, educate patients, and demonstrate effectiveness of therapies to third-party payers. Ideally, measures used in clinical trials and clinical practice would be one and the same, but until we have measures that can fulfill the differing needs of both situations, an interim goal is to develop reliable and comprehensive measures for clinical practice that correlate highly with those used in clinical trials. GRAPPA members specifically identified the need to develop assessment measures simple enough to be used by rheumatologists to monitor the effectiveness of therapy, to encourage dermatologists to track and quantify disease activity and initiate and adjust therapy (to the extent they are comfortable in doing so) for other aspects of PsA besides the skin, and to improve patient compliance with therapy as they are tracking their disease activity.

The core set of domains, identified by the Outcome Measures in Rheumatology Clinical Trials (OMERACT) PsA working group for inclusion in all clinical trials of PsA, include joints, skin, patient global, pain, function, and health-related quality of life (HRQOL; Figure 1)[1,2]. Domains considered important to measure, but not necessarily in all clinical trials, included dactylitis, enthesitis, fatigue, nails, spine, clinician global, acute-phase reactants, and radiography. Domains considered potentially important, but still needing research regarding their inclusion and how to assess them, included magnetic resonance imaging (MRI), computed tomography, ultrasound, tissue analysis (e.g., synovial and skin biopsy), and "participation." Table 1 lists the domains that have been assessed in PsA clinical trials and the assessments used for these domains, as reviewed[3-5].

Results

In plenary and breakout sessions at the 2007 GRAPPA meeting, the current status of measures used in clinical trials was reviewed, and the challenge of developing simplified measures for use in various types of clinical practice (rheumatology, dermatology, and general practice) was discussed. A variety of measures have been used in trials, including those that assess a single domain in a unidimensional fashion (e.g., swollen joint count), and composite measures, such as the American College of Rheumatology (ACR) 20/50/70 score, that assess multiple dimensions of the disease condition. Some measures assess both disease state and change obtained with therapy, such as the Disease Activity Score (DAS), and others assess only change of disease state, such as the ACR score. Some measures are performed by an evaluator, such as joint count by a physician, while others are questionnaires that the patient completes (patient reported outcomes). Some QOL measures, such as the PsAQOL, are disease-specific and therefore tailored to patients with PsA; others, such as the SF-36 (Medical Outcome Study Short-Form Survey 36), are used

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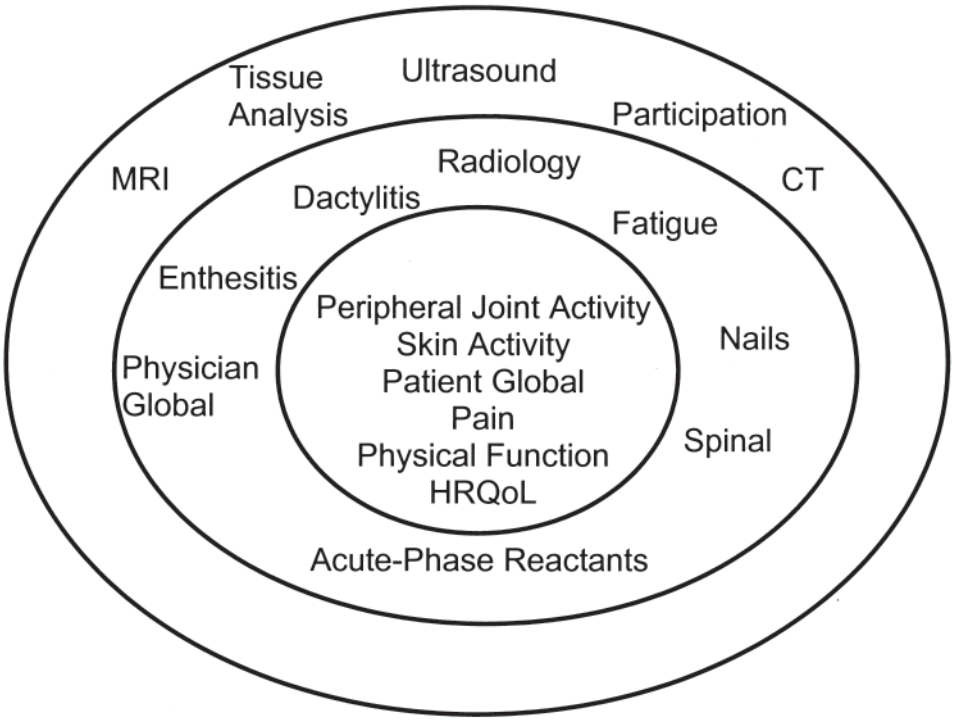

Figure 1. OMERACT proposal for domains in psoriatic arthritis trials[1,2]. Inner circle: must be included in clinical trials and longitudinal observational studies; middle circle: recommended for use but not mandatory; outer circle: the research agenda

Table 1. Assessment of psoriatic arthritis[4,5].

Domain of Assessment	Instrument
Joint	Tender/swollen joint count (78/76, 68/66), ACR, DAS variations, PsARC
Axial	BASDAI, BASFI, BASMI
Skin	PASI, target lesion, global
Pain	VAS
Patient global	VAS (global, skin + joints)
Physician global	VAS (global, skin + joints)
Function/QOL	HAQ, SF-36, PsAQOL, DLQI
Fatigue	FACIT, Krupp, MFI, VAS
Enthesitis	Mander Index, MASES, SPARCC, Leeds, Berlin, San Francisco, IMPACT (see Table 3)
Dactylitis	Leeds, present/absent, acute/chronic
Acute-phase reactant	ESR, CRP
Imaging	Radiography (modified Sharp or van der Heijde-Sharp), MRI, CT, US

ACR: American College of Rheumatology; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CRP: C-reactive protein; CT: computed tomography; DAS: Disease Activity Score; DLQI: Dermatology Life Quality Index; ESR: erythrocyte sedimentation rate; FACIT: Functional Assessment of Chronic Illness Therapy; HAQ: Health Assessment Questionnaire; MFI: Multidimensional FAtigue Inventory; MRI: magnetic resonance imaging; PASI: Psoriasis Activity and Severity Index; PsARC: Psoriatic Arthritis Response Criteria; PsAQOL: psoriatic arthritis quality of life; SF-36: Medical Outcome Study short form 36 health survey; US: ultrasound; VAS: visual analog scale.

in multiple diseases and thus can be compared across disease states. Most measures have been borrowed from other fields, e.g., rheumatoid arthritis (RA) and psoriasis, and have shown discrimination ability in placebo-controlled PsA trials with highly effective agents such as anti-tumor necrosis factor (TNF) agents; however, it is not known if they will be consistently discriminative in trials with all types of medications, including those with weak efficacy. Few of these measures have undergone formal validation procedures in PsA.

The core aspects of joint assessment are the tender and swollen joint counts. In OMERACT 8[1], the recommended number of tender joints to be assessed was 68 for tenderness and 66 for swelling (excluding evaluation of the hips). Although the DAS28 was reliable and discriminative when analyzed in two phase II trials of anti-TNF agents in patients with severe polyarticular disease[6], it is not known if it is reliable in patients with oligoarticular disease; if used as an inclusion criterion, it would have excluded about 20% of patients due to inadequate number of involved joints. In the IMPART study[7], in which patient evaluations by rheumatologists and dermatologists were assessed, both groups of physicians performed joint tenderness assessments reliably after a simple training session, although joint swelling was more reliably assessed by rheumatologists. Whether dermatologists who see psoriasis patients but who do not specialize in arthritis could perform such counts reliably without training is less certain. A training video could be helpful in lieu of hands-on training. In

discussions in Boston, emerging evidence was presented that a patient self-administered joint count has been shown to be reliable in RA; however, since the meeting, a study in PsA has been presented where this was not the case[8]. It is likely that some form of joint count will remain part of required assessments for quality measures. Most clinicians, however, direct their assessments to a few representative symptomatic joints and not a full 68/66. The 68/66 joint count is currently being employed in most registries, and will be assessed in a subset of the PsA patients in the large US data base, Consortium of Rheumatology Researchers of North America (CORRONA). The challenge and a subject of further research will be how to bridge the gap between comprehensive assessments of joints and the numbers that are realistically assessed in practice.

Other elements of composite assessments include patient global, physician global, patient pain, a function score such as the Health Assessment Questionnaire (HAQ), and an acute-phase reactant. The ACR score, DAS score, and PsA response criteria (PsARC) perform reliably and discriminatively in PsA trials[6]. However, they are cumbersome and impractical for clinical use because of the calculations involved (square roots in the case of DAS) and the need to wait for a laboratory result if an acute-phase reactant is employed. In RA, simpler measures have been proposed that are simple additive scores; results can be determined at the same clinic visit, except for the Simplified Disease Activity Index (SDAI), which includes an acute-phase reactant (Table 2). All of these have shown close correlation with the various versions of the DAS and ACR in RA. An exercise to determine the performance of these measures, applied retrospectively in data from various PsA trials, is under way. Because these measures can be done during a clinic visit, they potentially qualify both for clinical trials and for clinical practice. It is important to recall, however, that since they were developed for RA and measure only peripheral joint activity and not enthesitis, dactylitis, the spine, or the skin, they represent only a portion of the total experience of PsA patients. Thus, until a more comprehensive composite measure is developed that encompasses all these domains, additional individual assessments must be done to gain a complete picture.

Enthesitis is increasingly recognized as a key part of the pathophysiology of PsA, as evidenced by MRI and histology studies[9]. A number of outcome measures of enthesitis have been developed, which assess different enthesial insertion sites (Table 3)[10]. In the INSPIRE study, which involved experts in both PsA and ankylosing spondylitis (AS), all of the enthesial sites included in these various measures were assessed[10]. All had reasonable reliability, although the Canadian instrument (Canadian Rheumatology Association/ Spondyloarthritis Research Consortium of Canada, SPARCC) performed slightly better than others for PsA. These measures are being used in several current PsA trials, so we will have a greater sense of their performance in the near future.

Dactylitis, a very common feature of PsA, is usually measured as the presence or absence of swelling of a whole digit. A nuance is whether such a finding represents active inflammation, typically characterized by tenderness, or is inactive, in which the digit will usually not be tender. A newer measure, using a device that measures the circumference of the digit, has been developed in Leeds, providing quantification of this domain. Both enthesitis and dactylitis measures are simple to perform, but seem less likely to be widely adopted in routine practice settings than joint-count measures, unless their utility is demonstrated.

Spine assessments have not been done in PsA clinical trials because spine disease only occurs in a minority of patients, it is variable in its expression, and it requires imaging studies to confirm its presence (which adds to study expense), and it has been unclear how best to measure this domain. The INSPIRE study demonstrated that the measures of spine assessment developed for AS also function well in PsA patients with spine involvement[11].

Skin assessments used in PsA are those used in psoriasis studies, including the Psoriasis Area and Severity Index (PASI), the target lesion score, and static global assessment[12]. All have performed reliably in PsA studies. However, it should be noted that patients with PsA seen both in clinical studies and in practice tend to have low amounts of body surface area involvement; PASI scoring may not be as reliable in patients with low skin involvement and is not recommended in

Table 2. Clinical measures of rheumatoid arthritis activity.

Measure	DAS28	SDAI[17]	CDAI[17]	GAS	RAPID[18] PAS	ERAM[19]
Patient function	—	—	—	+	+	—
Patient pain	—	—	—	+	+	—
Patient global	+	+	+	—	+	+
Physician global	—	+	+	—	—	+
Tender joint	+	+	+	+	+	—
Swollen joint	+	+	+	—	—	+
ESR/CRP	+	+	—	—	—	—

CDAI: Clinical Disease Activity Index; CRP: C-reactive protein; DAS28: Disease Activity Score; ERAM: East Rheumatoid Arthritis Measure; ESR: erythrocyte sedimentation rate; PAS: Patient Activity Score; GAS: Global Arthritis Score; RAPID: Routine Assessment of Patient Index Data; SDAI: Simplified Disease Activity Index.

Table 3. Sites included in enthesitis indices. From Gladman, *et al*. J Rheumatol 2007;34:1740–5[10].

Descriptor	MASES[20]	Berlin[21]	SPARCC[22]	San Francisco[23]	Leeds[24]	IMPACT[25]
C1/C2	—		—	X	—	—
C7/T1	—		—	X	—	—
T12/L1	—		—	X	—	—
1st costochondral	RL		—	—	—	—
7th costochondral	RL		—	—	—	—
Lateral epicondyle humerus	—		RL	—	RL	—
Medial epicondyle humerus	—		RL	—	—	—
Posterior superior iliac spine	RL		—	—	—	—
Anterior superior iliac spine	RL		—	RL	—	—
Iliac crest	RL	RL	—	—	—	—
5th lumbar spinous process	X	—	—	X	—	—
Ischial tuberosity	—	—	—	RL	—	—
Proximal Achilles	RL	RL	RL	RL	RL	RL
Greater trochanter	—	RL	RL	RL	—	—
Medial condyle femur	—	RL	—	—	RL	—
Lateral condyle femur	—	RL	—	—	—	—
Insertion plantar fascia	—	RL	RL	RL	—	RL
Supraspinatus patella	—	—	RL	—	—	—
Quadriceps insertion patella	—	—	RL	—	—	—
Inferior pole patella	—	—	RL	—	—	—
Tibial tubercle	—	—	RL	—	—	—

X: site present; R: right; L: left; —: not included. MASES: Maastricht AS Enthesitis Score; SPARCC: Canadian Rheumatology Association/Spondyloarthritis Research Consortium; Leeds: Leeds Enthesitis Index; IMPACT: Infliximab Multinational Psoriatic Arthritis Controlled Trial.

patients with less than 3% surface area involvement. Nail involvement has been evaluated utilizing the modified Nail Psoriasis Severity Index (NAPSI) score[7].

Radiographic assessment is performed in clinical trials to assess the ability of a drug to inhibit progression of structural damage (joint space narrowing and erosions). The measures used in RA, including the van der Heijde modification of the Sharp score, modified in turn for PsA, have been discriminative[5].

Patient reported outcome measures of function, QOL, and fatigue have shown good psychometric characteristics in PsA trials[13,14]. The most commonly used measure is the HAQ; studies have shown the minimum clinically important difference of this instrument to be 0.3 (unlike 0.22 in RA)[15], and it functions reliably[16]. The SF-36 and Dermatology Life Quality Index (DLQI) also have been used as QOL measures in PsA. The PsAQOL, a disease-specific measure, has not yet been tested for discriminative power in a large clinical trial. The Functional Assessment of Chronic Illness Therapy (FACIT) system has shown discrimination as a fatigue measure in PsA clinical trials[4]. The Fatigue Severity Scale, although not used in trials, has been validated in PsA[3,4].

Conclusion

Future goals of the GRAPPA group are to validate measures being reliably used in clinical trials and to adapt and introduce simpler measures into routine clinical practice, thus facilitating more accurate and quantitative assessment of disease state and therapeutic change and ultimately improving outcomes and the control of PsA.

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