
Psoriatic arthritis indices

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ABSTRACT

The approach to measuring psoriatic arthritis (PsA) is still very variable. However, consistently assessed disease activity enables the determination, documentation and communication of treatment success or failure and facilitates the comparison of outcomes between trial populations and real-life patients. Consequently, homogeneously applied measures are desirable to optimise patient care. In the following, we present a brief overview of single disease activity measures and compound scores for PsA.

Measurement and documentation of PsA disease activity still differs considerably. In addition to treatment-related questions, the extent and frequencies of control examinations, and most importantly, the types of disease activity assessment lack consistency. Especially in the light of needed therapeutic aims for a treat to target strategy (1) homogeneously applied disease activity measures are required. To assure high-quality patient care, these indices should be implemented in randomised controlled trials (RCTs), longitudinal observational databases, and every-day clinical care, alike.

The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) (2) and the OMERACT initiative (3) published mandatory outcome measures for clinical trials (4) (Fig. 1): Participants voted on a core set of single variables and selected the following: peripheral joint activity, patient global and pain assessment on a visual analogue scale (VAS), physical function, skin disease, and quality of life (4). Spinal affection, enthesitis and dactylitis, acute phase reactants (APR), as well as structural damage, were not part of this “inner circle”, of obligatory assessments. The same is true for fatigue and nail involvement. Participation, tissue analysis, magnetic resonance imaging (MRI), computed tomography (CT)

and sonography were classified as part of a research agenda (Fig. 1) (4).

For several of the above mentioned single variables, validated measures have been repeatedly validated and successfully applied in clinical trials (5-8). However, many of them are transferred from other rheumatic diseases, like peripheral joint counts using a 28 joints model from rheumatoid arthritis (RA), or spinal assessments primarily developed for ankylosing spondylitis (AS). Concerns have been repeatedly expressed, whether these “borrowed” assessments are adequate: joint counts with a 28 joint pattern omit the distal interphalangeal joints (DIPs) that are often affected by PsA. Also, oligoarticular variants of PsA might be underrepresented by a score developed for the polyarticular disease RA (9). Similarly, it might be questioned, whether spinal assessments adopted from AS, that always affects the spine, works adequately in PsA, that is characterised by only facultative, and generally less severe axial involvement (9).

However, the “inner circle” of assessments should be accomplished at each visit not only in clinical trials, but also in every-day practice and long term observational datasets to objectify and document treatment success.

Compound scores

Single variables should be ideally combined into integrated scores, since compound measures of disease activity minimise between-patient and within-patient variability over time (10, 11) but still are responsive and discriminative between placebo and treatment arm in clinical trials (12). Moreover, they also carry advantages in clinical practice: Pooled indices display overall disease activity and the need for treatment escalation in a comprehensive and perceptible manner for doctors and patients alike. Thereby, patient empowerment and shared decision-making is facilitated, and patients presumably are

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encouraged to be compliant to therapy throughout their chronic condition. The acceptance of compound scores varies in clinical practice (13, 14) but their use should be further emphasised (1).

The *Disease Activity Score using 28 joint counts (DAS28)* was originally developed for patients with RA (15), but proved to be a highly responsive and discriminating instrument also in PsA patients (7, 12, 16, 17). It comprises four variables, namely tender and swollen joint count, erythrocyte sedimentation rate (ESR), and Patient Global Assessment (PtG) (see Table I). However, the 28 joint pattern does not capture joints commonly affected in PsA, including DIP joints of the hand, and joints of the ankle and foot. Therefore it may miss important elements of disease activity in many PsA patients (18).

Significant effort has been put in the development of PsA-specific compound scores: this is particularly challenging, firstly because of frequent spinal and enthesial involvement (18), secondly, because also peripheral joint involvement is highly variable when compared to other arthritides. This heterogeneity makes it difficult to account for the whole spectrum of clinical manifestations using one instrument. The association with a dermatologic condition that significantly impacts quality of life (19, 20) is further complicating the definition of meaningful outcomes and compound scores.

In a principal component analysis (PCA), the following three components reflected disease activity best (21): (i) patient reported outcomes, among these, most strongly pain assessment (PP) and PtG; (ii) joint involvement, especially the 66 swollen and 68 tender joint count; and (iii) acute phase response, represented best by C-reactive protein. Four of these variables (number of tender and swollen joints, PtG and PP) were also promoted to be key outcomes in OMERACT publications (Fig. 1) (4, 7, 22).

The *Disease Activity index for Psoriatic Arthritis (DAPSA)* (23) was originally developed for reactive arthritis (ReA), another seronegative spondylarthropathy often affecting the DIPs. Consequently, it applies a 66/68 joint count.

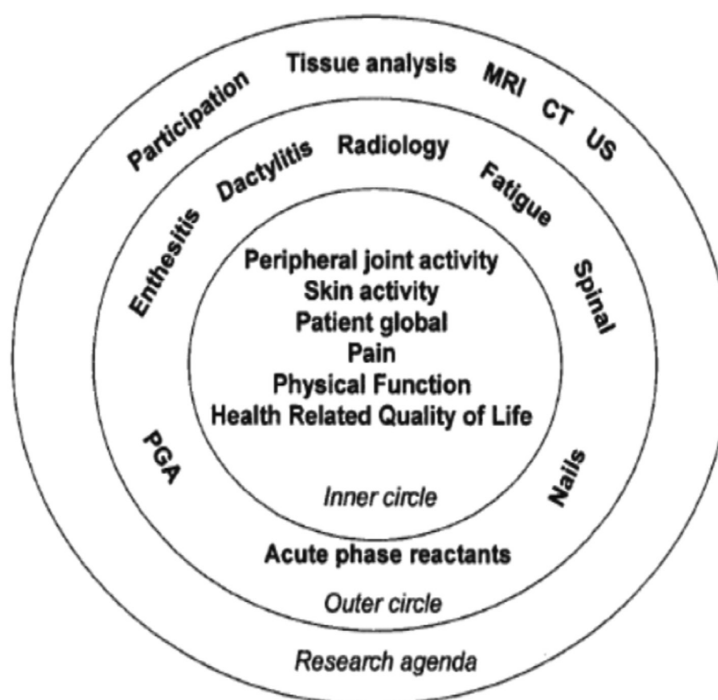


Fig. 1. Domains for Psoriatic Arthritis assessment in 3 categories: Items in the inner circle must be included in all RCTs and longitudinal studies. Other domains are recommended but not mandatory. Participation, Tissue analysis, MRI, CT, and US are part of research agenda. CT: Computed tomography; PGA: Physician global assessment; US: Ultrasound. Source: *Curr Opin Rheumatol* © 2009; Gladman *et al.* Consensus on a Core Set of Domains for Psoriatic Arthritis (4).

It is based on the numerical summation of five disease activity variables: tender and swollen joints (TJC, SJC), patient global and pain assessment on a 10 cm VAS, as well as C-reactive protein (CRP) (Tab. I). DAPSA exhibited good correlational, discriminatory and criterion validity for patients with PsA, and was sensitive to change both in the clinical trial setting and in an observational cohort (24). Of note, it also correlates with ultrasound assessed synovitis (25). Also the *Composite Psoriatic Disease Activity Index (CPDAI)* (26) uses a joint count including DIPs (range 0–66 for swollen, and 0–68 for tender joints). Moreover, it considers dactylitis, by assessing number of digits and function (Health Assessment Questionnaire; HAQ (27)), enthesitis (Leeds Enthesitis Index; LEI (6)), and axial disease (Bath Ankylosing Spondylitis Disease Activity Index; BASDAI (28)) and Ankylosing Spondylitis Quality of Life; ASQoL (29)). The CPDAI furthermore incorporates skin affection by use of Psoriasis Area Severity Index (PASI) (30) and Dermatology Life Quality Index (DLQI) (31) (Table I). Each aspect

is rated on a scale of 0–3, depending on the specific affection. The single domains are summarised and added up to a total score that reflects overall disease activity ranging from 0–15 (26) (Table I). The *modified CPDAI* omits spinal disease and consequently results in a 12-point maximum. Another variation, the CPDAI includes joint count, enthesitis and dactylitis (CPDAI-JED). Other than the DAPSA, the CPDAI and CPDAI-JED both failed to discriminate between patients with signs of sonographic synovitis and those without (25).

The *Psoriatic Arthritis Disease Activity Score (PASDAS)* (22) covers Physician and patient global VAS assessment, the physical component score (PCS) of the Medical Outcomes Survey-Short Form-36 (SF-36), a 66/68 joints count, enthesitis and dactylitis, as well as CRP (Table I). Finally, the *AMDf* (22) constitutes the *arithmetic mean of desirability functions* for tender and swollen joints, HAQ and PtG, as well as patient VAS ratings for skin and joints, PASI, and Psoriatic Arthritis Quality of Life Index (PsAQoL).

Table I. Summary of Compound Disease Activity State Scores in Psoriatic Arthritis.

Score	Formula	Includes		
		Joint Count	Skin	Spine
DAS28 ¹⁵	$0.56\sqrt{TJC} + 0.28\sqrt{SJC} + 0.70 \ln(\text{ESR}) + 0.014 * \text{PtG}$	28	–	–
DAPSA ²³	SJC + TJC + PtG + PP + CRP [mg/dl]	66/68	–	–
PASDAS ²²	$((((0.18 * \sqrt{\text{EGA}}) + (0.159 * \sqrt{\text{PtG}}) - (0.253 * \sqrt{\text{SF36/PCS}}) + (0.101 * \text{LN}(\text{SJC} + 1)) + (0.048 * \text{LN}(\text{TJC} + 1))) + (0.23 * \text{LN}(\text{LEI} + 1))) + (0.377 * \text{LN}(\text{TDC} + 1))) + (0.102 * \text{LN}(\text{CRPmg/dl} + 1))) * 1.5$	66/68	–	–
CPDAI ²⁶	peripheral arthritis (joint count and HAQ) + skin disease (PASI and DLQI) + enthesitis (LEI and HAQ) + dactylitis (digit count and HAQ) + axial disease (BASDAI and ASQoL)	66/68	x	–
mCPDAI ²⁶	peripheral arthritis (joint count and HAQ) + skin disease (PASI and DLQI) + enthesitis (LEI and HAQ) + dactylitis (digit count and HAQ)	66/68	x	x
CPDAI-JED ²⁶	peripheral arthritis (joint count and HAQ) + enthesitis (LEI and HAQ) + dactylitis (digit count and HAQ)	66/68	–	–

DAS28: Disease Activity Score 28 Joints; DAPSA: Disease Activity in Psoriatic Arthritis; PASDAS: Psoriatic Arthritis Disease Activity Score; CPDAI: Composite Psoriatic Disease Activity Index; mCPDAI: modified CPDAI; CPDAI-JED: CPDAI joints, entheses, dactylitis; TJC: tender joint count, SJC: swollen joint count, ln: natural logarithm; ESR: erythrocyte sedimentation rate; PtG: patient global assessment; PP: patient pain; CRP: C-reactive protein; EGA: physician global assessment; SF36/PCS: Medical Outcomes Survey Short Form-36 / Physical Component Score; LEI: Leeds Enthesitis Index; TDC: tender dactylitis count; HAQ: Health Assessment Questionnaire; PASI: Psoriasis Area Severity Index; DLQI: Dermatology Life Quality Index; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; ASQoL: Ankylosing Spondylitis Quality of Life.

All of the above mentioned PsA-specific compound scores performed well in clinical trials and observational datasets (22, 23).

Response criteria

Among available response scores, the *American College of Rheumatology (ACR) criteria* (32) are frequently used in PsA trials. Similarly to the DAS28, they were originally developed for RA, but are valid in PsA (7, 12, 16, 17). They require a 20/50/70 percent (ACR20/50/70) reduction of both tender and swollen joint counts, plus 3 of the following five items: evaluator and patient global VAS rating, pain assessment, HAQ, and APR. For some PsA studies a 78 joint count was used. The *European League Against Rheumatism (EULAR) response criteria* (33) are based on DAS28 improvement. They have originally been derived for RA assessment and were then validated also in PsA patients (7). They differentiate good or moderate response, and non-response. The more disease-specific *Psoriatic Arthritis Response Criteria (PsARC)* (34) include 66/68 tender and swollen joint counts as well as EGA and PtG, both on a 0–5 Likert rating scale. Response in the joint counts is defined as 30 percent improvement, whereas response on the Likert scale is determined by a 1-point reduction. The PsARC omits APR and pain assessment. The *Psoriatic Arthritis Joint*

Activity Index (PsAJAI) (35) is a response measure using a 30% reduction in physical function, PtG and pain assessment, physicians global assessment and APR.

Among the above mentioned, EULAR performed better than ACR20, and both better than PsARC (12). However, response criteria do not allow quantification of disease activity, but rather determine changes from baseline.

Discussion

PsA evaluation poses specific challenges due to its variety of clinical presentations, and the definition of meaningful single or compound outcomes that reflect overall disease activity is difficult. Compound scores are helpful and facilitate target-oriented therapy. However, which single variables should be integrated still needs consideration (4, 21). Principal component analyses enable rankings of single disease activity domains. Variables best represented in the PCA should be included in composite disease activity indices. Many of the currently employed scores have been originally developed for RA or AS, and thereby might miss specific disease characteristics. Most importantly, the fact that PsA frequently involves the DIPs endorses the use of a 66/86 joint count. Some of the items of particular interest for the decision which of the available compound scores should be favoured, are:

1. Score comprehensiveness; inclusion of skin assessment

DAS28 and DAPSA focus on the assessment of peripheral joint activity, whereas other compound scores implement several additional disease manifestations. A particularly significant question is whether to include skin assessments, as in CPDAI and AMDf. Higher comprehensiveness can certainly be argued to be of advantage, however, given the fact that various therapies have different efficacy in skin versus spinal, enthesal or peripheral joint disease (36) and that it is not yet clear if the pathogenesis of these symptoms is the same, a skin-inclusive score potentially increases the heterogeneity of responsiveness and reduces discriminatory capacity (36). Joint and skin disease do not necessarily correlate in terms of disease activity (37–39). Therefore, it seems arguable to employ a composite instrument for peripheral joint involvement and capture skin affection by additional instruments to allow evaluating therapies which are efficacious for certain but not other characteristics of this complex and heterogeneous disorder (40).

2. State measures versus response criteria

Disease activity state measures should be preferred because they can be used as thresholds for target-oriented treatment and related to long-term outcomes.

3. Feasibility

Lastly, feasibility of measurements should be considered. This is true in terms of time and effort necessary for single assessments, as well as for the practicability of compound scores. Scores that utilise simple summation of disease activity variables provide a useful and easy to calculate instrument both in the clinic and in trials (41). It is true that more complex formulae can be implemented by spreadsheet or web-based tools, however, face validity and transparency for patients and doctors presumably suffer by weighting and transformation of indices, and this might be a key factor for implementation in everyday practice.

Conclusion

In conclusion, high quality care that ensures homogeneous, guideline-oriented treatment for all PsA patients, requires regular assessment of validated scores. Comparability of outcomes and a treat to target approach to disease management make homogeneous use of compound disease activity state indices desirable. However, unequivocally accepted and reliable instruments that are ideally feasible in the assessment of “real-life” patients and long-term databases, as well as in the clinical trial setting, are desirable in PsA, but have not been ultimately provided.

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