Disease activity and response assessment in psoriatic arthritis using the Disease Activity index for PSoriatic Arthritis (DAPSA). A brief review

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ABSTRACT

In this review we provide reasons to use joint specific composite measures of disease activity for psoriatic arthritis (PsA) rather than composite scores that combine several manifestations of psoriatic disease, including skin involvement. Based on a principal component analysis, which, indeed, excluded skin involvement as a major factor in PsA, the Disease Activity index for PSoriatic Arthritis (DAPSA) was validated using clinical trial and observational data. Further, disease activity states and response criteria were recently defined. The DAPSA is simply calculated by summing swollen + tender joint counts + patient pain + patient global assessments + CRP, using 66/68 joint counts. DAPSA has meanwhile been validated in other studies and has shown to have a very high level of validity, also when compared with joint sonography. Thus, DAPSA is useful in clinical practice, clinical trials and observational studies.

Introduction

Psoriatic arthritis (PsA) is a multifaceted systemic disease with a main focus on the musculoskeletal system. Indeed, its complexity exceeds that of most other inflammatory joint diseases, since it may involve peripheral joints, the axial skeleton as well as entheses and dactylitis, beyond its characteristic skin and potential nail involvement and the comorbidities that can occur with this and other chronic diseases (1). Assessing PsA disease activity is therefore quite challenging, and various aspects and measures have been previously reviewed (2-4). These are also addressed in articles in this supplement. Most of the currently employed indices include non-arthritic manifestations, such as skin involvement and/or entheseal or axial involvement when assessing disease activity of PsA.

What should we measure when assessing disease activity in PsA, and how does DAPSA help?

For many years, the rheumatology community has taken the position that the different manifestations of PsA can be assessed quantitatively using a variety of validated measures, such as for axial disease (BASDAI, ASDAS) (5, 6), enthesitis (MASES) (7), dactylitis (8), skin (PASI) (9) and nail (10) involvement, and that the joints should be assessed separately (11). One reason behind this contention was the absence of insight regarding the similarity or disparity of pathogenetic events leading to the different clinical manifestations of PsA, and, indeed, different therapies have variable effects on distinct manifestations, rather suggesting a disparity (12). Also, the different manifestations may not have comparable significance regarding their structural and functional implications, as for example skin lesions have a high impact on quality of life, but can heal without scarring and do not induce physical disability, while inflammation of the joints, has cumulative effects, leading to potentially permanent destruction and impairment of physical function.

We feel that using composite measures which comprise different manifestations of psoriatic disease rather than focussing assessment of psoriatic arthritis on the joint and leave other manifestations to other, symptom-specific, validated, established scores will be helpful for clinical practice, clinical trials and observational studies in the field. In rheumatoid arthritis, composite measures of disease activity did not include vasculitis or nodules, and in ankylosing spondylitis, despite the frequent occurrence of peripheral joint disease, uveitis, psoriasis and inflammatory bowel disease, the main assessment continues to be specific for spinal disease. No one

Table I. Generalised results of the principal component analysis (11).

Component				
1	2	3	4	Loading in PCA
VAS PtGA				**>0.85**
VAS Pt Pain				0.5-0.85
BASDAI	BASDAI			*<0.5*
HAQ	HAQ			
TJC68	**TJC68**			
Enthesitis	**SJC66**			
	Enthesitis			
		CRP		
		ESR	ESR	
			PASI	

BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; HAQ: Health Assessment disability Questionnaire; PASI: Psoriasis Area and Surface Index; PCA: principal component analysis; PtGA: patient global assessment; Pt Pain: patient assessment of pain; SJC66: swollen joint count using 66 joints; TJC68: tender joint count using 68 joints; VAS: visual analogue scale. Factor 4 did not reach statistical significance.

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Moreover, although various musculoskeletal disease manifestations may have different implications when it comes to the patient's subjective perception or consequences of disease, they might not be contributing distinct information when it comes to quantifying overall disease activity. In fact, when we performed a principal component analysis of the various PsA manifestations (11), it turned out that the major factor that could be extracted was "pain", followed by "joints", "acute phase", and "skin" (Table I). BASDAI, patient global, joint tenderness, function (HAQ), and enthesitis (to a smaller extent) all loaded to the pain component. Using traditional and established instruments, such as a visual analogue scale for pain or patient global assessment may therefore also well represent the remaining variables on the pain component. At the same time, the issue of how to weigh in different manifestations, such as the extent and severity of enthesitis, in an overall assessment is mostly resolved with the patient pain and global assessments, since it is comprised within them.

Ideally, at least one variable from each factor should be included to cover all important domains of the disease (13-16). For the DAPSA this has been done; in fact, that the DAPSA score (see below) includes both, pain AND patient global assessment, significantly weighs in musculoskeletal manifestations. However, the skin domain is not included in the DAPSA score because it may be independent of musculoskeletal activity in improvement or worsening in PsA, and also may require a need for different therapeutic approaches, such as UV-irradiation or fumarates that are not efficacious for arthritis.

Interestingly, the principal component analysis also identified the same variables (marked in bold/dark grey in Table I) that had been comprised in a score developed for the use in reactive arthritis, another one of the spondylarthritides (17). This score was subsequently validated in PsA using clinical trial and clinical practice data, and was renamed Disease Activity index for PSoriatic Arthritis (DAPSA) (18). Indeed, hitherto the tools used for the assessment of joint involvement in PsA had mostly not been developed for PsA, since in most clinical trials scores or response criteria were employed that had been borrowed from rheumatoid arthritis (RA) assessment. Examples are the DAS28 which includes only 28 joints, and excludes both distal interphalangeal joints (DIPs) and foot joints or the ACR response criteria (11). DAPSA is thus defined as: TJC68 + SJC66 + PtGA (in cm VAS) + PtPain (in cm VAS) + CRP (mg/dl). A 68/66 joint count incorporates a pattern of peripheral arthritis that often is encountered in PsA and appears preferable to a 28 joint count for this disease. In analogy to SDAI and CDAI (19, 20) a clinical DAPSA (cDAPSA) has been validated, comprising all of the above items with exception of CRP (for explanations of abbreviations see footnote to Table I).

"Treat-to-Target!" (T2T) – but what is the target in PsA?

It is well established in RA that treating patients to a target of remission (REM) or at least low disease activity (LDA) conveys the best outcomes in clinical, functional and structural terms; the T2T recommendations for RA have recently been updated to expand this approach to established disease and consider work productivity and participation (21). Recently, an international task force has developed similar recommendations also for psoriatic arthritis (22), with remission/inactive disease defined as the major treatment target and LDA or minimal disease activity (MDA) as an alternative target. However, hitherto only MDA has been defined and validated (23) this definition is based on several individual items with specific thresholds to be achieved to fulfill the definition. Thus, except for those borrowed from RA, no validated definitions of the major disease activity states (high, moderate and low disease activity as well as remission) existed for PsA to date.

Recent analyses using the composite score DAPSA allowed defining remission as well as all other disease activity states (24). Based on survey data as well as analyses of clinical trial and observational data, and the multiple analyses performed in this study, the following distinct cut points for the classification of disease activity states were derived: REM: ≤4; 4<LDA≤14; 14< moderate disease activity (MDA) ≤28; high disease activity (HDA) >28. For cDAPSA the respective cut points derived are 4, 13 and 27 (24). With this advancement, PsA can now not only be assessed using a continuous measure, but also targeting various disease activity states including remission.

Which response criteria reflect therapeutic success in PsA?

In most clinical trials of the recent years, response criteria like disease activity assessments were borrowed from RA, with the exception of the PsARC (25); however, the latter does not distinguish between major and minor responses. In the above mentioned study, also new disease specific response criteria using the DAPSA (and cDAPSA) were presented (24) that allow the definition of a minor response at a 50% DAPSA change; of a moderate response as a 75% change; and of a major response as a 85% change from baseline. Importantly, the DAPSA level at baseline had little influence on the validity of these cut points and thus the definitions of relative response.

Conclusion

In this brief review we have presented data on the DAPSA score, including newly derived cut points for disease activity states as well as on response categories. Thus, two important items on the research agenda elaborated for the T2T-PsA recommendations, namely the definition of remission and low disease activity (22), as well as response criteria have now been accomplished and can be further validated and employed in clinical trials. Interestingly, in various recent assessments the discriminative capacity and construct validity of DAPSA was reported to be very good compared to both other clinical scores and to sonography (4, 26). These data as well as those summarised here suggest that the DAPSA and its sibling, the cDAPSA, can be effectively and widely employed in PsA clinical trials and practice.

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