

The Psoriasis Area and Severity Index Is the Adequate Criterion to Define Severity in Chronic Plaque-Type Psoriasis

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Key Words

Plaque-type psoriasis · Psoriasis Area and Severity Index · Dermatology Life Quality Index

Abstract

Background: Chronic plaque-type psoriasis is a major dermatosis, but a significant question is still unanswered: What defines severity in chronic plaque-type psoriasis? While objective assessments like the Psoriasis Area and Severity Index (PASI) have frequently been used in clinical trials, quality of life (QOL) questionnaires are currently becoming more and more popular. **Objective:** This article summarizes the most important objective and subjective measurements of severity in psoriasis. For every dermatologist it is critically important to distinguish between severe psoriasis and psoriasis that severely affects QOL. Even if the PASI also has disadvantages, it is the most adequate instrument available to evaluate severity in plaque-type psoriasis. **Result:** We provide reasons why PASI >12 defines severe, PASI 7–12 moderate and PASI <7 mild chronic plaque-type psoriasis.

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Introduction

Psoriasis is considered as a genetic, immunological, systemic disorder [1, 2]. With a prevalence of 1–3% and estimated annual costs between 650 and 800 USD per patient, its socioeconomic impact is remarkable [3]. Recently developed and upcoming biological treatments offer new therapeutic approaches, but also bring up the old, yet still unanswered question: What determines severity in psoriasis?

Only severe diseases justify the application of agents with significant adverse drug reaction (ADR) profiles. Systemic treatments are frequently approved exclusively for severe or moderate to severe psoriasis. The lack of a unanimous definition of severity in psoriasis might be one of the reasons for the restrictive use of systemic treatment modalities in psoriasis.

Generally, there is a consensus that clinical manifestations like psoriatic arthritis, psoriasis pustulosa, psoriatic erythroderma as well as some cases of psoriasis palmo-plantaris and inverse psoriasis per se are to be considered as severe.

However, there is much confusion about the definition of severity in chronic plaque-type psoriasis, which by far is the most common clinical manifestation of psoriasis.

Severity Assessments in Plaque-Type Psoriasis

The characteristic red, scaly, indurated lesion of plaque-type psoriasis varies over time in intensity, extent, distribution and associated symptoms, e.g. pruritus. In some patients, psoriasis severely affects everyday life and self-confidence, and leads to social stigmatization [4]. The response to and amount of previous remedies, as well as the time needed for daily treatment are additional factors influencing disease severity. Unfortunately, laboratory tests that accurately measure severity in psoriasis do not exist.

In order to define inclusion criteria in clinical trials, several so-called objective assessments have been developed to measure the severity of psoriasis. Concerns about the clinical relevance of an improved objective score led to the introduction of instruments to measure the patient's well being/quality of life (QOL). Additionally, scores combining objective and subjective subscales have been introduced to evaluate the different aspects of disease severity in a single assessment.

Disease-associated discomfort, disability and impaired QOL are continuous variables. However, in assessments that focus on whether clinical action should be taken, it is more practical to translate this continuum into dichotomous or polychotomous variables and thereby assume a threshold.

As in diagnostic screening tests, validity and reliability are important concerns in clinical measures. Evaluating the validity of a clinical score might be difficult, as no 'gold standard' exists. As a surrogate, the validity can be determined by the independent judgment of experienced clinicians. The intra- and interobserver reliability of clinical assessments should also be formally tested before their broader application.

In the following, the most common instruments to measure disease severity in psoriasis are shortly summarized. Because of the plethora of different instruments it is not possible to mention them all.

Body Surface Area

Several objective assessments incorporate an estimation of the involved body surface area (BSA) [5]. The BSA is easily evaluated either by the 'rule of nines' method or by the number of patient's hand areas affected. For decades, the area of one side of a flat closed patient's hand has been counted for 1% of his total BSA [6]. However,

planimetric investigations suggested that one hand actually represents 0.70–0.76% of the BSA [7]. This might be one reason why the affected BSA is often overestimated.

High interobserver variability is an important concern [8]. As a single instrument, BSA is not adequate to define the severity of plaque-type psoriasis, as it does not consider the intensity of the psoriatic lesion.

Psoriasis Area and Severity Index

The Psoriasis Area and Severity Index (PASI) was developed by Fredriksson and Pettersson [9] in 1978 to assess the effect of retinoid treatment in chronic plaque-type psoriasis. For other clinical manifestations of psoriasis, the PASI is not adequate. Both intensity and extent (BSA) of the psoriatic plaques are calculated separately for four anatomical regions (head, trunk, upper and lower extremities) by the physician. The intensity of erythema, desquamation and induration is rated on a 5-point scale with 0 indicating no involvement, 1 slight, 2 moderate, 3 severe and 4 very severe characteristics. The percentage of involvement of the four anatomical regions is assigned a numerical value of 0–6 with 0 indicating no involvement, 1 = 1–9%, 2 = 10–29%, 3 = 30–49%, 4 = 50–69%, 5 = 70–89% and 6 = 90–100% BSA involvement. When calculating the PASI, the four anatomical regions are evaluated according to their proportion of the whole integument. The PASI score varies from 0 to 72. Higher scores indicate severer conditions. Table 1 summarizes well-known advantages and disadvantages of the PASI.

Self-Administered PASI

The Self-Administered PASI (SAPASI) was designed in order to let the patient calculate the objective severity of his current psoriatic plaques [10]. It consists of a silhouette of the body to shade in the affected areas and of three visual analogue scales to rate the erythema, induration and scaliness of one's own average lesion. A third person transforms the patient's ratings into the intensity and extent scales of the PASI. The SAPASI is well validated and has a high test-retest reliability ($r = 0.82$) [5]. As an objective score, it is suitable for epidemiological studies, when the assessment cannot be performed by a physician [11].

Table 1. Advantages and disadvantages of the PASI

Advantages of the PASI

'Gold standard' in clinical trials [25]
Allows historical comparison with several treatments
Good correlation with other objective outcome measures [5, 23, 28]
Most validated objective measurement of psoriasis severity [24]
Good interobserver correlation when measured by trained observers [22]
Test-retest variability is less than 2% [11]
Easy performance

Disadvantages of the PASI

No correlation with QOL [18]
Does not always accurately predict severity from the patient's point of view [24]
Concerns about interrater reliability in BSA calculation [8]
No linear relationship to severity
Redundance of half of the range (scores of 35 or more are rare)
Majority of patients are included in the lowest area category (1–9% BSA)
Does not translate value ranges into the categories mild, moderate, severe
Erythema and scaling are influenced by temperature, humidity and recent application of emollients [5]
No reflection of the course over time
No reflection of the response to former therapies
No special consideration of particular locations, e.g. hands, feet, face, genitals
Certain therapies (e.g. anthralin) induce erythema and initially cause increased scores [29]

Physician's Global Assessment/Physician's Static Global Assessment

Compared to the mentioned assessments the Physician's Global Assessment (PGA)/Physician's Static Global Assessment provides a more subjective evaluation of overall disease severity. Unfortunately, the term PGA is used for two different instruments [12, 13]: in clinical trials, the PGA is frequently used to evaluate improvement relative to baseline severity [11]. Recently, the Food and Drug Administration has criticized that correct PGA assessment depends on the investigator's exact memory of baseline severity [14]. The other version of the PGA – sometimes also called Physician's Static Global Assessment – evaluates the overall severity without respect of baseline characteristics. 5-, 6-, 7- or 8-point scales are used, and there is no consensus about scale definition. For example, a score of '3' can either mean 'mild' or 'moderate' disease [11, 13].

Dermatology Life Quality Index

The Dermatology Life Quality Index (DLQI) is a widely used, simple and practical dermatology-specific QOL instrument. Patients answer 10 questions considering their QOL during the previous week on a 4-point scale, indicating 'not at all', 'a little', 'a lot' and 'very much', respectively [15]. The total DLQI score represents the sum of the scores for each question and ranges from 0 to 30 with higher scores reflecting worse QOL. Internal consistency and construct validity are strong [11]. Thus, the DLQI is an adequate instrument to assess the QOL in psoriasis patients [16].

Psoriasis Disability Index

The Psoriasis Disability Index (PDI) is a validated self-administered psoriasis-specific questionnaire originally consisting of 10 questions about aspects of the patient's functional disability during the previous 4 weeks [17]. Versions of the PDI using 15 questions have also been used [18]. The questions reflect daily activities, work, personal relationship and treatment. Answers are recorded on a 4-point scale, indicating grades from 'not at all' to 'very much' [19]. The PDI correlates strongly with the DLQI but does not correlate better than the DLQI with objective scores like the PASI or SAPASI [18].

Psoriasis Life Stress Inventory

The Psoriasis Life Stress Inventory has been developed in order to investigate which specific behavioral and social factors account for the decreased QOL in psoriasis patients [20]. The 15-item questionnaire evaluates the patient's level of stress experienced over the previous month on a 4-point scale, from 'not at all' to 'a great deal'. It measures psoriasis-specific psychological/psychosocial problems, many of which arise from anticipation of other people's reactions [21]. The Psoriasis Life Stress Inventory strongly correlates with the DLQI and the PDI, but not with the PASI and SAPASI [18].

Table 2. Definition of severity of chronic plaque-type psoriasis in RCTs

RCT therapy	phase	Inclusion criteria		Approved indication
		PASI/BSA	termed severity	
Alefacept [13]	III	BSA \geq 10	chronic plaque-type psoriasis	moderate to severe chronic plaque-type psoriasis
Efalizumab [30]	III	PASI \geq 12 BSA \geq 10	moderate to severe chronic plaque-type psoriasis	moderate to severe chronic plaque-type psoriasis
Etanercept [31]	III	PASI \geq 10 BSA \geq 10	moderate to severe chronic plaque-type psoriasis	to date not approved for plaque-type psoriasis
Infliximab [32]	II	PASI \geq 12 BSA \geq 10	moderate to severe chronic plaque-type psoriasis	to date not approved for plaque-type psoriasis

Salford Psoriasis Index

The Salford Psoriasis Index is a 3-component system incorporating the current objective severity based on the PASI, a psychosocial compound and the treatment history. Each subscore is reported separately on an 11-point scale (0–10) [22]. The PASI is transformed into the so-called extent subscore. A visual analogue scale is used to evaluate the psychosocial impact. The treatment history subscore is calculated by counting 1 point for each systemic therapy applied shorter and 2 points for each applied longer than a year. Every 5 admissions for inpatient treatment, as well as every episode of erythrodermia count 1 point. Additionally, a total cumulative dose of PUVA exceeding 200 treatments or 1,000 J cm² is worth 1 point.

Extent and psychosocial impact subscores both have a high test-retest reliability [11]. The extent subscore does not correlate with the other two components of the Salford Psoriasis Index, but with the PASI and SAPASI. There is a strong correlation between the psychosocial subscore and the PDI, PASI and SAPASI [23]. Although the Salford Psoriasis Index was designed to assist the clinician in everyday practice, at least the third component seems to be too difficult to be applied regularly [11].

Data from Clinical Trials

An indirect definition for ‘mild’, ‘moderate’ and ‘severe’ chronic plaque psoriasis can be derived from randomized controlled trials (RCTs). When a drug is approved, data from the corresponding clinical trial become critically relevant: safety and efficacy have been proven evidently only for the included population. The investigated drug is approved for the disease profile studied in the phase III RCT. Table 2 lists data from relevant RCTs concerning the severity definition of plaque-type psoriasis. As we cannot assume a Gaussian distribution of psoriasis severity in the patients treated in these trials, it is not possible to derive an exact definition of severity of psoriasis from the dispersion of the accordant data.

Proposed Definition

Generally, only patients with severe diseases are candidates for remedies with significant ADR profiles. Ethical considerations permit the application of such drugs only in patients who will probably benefit from them.

If the objective intensity and extent of a patient’s plaque-type psoriasis is mild, but psoriasis has significant impact on his QOL and self-confidence, none of the systemic treatment modalities is likely to improve his situation significantly. By contrast, the ADR profile of the common systemic antipsoriatic remedies would prohibit their use. For the mentioned patient, teaching of

coping strategies combined with topical drugs would be adequate.

Thus, it is extremely important to distinguish between severe psoriasis and psoriasis that severely affects QOL. This differentiation is necessary due to ethical considerations and shall not lead to an underestimation of the patient's point of view. Severe plaque-type psoriasis is characterized by the intensity and extent of psoriatic plaques. Although there are several disadvantages (table 1), the PASI is the best and most common instrument available to measure the mentioned characteristics [24, 25]. Thus, we propose to define severity of chronic plaque-type psoriasis by means of the PASI.

In doing so, defined PASI ranges have to be translated into the terms 'mild', 'moderate' and 'severe'.

- A psoriatic plaque is clinically significant if either erythema, induration or scaling is at least 'severe', and the other two characteristics are at least 'moderate'. In terms of the PASI, the minimum total plaque intensity of such a lesion is 7 [24].
- Patients with a PASI >12 have either 10–29% of their skin covered with clinically significant plaques or a BSA involvement of at least 30% without respect of the plaque intensity. Patients meeting these criteria definitely have severe psoriasis.
- A patient with a single deep red, very thick and scaly plaque on the back, the extremities and the scalp has a PASI = 12, unless BSA involvement is only 1%. This patient does not meet the criteria of severe psoriasis. Thus, we propose PASI = 12 as the upper limit of moderate plaque-type psoriasis.
- Clinically significant plaques covering less than 10% of the integument define the lower limit of moderate plaque-type psoriasis and result in a PASI = 7.
- If a patient's plaques are not clinically significant and BSA involvement is less than 10%, the PASI is less than 7 and the severity of plaque-type psoriasis is to be considered as mild.

We propose to define:

PASI >12 as severe chronic plaque-type psoriasis;

PASI 7–12 as moderate chronic plaque-type psoriasis;

PASI <7 as mild chronic plaque-type psoriasis.

Discussion

The proposed definition is useful exclusively for chronic plaque-type psoriasis. Other clinical manifestations like psoriatic arthritis, psoriasis pustulosa, psoriatic eryth-

roderma as well as some cases of psoriasis palmoplantaris and inverse psoriasis are generally to be considered severe.

Feldman [24] has recently stated that PASI and BSA define severity of chronic plaque-type psoriasis in RCTs, while the impact on the patient's QOL defines severity in clinical practice. He differentiates between 'severe disease' (objective criteria) and 'really severe disease' (subjective criteria). Two definitions of severity of one and the same disease – one for clinical trials and one for clinical practice – are not rational and necessarily lead to questioning the idea of evidence-based medicine.

As BSA involvement is not the critical criterion from the patient's point of view, Krueger et al. [26] propose a more comprehensive, patient-related definition of severity in psoriasis in clinical trials. From the patient's point of view 'embarrassment over appearance' is considered as very characteristic of severe psoriasis, whereas a positive family history is regarded as beneficial [27]. These factors are certainly not adequate to define disease severity in the context of indications for drug treatment.

Both the European Agency for the Evaluation of Medical Products and the Food and Drug Administration consider PASI and BSA as adequate to define severity in psoriasis (<http://www.emea.eu.int/pdfs/human/ewp/245402en.pdf>). A major advantage of the PASI is that it enables historical comparison between different clinical trials. Since the change of the millennium, the PASI has become even more popular: while used in 33.3% of all RCTs evaluating psoriasis therapy between 1977 and 2000, the PASI was adopted by 59.2% of the RCTs between 2001 and 2003 [25]¹. Despite the above-mentioned disadvantages (table 1), the PASI is the best-evaluated objective method that we have to define disease severity in plaque-type psoriasis [24]. In order to reduce the variability of the PASI, it would be rational to standardize the time interval between the application of emollients and PASI evaluation.

Patients with a PASI greater than 12 definitely have severe psoriasis and are most likely to benefit from systemic remedies. The chance to significantly improve the severity of their psoriatic lesions justifies possible ADRs of systemic agents like cyclosporine or methotrexate.

The major concern about the PASI is that its reduction is *not in all patients* translated into an improvement of QOL [4, 18, 24]. On the other hand, QOL correlates with

¹ Naldi L: The EDEN Psoriasis Project (oral presentation). EDEN Symposium – How to Perform Effective Clinical Trials for Psoriasis, Geneva, April 2004.

psoriasis-related stress. That again mainly derives from the patient's ability to anticipate the reactions of others and might be improved by adequate coping strategies [21]. Furthermore, psychological distress often has a detrimental effect on treatment outcome.

If a patient's QOL is very much affected, but the PASI is low, the success of a conventional therapeutic intervention is unlikely. Thus, it seems to be logical that patients with a disproportionate impact on QOL might benefit significantly from coping strategies. With respect to evidence-based medicine, however, this hypothesis should be evaluated in a randomized controlled trial.

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