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SHORT REPORT

Psoriasis severity: commonly used clinical thresholds may not adequately convey patient impact

N.M. Golbari,[1] J.M. van der Walt,[2] A. Blauvelt,[3] C. Ryan,[4] P. van de Kerkhof,[5] A.B. Kimball[6,*]

[1]Downstate Medical Center, Brooklyn, NY, USA
[2]PRI Healthcare Solutions, Paramus, NJ, USA
[3]Oregon Medical Research Center, Portland, OR, USA
[4]Charles Institute of Dermatology, University College Dublin, Dublin, Ireland
[5]International Psoriasis Council, St. Louis, MO, USA
[6]Harvard Medical School and Beth Israel Deaconess Medical Center, Boston, MA, USA
*Correspondence: A.B. Kimball. E-mail: clears@bidmc.harvard.edu

Abstract

Background Psoriasis severity is usually evaluated using quantitative and qualitative measures, including per cent body surface area (BSA) involvement, the Psoriasis Area and Severity Index (PASI) and the Dermatology Life Quality Index (DLQI), a patient-reported questionnaire. However, standardized definitions for psoriasis severity categories have not been well established. A PASI of 10 or 12 has remained the minimal severity threshold defining eligibility for psoriasis treatments. In the present study, the validity of this cut-off was re-evaluated in the context of quality of life.

Objective To determine whether the thresholds commonly used to define moderate psoriasis (PASI of 10–12 and BSA of 10) are supported by patient-reported DLQI data.

Methods A systematic review of randomized controlled trials that enrolled mild or moderate patients published between January 2000 and June 2017 was used to assess correlations between provider and patient-generated severity at baseline.

Results For subject groups with high impact on quality of life (DLQI > 10), the mean weighted BSA was 7.6 (Range: 7.1–8.4) and the mean weighted DLQI was 11 (Range: 10.2–12.2). Similarly, the mean weighted PASI for patients with DLQI > 10 was 8.7 (Range: 7.1–10.1) and the mean weighted DLQI was 10.9 (Range: 10.1–12.2).

Conclusion Patients with PASI or BSA scores less than 10 can have major quality of life impairment. In general, the objective measures of BSA and PASI alone, when excluding DLQI, may not fully capture the impact of disease severity.

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Conflicts of Interest

Dr. Nicole Golbari and Dr. van der Walt have no conflicts of interest to report. Dr. Blauvelt has served as a scientific adviser and/or clinical study investigator for AbbVie, Almirall, Arena, Athenex, Boehringer Ingelheim, Bristol-Myers Squibb, Dermavant, Eli Lilly and Company, Forte, Galderma, Incyte, Janssen, Leo, Novartis, Pfizer, Regeneron, Sanofi Genzyme, Sun Pharma and UCB Pharma, and as a paid speaker for AbbVie. Dr. Ryan has received compensation as a speaker, consultant or advisor for AbbVie, Boehringer Ingelheim Dermira, Dr Reddys, Janssen, Leo, Lilly, Novartis, Regeneron-Sanofi and UCB. Dr. van de Kerkhof received compensation for consultancy services and presentations from Celgene, Allmirall, AbbVie, Lilly, Novartis, Janssen, Leo, Bristol Mayer Squibb, Dermavant and UCB. Dr. Kimball has received compensation as a consultant and an investigator for Novartis, AbbVie, UCB, Lilly and Janssen and has received fellowship funding from Janssen and AbbVie.

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Introduction

Psoriasis is a chronic, immune-mediated disease, manifesting in skin symptoms that greatly impact patient quality of life (QoL). Severity has typically been classified into either three categories (mild, moderate and severe) or two categories (mild and moderate-to-severe). Historically, these categories have been important

in determining treatment options: 'mild' patients have traditionally been defined as those who can be appropriately treated with topical therapies, while 'moderate-to-severe' patients have been candidates for systemic treatment.[1]

A multitude of quantitative severity measures are available for clinical use. However, these assessment tools lack uniformity, some are not well validated, and some are challenging to use in clinical settings.[2] Due to ease of implementation and established use in randomized controlled trials (RCTs), body surface area (BSA) and Psoriasis Area Severity Index (PASI) are most frequently employed for severity in RCT and office settings.[3,4]

The 'Rule of Tens' has been used to define severe psoriasis in the European literature: BSA > 10, PASI > 10 or Dermatology Life Quality Index (DLQI) >10.[5] Similarly, psoriasis severity eligibility criteria for RCTs of newer psoriasis therapies have generally been set at 10% or more BSA involvement.

Treatment decisions using artificially designated cut-offs based on quantitative measures such as BSA may leave patients who are significantly impacted by their disease undertreated. For example, it is well established that patients with niche psoriasis subtypes with involvement of the face, genitalia, palms and soles, scalp, and nails can suffer greatly from their localized psoriasis, but may not fit the traditional definition of severe disease if skin involvement is not at least 10% BSA.

The PASI also has similar limitations. It becomes less sensitive to change at BSAs lower than 10% and therefore may be inadequate in measuring mild-to-moderate disease with low BSA involvement, or improvement of disease relative to baseline with therapy. Moreover, like BSA, it does not capture or quantify the impact of localized sites.[6,7] A 2012 Swedish registry study examining health-related QoL outcome measures reported only moderate correlation between DLQI and PASI and also found that PASI correlated weakly with the EuroQol 5D, an instrument often employed to measure the health-related QoL in cost-effectiveness analysis.[8] While other studies have demonstrated strong correlation in change between PASI and DLQI in moderate-to-severe psoriasis,[9] the correlation at the lower end of the severity scale (mild-to-moderate) has not been fully determined.

The treatment decision cut-offs based on the Rule of 10s that is used in RCT and clinical settings may lead to decreased access to treatment for patients with psoriasis.[3,10] Consistent with these gaps, a National Psoriasis Foundation survey from 2003 to 2011 revealed that 30% of 'moderate psoriasis' (defined as 3–10% BSA) received treatment solely with topical medications and 24–36% of moderate psoriasis felt that they were untreated.[11]

In this research, we examined correlations between PASI, BSA and DLQI, in studies that enrolled mild-to-moderate patients to determine whether PASI 10 and BSA 10% are meaningful cut-offs to use when deciding whether to utilize systemic therapies in psoriasis patients.

Methods

We performed an English-based systematic search using two strategies for RCTs that assessed efficacy of topical, conventional oral or biologic medications in psoriasis patients with mild-to-moderate disease. The first strategy employed the use of the PubMed database to search for studies published from January 2012 through June 2017. Phase I–III studies included mild, moderate or mild-to-moderate psoriasis patients and subtypes (scalp, palmoplantar). The second search strategy employed Cochrane Central Register of Controlled Trials, Embase, Ovid and Medline databases. RCTs published January 2000–June 2017 were included. Conference abstracts and non-RCT studies were excluded. Two investigators independently reviewed the publications. Mean baseline scores for BSA, PASI and DLQI were plotted against each other in three analyses. Pearson's correlation coefficients (r) and weighted correlation coefficients (Wr), which account for the number of subjects in each patient cohort assessed, were calculated for each comparison of variables. P-values of Wr are reported, and values < 0.05 were considered significant.

Results

The combined searches resulted in 134 studies after duplicates were removed. In general, DLQI, BSA and PASI were not reported in the same publication, which limited the number of studies for analysis. Specifically, 118 studies were excluded, since only one of the 3 assessment measures were reported. Sixteen remaining publications met inclusion criteria (Table 1).

PASI vs. BSA

Mean BSA scores were plotted against mean PASIs from 10 studies (n = 3075 [27 treatment arms]) and as expected strong correlation was observed (r = 0.923; Wr = 0.876; $P < 0.00001$; Fig. 1).

BSA vs. DLQI

BSA versus DLQI (n = 2487 across 4 studies [12 treatment arms])) also yielded strong correlation (r = 0.951; Wr = 0.966; $P < 0.00001$) (Fig. 2.1). Since a DLQI above 10 is a threshold designating a very large impact on quality of life, correlations between BSA and DLQI were assessed for subject groups with DLQI > 10. The mean weighted BSA for this cohort of treatment arms in which both BSA and DLQI were available as outcome measures (n = 510) was 7.6 (range: 7.1–8.4) and the mean weighted DLQI was 11 (range 10.2–12.2). In addition, the correlation coefficient was weak and inverted ($r = -0.13$; Wr = −0.13; P = 0.81) (Fig. 2.2).

PASI vs. DLQI

Similar analyses were performed for mean PASI versus mean DLQI (n = 2991 in 23 treatment arms), which again correlated

Table 1 Summary table of studies

Article	*N*	BSA% Mean (SD)	PASI Mean (SD)	DLQI Mean (SD)
Strober *et al.* (2017)	73	7.1 (1.8)	8 (3.2)	11.1 (6.5)
	148	7.2 (1.6)	8.2 (4)	11 (6.5)
Papp *et al.* (2016)	71	7.6 (4.6)	9.5 (5.1)	10.6 (5.9)
	70	6.4 (3.8)	8.5 (3.3)	8.6 (5.5)
	71	6.5 (4.1)	8.5 (3.6)	9.3 (6)
	70	7.8 (4.3)	9.9 (4.1)	12.2 (7.4)
	74	8.4 (4.9)	10.1 (4.4)	10.9 (7.2)
	74	8 (4.5)	9.6 (3.8)	10.2 (6.5)
Reich *et al.* (2017)	893	5.1 (2.7)	4.5 (2.2)	5.2 (4.7)
	897	5 (2.6)	4.5 (2.2)	5(4.5)
Pfaff *et al.* (2015)	24	3.8 (2.1)	4.4 (2.1)	4.3 (2.7)
	22	3.6 (1.8)	4.2 (1.8)	3.8 (2.7)
Bissonnette *et al.* (2010)	29	–	7.1 (3.1)	6
	7	–	7.3 (2.1)	5.3
Jensen *et al.* (2011)	30	–	7.3 (3.8)	6.3 (5.3)
Mease *et al.* (2005)	162	–	8.3 (7.2)	10.1
(Psoriatic arthritis)	151	–	7.4 (6)	8.6
Bissonnette *et al.* (2011)	12	–	6.5 (3)	9.8 (4.4)
(Palmoplantar psoriasis)	12	–	7.1 (3.3)	11.9 (6.9)
Drouin *et al.* (2008)	10	–	9.7 (3.7)	4 (2.7)
	16	–	7.5 (1.9)	5.1 (5)
Choonhakarn *et al.* (2010)	37	–	11.6 (2.9)	8.6 (1.7)
	38	–	10.3 (3.1)	8.1 (1.8)

References cited are present in supporting information.

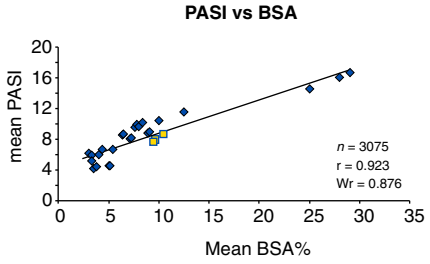

Figure 1 Correlation between mean PASI and mean BSA at baseline. Yellow square markers indicates studies that were not limited to patients with only plaque psoriasis. PASI, Psoriasis Area Severity Index; BSA, Body Surface Area; *n*, subjects; *r*, correlation coefficient; Wr, weighted correlation coefficient.

strongly ($r = 0.556$, Wr = 0.901; $P < 0.00001$ Fig. 3.1). When looking at patient groups with a DLQI > 10 for the treatment arms in which both PASI and DLQI were available as outcome measures ($n = 808$), the mean weighted PASI for this cohort was 8.7 (range: 7.1–10.1) and the mean weighted DLQI was 10.9 (range 10.1-12.2). Additionally, a weak and inverted correlation ($r = -0.302$, Wr = −0.064; $P = 0.86$) was observed (Fig. 3.2).

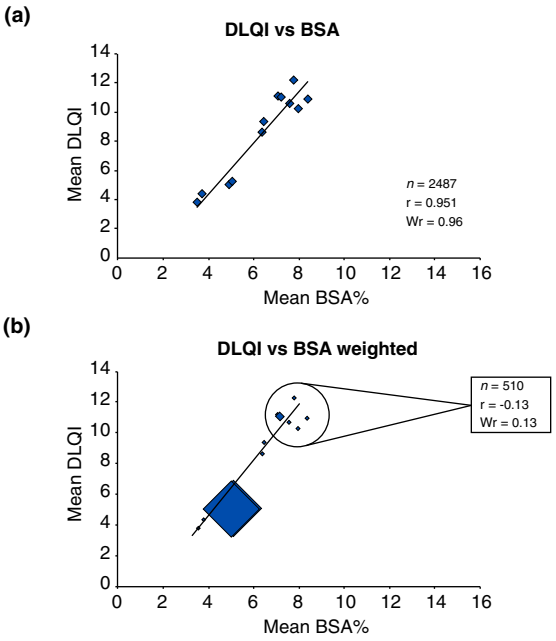

Figure 2 DLQI vs BSA. (2.1) Correlation between mean DLQI and mean BSA at baseline. (2.2) Weighted DLQI vs BSA: Subset analysis DLQI > 10. DLQI, Dermatology Life Quality Index; BSA, Body Surface Area; *n*, subjects; *r*, correlation coefficient; Wr, weighted correlation coefficient.

Discussion

In this study, the correlation between mean DLQI and mean BSA at baseline was high. However, BSA and DLQI were not well correlated at values of DLQI > 10. Importantly, many patients with BSA < 10 (range: 7.1–8.4) reported a significant impact on quality of life (DLQI range: 10.2–12.2). Similarly, patients with DLQIs > 10 (range: 10.1–12.2) also reported PASI mostly below 10 (range: 7.1–10.1). In general, the objective measures of BSA and PASI alone, when excluding DLQI, did not fully capture the impact of disease severity.

The PASI is used by European clinicians to assess psoriasis severity and to guide therapeutic decision making and reimbursement. In fact, the European S3 guidelines for systemic therapy treatment define moderate-to-severe psoriasis as PASI > 10.[12] Similarly, the National Psoriasis Foundation recommends treat-to-target goals based on BSA thresholds, but also supports the use of validated patient-reported outcome measures in treatment decisions.[13]

The findings in this study highlight the concern that treatment decisions based on threshold assessments of disease measures alone, such as BSA or PASI, may result in the under treatment of a subset of patients that experience a high burden of disease. A large multinational study reported that physician and patient perceptions of psoriasis disease severity differ.[14,15]

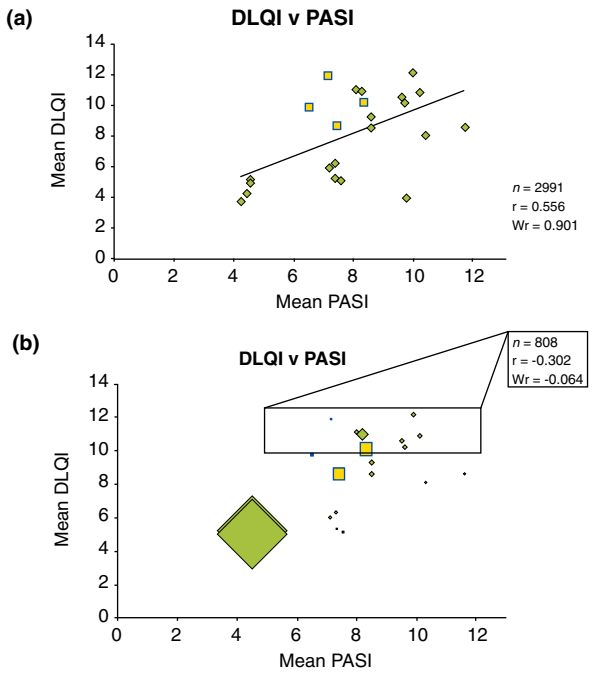

Figure 3 DLQI vs PASI. (3.1) Correlation between mean DLQI and mean PASI at baseline. (3.2) Weighted DLQI vs PASI: Subset analysis DLQI > 10. Yellow square markers indicates studies that were not limited to patients with only plaque psoriasis. DLQI, Dermatology Life Quality Index; PASI, Psoriasis Area Severity Index *n*, subjects; *r*, correlation coefficient; Wr, weighted correlation coefficient.

Indeed, according to the 'Rule of Tens', if the patient groups examined in this study were to be assessed by objective severity measures alone, as is done in most clinical settings,[5] they would likely have been classified as 'mild-to-moderate' and treated with topical therapies alone, even though their DLQIs indicated high impact or severe disease.

Other data support this hypothesis. In a Swedish registry study, decisions for biologic treatment were more strongly associated with PASI than DLQI in moderate-to-severe patients.[16] While patients in this study with low PASIs and high DLQI did not benefit from biologic treatment, another retrospective study demonstrated that mild psoriasis patients with high DLQIs benefited from conventional systemic therapy, even when baseline PASIs were 6 or less.[17] In addition, according to a European consensus, although PASI $\leq$ 10 is typically used to describe mild psoriasis, several additional criteria can be taken into consideration, including the involvement of special sites such as the genitals, face, palms or soles, or if patient symptoms such as pruritus are significant. The presence of these elements would then escalate classification of disease to moderate-to-severe disease.[18]

Limitations of this study include a small number of RCTs, which included plaque and niche RCTs, and population heterogeneity. Since patient level data were not available, averages from subgroup analyses were used.

Definitions of psoriasis severity are inconsistent across RCTs, cohort studies and clinical settings. Despite this, objective severity scores alone continue to be used to enrol patients in clinical trials as well as by physicians and some payers in clinical practice to determine systemic treatment eligibility. Although clinicians may not routinely use patient-reported outcomes such as the DLQI to measure impact of disease for their patients, the results from this review support the view that objective physician-assessed outcome measures alone may be insufficient for evaluating disease severity. Increasing clinical use of subjective scoring systems that are more specific to the symptoms encountered by patient with psoriasis, such as the DLQI-R or the PSI, could be useful in characterizing the impact of disease with lower BSA or lower PASI and improving access to care.[19,20] More real-world evidence and expert consensus are needed to develop more patient-centred guidelines for the initiation of systemic therapies in real-world settings.

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Supporting information

Additional Supporting Information may be found in the online version of this article:

Supplemental Citations (Figures 1-4)