Initial validation of the product of the signs global assessment and body surface area in atopic dermatitis

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Background: Current valid instruments that measure the signs of atopic dermatitis in clinical trials may not be suitable for clinical practice because of their complexity. The product of a clinician-derived 5-point signs global assessment and body surface area (SGA × BSA) may represent a simple approach to quickly assess the severity of signs in patients with atopic dermatitis in clinical practice.

Objectives: Evaluate the basic measurement properties of the SGA × BSA.

Methods: Retrospective chart review of patients with atopic dermatitis treated in an outpatient dermatology clinic at Oregon Health & Science University from 2015 to 2018 who had a recorded BSA and SGA.

Results: We identified 138 patients completing 325 clinic visits. SGA × BSA demonstrated strong and statistically significant ($P < .001$) correlations with the Eczema Area and Severity Index ($r = 0.91$, n = 19), average daily pruritus ($r = 0.71$, n = 177), patient global assessment ($r = 0.74$, n = 170), and a derived global scale composed of the average of 4 signs rated between 0 and 3 ($r = 0.77$, n = 282). Acceptability, responsiveness, and floor or ceiling effects of the measure were deemed adequate. Severity banding was maximized at 1, 21, and 87 ($\kappa = 0.4902$).

Limitations: The patient cohort was gathered exclusively from a tertiary care clinic setting in the Pacific Northwest and lacked ethnic diversity.

Conclusions: The results from this study suggest that SGA × BSA is a valid and feasible instrument for atopic dermatitis signs in clinical practice. (J Am Acad Dermatol 2021;84:283-9.)

INTRODUCTION

Identifying methods to measure atopic dermatitis severity enables adequate assessment and recording of disease activity for optimal disease management. Various clinical outcome measurement instruments exist to assess atopic dermatitis severity. However, they were designed primarily for the clinical trial setting and not all instruments show adequate validation in standard clinical practice.[1]

In 2014, the Harmonising Outcome Measures in Eczema group recommended the Eczema Area and Severity Index (EASI) as the preferred instrument to measure the signs of atopic dermatitis in clinical trials.[2] Although the EASI is a valid and responsive measure for assessing the signs of atopic dermatitis in clinical trials, it may be too time consuming and complex for general use in the clinical practice setting.[3] In addition to the complex nature of the EASI measurement, the tool may demonstrate

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difficulty in assessing patients with more limited disease.[4]

In a 2018 review of atopic dermatitis outcome measures by Chopra and Silverberg,[3] the authors suggested that the gestalt global assessment may be more feasible than the EASI for clinical practice but requires validation. The signs global assessment (SGA) is a 5-point static global assessment recorded by an investigator that primarily assesses signs of atopic dermatitis, akin to the gestalt global assessment but with a focus on only signs. As a stand-alone instrument, however, the SGA does not adequately assess the body surface involvement. Alternatively, although the body surface area (BSA) measure assesses area of involvement, it does not reflect the intensity of atopic dermatitis lesions and is therefore not suitable as a sole measure of signs. Schmitt et al[1] identified both lesion intensity and extent of the skin lesions to be components of atopic dermatitis that are very important to both patients and clinicians. Similar work by Charman et al[5] identified 3 clinical signs—erythema, papulation, and excoriation—to be independent predictors of patient-reported disease severity. Furthermore, a recent international survey of 1,111 patients found the extent of atopic dermatitis involvement to be "quite important" or "very important" to the majority of patients.[6]

CAPSULE SUMMARY

- This study provides initial validation of a novel outcome measure for assessing the signs of atopic dermatitis in clinical practice.
- This is a valid and feasible outcome measure for quickly measuring the signs of atopic dermatitis in clinical practice, improving patient assessment and follow-up.

The product of a physician-derived SGA and BSA has been proposed as an instrument to quickly assess the severity of signs in psoriasis in clinical practice and has shown good validity.[7-10] A similar outcome measure was recently proposed as a severity measure for pediatric atopic dermatitis, and correlated well with the EASI.[11] We conducted a single-center, retrospective case series with the aim to investigate the construct validity, floor or ceiling effects, ease of use (acceptability), responsiveness, and interpretability of the product of the SGA and BSA (SGA × BSA) in both pediatric and adult patients.

MATERIALS AND METHODS

Study design

We performed a retrospective chart review of pediatric and adult patients with atopic dermatitis defined according to a dermatologist's diagnosis.[12] Patients treated in an outpatient dermatology clinic at Oregon Health & Science University between January 2015 and December 2018 were identified through an electronic medical record search with the diagnosis of atopic dermatitis (L20). Only patients who had a clinician-confirmed atopic dermatitis diagnosis and a recorded BSA and SGA at the same encounter were included—both SGA and BSA are standard assessments for all patients. SGA is a 5-point, static global assessment scale recorded by an investigator, ranging from 0 (clear) to 4 (severe), that takes into account 4 signs: erythema, papulation, lichenification, and excoriation. Total BSA was calculated from regional BSAs, in which each region was weighted by converting regional BSA to total BSA through a summation of regional exact percentiles multiplied by a weighted factor (0.1 for head and neck, 0.2 for upper extremities, 0.3 for trunk, and 0.4 for lower extremities). The total BSA was then calculated by summing the final regional percentages.

In addition to BSA and SGA, we recorded any documented EASI score, average daily Itch Numeric Rating Scale score, patient global assessment, and the static physician global assessment. The Itch Numeric Rating Scale is a patient-reported numeric scale rating of average daily pruritus, ranging from 0 (no itch) to 10 (worst itch imaginable). The patient global assessment is a 3-point assessment scale reported by patients, ranging from 1 (mild) to 3 (severe). Last, the static physician global assessment is a derived global scale, similar to that used in psoriasis trials, composed of the average of 4 total body signs—erythema, papulation, lichenification, and excoriation—rated between 0 and 3. The static physician global assessment and SGA are very similar conceptually because they both provide an average severity of clinical signs.

All data were entered into the Research Electronic Data Capture application (Vanderbilt University, Nashville, TN). Analysis was performed in Stata, version 15 (StataCorp, College Station, TX). Comparisons of continuous data were performed with Wilcoxon's rank sum and Kruskal-Wallis tests unless otherwise indicated.

Consistent with the Consensus-based Standards for the Selection of Health Measurement Instruments guidance for determining construct validity, we hypothesized that SGA × BSA would demonstrate convergent validity with existing outcome measures,

Abbreviations used:

BSA: body surface area
EASI: Eczema Area and Severity Index
SGA: signs global assessment

including EASI, the Itch Numeric Rating Scale, patient global assessment, and static physician global assessment. Additionally, we hypothesized that the SGA × BSA measure would exhibit adequate floor or ceiling effects, ease of use (acceptability), and responsiveness to further suggest its use as a valid and feasible outcome measure for clinical practice.

The following parameters were assessed:

Construct validity

Construct validity was assessed by investigating convergent validity and cross-cultural validity. To assess convergent validity, we analyzed the Spearman rank correlations between SGA × BSA and EASI, static physician global assessment, patient global assessment, and Itch Numeric Rating Scale. Cross-cultural validity was assessed by analyzing correlation coefficients of relevant subgroups, including age, sex, and race. The a priori hypotheses were that the SGA × BSA would positively correlate with the aforementioned measures, and relevant subgroups, better than SGA or BSA alone, and with a correlation coefficient of at least 0.5.

Floor or ceiling effects

Floor or ceiling effects were rated as absent if less than or equal to 15% of the records achieved the lowest or highest possible score (0 or 400).

Acceptability/ease of use

To assess acceptability of the instrument, we prospectively measured and recorded the time it took to administer SGA and BSA for a subset of 20 patients. Acceptability was considered adequate if the mean time to administer the outcome measures was less than 2 minutes.

Responsiveness

Responsiveness to change was calculated by correlating changes in SGA × BSA to changes in patient global assessment, an independent anchor from SGA × BSA. Intrapatient changes in SGA × BSA scores between visits were calculated and compared with corresponding changes in patient global assessment, using Spearman rank correlations.

Table I. Demographics and atopic dermatitis severity

Sex*	n (%)
Men	82 (59.9)
Women	55 (39.8)
Age*	Years
Mean (SD)	37.2 (17.4)
Range	4.4, 77.9
Ethnicity*	n (%)
Non-Hispanic	127 (92)
Hispanic	8 (5.8)
Race*	n (%)
White	84 (60.9)
Black	5 (3.6)
Asian	29 (21)
Alaskan	2 (1.5)
Multiracial	12 (8.7)
AD severity	Median (IQR)
SGA (n = 325)	3 (2—4)
BSA (n = 325)	19.6 (6—42.5)
EASI (n = 20)	15.4 (8.9—27.7)
sPGA (n = 302)	7 (4—8)
PtGA (n = 186)	4 (3—5)
iNRS (n = 192)	5 (2—7)
SGA score (n = 325)	n (%)
0	17 (5.2)
1	35 (10.8)
2	43 (13.2)
3	128 (39.4)
4	102 (31.4)

AD, Atopic dermatitis; *BSA*, body surface area; *EASI*, Eczema Area and Severity Index; *iNRS*, Itch Numeric Rating Scale; *IQR*, interquartile range; *PtGA*, Patient Global Assessment; *SD*, standard deviation; *SGA*, signs global assessment; *sPGA*, static physician global assessment.
*Categories failing to add to 138 indicate missing data.

Interpretability

We used an anchor-based approach to assess interpretability, in which the measure to be interpreted is compared, or anchored, with a global assessment recorded simultaneously.[13] The score to be interpreted is stratified with numeric cutoffs into severity bands comparable to the global assessment score. We used the patient global assessment as a global severity score, and using the patient global assessment's defined severity strata, the SGA × BSA was stratified with numeric cutoffs into comparable severity strata. Agreement between SGA × BSA severity bands and patient global assessment scores were calculated with Cohen κ at multiple candidate score ranges.

RESULTS

We identified 138 patients completing 325 clinic visits with recorded SGA and BSA (mean patient

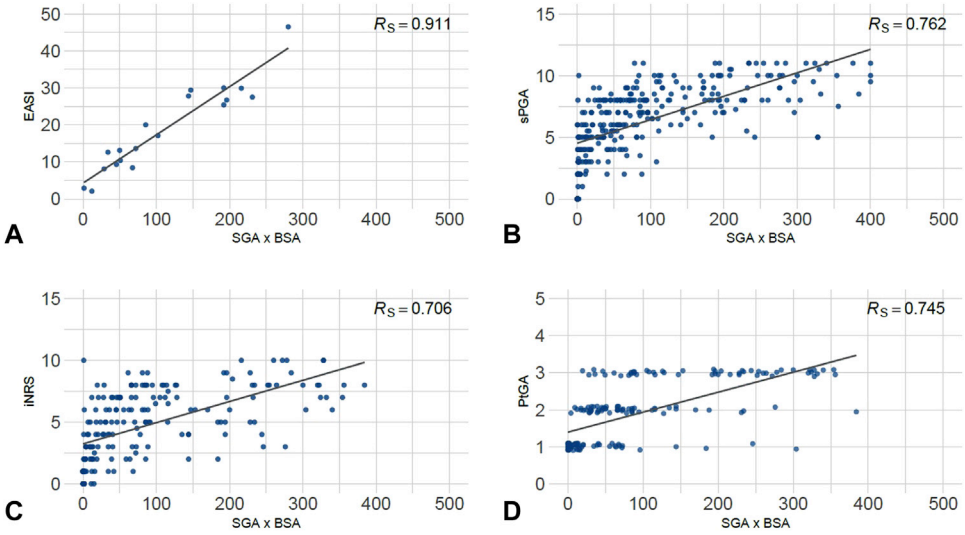

Fig 1. Scatter plots. Correlation of signs global assessment and body surface area with **(A)** Eczema Area and Severity Index, **(B)** static physician global assessment, **(C)** Itch Numeric Rating Scale, and **(D)** patient global assessment, lightly jittered to improve visibility of the distribution. *BSA*, Body surface area; *EASI*, Eczema Area and Severity Index; *iNRS*, Itch Numeric Rating Scale; *PtGA*, Patient Global Assessment; *SGA*, signs global assessment; *sPGA*, static physician global assessment.

visits 2.3 ± 1.6; median 2; range 1-10). The mean age of the cohort was 37.2 ± 17.4 years and consisted of 82 men (59.9%). The cohort was predominantly non-Hispanic white adults with moderate to severe disease (Table I).

Construct validity

We observed strong and statistically significant correlations between SGA × BSA and EASI (r = 0.911; $P < .001$; n = 19) (Fig 1, *A*). SGA × BSA also showed strong correlations with the static physician global assessment, Itch Numeric Rating Scale, and the patient global assessment (Table II and Fig 1, *B* to *D*). All correlations were greater than or equal to 0.5. SGA × BSA correlations with all the aforementioned measures were better than their correlations to either BSA or SGA alone (Table II). SGA × BSA's correlation with patient global assessment revealed a correlation coefficient less than the proposed 0.5 for the child group (<18 years) but otherwise demonstrated adequate cross-cultural validity for adults, male sex, female sex, Hispanics, and non-Hispanics (Table II).

Floor or ceiling effects

Seventeen patients (5.2%) received a minimum score of 0 and only 3 (0.9%) received a maximum score of 400. Therefore, no floor or ceiling effects were observed.

Table II. Outcome measure correlations and cross-cultural validity*

	sPGA		iNRS		PtGA	
	n	*r*	n	*r*	n	*r*
SGA × BSA	302	0.762	192	0.706	186	0.745
Age						
Child (<18 y)	37	0.682	18	0.09†,‡	15	0.458†,§
Adult	249	0.773	159	0.75	155	0.761
Sex						
Male patient	178	0.765	105	0.705	102	0.705
Female patient	123	0.75	86	0.711	83	0.782
Race						
White	193	0.769	123	0.74	120	0.802
Nonwhite	103	0.725	65	0.622	62	0.629
SGA	302	0.735	192	0.701	186	0.714
BSA	302	0.745	192	0.686	186	0.733
EASI	21	0.922	15	0.622	16	0.866

BSA, Body surface area; *EASI*, Eczema Area and Severity Index; *iNRS*, Itch Numeric Rating Scale; *PtGA*, Patient Global Assessment; *SGA*, signs global assessment; *sPGA*, static physician global assessment.
*All $P < .001$ unless denoted by †.
‡$P = .09$.
§$P = .72$.

Acceptability/ease of use

The mean time to administer the SGA × BSA was 1.5 ± 0.43 minutes (range 0.62-2.45 minutes). Comparison of administration times revealed no significant difference between adults aged 18 years or older and children (adult [n = 16] mean time 1.5 ± 0.2 minutes; children [n = 4] mean time

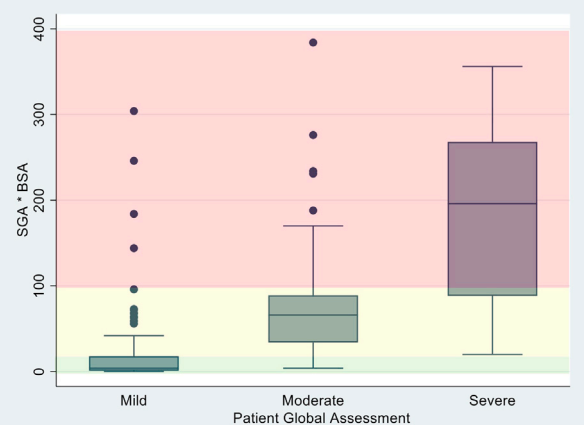

Fig 2. Severity banding. Distribution of the signs global assessment and body surface area by patient global assessment score. *BSA*, Body surface area; *SGA*, signs global assessment.

1.3 ± 0.3 minutes; $P = .30$ for t test). The subgroup of 20 patients timed for acceptability analyses consisted of an array of atopic dermatitis severity, with 1 clear patient, 3 almost clear, 4 mild, 6 moderate, and 5 severe.

Responsiveness

The mean change in patient global assessment was correlated to the mean change in SGA × BSA ($r = 0.577$).

Interpretability

The distribution of SGA × BSA scores stratified by patient global assessment scores is depicted in Fig 2. Different banding options were tested according to the mean and median patient global assessment scores per SGA × BSA, and κ coefficients of agreement were calculated for each band. Maximum agreement between patient global assessment and SGA × BSA was achieved at SGA × BSA scores of 1, 21, and 87 ($\kappa = 0.4902$) (Fig 2). Scores of 1, 20, and 100 did not significantly reduce agreement ($\kappa = 0.4902$). The analyses included 77 patients with a patient global assessment of mild, 57 moderate, and 52 severe. With the proposed aforementioned cutoffs, our cohort included 98 patients with a mild SGA × BSA score, 123 with a moderate one, and 109 with a severe one.

DISCUSSION

The results of this study suggest that the SGA × BSA correlates well with several valid and well-recognized investigator- and patient-reported outcome measures for atopic dermatitis in the outpatient setting. These results provide evidence of construct validity, or adequate correlation with other measures that one would assume a signs score should correlate with, such as itch, a patient global assessment, and more detailed signs score measures. Multiple studies in psoriasis investigating the measurement properties of physician global assessment × BSA, and a recent study by Suh et al,[11] have also demonstrated adequate validity in clinical practice.[7-11] The correlations observed in this study are consistent with that of these previous studies, further supporting the validity of the SGA × BSA. Cross-cultural validity analyses revealed that the proposed instrument correlated well with relevant groups besides children. The lack of correlation in children may be in part due to the small pediatric sample size, as well as possible lack of validity of the patient global assessment and Itch Numeric Rating Scale assessments in the pediatric population. Suh et al found that the product of Validated Investigator Global Assessment for AD, an SGA similar to the SGA that incorporates oozing/crusting rather than excoriation, and BSA demonstrated adequate validity in a strictly pediatric atopic dermatitis cohort.[11]

Although content validity was not directly assessed in this study, previous studies have suggested that several signs—including erythema, edema/papulation, and intensity of excoriations—as well as lesional intensity and extent of atopic dermatitis are very important to patients, all of which are encompassed by the SGA × BSA instrument.[1,5,6] Furthermore, the SGA × BSA's correlation with patient-reported itch and global disease severity confirms its ability to capture a measurement of disease severity important to patients. The SGA and BSA alone also demonstrated strong correlations with other measures and could potentially be used as individual assessments. The advantage of using the SGA × BSA, however, is that the instrument had better correlations with all measures compared with BSA and SGA alone, and provides more information to the provider relevant to therapeutic decision making.

The SGA × BSA was found to be acceptable regarding ease of use, with an average administration time of 1.5 minutes. The SGA × BSA also demonstrated responsiveness to change, or the ability of an instrument to detect changes over time, when the patient global assessment was used as the reference standard. Absence of floor or ceiling effects further validates that the instrument is suitable for longitudinal data collection.

This study also provides data regarding interpretability of the SGA × BSA using the patient global assessment as an anchor. Interpretability is the ability to translate a quantitative score (eg, EASI score of 14

to a qualitative meaning, eg "moderate disease"). The results of this study suggest SGA × BSA banding scores of 1, 21, and 87. We propose using the following severity strata for simplicity: 1.0 to 19.9 = mild, 20.0 to 99.99 = moderate, and 100 to 400 = severe.

Accurately measuring and recording the signs of atopic dermatitis in clinical practice has several potential benefits. Clinicians will have a more accurate assessment of disease severity that will aid in determining treatment responses and improve patient monitoring. Additionally, it would allow better documentation of the patient's disease burden, which may help in obtaining the most appropriate, patient-specific therapies. With the recent increase in drug development for atopic dermatitis and the possible emergence of costly medications, accurately documenting the skin disease burden by using both clinician- and patient-reported outcomes will become increasingly important. The Harmonising Outcome Measures in Eczema group recently identified 2 instruments that were deemed valid and feasible in clinical practice to measure the symptoms of atopic dermatitis.[14] No such recommendations have been made for measuring clinician-reported disease signs in clinical practice. Although the EASI is the preferred instrument for measuring the signs of atopic dermatitis in clinical trials, it is likely too time consuming to be used routinely in clinical practice.[3] The SGA × BSA is a quicker, more simple measurement that correlates well with the EASI, as shown by the results of this study.

Although the SGA × BSA used in this study performed well, there is a potential for variability in how the instrument is used. For example, multiple investigator global assessments exist for atopic dermatitis.[3] The SGA used in this study took into account 4 signs: erythema, papulation, lichenification, and excoriation. Some SGAs take into account only erythema and papulation, whereas other global assessments may take into account more domains than just the intensity of signs (eg, a gestalt global assessment). Additional variability may stem from how the BSA assessment is performed. In this study, we calculated a total BSA derived from regional BSA percentages. The rule of nines and using palm prints, however, are alternative valid methods for assessing BSA. It is unclear whether using different global assessments or methods of BSA calculation would change the measurement properties of this instrument. When the SGA × BSA is used in atopic dermatitis, we recommend using an SGA that takes into account the 4 most important signs of the disease multiplied by the BSA measurement method of the provider's choice.

The present study has limitations. The cohort was gathered exclusively from a tertiary care clinic setting, composed predominantly of patients with moderate to severe disease activity as determined by SGA. Our cohort, however, did include 95 patients (29.2%) in the clear, almost clear, and mild categories, which allowed for adequate analysis and validation of the instrument in groups with lower disease severity. This study lacked ethnic diversity, which may restrict its generalizability. Another limitation is the small number of patients with full EASI measurements included in analyses. Finally, interrater reliability was not assessed, given that a single investigator performed all clinical assessments used in this study's analyses. Future studies in ethnically diverse populations and including more EASI assessments are needed to further validate the instrument. Additional studies would provide opportunities to evaluate content validity and interrater reliability.

In summary, our study suggests that the SGA × BSA is a valid and feasible outcome measure to measure atopic dermatitis signs severity that may be used as a proxy for the EASI in clinical practice. The SGA × BSA demonstrated evidence of convergent validity with patient-reported outcomes, further emphasizing its utility in an actual clinical setting.

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