Product of Investigator Global Assessment and Body Surface Area (IGAxBSA): A practice-friendly alternative to the Eczema Area and Severity Index to assess atopic dermatitis severity in children

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Background: Accurately documenting pediatric atopic dermatitis (AD) severity is important, but research tools, such as Eczema Area and Severity Index (EASI), are too time consuming for clinical settings. Product of the Physician Global Assessment and affected percentage of body surface area (PGA×BSA) is a new, rapid measure of psoriasis severity.

Objective: To evaluate an Investigator Global Assessment and body surface area product (IGA×BSA) as an easy-to-use severity measure for pediatric AD.

Methods: Patient-reported and objective disease severity measures were collected from 195 caretaker/child dyads (child age range, 5-17 years) with almost clear (Validated Investigator Global Assessment for AD [vIGA] of 1) to severe (vIGA of 4) AD. Data were assessed with Spearman coefficients and plots. Severity strata were proposed by using an anchoring approach based on the EASI.

Results: IGA×BSA correlates better with the EASI than IGA alone (r = 0.924 vs r = 0.757, $P < .001$). Bland-Altman plot indicates high and consistent agreement between IGA×BSA and the EASI. Suggested severity strata for IGA×BSA are 0-30, mild; 30.1-130, moderate; and 130.1-400, severe (κ = 0.760).

Limitations: The patient cohort was predominantly from the midwestern United States.

Conclusions: IGA×BSA (using the vIGA) is a simple measure that correlates well with the EASI in patients with mild to severe pediatric AD. Future work is needed to affirm reliability across IGA scales and responsiveness to change. (J Am Acad Dermatol 2020;82:1187-94.)

Key words: adolescent; disease severity; eczema; pediatric; pruritus; quality of life.

Disease severity assessment is important in directing treatment choices in atopic dermatitis (AD). Recommendations and guidelines emphasize disease severity assessment as the basis for increasing therapy potency.[1] The Eczema Area and Severity Index (EASI)[2] and Scoring

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Atopic Dermatitis (SCORAD)[3] tools have been recommended as core physician-based outcome measures for assessing severity in trials, but they are complicated, time consuming, and unsuited for clinical use in a busy office practice.[4] The Investigator Global Assessment (IGA) offers a rapid severity assessment that maps to easy-to-understand terms (clear, almost clear, mild, moderate, and severe) and is thus easily interpreted by both clinicians and patients. It also serves as the primary endpoint required by the US Food and Drug Administration for new drug approval trials[5] and has recently been validated.[6,7] However, the IGA does not include extent of disease (percentage of body surface area [BSA] affected) and, as a result, fails to capture an important aspect of severity captured by other disease measures.[8]

CAPSULE SUMMARY

- Atopic dermatitis severity measures for clinical research are time consuming, but simple measures (Global Assessment and body surface area) are incomplete and complementary.
- The product of Investigator Global Assessment and body surface area provides a rapid office-based severity measurement of pediatric atopic dermatitis that compares well with more cumbersome assessments.

PGA×BSA, the multiplied product of the Physician Global Assessment (PGA) and BSA is an emerging disease severity measure in psoriasis that is simpler and more intuitive than the Psoriasis Area and Severity Index (PASI), the most commonly used measure of psoriasis severity.[9-13] PGA×BSA is strongly correlated with the PASI and similarly able to capture changes in disease severity, and it is more sensitive than the PASI in patients with mild disease (BSA < 10%).[9-12] As such, PGA×BSA is being touted as a potential alternative for the PASI in clinical practice.[14,15] A similar measure for pediatric AD has yet to be evaluated.

Given that the IGA is a simple tool required by the US Food and Drug Administration for studies but is limited by its failure to include the extent of involvement (as encompassed by BSA) in determining severity, we hypothesized that IGA×BSA would perform similarly well to the EASI in evaluating disease severity of AD in children, the largest affected group.

METHODS

Primary caretaker/child dyads were recruited at the Ann and Robert H. Lurie Children's Hospital of Chicago (LCH) allergy and dermatology clinics, as well as from the National Eczema Association's Eczema Expo in Chicago, Illinois, from June 21 through 24, 2018. Parents and children 12 years of age and older provided written informed consent and assent, respectively, after study approval by the Ann and Robert H. Lurie Children's Hospital of Chicago institutional review board. Inclusion criteria included children ages 5 through 17 years old with active AD of any severity (dyads for ages 8 years and older; parent proxy for children 5 to <8 years old). The patients and enrolled caretaker had to speak English. Exclusion criteria included a developmental delay and/or a behavioral disorder that would preclude the ability to complete the assessment tools.

Assessments

At the 1-time visit for this study, demographics, medical information, disease severity measures, and patient-reported outcomes were captured. Patients and caretakers were allowed to complete questionnaires online within 48 to 72 hours if not finished at the visit. The selected IGA tool was the recent Validated Investigator Global Assessment for AD (vIGA-AD) with descriptors to help standardize the assessed severity of erythema, induration/papulation, lichenification, oozing/crusting at each grade of severity (clear: IGA, 0; almost clear: IGA, 1; mild: IGA, 2; moderate: IGA, 3; and severe: IGA, 4).[6,7] In addition to our choice to use an IGA scale, rather than a PGA (which is nonstandardized), we selected the new vIGA because it was generated by experts in AD management assessment and is increasingly used in clinical trials. BSA was estimated based on the rule of nines[16] and/or the palmar rule.[17] Parent/child dyads or 1 parent by proxy (if the child was younger than 8 years) completed questionnaires for disease severity (Patient-Oriented Eczema Measure (POEM),[18] quality of life (Children's Dermatology Life Quality Index [CDLQI] if 16 years or younger; Dermatology Life Quality Index [DLQI] if older than 16 years),[19] and an itch questionnaire (Average Pruritus Numerical Rating Scale [NRS]: *Please rate the average itch severity due to your atopic dermatitis in the past 7 days*, with 0 being *no itch* and 10 being *worst imaginable itch*).[20] To be able to include results from children 5 years of age and older and have a consistent source, only parent/caretaker responses were analyzed. Other physician assessments included the EASI,[21] BSA, and SCORAD.[22,23] The objective SCORAD (oSCORAD) was calculated by subtracting the scores for the

Abbreviations used:

AD:	atopic dermatitis
BSA:	body surface area
CDLQI:	Children's Dermatology Life Quality Index
DLQI:	Dermatology Life Quality Index
EASI:	Eczema Area and Severity Index
IGA:	Investigator Global Assessment
IGA×BSA:	product of Investigator Global Assessment and body surface area
NRS:	numerical rating scale
oSCORAD:	objective Scoring Atopic Dermatitis
PASI:	Psoriasis Area and Severity Index
PGA:	Physician Global Assessment
PGA×BSA:	Product of Physician Global Assessment and body surface area
POEM:	Patient-Oriented Eczema Measure
SCORAD:	Scoring Atopic Dermatitis
vIGA:	Validated Investigator Global Assessment for Atopic Dermatitis

subjective symptoms, pruritus and sleep loss, from the total SCORAD.[24]

Statistical analysis

The EASI was the reference measure for comparisons across different measures. Means and standard deviations were provided for key demographic data and measures of interest. Spearman rank correlation coefficients were calculated to compare AD disease measures of interest (IGA×BSA, IGA, BSA, EASI, oSCORAD, SCORAD, POEM, Average Pruritus NRS, and CDLQI) and to assess by hypothesis testing the construct validity of IGA×BSA with other currently used assessments, particularly the EASI. We hypothesized that IGA×BSA would correlate more strongly with the EASI than either IGA or BSA alone with the EASI. The Steiger *Z* test was used to compare the significance of the difference between 2 related correlation coefficients with a common variable.[25,26] Scatterplot and Bland-Altman plots were used to compare IGA×BSA with the EASI. Although IGA×BSA scores range from 0 to 400, for purposes of statistical analysis,[10] we rescaled by a constant factor of 5.556 to compare this measure with the EASI scale (range, 0-72). The Bland-Altman plot was constructed by plotting the difference between the EASI and rescaled IGA×BSA against the mean of the 2 measures.[27] Statistical analysis was performed with SPSS for Windows, version 25.0 (IBM, Armonk, NY). A 1-sided *P* value of less than .05 was considered significant.

Anchor-based severity strata

An anchor-based approach to severity strata was applied to IGA×BSA, with the EASI as the anchor variable, similar to previous studies that determined strata for other severity measures.[18,28,29] The mean, median, and mode of the EASI score were determined for each potential threshold point of IGA×BSA. The nonscaled scores of IGA×BSA have a wide range of values (range, 0-400), so increments of 5 were used between the possible threshold points. Once possible threshold values were determined, a kappa coefficient of agreement was calculated to determine which IGA×BSA threshold values had the highest coefficient of agreement with EASI strata. In this study, a score of 1 on IGA (almost clear, n = 7) was included in the mild severity strata.

RESULTS

Participant characteristics

Participant characteristics stratified by EASI severity are shown in Table I. Overall, 195 children were enrolled, including 23.6% with mild, 48.7% with moderate, and 27.7% with severe disease. The mean ± standard deviation age of participants was 10.3 ± 3.5 years, with 41.5% male, and these characteristics were not significantly different across severity strata. Poorer quality of life, based on CDLQI (or DLQI for those older than 16 years [n = 6]), correlated with worsening disease severity (CDLQI/DLQI vs IGA×BSA: r = 0.354, $P < .001$, n = 195). The percentage of patients with a "very large effect" (CDLQI ≥ 13)[30] on their quality of life increased from 10% in patients with mild disease to 29% in those with moderate and 43% in those with severe disease.

Correlation of IGA×BSA with other disease severity measures

Fig 1 displays a heatmap of correlations between various measures of pediatric AD severity and quality of life. In comparing the IGA×BSA with other disease severity assessments, we found very strong correlations with the more cumbersome EASI and SCORAD severity measures. IGA×BSA correlated significantly more strongly with the EASI than IGA (vIGA-AD) alone with the EASI (r = 0.924 vs r = 0.757; $P < .001$, as evaluated by Steiger *Z* test).[26] IGA×BSA correlated almost as well with the physician-assessed oSCORAD (r = 0.77, $P < .001$) and SCORAD (r = 0.774, $P < .001$) and comparably with the EASI and these measures (r = 0.780 and r = 0.779, $P < .001$, respectively). Correlations with the POEM (r = 0.449, $P < .001$), Average Pruritus NRS (r = 0.332, $P < .001$), and CDLQI (r = 0.354, $P < .001$) were significant but not as strong. There were no significant differences in correlations between IGA×BSA and POEM, IGA×BSA and Average Pruritus NRS, or IGA×BSA and CDLQI between proxy-reported and patient

Table I. Participant characteristics*

Characteristics	Total participants	Disease severity by EASI		
		Mild (≤7)	Moderate (7.1-21)	Severe (>21)
Size of group, n	195	46	95	54
Male sex, n (%)	81 (41.5)	14 (30.4)	44 (46.3)	23 (42.6)
Age in years at enrollment, mean (SD)	10.3 (3.5)	10.5 (3.7)	10.3 (3.5)	10.1 (3.5)
Hispanic ethnicity, n (%)	43 (22.1)	14 (30.4)	17 (17.9)	12 (22.2)
Race, n (%)				
White alone	74 (37.9)	17 (37.0)	37 (38.9)	20 (37.0)
Black alone	44 (22.6)	9 (19.6)	26 (27.4)	9 (16.7)
Asian alone	36 (18.5)	7 (15.2)	18 (18.9)	11 (20.4)
Other	41 (21.0)	13 (28.3)	14 (14.7)	14 (25.9)
Highest level of parent's education, n (%)				
Less than high school	14 (6.7)	5 (10.9)	7 (6.4)	2 (3.7)
High school graduate	31 (16.0)	7 (15.2)	13 (13.8)	11 (20.4)
Some college	31 (16.0)	7 (15.2)	19 (20.2)	5 (9.3)
College graduate	73 (37.6)	18 (39.1)	33 (35.1)	22 (40.7)
Graduate school	46 (23.7)	9 (19.6)	23 (24.5)	14 (25.9)
IGA, mean (SD)*	3.0 (.75)	2.1 (.64)	3.0 (.47)	3.6 (.53)
oSCORAD, mean (SD)*	37.4 (15.4)	21.8 (10.0)	36.8 (10.4)	51.7 (13.2)
SCORAD, mean (SD)*	47.0 (18.2)	27.7 (11.1)	46.5 (11.6)	64.3 (15.3)
POEM, mean (SD)*	14.5 (7.3)	9.6 (6.2)	14.5 (6.5)	18.6 (7.1)
Average pruritus NRS, mean (SD)*	5.4 (2.7)	3.7 (2.4)	5.6 (2.8)	6.5 (2.3)
CDLQI score, mean (SD)*	9.5 (7.2)	6.2 (5.5)	9.2 (6.6)	13.0 (8.0)
IGA×BSA, mean (SD)*	92.2 (80.3)	16.0 (12.1)	74.4 (33.8)	188.5 (79.9)

BSA, Body surface area; *CDLQI*, Children's Dermatology Life Quality Index; *EASI*, Eczema Area and Severity Index; *IGA*, Investigator Global Assessment; *IGA×BSA*, product of Investigator Global Assessment and body surface area; *NRS*, numeric rating scale; *oSCORAD*, objective Scoring Atopic Dermatitis; *POEM*, Patient-Oriented Eczema Measure; *SCORAD*, Scoring Atopic Dermatitis; *SD*, standard deviation.
**P* values of characteristics in bold are statistically significant ($P < .001$).

(≥8 years old)-reported outcomes (Steiger Z tests: $P = .613$, $P = .438$, and $P = .729$, respectively).

When visually represented (Fig 2), the association between an adjusted IGA×BSA and the EASI appears strong, because most data points are clustered around the diagonal line of agreement. However, as disease severity increases, there is a slight tendency for IGA×BSA to overestimate the severity compared with the EASI. Bland-Altman plots show a slight trend of points falling below the 95% confidence band as the mean severity scores increased, but most data points fell within the 95% confidence band, with the mean difference value (0.077 ± 11.891) near 0, indicating that the 2 measures have strong agreement, with no discernible bias toward one measure or the other (Fig 3).

Proposed disease severity strata for IGA×BSA

Using the anchor-based approach, possible thresholds of IGA×BSA were determined by observing when the mean, median, and mode EASI score corresponded with the EASI threshold values (mild/moderate, 7; moderate/severe, 21).[25] Potential mild/moderate (25, 30, 35) and moderate/severe (125, 130, 135) threshold values were identified. An IGA×BSA severity strata of mild, 0 to 30; moderate, 30.1 to 130; and severe, 130.1 to 400 had the highest kappa coefficient ($\kappa = 0.760$, $P < .001$) (Table II). As such, these proposed severity strata for IGA×BSA have much greater agreement than the previously established IGA severity strata with EASI severity strata ($\kappa = 0.546$, $P < .001$).[6,25]

DISCUSSION

We examined the accuracy of IGA×BSA in determining the severity of AD, using the EASI score as the standard for accuracy, and also compared IGA×BSA with other widely used research severity measures (SCORAD, oSCORAD, and POEM). IGA×BSA can be performed quickly in the busy office setting, in contrast to time-consuming severity measures, such as the EASI and SCORAD. IGA×BSA had a significantly stronger correlation with EASI than IGA alone. This relationship remained consistent across increasing severity, as evidenced by the scatterplot and Bland-Altman plot.

In this study, both the rule of nines and the palmar method were used to estimate BSA; we found that the quicker method of the palmar rule is similarly accurate and easier to perform in clinical practice for more localized disease (1 full palmar area of the patient, including fingers = 1% of BSA).[17] Rather

	IGA×BSA	IGA	BSA	EASI	oSCORAD	SCORAD	POEM (proxy)	POEM (child)†	Average pruritus NRS (proxy)	Average pruritus NRS (child)†	CDLQI (proxy)	CDLQI (child)†
IGA×BSA		0.821	0.984	0.924	0.775	0.774	0.449	0.417	0.332	0.388	0.354	0.327
IGA	0.821		0.72	0.757	0.711	0.736	0.445	0.38	0.43	0.428	0.39	0.29
BSA	0.984	0.72		0.914	0.741	0.735	0.42	0.405	0.285	0.371	0.322	0.328
EASI	0.924	0.757	0.914		0.78	0.779	0.426	0.452	0.313	0.415	0.347	0.36
oSCORAD	0.775	0.711	0.741	0.78		0.964	0.387	0.413	0.268	0.321	0.32	0.272
SCORAD	0.774	0.711	0.735	0.78	0.964		0.477	0.526	0.414	0.445	0.392	0.383
POEM (proxy)	0.449	0.445	0.42	0.426	0.387	0.477		0.649	0.5	0.649	0.651	0.5
POEM (child)†	0.417	0.38	0.405	0.452	0.413	0.526	0.649		0.46	0.507	0.634	0.716
Average pruritus NRS (Proxy)	0.332	0.43	0.285	0.313	0.268	0.414	0.5	0.46		0.575	0.411	0.612
Average pruritus NRS (Child)*	0.388	0.428	0.371	0.415	0.321	0.445	0.649	0.716	0.575		0.645	0.455
CDLQI (proxy)	0.354	0.39	0.322	0.347	0.32	0.392	0.651	0.634	0.411	0.645		0.513
CDLQI (child)†	0.327	0.29	0.328	0.36	0.272	0.383	0.5	0.507	0.612	0.455	0.513	

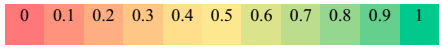

Fig 1. Heatmap of correlation coefficients (Spearman rho) between disease measures. *All correlations have *P* values < .001. N = 195, unless noted. †n = 140. *BSA*, Body surface area; *CDLQI*, Children's Dermatology Life Quality Index; *EASI*, Eczema Area and Severity Index; *IGA*, Investigator Global Assessment; *IGA×BSA*, product of Investigator Global Assessment and body surface area; *NRS*, numeric rating scale; *oSCORAD*, objective Scoring Atopic Dermatitis; *POEM*, Patient-Oriented Eczema Measure; *SCORAD*, Scoring Atopic Dermatitis.

than using a gestalt physician-performed global assessment without standardization, we used the vIGA,[6] which was recently been developed by experts in AD and is available through the International Eczema Council website.[7] This easy 5-point scale has specific morphologic descriptors and strong interrater and intrarater reliability. Because we wanted to include children as young as 5 years to less than 8 years old, for whom there was only parent proxy available, we decided to use parent-reported outcomes for children of all ages. We found no significant difference in correlations of patient-reported outcomes and IGA×BSA versus caretaker-reported outcomes and IGA×BSA.

Based on our cohort, we were able to stratify IGA×BSA into severity scores as mild (0-30), moderate (30.1-130), and severe (130.1-400), and these strata had higher agreement with current EASI strata than IGA alone. As such, disease severity strata

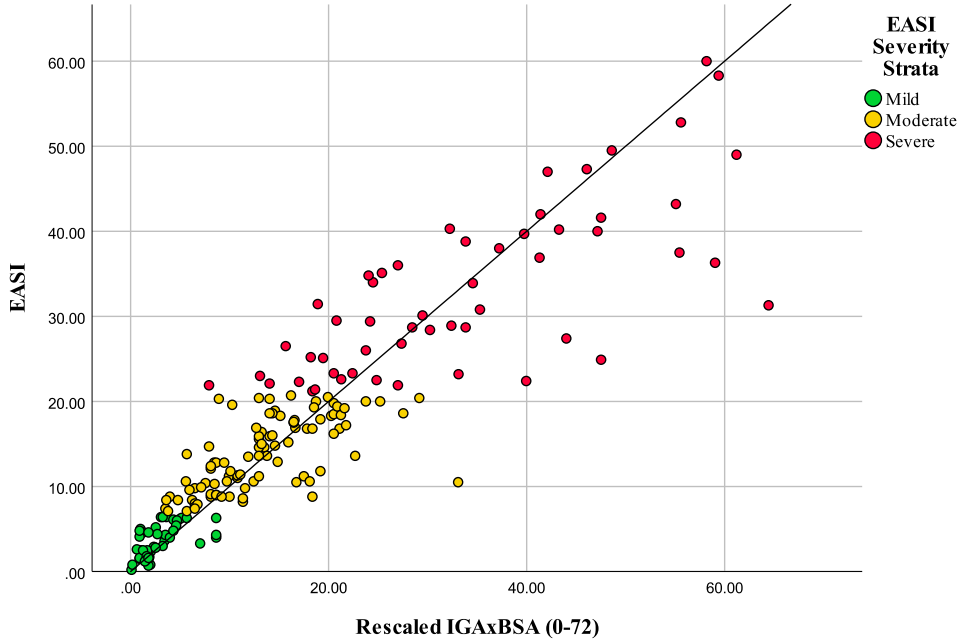

Fig 2. Scatterplot of the rescaled IGA×BSA (range, 0-72) and EASI. The IGA×BSA was rescaled from 0 through 400 to 0 through 72 to be able to compare it with the EASI (range, 0-72). This allowed a diagonal line of agreement to be drawn on the scatterplot to observe the trend for IGA×BSA to overestimate or underestimate the EASI. *EASI*, The Eczema Area and Severity Index; *IGA×BSA*, product of Investigator Global Assessment and body surface area.

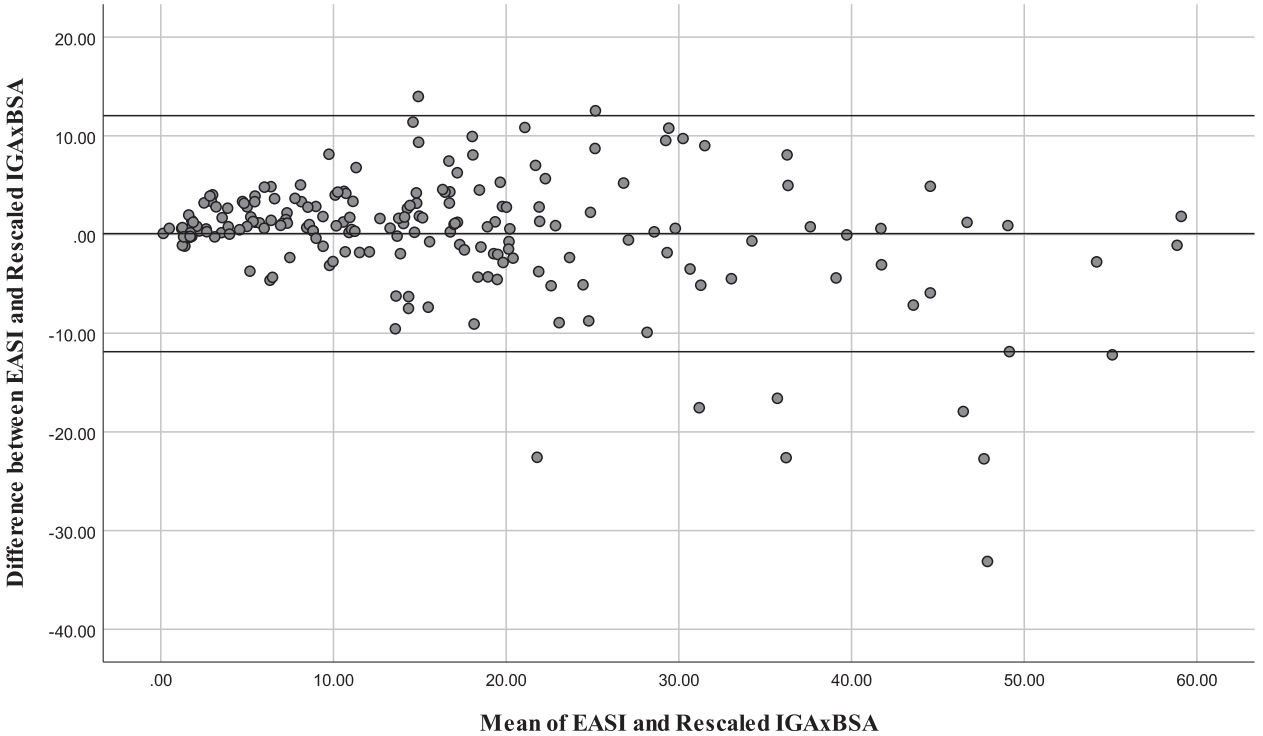

Fig 3. Bland-Altman plot of the rescaled IGA×BSA (0-72) and EASI. The IGA×BSA was rescaled from 0 through 400 to 0 through 72 to be able to compare it with the EASI (range, 0-72). Horizontal lines are drawn to denote the mean difference and 95% limit of agreement (the mean difference ± 1.96 × standard deviation). Good agreement is indicated by the low mean differences (closer to 0), low dispersion around the mean difference (largely within the dotted lines), and lack of correlation between the mean (*x*-axis) and difference between the measures (*y*-axis), as shown by the horizontal spread of data. *EASI*, The Eczema Area and Severity Index; *IGA×BSA*, product of Investigator Global Assessment and body surface area.

Table II. Proposed IGA×BSA strata (bolded) with the EASI as anchor variable

IGA×BSA strata			*Kappa* coefficient of agreement	*P*
Mild	**Moderate**	**Severe**		
0-25	25.1-125	125.1-400	0.725	<.001
0-25	25.1-130	130.1-400	0.733	<.001
0-25	25.1-135	135.1-400	0.714	<.001
0-30	**30.1-130**	**130.1-400**	**0.760**	**<.001**
0-35	35.1-130	130.1-400	0.731	<.001

EASI, Eczema Area and Severity Index; *IGA×BSA*, product of Investigator Global Assessment and body surface area.

using IGA×BSA may be useful in clinical practice to direct disease-appropriate therapy. The range of values in IGA×BSA allows for more interpretation within each severity category as well. This may be most important in patients with milder disease, in whom increases in BSA extent have been associated with higher patient-reported severity.[31]

IGA×BSA also correlates with other AD severity measures, including oSCORAD, SCORAD, and POEM. As expected, IGA×BSA (with its 2 objective signs) more strongly correlates with measures that include objective clinical signs, such as oSCORAD and SCORAD, than with patient-reported outcomes such as the POEM and Average Pruritus NRS (low to moderate correlation), because the extent of sleep loss and itch (2 of the 7 questions in the POEM) are well recognized to be distinct in some patients from their extent and intensity of disease.[32,33] In addition, patient-reported outcomes may be subject to coping strategies, comorbidities, and impact on quality of life.[3,34] Objective measures also showed low to moderate correlation with the CDLQI. Only the POEM showed moderate to strong correlation with the CDLQI, highlighting the ability of patient-reported measures to include the personal impacts on quality of life beyond the observable clinical presentation. In addition, the stronger correlation likely reflects the overlap in instrument items, such as itch and sleep loss measures, in both the POEM and CDLQI.

A limitation of our study was the predominantly midwestern US cohort, which included racial and economic diversity but not geographic diversity. Another potential limitation of the scale is its greater sensitivity to change in disease extent than either IGA or the EASI alone, given the broad spectrum of BSA (0%-100% vs 0-4 for IGA), which may have contributed to the slight overestimation compared with the EASI score. Finally, the vIGA-AD considers extent in determining severe disease or borderline cases, which may lead IGA×BSA using vIGA-AD, in contrast to other scales with no extent among descriptors, to overestimate severity. Future studies will test IGA×BSA by using a different IGA scale that includes no extent in its descriptors and will evaluate the reliability and responsiveness of IGA×BSA through assessing children during disease flares and improvement, including during a clinical trial.

In conclusion, our data support the use of IGA×BSA as a quick and easy-to-interpret alternative to the EASI in clinical practice and possibly even in clinical research trials. IGA×BSA is also able to capture differences in extent within severity groups better than the EASI with its strata of extent. Suggested severity strata for IGA×BSA indicate high agreement with currently accepted mild, moderate, and severe categories in the EASI. Because justification of severity will likely be required for prescribing new therapeutic agents for moderate to severe disease, we recommend institution of the IGA×BSA for routine assessment and monitoring of pediatric patients with AD.

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