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**What the EASI score tells us about the severity of atopic dermatitis - an interpretability
study**

Running head: EASI score

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What's already known about this topic?

- The Eczema Area and Severity index (EASI) is one of the best validated outcome instruments for atopic dermatitis.

What does this study add?

- The severity of atopic dermatitis can now be interpreted from the EASI numerical score.
- The EASI takes a short time to administer.
- Our study supports the use of EASI as an outcome tool in clinical trials by providing the first guide for interpreting the score and confirming its ease of use.

Abstract

Background: The EASI (Eczema Area and Severity Index) is an investigator-assessed instrument measuring the severity of clinical signs in atopic dermatitis (AD). The EASI was identified as one of the best validated outcome measures for AD; however, no previous studies address how to interpret the EASI score for clinical use.

Objectives: To evaluate the interpretability and the ease of use of the EASI.

Methods: A retrospective analysis of pediatric and adult patients with AD was performed. Interpretability was evaluated by stratifying the EASI scores according to the Investigator's Global Assessment. The severity strata displaying the highest kappa coefficient of agreement were then selected as the recommended EASI band. The time to administer the EASI was recorded in a subgroup of patients.

Results: The suggested severity strata for the EASI are: 0=clear; 0.1-1=almost clear; 1.1-7=mild; 7.1-21=moderate; 21.1-50=severe; 50.1-72=very severe, $\kappa = 0.75$. The EASI was also found to be acceptable in terms of ease of use, with assessments by trained investigators taking approximately six minutes.

Conclusions: Our study provides the first guide for interpreting the EASI score. It enables translation of the EASI numerical output into an AD global severity state that should be more meaningful to providers and patients. Along with a short administration time, the EASI demonstrates adequate feasibility, further supporting its use in clinical trials.

Introduction

The EASI (Eczema Area and Severity Index) is an investigator-assessed instrument measuring the severity of clinical signs in atopic dermatitis (AD). The EASI was developed in 1998 based upon the PASI (Psoriasis Area and Severity Index) scoring system used in psoriasis.¹ While there are over 25 named instruments for measuring the severity of AD, the EASI was identified as one of the three best validated outcome measures for AD.² Most recently, the EASI was chosen by the international Harmonizing Outcomes Measures in Eczema (HOME) group as one of four instruments to be included in an AD clinical trial core outcome set after an extensive systematic evaluation of its measurement properties.^{3,4}

Validation studies confirm the EASI displays adequate reliability, validity, and responsiveness – key performance properties needed for any outcome instrument.⁵

However, some important instrument properties have not been formally studied for the EASI. For example, data regarding how a clinician would translate an EASI score into clinically meaningful information is not available – a measurement property termed *interpretability*. Additionally, no studies have addressed the ease of use (acceptability) which refers to the practicalities of usage – time to administer, cost, and additional tools required for applying

the instrument. Finally, the floor and ceiling effects have not been assessed for the EASI, which evaluates whether scores are skewed to the extreme ends of the scale. The objectives of this project were to study the interpretability and acceptability of the EASI instrument and to assess for floor and ceiling effects.

Materials and Methods

Study Design

This is a retrospective study of pediatric and adult patients with AD defined according to the Hanifin and Rajka criteria.⁶ Subjects seen in the Department of Dermatology at Oregon Health & Science University (OHSU) between 4/2013-3/2014 were identified through an electronic medical record search with the diagnosis of Atopic Dermatitis (691.8). Only patients who had documentation of both the Investigator Global Assessment (IGA) and EASI scores at the same encounter were included. At least one of the four authors, all dermatologists, performed both IGA and EASI scoring per patient in a single visit. JMH trained all other authors on the administration of the scales. The time it took to administer the EASI was recorded for a subset of patients. No criteria have been defined for the required sample size of studies assessing measurement properties, although at least 50 patients have been suggested.⁷ We estimated that a minimum of 100 questionnaires would be needed to accurately categorize the EASI scores into six bands.

The following parameters were assessed:

- 1. Interpretability** was evaluated by stratifying the EASI against the IGA acting as a severity anchor,^{8,9} based on a previous study.¹⁰ In an anchor-based approach the measure to be interpreted is compared, or anchored, to a global assessment performed at the same time. The score is then stratified using numerical cut-offs into the severity bands represented by the global score. As a global severity score we used the IGA which

evaluates the overall severity of AD at a given time in a static fashion - assessing only the current disease severity regardless of the disease course or the severity in previous encounters. In our clinic it is performed as a rapid, global evaluation of severity that takes into account all aspects of the disease. This is a gestalt assessment that is assessed separately from the EASI, thus can be used as an independent anchor. In our clinic the IGA consists of a six-point scale, ranging from clear (0) to very severe AD (5) (see Table 1). Interpretability assessment was performed in accordance with the Consensus-based Standards for the Selection of Health Measurement Instruments (COSMIN) guidelines.¹¹

- 2. Acceptability/ease of use** was considered adequate if the mean time to administer the EASI was under 7 minutes.³
- 3. Floor and ceiling effects** were rated as adequate (i.e., absent) if $\leq 15\%$ of the respondents achieved the lowest or highest possible score.³

Approval for the study was given by the OHSU Institutional Review Board.

Data processing and statistical analysis

Data were analyzed using Stata statistical software (StataCorp 2013, College Station, TX: StataCorp LP). The distribution of each of the score variables was summarized using means and standard deviations. Medians and ranges were also computed. Associations were assessed by the *t*-test and ANOVA for the EASI, and by non-parametric methods for the IGA.

For each EASI score (0-72), the corresponding mean and median IGA scores were calculated and tabulated. All of the EASI scores which corresponded to a one-step increase in mean or median IGA were considered possible cut-off values. For each different combination of

possible cutoff EASI values (i.e. a band) the kappa (k) coefficient of agreement was calculated.

Results

A total of 170 AD patients were included in the study. The majority of the participants were non-Hispanic Caucasian adults, though children (0 to 16 years) represented a third of the patient population.

The distribution of EASI and IGA scores are shown in Table 1, with a trend towards higher EASI and IGA scores in males. No significant differences in EASI or IGA scores were noted between children and adults, different ethnicities or races. The Spearman rank correlation coefficient showed a strong and highly statistically significant correlation between EASI scores and the IGA ($r = 0.91$, $p < 0.0001$), which were not affected by age, gender, ethnicity or race.

Interpretability

The distribution of the EASI scores stratified by IGA scores is depicted in Fig. 1. Based on the mean and median IGA per EASI score, different banding options were suggested and Kappa coefficients of agreement were calculated for each band (Table 2). The first banding option had the highest kappa and was selected as the final severity band.

Subgroup analysis

Overview of EASI scores falling outside the proposed banding: No patients showed an IGA score > 1 points outside of that predicted by the final EASI severity band. There were 10 patients (6%) whose actual IGA score was one point lower than the final severity band would have predicted from their EASI score. There were 21 patients (12%) whose actual

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IGA score was one point higher than the final severity band would have predicted. The patients falling outside the suggested banding had a similar distribution of gender, age, race and ethnicity as the original study population.

Accessibility/ease of use: In a subgroup of 32 patients, the time it took to administer the EASI was recorded in a prospective fashion, with a mean of six minutes (SD 4.5 minutes, range 2-20 minutes). There were no significant differences in administration times between adults ≥ 16 years and children (adults, $n=23$, mean time 5.6 ± 0.6 minutes; children, $n=9$, mean time 7.7 ± 2.3 minutes; $p=0.24$ for t -test). There were no significant differences in administration times between ethnicities (Hispanics, $n=9$, mean time 6 ± 1.8 minutes; non-Hispanics, $n=20$, mean time 5.4 ± 0.7 minutes; $p=0.72$ for t -test) or between different races ($p=0.67$ for F test).

Floor/ceiling effects: Only three patients (1.8%) received an EASI score of 0, while none received an EASI score of 72, therefore no floor or ceiling effects were demonstrated.

Discussion

This study provides the first data regarding interpretability of the EASI instrument using the IGA as an anchor. While EASI scores provide valid and reliable numerical data on the severity of clinical signs, until now the clinical significance of a particular EASI score was not readily apparent. With the increased use of this outcome measure in AD trials, data from this study will assist clinicians in interpreting clinical trial results.

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The suggested severity strata for the EASI are as follows: 0=clear; 0.1-1=almost clear; 1.1-7=mild; 7.1-21=moderate; 21.1-50=severe; 50.1-72=very severe. As can be seen from the selected banding, the distribution of severity scores across strata is not equal. The range of EASI scores becomes larger as the IGA increases. This is consistent with the findings of a previous study examining the minimal clinically important difference of the EASI.¹² In that study, a one-point improvement in the IGA correlated with an overall mean decrease in the EASI of 6.6 points. However, this decrease was uneven across the severity scores, ranging from a mean one-point change in the EASI to improve the IGA in the low severity levels to a mean 8.6 change in the EASI to improve the IGA in patients with severe disease. This skewing of the severity strata may reflect the non-linear relationship between disease extent and perceived severity found in previous studies.¹³ Thus changes in EASI score at the lower end of the scale are slightly more clinically significant than at the higher end of the scale.

The proposed interpretation of EASI scores into global assessments functions primarily as a general guide. While there was substantial agreement between the observed global severity compared to that predicted by our banding, there still remained patients whose global assessment fell outside of that predicted by our banding. Specifically, there were 31 patients (18%) whose IGA scores differed from the IGA predicted by their EASI score. These outliers were no different in any demographic variables when compared to the patients whose EASI score did accurately predict the IGA. These outliers likely reflect the additional factors that determine overall disease severity that reside outside of clinical signs (and thus not captured by the EASI score) such as pruritus, involvement of high visibility areas, and impact on quality of life. Nevertheless, the suggested banding allows for a useful interpretation of an EASI score given the obvious limitations.

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The EASI was also found to be acceptable³ in terms of ease of use with assessments by trained investigators taking approximately six minutes. The EASI does not require special instruments and is free of charge. An unrestricted EASI training module for investigators could be beneficial in future clinical trials to enhance uniformity in scoring. Further standardized instructions for implementing the EASI in various skin types is under development.

One limitation of our study is that the study population was comprised of patients with limited ethnic diversity, potentially restricting its generalizability. Future studies on more diverse populations are needed to test the general applicability of this banding. Another limitation is the recruitment of subjects from a tertiary care clinic setting, which could lead to an over-representation of moderate to severe AD patients. However, a third of our patient population had an IGA of either mild or almost clear, allowing for adequate analysis of the lower severity strata. Inter-rater variability between the investigators was a concern, therefore all were trained extensively on performing the scoring process in a similar manner to minimize variability in outcomes.

In summary, our study serves to better characterize the performance characteristics of the EASI outcome measure. Previous studies found that the EASI met many of the requirements put forth by the COSMIN group.⁷ Our study further supports the use of EASI by providing the first guide for interpreting the score and confirming its ease of use and lack of floor and ceiling effects.

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Figure Legends

Figure 1. Distribution of EASI by IGA scores

Table 1. Distribution of EASI and IGA scores overall and by demographics

		N	EASI			IGA**		
			Mean (SD)	Median (IQR)	P	Mean (SD)	Median (IQR)	P
All patients		170	15.2 (15.7)	9.1 (4.6-22.8)		2.9 (1.1)	3 (2-4)	
Gender	Female	92	13.3 (14.9)	8.2 (4.4-17.4)	0.08	2.8 (1.0)	3 (2-3)	0.09
	Male	78	17.5 (16.4)	11.1 (5.7-28.6)		3.0 (1.2)	3 (2-4)	
Age	Child <16 years	54	12.8 (13.9)	7.85 (3.8-16.4)	0.17	2.6 (1.1)	3 (2-3)	0.12
	Adult	116	16.4 (16.4)	10.2 (5.1-23)		3.0 (1.0)	3 (2-4)	
Ethnicity	Non-Hispanic	104	15.2(16)	8.8 (4.2-21.8)	0.72	2.8 (1.1)	3 (2-3.5)	0.92
	Hispanic	32	16.3 (15.6)	10.5 (5.4-23.5)		2.8 (1.1)	3 (2-3.5)	
	Not provided	34	14.4 (15.1)	9.1 (4.9-17.4)		3.0 (1.0)	3 (2-4)	
Race	White	106	15.9 (16.6)	9.2 (4.6-22.9)	0.54	2.9 (1.1)	2 (2-4)	0.34
	Asian	19	11.8 (11.6)	8 (2.2-18.8)		2.4 (1.2)	3 (2-3)	
	Other*	11	17.1 (16.0)	11.8 (5.6-23.4)		3.1 (0.8)	3 (3-3)	
	Not provided	34	14.4 (15.1)	9.1 (4.9-17.4)		3.0 (1.0)	3 (2-4)	

EASI - Eczema Area and Severity index; IGA – Investigator’s global assessment; IQR - interquartile range; SD – standard deviation.

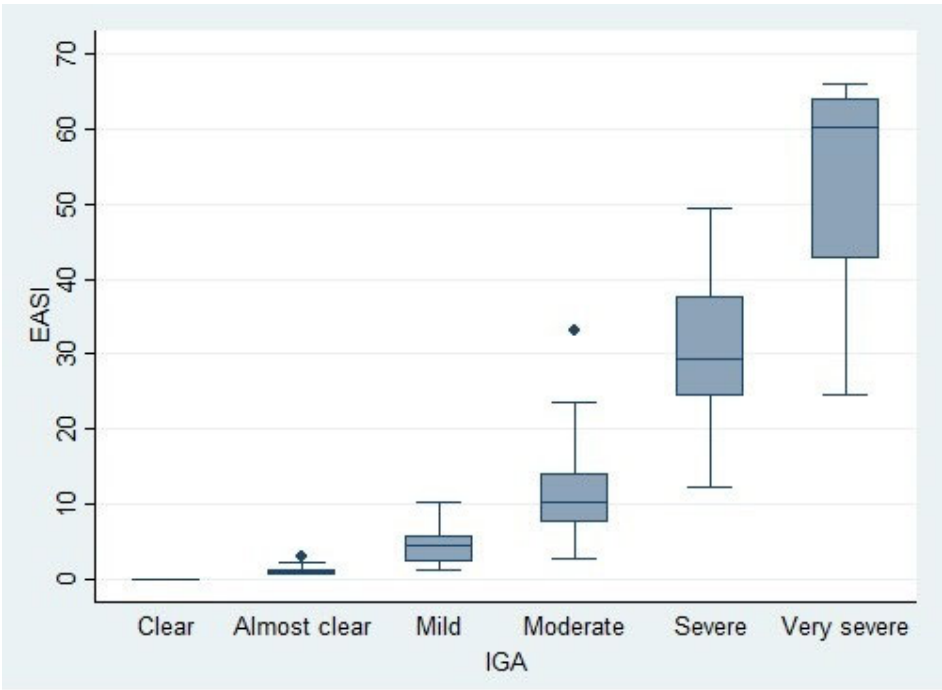
*Multiracial n=9; African-American n=1; Indian-American n=1.

**IGA: 0 = clear; 1 = almost clear; 2 = mild; 3 = moderate; 4 = severe; 5 = very severe

Table 2. Kappa coefficients of agreement for different proposed sets of EASI severity bands

Possible EASI bandings						K coefficient of agreement
Clear	Almost clear	Mild	Moderate	Severe	Very severe	IGA
0	0.1-1	1.1-7	7.1-21	21.1-50	50.1-72	0.75, p<0.0001
0	0.1-1	1.1-6	6.1-21	21.1-50	50.1-72	0.74, p<0.0001
0	0.1-1	1.1-7	7.1-20	20.1-50	50.1-72	0.74, p<0.0001
0	0.1-1	1.1-6	6.1-20	20.1-50	50.1-72	0.73 p<0.0001

EASI – Eczema Area and Severity index; IGA – Investigator’s global assessment.



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