

The Self-Administered Eczema Area and Severity Index in Children with Moderate to Severe Atopic Dermatitis: Better Estimation of AD Body Surface Area Than Severity

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Abstract: The Self-Administered Eczema Area and Severity Index (SA-EASI) is one of the few patient based atopic dermatitis (AD) disease activity scores and was found to be highly correlated with the EASI. Correlation with other frequently used scoring methods has not been investigated. The aim of this study was to evaluate the relation of the SA-EASI with two physician-based disease activity scores (objective SCORAD and SASSAD score) and with a serum marker for AD (Thymus and Activation-Regulated Cytokine [TARC]) in children with AD. Sixty children with moderate to severe AD were included. The SA-EASI was completed by caregivers, and the objective SCORAD and SASSAD scores were measured successively on the same day by a trained investigator. Blood for serum TARC measurement was drawn. The correlation between the SA-EASI and the objective SCORAD was high ($\rho = 0.61$, $p = <0.001$), mainly based on high correlation between the body surface area (BSA) measurements of both scores ($\rho = 0.50$, $p = <0.001$). The correlation with the SASSAD score (only severity measurement) was 0.43 ($p = <0.001$). The correlation with serum TARC levels was 0.46; $p = <0.001$, mainly based on the BSA score of the SA-EASI ($\rho = 0.42$, $p = <0.001$). Parents may have more difficulty in scoring severity of AD than scoring BSA involved. Educating parents in severity scoring of AD may improve agreement of the SA-EASI and the objective SCORAD, TARC, and SASSAD score. Additional use of the SA-EASI in routine clinical practice or in trials may then facilitate more frequent but still accurate assessment of AD.

Measuring disease activity of atopic dermatitis (AD) is important to determine the effect of treatment. Not only in clinical trials, but also in routine clinical practice

dermatologists should be able to assess disease activity (1). Many different clinical scoring systems have been developed to visually evaluate the severity of AD. Both

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objective (disease extent and severity) and subjective (pruritis and sleep loss) symptoms can be measured (1,2).

Most of the objective skin scoring systems require trained investigators to administer the instrument correctly, and some scoring systems are too complicated and time consuming for routine clinical use. Self-assessment of AD can facilitate scoring of AD in a cost effective manner (3) and will enable AD disease activity assessments at home between visits to the clinic. In this way, disease course can be followed more precisely during treatment. The Self-Administered Eczema Area and Severity Index (SA-EASI) is developed to allow the patient or patients' parent/caregiver to evaluate both the extent and severity of AD at any moment (3).

The SA-EASI is derived from the Eczema Area and Severity Index (EASI), which is a thoroughly validated scoring system for AD (4). The main difference between the EASI and the SA-EASI is that severity characteristics of AD are scored 0–3 by the physician in the EASI, and 100 mm visual analog scales (VAS) are marked by the patient in the SA-EASI (3,5). The SA-EASI is highly correlated to the EASI and can be used in grading the severity of AD and track changes over time (3). The correlation between the EASI and the total SCORAD index is also high ($\rho = 0.88$, $n = 42$) (6). The SA-EASI has not been related with other frequently used and most widely validated AD scoring systems such as the objective SCORAD and the SASSAD score (4). This will be useful in comparing results of studies using different AD scoring systems.

The objective SCORing Atopic Dermatitis (SCORAD) combines both disease extent and severity, is validated adequately on construct validity, interobserver reliability, and sensitivity to change, and is developed both for children and adult patients with AD (4,7). The Six Area Six Sign Atopic Dermatitis (SASSAD) severity score (8) measures six different severity signs on six different body parts, has been shown to have adequate interobserver reliability (4), and has proved to be equally applicable to children and adults (9,10). Both scoring systems have been used widely in randomized controlled trials assessing therapeutic interventions in AD (11,12).

Several laboratory markers such as sE-selectin (13), interleukin-16 (IL-16) (14), and Thymus and Activation-Regulated Chemokine (TARC) (15,16) have been described to play a role in the pathogenesis of AD and to correlate with clinical disease activity of AD. Thymus and Activation-Regulated Chemokine (TARC) is a ligand for CC chemokine receptor 4 (CCR4) that is selectively expressed on Th2 cells and has shown to induce the selective migration of Th2 cells. Endothelial cells and keratinocytes have been shown to produce TARC (17), and infiltration of Th2 cells in the skin is an

important feature in the pathogenesis of AD. Serum TARC levels are selectively elevated in patients with AD compared to healthy controls, patients with allergic respiratory diseases, or patients with psoriasis (15,17). Furthermore, levels of serum TARC correlate with disease activity measured by the Leicester Sign Score (extensive version of SASSAD score) (15,18), SCORAD index (17), and parallel disease severity during treatment with cyclosporine, mycophenolate sodium, or topical corticosteroids (15,16). This makes serum TARC an attractive biomarker for disease activity measurement in AD.

This study investigates the relation of the SA-EASI with two physician-based objective disease activity scores (the objective SCORAD and SASSAD score) and with a serum marker for AD (TARC) in children with moderate to severe AD.

PATIENTS AND METHODS

Patients

Sixty children (age between 5 and 16 yrs) with moderate to severe AD were studied. The diagnosis of AD was made according to the criteria of Hanifin and Rajka (19). Evaluation of disease activity by the SA-EASI, objective SCORAD, SASSAD score, and serum TARC was done successively on the same day. Patients were not asked to stop topical corticosteroid use or other therapy for AD before evaluation of disease activity. The local medical ethical committee approved this study, and patients (and their parents or caregivers) gave their written informed consent.

Self-Administered Eczema Area and Severity Index (SA-EASI)

The SA-EASI was completed by the parents/caregivers at the outpatient clinic (sometimes with help of the child). The parents/caregivers were told to assess the current severity and extent of AD. Furthermore, a short explanation (approximately 5 minutes) was given on how to shade the areas currently affected by AD and on how to use a VAS scale. The SA-EASI has been described previously by Housman et al (3). In short, the first part of the SA-EASI consists of an estimation of the amount of body surface affected by AD of four different areas: head, upper extremities, trunk, and lower extremities. Each area score is multiplied by a figure assigned to the corresponding body area which differs between children ≤ 7 years and children > 7 years old. The second part of the SA-EASI consists of five 100 mm visual analogue scales (VAS) each representing an AD severity

characteristic (redness, thickness, dryness, and scratches of an AD lesion). By multiplying the total area score by the VAS scores of all severity characteristics a total score (maximum of 96) for the SA-EASI is calculated (3). The score for itchiness is not part of the total SA-EASI score.

Objective SCORing Atopic Dermatitis (SCORAD)

The objective SCORAD was completed by a trained physician. In the objective SCORAD, the subjective items (pruritis and sleep loss) have been eliminated (7). The first part of the objective SCORAD consists of grading the extent of BSA affected by AD by the rule of nines. The second part consists of scoring the intensity of six AD severity characteristics (erythema, edema/papulation, oozing/crusts, excoriations, lichenification, and dryness). Total objective SCORAD (maximum of 83) was obtained by the sum of [BSA divided by 5] and [total severity score multiplied by 3.5] (7).

Six Area, Six Sign Atopic Dermatitis Severity Score (SASSAD score)

The SASSAD score was completed by the same investigator as the objective SCORAD. The SASSAD score comprises assignment of six signs (erythema, exudation, dryness, cracking, and lichenification) on six sites (arms, hands, legs, feet, head and neck, trunk); each on a scale of 0 (absent); 1 (mild); 2 (moderate); and 3 (severe). Total SASSAD score (maximum of 108) is calculated by adding all severity scores on each site (8).

Thymus and Activation-Regulated Cytokine (TARC)

Thymus and Activation-Regulated Chemokine (TARC) was measured using a quantitative sandwich enzyme immunoassay technique via precoated microplates with a TARC specific monoclonal antibody (Quantikine Human TARC immunoassay; R&D Systems Inc., Minneapolis, MN). Blood for TARC measurement was drawn on the same day disease severity was scored.

Statistical Analysis

Statistical analysis was performed using the program SPSS for Windows (version 15.0, 2006; SPSS inc., Chicago, IL). Data were expressed as frequencies (number of patients or percentages) for categorical variables and as a mean $\pm$ SD for continuous variables. To analyze the relationship between SA-EASI and other severity scoring indexes the correlation between the total SA-EASI score and the objective SCORAD, the SASSAD score and serum TARC levels was calculated. Furthermore,

the total area score and severity score from the SA-EASI were correlated separately with the BSA and severity score from the objective SCORAD and with serum TARC levels to investigate the level of agreement between segments of these different scoring methods. Linear regression analysis was done to investigate if the objective SCORAD could be predicted by the total SA-EASI score. The levels of serum TARC were log transformed (Ln) to obtain a normally distributed variable. Most variables were normally distributed, and correlations were investigated using Pearson correlation coefficient; otherwise Spearman correlation coefficient was used. A correlation coefficient (ρ) of 0.10–0.29 indicates a small correlation, 0.30–0.49 a moderate correlation, and 0.50–1.0 a high correlation (20).

RESULTS

Baseline characteristics of the study population are presented in Table 1. Sixty children, 24 boys, and 36 girls; age 5–16 years, with AD were studied.

Relation Between Total SA-EASI and Objective SCORAD

A strong positive correlation between the total SA-EASI and the objective SCORAD ($\rho = 0.61$, $n = 60$, $p = <0.001$) was seen (Fig. 1). An increase in total SA-EASI score of 1 point indicated an increase in objective SCORAD of 0.64 points (objective SCORAD = $20.5 + \text{total SA-EASI score} \times 0.64$; $p = <0.001$, $R^2 = 0.37$). Addition of other variables such as sex and age did not improve this model.

The correlation between the BSA calculated from the SA-EASI and the BSA calculated from the objective SCORAD was 0.50 ($n = 60$, $p = <0.001$) (Table 2). When the total severity score of the SA-EASI was correlated with the severity score of the objective

TABLE 1. Baseline Characteristics of AD Patients

Number of AD patients	60
Gender (no. of patients)	
Boys	24 (40%)
Girls	36 (60%)
Age (yrs $\pm$ SD)	10.5 $\pm$ 3.4
Disease activity	
SA-EASI (score $\pm$ SD)	15 $\pm$ 12
Objective SCORAD (score $\pm$ SD)	30 $\pm$ 12
Objective SCORAD $< 15^*$	4 (6.7%)
Objective SCORAD 15–40	45 (75%)
Objective SCORAD > 40	11 (18.3%)
SASSAD score (score $\pm$ SD)	27 $\pm$ 11
TARC (pmol/L $\pm$ SEM)	2018 $\pm$ 393

*Objective SCORAD < 15 indicates mild, 15–40 moderate, and > 40 severe disease activity (7).

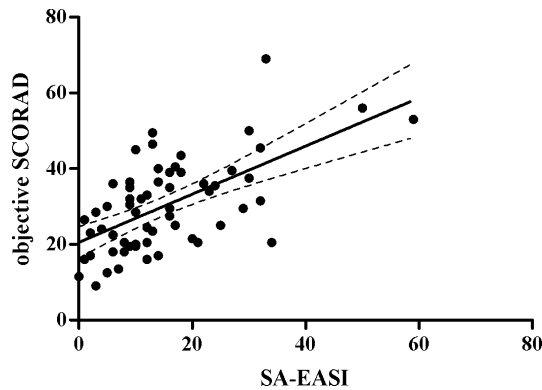


Figure 1. Correlation between SA-EASI and objective SCORAD. Scatter plot shows linear regression line and 95% confidence band; $R^2 = 0.37$; $r = 0.61$; $p = <0.0001$.

TABLE 2. Correlations Between SA-EASI and: Objective SCORAD, SASSAD, and TARC

	Correlation coefficient (ρ)	p
Total SA-EASI vs objective SCORAD	0.61	<0.001
BSA SA-EASI vs BSA objective SCORAD	0.50	<0.001
Severity score SA-EASI vs severity score objective SCORAD	0.37	0.003
Total SA-EASI vs SASSAD score	0.43	<0.001
Total SA-EASI vs logTARC	0.46	<0.001
BSA SA-EASI vs logTARC	0.42	0.001
Severity score SA-EASI vs logTARC	0.36	0.005

SCORAD, only a moderate correlation was found ($\rho = 0.37$, $n = 60$, $p = 0.003$).

Correlation Between Total SA-EASI and SASSAD Score

The correlation between the total SA-EASI and the SASSAD score was moderate ($\rho = 0.43$, $n = 60$, $p = <0.001$).

Correlation Between Total SA-EASI and Serum TARC Levels

The correlation coefficient between the total SA-EASI and log TARC was 0.46, suggesting a moderate correlation ($n = 60$, $p = <0.001$). The correlation coefficient between the BSA of the SA-EASI and log TARC was 0.42 ($n = 60$; $p = 0.001$), and the correlation between the severity score of the SA-EASI and log TARC was 0.36 ($n = 60$; $p = 0.005$).

Additionally, the correlation between log TARC and objective SCORAD was 0.51 ($n = 60$; $p = 0.001$), the

correlation between log TARC and the BSA/severity score of the objective SCORAD were respectively 0.44 and 0.49 ($n = 60$; $p = 0.001$). The correlation between log TARC and SASSAD was 0.42 ($n = 60$; $p = 0.001$).

DISCUSSION

We investigated whether the SA-EASI was related with validated and well used investigators' assessment scores for AD (objective SCORAD and SASSAD score) and with a laboratory marker for AD (TARC). We found a high correlation ($\rho = 0.61$) between the total SA-EASI and the objective SCORAD. Moderate correlations were found between the SA-EASI and the SASSAD score and the SA-EASI and serum TARC levels ($\rho = 0.43$ and $\rho = 0.46$). The BSA score of the SA-EASI correlated best with the BSA score of the objective SCORAD and TARC. Correlations between the severity scores of the disease activity scores were lower.

Both the EASI and the objective SCORAD are composite indexes including assessment of both disease severity and extent without subjective symptoms (5,21). A high correlation between the EASI and SCORAD index has been found (6). Housman et al found a high correlation between the total SA-EASI and the EASI (3). When individual severity scores (e.g., erythema) of the SA-EASI were correlated with the corresponding scores of the EASI, correlations were small to moderate. Only with the addition of the BSA score next to the severity scores in the SA-EASI, the correlations between the SA-EASI and the EASI increased. In accordance, we found that the high correlation between the SA-EASI and the objective SCORAD is mainly based on a high correlation between the BSA scores. The correlation between the severity scores of both skin scoring systems was lower.

The SASSAD score is only based on a severity measurement of several body sites, and assessment of BSA is not included (8). The lack of a BSA measurement may explain why a moderate correlation with the SA-EASI was found.

Apparently, parents have more difficulty in assessing the severity of their child's AD than the BSA involved. The assessment of severity in the SA-EASI is done by a 100 mm VAS, whereas in the objective SCORAD and SASSAD, only a 4-point scale is used. It may be more difficult to assess severity in the SA-EASI because a VAS gives a wider range to choose from, compared to a 0–3 score of the SCORAD or SASSAD. This could explain why a lower correlation between the severity scores of the SA-EASI and the SCORAD/SASSAD was found in this study.

Thymus and Activation-Regulated Chemokine (TARC) levels correlated well with AD disease activity

in adults as scored by the LSS, a skin scoring system related to the SASSAD ($\rho = 0.56$; $n = 177$) (15), and also with the objective SCORAD ($\rho = 0.60$; $n = 40$) (17). In accordance with Kakinuma et al (17), we found a large correlation between the objective SCORAD and TARC levels in children. Additionally, both the BSA score and the severity score of the objective SCORAD correlated equally well with serum TARC levels ($\rho = 0.44$ and $\rho = 0.49$; $n = 60$). We found a moderate correlation of 0.46 between SA-EASI and TARC, mainly based on BSA estimate of the SA-EASI. This also suggests that parents can more accurately assess the extent of their child's AD. Possibly, better education/training for the parents or patients' caregivers on how to assess the severity of AD can enhance the correlation between the SA-EASI and objective SCORAD, but also the correlation between SA-EASI and TARC. For example, use of example photographs of severity characteristics of AD can be of help in training parents or patient's caregivers in grading AD severity. Use of reference photographs of severity characteristics has been used for education and training on the SCORAD (21).

A limitation of this study is that the majority of the patients in this study had moderate or severe AD at the moment of scoring according to the objective SCORAD. Active AD might be differently assessed by the patient or patients' caregiver than mild AD, and one has to be careful to extrapolate the results from this study to patients with mild AD. In addition, parents of children with mild AD may have more difficulty in assessing severity as they may have not had exposure to severe AD to act as a comparator in the way that a clinician would. Furthermore, this is a single time-point study. When multiple SA-EASI measurements are done to reflect disease course during treatment, patients and patients' caregivers may become more experienced in performing the SA-EASI. This could lead to higher correlations between both the BSA and severity characteristics of the SA-EASI and objective SCORAD.

Comparison of the SA-EASI with other tools in measuring AD from the patients' perspective, such as the Patient-Oriented Eczema Measure (POEM) (22) and the Patient-Oriented SCORAD (PO-SCORAD) (23), was not done in this study but could be useful to investigate in future studies.

In conclusion, the SA-EASI has a good correlation with the objective SCORAD in assessing disease activity in children with AD. This correlation is mainly based on good agreement between the BSA scores of the SA-EASI and the objective SCORAD. Less agreement was found between the SA-EASI and serum TARC levels; BSA score of the SA-EASI correlated better with TARC than the severity score of the SA-EASI. Also, less agreement

was found between the SA-EASI and the SASSAD score where assessment of BSA is not included. The lower correlations between the severity scores of the SA-EASI and objective SCORAD/TARC suggest that parents may have more difficulty in scoring severity of AD than scoring BSA involved. Training parents in assessing the severity of AD may improve agreement between the SA-EASI and other AD scoring systems. Additional use of the SA-EASI in routine clinical practice or in trials may then facilitate more frequent but still accurate assessment of AD disease activity.

REFERENCES

1. Finlay AY. Measurement of disease activity and outcome in atopic dermatitis. *Br J Dermatol* 1996;135:509–515.
2. Charman C, Williams H. Outcome measures of disease severity in atopic eczema. *Arch Dermatol* 2000;136:763–769.
3. Housman TS, Patel MJ, Camacho F et al. Use of the self-administered eczema area and severity index by parent caregivers: results of a validation study. *Br J Dermatol* 2002;147:1192–1198.
4. Schmitt J, Langan S, Williams HC. What are the best outcome measurements for atopic eczema? A systematic review. *J Allergy Clin Immunol* 2007;120:1389–1398.
5. Hanifin JM, Thurston M, Omoto M et al. The eczema area and severity index (EASI): assessment of reliability in atopic dermatitis. EASI Evaluator Group. *Exp Dermatol* 2001;10:11–18.
6. Rullo VE, Segato A, Kirsh A et al. Severity scoring of atopic dermatitis: a comparison of two scoring systems. *Allergol Immunopathol (Madr)* 2008;36:205–211.
7. Oranje AP, Glazenburg EJ, Wolkerstorfer A et al. Practical issues on interpretation of scoring atopic dermatitis: the SCORAD index, objective SCORAD and the three-item severity score. *Br J Dermatol* 2007;157:645–648.
8. Berth-Jones J. Six area, six sign atopic dermatitis (SASSAD) severity score: a simple system for monitoring disease activity in atopic dermatitis. *Br J Dermatol* 1996;135(Suppl 48):25–30.
9. Berth-Jones J, Graham-Brown RA, Marks R et al. Long-term efficacy and safety of cyclosporin in severe adult atopic dermatitis. *Br J Dermatol* 1997;136:76–81.
10. Berth-Jones J, Finlay AY, Zaki I et al. Cyclosporine in severe childhood atopic dermatitis: a multicenter study. *J Am Acad Dermatol* 1996;34:1016–1021.
11. Charman C, Chambers C, Williams H. Measuring atopic dermatitis severity in randomized controlled clinical trials: what exactly are we measuring? *J Invest Dermatol* 2003;120:932–941.
12. Msika P, De BC, Piccardi N et al. New emollient with topical corticosteroid-sparing effect in treatment of childhood atopic dermatitis: SCORAD and quality of life improvement. *Pediatr Dermatol* 2008;25:606–612.
13. Gutgesell C, Heise S, Seubert A et al. Comparison of different activity parameters in atopic dermatitis: correlation with clinical scores. *Br J Dermatol* 2002;147:914–919.
14. Angelova-Fischer I, Hipler UC, Bauer A et al. Significance of interleukin-16, macrophage-derived chemokine,

- eosinophil cationic protein and soluble E-selectin in reflecting disease activity of atopic dermatitis—from laboratory parameters to clinical scores. *Br J Dermatol* 2006;154:1112–1117.
15. Hijnen D, de Bruin-Weller M, Oosting B et al. Serum thymus and activation-regulated chemokine (TARC) and cutaneous T cell-attracting chemokine (CTACK) levels in allergic diseases: TARC and CTACK are disease-specific markers for atopic dermatitis. *J Allergy Clin Immunol* 2004;113:334–340.
16. Fujisawa T, Nagao M, Hiraguchi Y et al. Serum measurement of thymus and activation-regulated chemokine/CCL17 in children with atopic dermatitis: elevated normal levels in infancy and age-specific analysis in atopic dermatitis. *Pediatr Allergy Immunol* 2009;20:633–641.
17. Kakinuma T, Nakamura K, Wakugawa M et al. Thymus and activation-regulated chemokine in atopic dermatitis: serum thymus and activation-regulated chemokine level is closely related with disease activity. *J Allergy Clin Immunol* 2001;107:535–541.
18. Berth-Jones J, Graham-Brown RA. Placebo-controlled trial of essential fatty acid supplementation in atopic dermatitis. *Lancet* 1993;341:1557–1560.
19. Hanifin JM, Rajka G. Diagnostic features of atopic dermatitis. *Arch Dermatol Venereol (Stockh)* 1980; 92(Suppl):44–47.
20. Pallant J. *SPSS Survival Manual*, 3rd edn. Berkshire, England: Open University Press, 2009:132.
21. Severity scoring of atopic dermatitis: the SCORAD index. Consensus Report of the European Task Force on Atopic Dermatitis. *Dermatol* 1993;186:23–31.
22. Charman CR, Venn AJ, Williams HC. The patient-oriented eczema measure: development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. *Arch Dermatol* 2004;140:1513–1519.
23. Vourc'h-Jourdain M, Barbarot S, Taieb A et al. Patient-oriented SCORAD: a self-assessment score in atopic dermatitis. A preliminary feasibility study. *Dermatol* 2009;218:246–251.