Utility of serum thymus and activation-regulated chemokine as a biomarker for monitoring of atopic dermatitis severity

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Background: Serum thymus and activation-regulated chemokine (sTARC) levels reflect disease severity of atopic dermatitis (AD) in small study populations. It remains unclear whether sTARC is a reliable outcome measurement for AD severity in heterogeneous AD populations in daily practice.

Objective: We sought to assess the utility of sTARC as a biomarker for monitoring AD severity in adults in daily practice.

Methods: sTARC, clinical skin score (Six Area, Six Sign AD [SASSAD]), and body surface area measurements were collected from all adult patients with AD visiting our clinic between March 2009 and March 2012, at first visit or exacerbation (baseline). In addition, data from short-term and long-term follow-up visits were collected.

Results: At baseline sTARC levels ranged widely (n = 320; minimum-maximum: 3-50,400 pg/mL) and sTARC and SASSAD or body surface area correlated moderately. In the majority of patients, sTARC and SASSAD or body surface area changed congruently during follow-up.

Limitations: Data were collected retrospectively.

Conclusion: sTARC may represent a suitable biomarker for monitoring of AD severity in daily practice. (J Am Acad Dermatol 2014;71:1160-6.)

Key words: atopic dermatitis; body surface area; disease severity; follow-up; serum thymus and activation-regulated chemokine; Six Area; Six Sign Atopic Dermatitis.

Atopic dermatitis (AD) is a chronic inflammatory skin disease with high prevalence,[1-3] considerable morbidity, and profound effect on quality of life.[4] Treatment options include topical steroids, topical immunomodulatory agents, ultraviolet therapy, and systemic immunosuppressive drugs. The choice of therapy depends on different factors, such as disease severity, previous treatment responses, and side effects.[5]

Assessment of AD disease severity is important for evaluating therapy effectiveness and is currently determined by clinical disease severity scores. There are a large number of AD severity scores (eg, SCORing

Abbreviations used:

AD:	atopic dermatitis
BSA:	body surface area
SASSAD:	Six Area, Six Sign Atopic Dermatitis
SCORAD:	SCORing Atopic Dermatitis
sTARC:	serum thymus and activation-regulated chemokine

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AD [SCORAD]; Three Item Score; Eczema Area and Severity Index; Six Area, Six Sign AD [SASSAD]). These severity scores weighted measures of the intensity of clinical lesions and/or the extent of clinically involved skin expressed as body surface area (BSA).[6,7] Unfortunately, these scores are subjective, characterized by high interobserver and intraobserver variations and studies comparing validity and reliability are lacking.[6-8] Disease severity scores are, therefore, less reliable in daily practice where different clinicians may monitor a single patient.

For these reasons, there is a need for an objective biomarker. To date, several serum cytokines and chemokines have been suggested as biomarkers for AD. Serum thymus and activation-regulated chemokine (sTARC) was found to correlate well with disease severity.[9-12] Thymus and activation-regulated chemokine is produced by different cell types, including dendritic cells and endothelial cells.[13-15] Thymus and activation-regulated chemokine is a chemoattractant for $CCR4^+$ T cells, which are known to play an important role in the pathogenesis of AD.[16-18] Elevated sTARC levels have also been described in other skin diseases such as cutaneous T-cell lymphoma and staphylococcal scalded skin syndrome.[12]

sTARC levels were found increased in patients with AD, but not in healthy control subjects or in patients with asthma, allergic rhinitis, or both.[9,11,19] This specificity within the atopy syndrome makes sTARC an attractive biomarker for AD. Furthermore, sTARC levels are significantly higher in patients with severe AD compared with mild or moderate AD.[9-12] Previously reported correlation coefficients between sTARC and disease severity scores (mainly SCORAD or SASSAD) varied between 0.39 and 0.99,[9,19-28] but were investigated in small study populations[9,20,21,23-26,29] predominantly in children.[20,23-28] Only a few small studies investigated sTARC in AD longitudinally.[9,19,20,22,29,30]

The aim of the current study was to validate sTARC as a biomarker for monitoring AD severity in adult patients in daily practice.

CAPSULE SUMMARY

- In small selected study populations, serum thymus and activation-regulated chemokine reflects atopic dermatitis (AD) severity.
- In this large heterogeneous AD population, serum thymus and activation-regulated chemokine levels and AD severity scores changed congruently during follow-up.
- In daily practice, serum thymus and activation-regulated chemokine may represent a suitable biomarker for monitoring AD severity.

METHODS

Patient population

This study is based on information gathered via the standard treatment protocol for patients with AD visiting our department. sTARC levels, clinical disease severity score SASSAD,[31] and BSA are determined routinely at baseline (first visit and/or exacerbation), short-term follow-up, and/or long-term follow-up visits. Exacerbation is defined as increased disease severity, requiring escalation of therapy.[32]

Medical records of all 579 patients visiting our department between March 2009 and March 2012 were screened. The following inclusion criteria were used: (1) diagnosis of AD, according to the criteria of Hanifin and Rajka[33]; and (2) sTARC level measurement and concomitant SASSAD and BSA determined at baseline. Exclusion criteria were: (1) systemic immunosuppressive treatment (other than systemic corticosteroids) in the 3 months before baseline; and (2) systemic corticosteroids 2 weeks before baseline. Of the 579 patient files screened, 259 patients were ineligible: 220 (85%) because of use of systemic immunosuppressive treatment within 3 months before baseline; 10% because of missing SASSAD and BSA scores at baseline; and 5% because of another diagnosis.

Follow-up

Short-term follow-up was defined as 1 to 6 weeks, and long-term follow-up as 7 to 36 weeks after baseline. In patients with multiple measurements within the defined periods, an interpolation algorithm was used to determine 1 time point within the short-term follow-up interval closest to 4 weeks, and within the long-term follow-up interval closest to 24 weeks.

Measurements

sTARC was determined using the human thymus and activation-regulated chemokine immunoassay (Quantikine, R&D Systems, Minneapolis, MN) according to the manufacturer's instructions. The reference range in healthy control subjects was 71 to 848 pg/mL.

The compiled data on SASSAD and BSA were determined by different doctors and nurses, who were trained in using SASSAD and BSA. Pearson correlation coefficient between SCORAD and SASSAD, and between SCORAD and BSA, was