Pellacani, G., Gupta, G., Micali, G., Malvehy, J., Stratigos, A. J., Casari, A., Cheseter, J., Kaleci, S. and Dirschka, T. (2018) Actinic keratosis area severity index (AKASI): reproducibility study and comparison with total lesion count. British Journal of Dermatology, 179(3), pp. 763-764.

PROFESSOR GIUSEPPE MICALI (Orcid ID : 0000-0002-5157-3939)
DR ALICE CASARI (Orcid ID : 0000-0002-3448-6008)

ACTINIC KERATOSIS AREA SEVERITY INDEX (AKASI): REPRODUCIBILITY STUDY AND COMPARISON WITH TOTAL LESION COUNT

G. Pellacani,[1] G. Gupta,[2] G. Micali,[3] J. Malvehy,[4,5] A. J. Stratigos,[6] A. Casari,[1] J. Cheseter,[1] S. Kaleci,[1] T. Dirschka[7]

1. Department of Dermatology, University of Modena and Reggio Emilia, Italy

2. Department of Dermatology, University Hospital Monklands, Lanarkshire, and University of Glasgow, UK

3. Dermatology Clinic, University of Catania, Italy

4. Dermatology Department, Melanoma Unit, Hospital Clínic de Barcelona, IDIBAPS, Universitat de Barcelona, Barcelona, Spain

5. Centro de Investigación Biomédica en Red en Enfermedades Raras (CIBERER), Valencia, Spain

6. First Department of Dermatology - Venereology, National and Kapodistrian University of Athens Medical School, Andreas Sygros Hospital, Athens, Greece

7. Centroderm Clinic, Wuppertal, and Faculty of Health, University Witten-Herdecke, Witten, Germany

Corresponding author: Alice Casari

Adress: Department of Dermatology, University of Modena and Reggio Emilia, Italy

email: alice.casari@gmail.com

DEAR EDITOR,

Actinic keratosis (AK) is caused by ultraviolet radiation exposure and is more likely to be subclinical than visible. AK can potentially progress to invasive squamous cell carcinoma (SCC).[1] All stages of AK and sometimes, invasive SCC[2] coexist in the "cancerization field" where further neoplastic changes can occur.[3] The current clinical or histological based classification systems are time consuming and are restricted by the presence of multiple lesions.[4,5]

The Actinic Keratosis Area Severity Index (AKASI) score evaluates sun damaged skin in defined regions of the head, estimating a grade of severity according to erythema, distribution and lesion thickness, along with the area affected. The head is divided into four areas and each region is given a weighting based on its approximate relative size as follows: scalp 40%; forehead 20%; left cheek, ear, chin and nose 20%; right cheek, ear, chin and nose 20%. For each region, the initial step is to estimate the percentage of the area that is affected by actinic damage, represented by a numerical value between 0 and 6. The three clinical signs of AK severity; distribution (none, isolated/scattered, clustered, clustered/confluent, all confluent), erythema (absent, slight, moderate, intense, very intense) and thickness (no palpability, just palpable, clearly palpable, thickened, very thickened) are assessed and scaled $(0 - 4)$.[6] An AKASI subscore is calculated for each of the four areas of the head by adding the area and severity scores, and multiplying the subtotal by the area coefficient. The subtotals together give a total AKASI score for the entire head. Total scores range from 0 (no AK / no actinic damage) to 18 (AK of the severest possible degree).[6]

In a pilot study of 30 consecutive patients, the reproducibility and accuracy of diagnosis with AKASI compared with Total Lesion Count (TLC), the current gold standard for AK severity reporting, was performed. Patients without previous skin cancer diagnosis and/or field and/or lesion treatments, on the area of evaluation were enrolled and examined by four dermatologists, blinded to colleagues' diagnoses, following a consensus discussion of what lesions constitute AKs.[7]

Most patients were men (n=23), with a mean age of 77 years (range $63 - 87$). Mean TLC results were 38.7 ±20.7 (0-94). The intra-class correlation coefficient (ICC) for intra-observer TLC and for each parameter was almost perfect (>80) but, when investigating the agreement between the observers according to TLC types, there was a lower correlation for AK type II compared to AK I and III. Type II lesions are discrete and are in part or totally covered by a scaly surface. Incorrectly classified Type II as Type III could be of particular importance for clinical trials, as most studies exclude Type III, suggesting that inclusion and exclusion criteria could be much more subjective than previously thought.

Mean AKASI results were 7.1 ±2.5 (0-12.6). When considering the single AKASI score there was an almost perfect correlation for intra-observer and for each parameter (area score, thickness and distribution). AKASI thickness seemed easier to score than TLC, probably due to the different scoring methodologies. The presence of 4 different grades of thickness (none, just palpable, palpable, thick and very thick) could permit a better classification than a triple choice (non-palpable, palpable, very palpable). Interestingly, the classification of erythema presented the greatest range of scores. By definition, erythema in AKASI pertains to that within a sun-damaged field, and not due to telangiectasia, dermatitis or eczema, which can arise or co-exist in the same area, potentially confounding the observer.

Inter-observer variability analysis of TLC and AKASI showed no significant differences between the 4 observers ($P > 0.05$). However, the ICC was slightly lower for TLC among the observers than for AKASI (0.92, 95% confidence interval (CI), 0.86-0.95; vs 0.94, 95% CI, 0.90-0.97, respectively). Disease severity was classified similarly by either method of evaluation, as evidenced by the global AKASI and TLC scores correlation in a linear fashion ($r=0.75$; 95% CI, 0.66-0.82, $p<0.00$; Figure 1).

According to Bland Altman analysis, the level of agreement (LoA) for both methodologies of classification by each observer was almost perfect, and as the differences within the mean and standard deviation were not clinically important, the two methods could be used interchangeably.

In this pilot study, AKASI seems to be a potential alternative scoring system for TLC in both clinical and future clinical trial settings. Cut-off thresholds could help standardize patient comparisons and assist in tailoring and assessing individual treatments. Further validation in multicentre/multi-observer settings is required.

REFERENCES

1. Green AC. Epidemiology of actinic keratosis. Curr Probl Dermatol. 2015; 46: 1-7.

2. Deltondo JA, Helm KF. Actinic keratosis: precancer, squamous cell carcinoma, or marker of field cancerization? G Ital Dermatol Venereol. 2009;144(4):441-444.

3. Olsen EA, Abernethy ML, Kulp-Shorten C et al. A double-blind, vehicle- controlled study evaluating masoprocol cream in the treatment of actinic keratoses on the head and neck. J Am Acad Dermatol 1991;24:738–743.

4. Weinstock MA, Bingham SF, Cole GW et al. Reliability of counting actinic keratoses before and after brief consensus discussion: the VA topical tretinoin chemoprevention (VATTC) trial. Arch Dermatol. 2001;137(8):1055-1058.

5. Dirschka T, Gupta G, Micali G et al. Real-world approach to actinic keratosis management: practical treatment algorithm for office-based dermatology. J Dermatolog Treat. 2017;28(5):431-442.

6. Dirschka T, Pellacani G, Micali G, Malvehy J, Stratigos AJ, Casari A, Schmitz L, Gupta G; Athens AK Study Group. A proposed scoring system for assessing the severity of actinic keratosis on the head: actinic keratosis area and severity index. J Eur Acad Dermatol Venereol. 2017;31(8):1295-1302

7. Lee KC. Lew R, Weinstock MA. Improvement in precision of counting actinic keratoses. Br J Dermatol. 2014;170(1):188-191.

FIGURE LEGEND

Figure 1. Correlation between the global AKASI scores and the global TLC scores for all 30 patients by 4 independent blinded observers.

r=0.75, p<0.001