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## Examining cutaneous disease activity as an outcome measure for clinical trials in dermatomyositis

*To the Editor:* Due to successful emerging therapies for psoriasis, total skin clearance has become a primary endpoint in clinical trials and has impacted trial design for other inflammatory skin conditions such as dermatomyositis.[1] However, insufficient evidence exists on the impact of total skin clearance from these patients' perspectives, and dermatomyositis patients might retain signs of inflammation and damage despite having an acceptable quality of life (QoL). For example, periungual telangiectasias are asymptomatic markers of disease activity in dermatomyositis but can be retained even when disease is well-controlled.[2] The effect of skin clearance on QoL was investigated in some studies by comparing patient-reported outcomes to validated measures of disease severity.[1] The current standardized QoL instruments, Skindex-29 and Dermatology Life Quality Index (DLQI), are shown to correlate with Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity scores and have been validated for use in clinical trials.[3] However, the Skindex-29 and DLQI scores have not been specifically examined in patients with mild disease (CDASI $\leq$14), who might have an acceptable QoL despite their cutaneous manifestations.[4] This is clinically important, as strict total clearance endpoints might impede development of much needed therapies that might provide substantial QoL benefit without complete resolution of skin findings. In this study, we aimed to identify CDASI cutoff values to be used as meaningful endpoints in clinical trials to optimize drug development for this difficult-to-treat and rare disease.

We performed a retrospective review of 171 patients enrolled in a prospective longitudinal dermatomyositis database. We evaluated the correlation of individual Skindex-29 and DLQI scores versus the CDASI activity scores in patients with dermatomyositis at their enrollment visit. A slope-changing linear model was fitted to determine the CDASI cutoff value, defined as the lowest CDASI score at which the instrument correlates well with QoL (Fig 1). The DLQI had the lowest CDASI cutoff value of 4, compared with the other Skindex-29 subscales (emotions 10, functioning 8, symptoms 7). Below these CDASI cutoff values, the Skindex-29 and DLQI were found to correlate poorly with cutaneous disease activity. Further improvement in CDASI activity score does not lead to further improvement in QoL. Our findings suggest that QoL is not directly affected by the minimal cutaneous disease activity below these CDASI cutoff values and, therefore, total clearance of skin findings might be irrelevant as a meaningful outcome for patients. In addition, the linear correlation of CDASI with QoL until the cutoff value suggests that changes in CDASI scores are relevant over the spectrum of disease activity above these cutoffs.

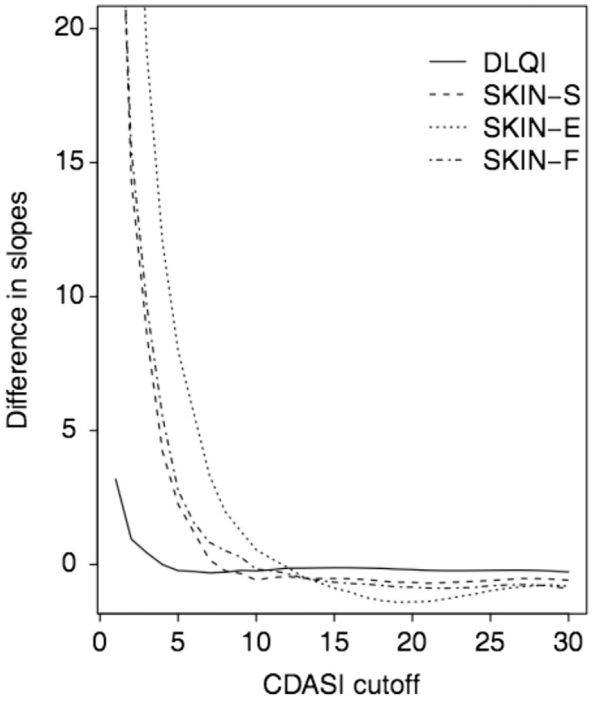


**Fig 1.** Slope-changing linear model of quality-of-life (QoL) instruments and CDASI values. A slope of 0 indicates a strong correlation whereas a slope >0 indicates a poor correlation. Therefore, CDASI cutoff values, or the lowest CDASI score at which the instrument correlates well with QoL, are determined by the inflection point for each QoL instrument. The cutoff values are 4 for DLQI, 7 for SKIN-S, 10 for SKIN-E, and 8 for SKIN-F. *CDASI*, Cutaneous Dermatomyositis Disease Area and Severity Index; *DLQI*, Dermatology Life Quality Index; *QoL*, quality of life; *SKIN-E*, Skindex-29 emotions subscale; *SKIN-F*, Skindex-29 functioning subscale; *SKIN-S*, Skindex-29 symptoms subscale.

Though the DLQI had the lowest CDASI cutoff value, a separate study by our group found that it is not sensitive in capturing QoL in the mild disease subgroup. Therefore, we propose the prioritization of the Skindex-29 subscale cutoff of 7 as a clinically meaningful endpoint. This study is limited as it was retrospective and performed at a single center. Future randomized controlled trials will be important to further examine CDASI cutoffs in a controlled trial setting. The results of this pilot study can be used to design trials to reach a meaningful clinical endpoint, instead of unnecessarily seeking total remission of skin findings in terms of QoL for patients. Using meaningful endpoints will optimize clinical trials and enable the development of essential treatments for dermatomyositis.

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## Keratoacanthomas: A review of excised specimens

*To the Editor:* The management of keratoacanthomas (KAs) is variable.[1] Although some clinicians believe these lesions will regress, others regard them as a variant of squamous cell carcinoma (SCC) and treat them.[2] Because no guidelines exist, our goal was to provide evidence that informs KA management. The primary aim of our study was to quantify postbiopsy residual cancerous tissue rates in KA and well-differentiated SCC excision specimens. The authors hypothesized that the presence of residual tumors would be similar between the 2 specimen types. Our secondary aim was to determine risk factors for residual tumors in excision specimens.