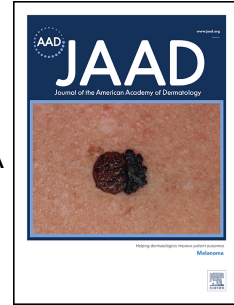


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Classification of Disease Damage and Activity in Cutaneous Lupus Erythematosus: A Cross-Sectional Analysis

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35 **Keywords:** Cutaneous Lupus Erythematosus; Cutaneous Lupus Disease Area and Severity Index; classification;

36 Disease activity; Disease damage; general dermatology; medical dermatology; autoimmune disease;

37 cutaneous lupus erythematosus

38

39 **Abbreviations:** CC: correctly classified; CLASI: Cutaneous Lupus Erythematosus Disease Severity and

40 Activity Index; CLASI-A: Cutaneous Lupus Erythematosus Disease Severity and Activity Index Activity

41 Score; CLASI-D: Cutaneous Lupus Erythematosus Disease Severity and Activity Index Damage Score; CLE:

42 Cutaneous Lupus Erythematosus; PGA: Physician's Global Assessment.

43 Classification of Cutaneous Lupus Disease Area and Severity Index (CLASI) scores provides a
44 framework for disease severity in patients with cutaneous lupus erythematosus (CLE). One prior study
45 classified CLASI activity (CLASI-A) scores using a small cohort, but no studies have been performed on
46 CLASI damage (CLASI-D) scores.¹ Our objective was to establish CLASI-D strata for mild, moderate, and
47 severe disease using a large, heterogeneous cohort, and compare characteristics between categories.

48 This was a cross-sectional analysis of CLE patients recruited prospectively at outpatient
49 dermatology clinics at University of Texas (UT) Southwestern and Parkland Hospital in Dallas, Texas, from
50 April 2009 to January 2020. This study was approved by the UT Southwestern Institutional Review Board.
51 CLASI-D and Physicians' Global Assessment (PGA) of damage were scored. PGA scores served as
52 anchoring measures to classify patients into mild, moderate, and severe categories. Receiver operating
53 characteristic curves were used to evaluate strata. Patients were classified into activity categories based
54 on CLASI-A strata published previously.¹ Patient characteristics were compared using Chi-square and
55 Kruskal-Wallis tests.

56 **Table 1** provides patient characteristics (N=270). Based on PGA scores, 49% of patients had mild,
57 35% moderate, and 16% severe disease damage, with examples shown in **Supplemental Figure 1**. CLASI-
58 D scores of 0-5, 6-16, and 17-56 corresponded to mild [sensitivity 86%, specificity 96%, correctly
59 classified (CC) 95%], moderate [sensitivity 73%, specificity 83%, CC 69%], and severe [sensitivity 65%,
60 specificity 90%, CC 56%] damage. Among the patients with CLASI-D scores of 0-5, 95% had mild disease.
61 Between 6 and 16, 69% had moderate disease. Among patients with a CLASI-D score of 17 or greater,
62 56% had severe disease damage.

63 Patients with moderate and severe disease damage experienced longer disease duration than
64 patients with mild damage (mild: 8.19±10.48 years; moderate: 11.01±11.21 years; severe: 10.93±8.46
65 years, p=0.003) (**Figure 1**). The correlation of disease damage with disease duration may be secondary to
66 patients with longer disease duration experiencing increased damage from prior active flares.² Patients

67 with severe disease damage were more likely to have discoid lupus erythematosus (DLE) (100% DLE vs
68 0% subacute CLE vs 0% acute CLE, $p < 0.0001$). DLE is characterized by significant disease damage,³ and
69 may predispose patients to worse disease damage independent of disease activity. Disease activity
70 severity did not appear to correlate with disease subtype (**Supplemental Figure 2**).

71 We have introduced CLASI damage severity strata using a large, diverse cohort, and highlighted
72 characteristics associated with different disease damage categories. This work proposes an anchor-
73 based technique for quantifying disease damage, instead of relying on individualized, subjective
74 descriptions of damage severity. This standardization can help providers contextualize CLE damage
75 severity in their patients, explore impact on their quality of life, and guide treatment decisions.^{2,4} The
76 identification of characteristics associated with worse disease damage severity, specifically longer
77 disease duration and DLE subtype, improves our understanding of disease course in CLE patients.
78 Limitations include single-center, single-rater, cross-sectional design, relatively low percentages of
79 severe disease, and subjective nature of PGA scores. Future multi-center larger studies will help validate
80 our data to define disease severity strata in CLE.

81

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83 Lupus Erythematosus Registry for their contributions to lupus research.

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97

98 **Figure Legends**99 **Figure 1. Mean disease duration (years) of patients with mild, moderate, and severe disease damage.**

100 This bar graph demonstrates that mean disease duration (\pm standard deviation) of patients with moderate
101 disease damage (11.01 ± 11.21 years) and severe disease damage (10.93 ± 8.46 years) was significantly
102 greater than those with mild damage (8.19 ± 10.48 years) ($p=0.003$). *: $p<0.05$

103 Abbreviations: ns = not significant

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105 **Table 1. Patient Clinical and Demographic Characteristics (N=270)**

Patient Characteristic	Mean or N	SD or %	
Age at visit, years	45.74	14.04	
Gender			107
Male	40	14.81%	
Female	230	85.19%	108
Race/Ethnicity			
Caucasian	84	31.11%	109
Black	140	51.85%	
Hispanic	30	11.11%	110
Asian	10	3.70%	
Other	6	2.22%	111
PGA Scores ^a			
PGA-A	7.58	1.93	112
PGA-D	7.18	2.31	113
CLASI Scores			
CLASI-A	5.9	6.60	114
CLASI-D	8.6	8.10	115
Disease Severity by PGA-A			116
Mild	153	57%	117
Moderate	87	32%	
Severe	29	11%	118
Disease Severity by PGA-D			
Mild	132	49%	119
Moderate	95	35%	120
Severe	43	16%	
Predominant CLE subtype			121
Acute CLE	25	9.26%	122
<i>Bullous LE</i>	3	1.11%	
Subacute CLE	33	12.22%	123
Chronic CLE	212	78.52%	124
<i>Discoid LE</i>	179	62.96%	
<i>Chilblains LE</i>	3	1.11%	125
<i>LE Tumidus</i>	26	9.63%	126
<i>LE Panniculitis</i>	4	1.48%	
Systemic Lupus Involvement			127
Present	149	55.19%	
Absent	121	44.81%	128
Smoking Status ^b			129
Non-smoker	135	50.00%	
Current smoker	46	17.04%	130
Past smoker	88	32.59%	131

133 ^a1 patient had missing PGA-A score.

134 ^b1 patient had missing smoking status.

135 **Abbreviations:**

136 ACLE: Acute Cutaneous Lupus Erythematosus; CCLE: Chronic Cutaneous Lupus Erythematosus; CLASI-A:

137 Cutaneous Lupus Erythematosus Disease Severity and Activity Index-Activity Score; CLASI-D: Cutaneous

138 Lupus Erythematosus Disease Severity and Activity Index-Damage Score; CLE: Cutaneous Lupus

139 Erythematosus; DLE = Discoid Lupus Erythematosus; LE: Lupus Erythematosus; PGA-A: Physician's Global

140 Assessment of Activity; PGA-D: Physician's Global Assessment of Damage; SD: standard deviation; SCL =

141 Subacute Cutaneous Lupus Erythematosus

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142 **Supplemental Figure Legends**

143 **Supplemental Figure 1. Representative patient clinical photographs demonstrating mild, moderate,**
144 **and severe disease damage by CLASI-D strata. (A)** A 40 year old female with facial lupus erythematosus
145 tumidus (LET) lesions, classified as having mild disease damage (CLASI-D of 0-5). **(B)** A 23 year old female
146 with disease damage from LET on bilateral thighs (left thigh pictured here) and hyperpigmentation and
147 scarring on bilateral arms (not pictured), classified as moderate disease damage (CLASI-D of 6-16). **(C)** A
148 78 year old male with severe disease damage from DLE on scalp (CLASI-D of 17+).

149 **Supplemental Figure 2. CLE subtypes in different severity groups of activity and damage. (A-B)** Bar
150 graphs compared different categories of CLE disease activity and damage in ACLE (n=28), SCLE (n=33),
151 and DLE patients (n=179). **(A)** Damage severity was found to be significantly different among disease
152 subtypes ($p < 0.0001$). Patients with DLE were more likely to have severe disease damage. **(B)** Activity
153 severity did not appear to be significantly associated with any particular subtype ($p = 0.36$).

154 Abbreviations: ACLE: acute cutaneous lupus erythematosus; DLE: discoid lupus erythematosus; SCLE:
155 subacute cutaneous lupus erythematosus

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