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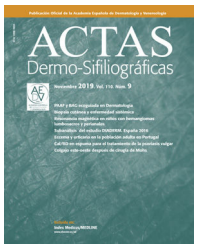

RESIDENT'S FORUM

[Translated article] RF-2019 Classification Criteria for Systemic Lupus Erythematosus

FR-Criterios de clasificación 2019 del lupus eritematoso sistémico

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Systemic lupus erythematosus (SLE) is a systemic autoimmune disease with a broad spectrum of clinical and immunological manifestations, that is difficult to diagnose. The classification criteria for SLE are essential for standardization of cohorts and reproducibility of clinical trials.[1]

In 2019, the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) drew up new classification criteria for SLE[2] (EULAR/ACR-2019). These were more sensitive and specific than the 1997 criteria of the ACR (ACR-1997) and the 2012 criteria of the Systemic Lupus International Collaborating Clinics (SLICC-2012). The methodology included an initial phase comprising a systematic review of the literature,[3] a Delphi exercise with 145 international experts,[4] a cohort of 616 patients with recent-onset SLE, and a survey of 339 individuals with SLE. In the second phase, 19 experts used the nominal group technique to reduce the number of classification criteria to 21.[5] In the third phase, the criteria were separated into clinical and immunological criteria. Weighting was based on a representative sample of patients with SLE, and pairs of criteria were compared using a multicriteria decision analysis. The last phase, of refinement and validation of the criteria, was based on a validation cohort comprising 1270 individuals (696 patients with SLE and 574 controls with diseases mimicking SLE). The sensitivity and specificity of the new criteria were 96.1% and 93.4%, respectively, which represents an improvement on the ACR-1997 and SLICC-2012 criteria,[2] thus enabling greater accuracy and a lower percentage of false positives and negatives.

The most relevant modification introduced by EULAR/ACR-2019 is the presence of antinuclear antibodies (ANA) at titers of $\geq$1/80 (measured as HEp-2 cells or equivalent) as an essential criterion, thus excluding patients with persistently negative ANA titers. This criterion is based on the results of a systematic review of 13 080 patients with SLE, in which an ANA titer $\geq$1/80 had 97.8% sensitivity.[3]

In addition, the clinical and immunological criteria were redesigned and are now subdivided into 7 clinical domains

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Table 1 Criteria for Systemic Lupus Erythematosus According to the New 2019 Classification of the European League Against Rheumatism and the American College of Rheumatology (EULAR/ACR-2019).

	EULAR/ACR-2019 Entry criterion: ANA at titers ≥ 1/80 Additive criteria: at least 1 clinical criterion and ≥ 10 points[a]	
Clinical domains		Weight
Constitutional	Unexplained fever > 38.5 °C[b]	2
Hematologic	Leukopenia	3
	Thrombocytopenia	4
	Autoimmune hemolysis	4
Neuropsychiatric	Delirium	2
	Psychosis	3
	Seizure	5
Mucocutaneous	Nonscarring alopecia	2
	Oral ulcers	2
	Subacute cutaneous or discoid lupus[c]	4
	Acute cutaneous lupus[c]	6
Serosal	Pleural or pericardial effusion	5
	Acute pericarditis	6
Musculoskeletal	Joint involvement	6
Renal	Proteinuria > 0.5 μg/d	4
	Renal biopsy class 2 or 5 lupus nephritis	8
	Renal biopsy class 3 or 4 lupus nephritis[d]	10
Immunological domains		Weight
Antiphospholipid antibodies	Anticardiolipin antibodies or anti-β2GP1 antibodies or lupus anticoagulant	2
Complement proteins	Low C3 or C4	3
	Low C3 and C4	4
SLE-specific antibodies	Anti-dsDNA antibody or anti-Smith antibody	6

Abbreviations: ANA, antinuclear antibody; anti-dsDNA, anti-double stranded DNA antibody; anti-β2GP1, anti-ß2 glycoprotein 1; EULAR/ACR-2019, 2019 classification of the European League Against Rheumatism and the American College of Rheumatology for SLE; SLE, systemic lupus erythematosus.

[a] The criteria are cumulative and do not need to be present simultaneously. Within each domain, only the highest-scoring criterion is counted for the total score.

[b] Unexplained fever > 38.3 °C is a new clinical criterion in this classification.

[c] Definitions:

a. Subacute cutaneous lupus: annular or papulosquamous (psoriasiform) cutaneous eruption, usually photodistributed.
- Skin biopsy: interface vacuolar dermatitis, perivascular lymphohistiocytic infiltrate, and/or dermal mucin.

b. Discoid lupus erythematosus:
- Erythematous-violaceous cutaneous lesions with atrophic scarring, dyspigmentation, follicular hyperkeratosis/plugging leading to scarring alopecia on the scalp.
- Skin biopsy: interface vacuolar dermatitis, perivascular and/or periappendageal lymphohistiocytic infiltrate. Plugs may be observed on the scalp, as may be mucin deposition in longstanding lesions.

c. Acute cutaneous lupus:
- Malar rash or generalized maculopapular rash.
- Skin biopsy: interface vacuolar dermatitis, perivascular lymphohistiocytic infiltrate, often with dermal mucin. Perivascular neutrophilic infiltrate may be present early in the course.

[d] Class 3 or 4 lupus nephritis itself indicates a total score of 10. ANA ≥ 1/80 is sufficient to classify a patient as having SLE.

(constitutional, hematologic, neuropsychiatric, serosal, mucocutaneous, musculoskeletal, and renal) and 3 immunological domains (antiphospholipid antibodies, low complement levels, and SLE-specific antibody). Unexplained fever was included as a constitutional clinical criterion. Within each domain, the criteria are weighted with values ranging from 2 to 10 according to their relative weight in the diagnosis of SLE based on available scientific evidence. Therefore, based on the new criteria, diagnosis of SLE requires a positive ANA titer ≥1/80, a clinical criterion, and a score ≥10. The changes in weighting make it possible to classify as having SLE patients with class 3–4 lupus nephritis as the only clinical manifestation and a positive ANA titer. As for mucocutaneous criteria, even if a patient presents with various cutaneous manifestations that are typical of SLE, only that with the highest value will be scored (Table 1). Therefore, in line with the new classification, it is not possible to classify an SLE patient based only on mucocutaneous findings.

The new EULAR/ACR-2019 classification criteria for SLE are more sensitive and specific and include major

modifications: positive ANA titers as an essential requirement, new clinical criteria, and changes in weighting. These are aimed at standardizing SLE cohorts and including individuals with a shorter disease course.

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