New 2019 SLE EULAR/ACR classification criteria are valuable for distinguishing patients with SLE from patients with pSS

The new 2019 SLE European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) classification criteria for systemic lupus erythematosus (SLE) have been recently published.[1] These criteria have been developed to find a better equilibrium between specificity and sensitivity compared with the previous criteria (SLE ACR-1997[2] and SLE Systemic Lupus International Collaborating Clinics (SLICC)[3]). Even if these criteria have been built for classification, they could be useful in clinical practice in patients with a suspicion of systemic autoimmune disease (AID) to differentiate patients with SLE from patients with another systemic AID, such as primary Sjögren's syndrome (pSS), scleroderma or myositis. SLE and pSS share biological and clinical similarities. In clinical practice, it is frequently difficult to differentiate these two diseases. Moreover, SLE and Sjögren's syndrome (SS) may overlap. The aim of this study was to explore the utility of the 2019 SLE EULAR/ACR criteria compared with the SLE ACR-1997[2] and SLE SLICC[3] criteria for differentiating patients with SLE from patients with pSS or with an overlap between SLE and SS in clinical practice.

This retrospective study was performed in the Department of Rheumatology, Hopitaux Universitaires Paris Sud, a French reference centre for rare systemic AID. The biological, immunological and clinical data were collected at diagnosis or at the first visit at the centre. We included three different groups of patients:

- Forty-nine patients with SLE (both inpatients and outpatients followed in the Department of Rheumatology) based on the diagnosis made by the clinician, with exclusion of patients with an association with another connective tissue disease.

Table 1 Patient characteristics

Characteristics		SLE	pSS	Overlap	P value
General features	Mean age at diagnosis, years (SD)	33 (11.88)	54 (13.96)	41 (16.43)	p < 10-4
	Female, n (%)	40 (81.6)	49 (100)	26 (100)	p = 0.001
	SLEDAI,[6] mean (SD)	11.32 (7.20) –	–	6.5 (5.34)	0.002
	Mean ESSDAI,[5] mean (SD)	x	5.55 (3.28)	9.65 (5.43)	p = 0.001
	Mean disease duration, years (SD)	14.2 (8.8)	14.4 (6.5)	14 (5)	p = 0.748
Clinical features	Fever, n (%)	9 (18.37)	1 (2.04)	3 (11.53)	p = 0.003
	Photosensitivity, n (%)	9 (18.37)	2 (4.08)	4 (15.38)	p = 0.082
	Acute/subacute lupus, n (%)	22 (44.90)	0 (0)	4 (15.38)	$p < 10^{-4}$
	Chronic lupus, n (%)	8 (16.32)	0 (0)	0 (0)	p = 0.001
	Oral ulcerations, n (%)	6 (12.24)	2 (4.08)	0 (0)	p = 0.083
	Non-scarring alopecia, n (%)	7 (14.29)	0 (0)	2 (7.69)	p = 0.024
	Pleurisy, n (%)	7 (14.29)	0 (0)	0 (0)	p = 0.003
	Pericarditis, n (%)	4 (8.16)	0 (0)	1 (3.84)	p = 0.121
	Adenomegalies, n (%)	10 (20.40)	3 (6.12)	5 (19.23)	p = 0.099
	Myalgias, n (%)	4 (8.16)	14 (28.57)	5 (19.23)	p = 0.034
	Arthralgias, n (%)	45 (91.84)	41 (83.67)	19 (73.08)	p = 0.097
	Synovitis, n (%)	26 (53.06)	3 (6.12)	8 (30.77)	$p < 10^{-4}$
	Cough, n (%)	0 (0)	12 (24.49)	9 (34.61)	p = 0.0001
Biological features	Leukopenia*, n (%)	9 (18.36)	3 (6.12)	4 (23.07)	p = 0.178
	Lymphopenia†, n (%)	16 (32.65)	7 (14.29)	13 (50)	p = 0.004
	Mean CRP, mg/L (SD)	13.68 (28.13)	9.32 (13.98)	7.66 (15.22)	p = 0.0004
Immunological features	ANA >1/80 IIF **, n (%)	48 (97.96)	36 (73.47)	25 (96.15)	p = 0.003
	Anti-DNA, n (%)	44 (89.80)	0 (0)	26 (100)	$p < 10^{-4}$
	Anti-Sm, n (%)	19 (38.77)	0 (0)	7 (26.92)	$p < 10^{-4}$
	RF positivity, n (%)	1 (2.04)	17 (34.69)	11 (42.30)	p = 0.001
	APL, n (%)	20 (40.82)	7 (14.28)	7 (26.92)	p = 0.013
	Hypocomplementaemia C3 ‡, n (%)	13 (26.53)	0 (0)	3 (11.54)	$p < 10^{-4}$
	Hypocomplementaemia C4§, n (%)	24 (48.98)	9 (18.36)	9 (34.6)	p = 0.006
	Hypergammaglobulinaemia ¶, n (%)	18 (58.06)	21 (43.75)	22 (88.46)	p = 0.0002
	Mean serum gammaglobulin level, g/L (SD)	15.4 (5.44)	14.3 (6.44)	19.1 (6.58)	p = 0.002
Renal features	Significant glomerular proteinuria, n (%)	17 (34.69)	0 (0)	1 (3.85)	$<10^{-4}$
Sets of criteria	SLE ACR-1997, n (%)	38 (77.6)	1 (2.1)	10 (38.5)	$p < 10^{-4}$
	SLE SLICC, n (%)	48 (97.9)	4 (8.3)	20 (76.9)	$p < 10^{-4}$
	2019 SLE EULAR/ACR, n (%)	48 (97.9)	2 (4.2)	22 (84.6)	$p < 10^{-4}$
	pSS ACR/EULAR 2016, n (%)	0 (0)	49 (100)	26 (100)	p=1.000

Significant glomerular proteinuria was defined by daily proteinuria ≥1 g/day.
*Leucopenia was defined by leucocyte count <4 $x10^9$/L
†Lymphopaenia was defined by lymphocyte count <1$x10^9$/L.
‡Hypocomplementaemia C3 was defined by seric C3 fraction level ≤0.5 g/L.
§Hypocomplementaemia C4 was defined by seric C4 fraction level ≤0.15 g/L.
¶Hypergammaglobulinaemia was defined by serum gammaglobulin level >13.5 g/L.
ACR, American College of Rheumatology; ANA, antinuclear antibodies;APL, antiphospholipid; CRP, C reactive protein; ESSDAI, EULAR Sjögren's syndrome Disease Activity Index;EULAR, European League Against Rheumatism; IFF, indirect immunofluorescence assay; pSS, primary Sjögren's syndrome; RF, rheumatoid factor ; SLE, systemic lupus erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLICC, Systemic Lupus International Collaborating Clinics.

- Forty-nine patients with pSS randomly chosen from the Paris Sud database and compared in a 1:1 ratio with the SLE group. All patients with pSS fulfilled the pSS ACR/EULAR 2016 criteria.[4] We excluded patients with an association with another connective tissue disease.
- Twenty-six patients with SLE/SS overlap based on clinical diagnosis. This last group was made of 13 patients diagnosed with SLE but also presenting objective signs of associated Sjögren's syndrome, including positive minor salivary glands biopsy (Focus Score ≥1), and/or objective sicca syndrome defined by a salivary flow <0.10 mL/min or a Schirmer test <5 mm at 5 min (n=13), and 13 patients diagnosed with Sjögren's syndrome, but associated with anti-DNA antibodies.

The characteristics of the patients are presented in table 1. Disease duration was equal between the three groups, and was around 14 years in each arm. Three sets of lupus criteria (SLE ACR-1997, SLE SLICC and 2019 SLE EULAR/ACR criteria) were tested in each group of patients. The 2019 SLE EULAR/ACR criteria were met in 97.9% of patients with SLE and in only 4.2% of patients with pSS. Thus this new set of criteria for SLE offered the best equilibrium between specificity and sensitivity compared with the older criteria and was able to discriminate patients with SLE and pSS in clinical practice.

Interestingly, patients from the overlap group fulfilled both the criteria for SLE and SS, confirming the mixed presentation and the capacity of the criteria to detect the overlap. The comparison of the three groups showed that some clinical and biological manifestations helped to differentiate the two conditions. Actually, skin involvement, serositis, synovitis, glomerular involvement, lymphopaenia and systemic inflammation were more frequent in SLE. Conversely, cough, myalgia and rheumatoid factor positivity at diagnosis were more frequent in pSS. Systematic assessment of sicca symptoms is easy and might help to differentiate the two conditions. Interestingly, patients with overlap syndrome were likely to present with a more systemic disease than patients with pSS alone as assessed by the EULAR Sjögren's Syndrome Disease Activity Index.[5]

To sum up, this study shows that the new 2019 SLE EULAR/ACR criteria for SLE can be useful in clinical practice helping to differentiate between SLE and pSS and detecting overlap presentations.

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REFERENCES

1 Aringer M, Costenbader K, Daikh D, *et al*. 2019 European League against Rheumatism/American College of rheumatology classification criteria for systemic lupus erythematosus. *Ann Rheum Dis* 2019;78:1151–9.
2 Hochberg MC. Updating the American College of rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997;40.
3 Petri M, Orbai A-M, Alarcón GS, *et al*. Derivation and validation of the systemic lupus international collaborating clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheumatism* 2012;64:2677–86.
4 Shiboski CH, Shiboski SC, Seror R, *et al*. 2016 American College of Rheumatology/European League against rheumatism classification criteria for primary Sjögren's syndrome: a consensus and data-driven methodology involving three international patient cohorts. *Arthritis Rheumatol* 2017;69:35–45.
5 Seror R, Theander E, Brun JG, *et al*. Validation of EULAR primary Sjögren's syndrome disease activity (ESSDAI) and patient indexes (ESSPRI). *Ann Rheum Dis* 2015;74:859–66.
6 Bombardier C, Gladman DD, Urowitz MB, *et al*. Derivation of the SLEDAI. A disease activity index for lupus patients. The Committee on prognosis studies in SLE. *Arthritis Rheum* 1992;35:630–40.