New 2019 SLE EULAR/ACR classification criteria are valid for identifying patients with SLE among patients admitted for pericardial effusion

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 Seritis is a prominent—often inaugural—feature of active SLE. Low titers of antinuclear antibodies (ANA) have been frequently reported in patients with idiopathic pericarditis.^{2,3} Of note, ANA positivity at a titer $\geq 1/80$ is now mandatory as an entry criterion in the 2019 SLE EULAR/ACR classification criteria. Although classification criteria have theoretically no individual diagnostic purpose, we aimed at testing this new criteria set in unselected patients with pericardial effusion.

In a retrospective study performed in the Department of Internal Medicine, University Paris Diderot, a French competence centre for rare systemic autoimmune diseases (AIDs), all consecutive adult patients hospitalised from January 2009 to January 2019 for pericardial effusion were reviewed. Clinical and biological data collected at time of the diagnosis of pericardial effusion were analysed.

Over a 10-year period, 137 patients were admitted for pericardial effusion. Search for ANA was systematically performed at diagnosis in all but 8 ($n=129$) and measured at a titer $\geq 1:80$ on Hep-2 cells in 49 patients (38%) that were eventually separated in three groups:

1. Seventeen (34.7%) patients with a final diagnosis of SLE based on senior clinician judgement.
2. Six (12.2%) patients with a final diagnosis of AID other than SLE including primary Sjögren's syndrome ($n=2$), undifferentiated connective-tissue disease ($n=2$) and systemic sclerosis ($n=2$).
3. Twenty-six (53.1%) patients with a diagnosis of idiopathic pericarditis after exclusion of malignancy, tuberculosis and systemic inflammatory diseases with a median 12.3 (1.6–29.8) months follow-up

The characteristics of the patients are listed in table 1. Three sets of lupus criteria (SLE ACR-1997,⁴ SLE SLICC⁵ and 2019 SLE EULAR/ACR criteria) were applied in all ANA-positive patients. The 2019 SLE EULAR/ACR criteria were met in 100% of patients with SLE, 33.3% of patients with non-SLE AID and 11.5% of patients with idiopathic pericarditis. Thus, this new set of criteria for SLE offered a higher sensitivity (100%) but a lower specificity (84.38%) as compared with the former criteria, for the diagnosis of SLE in patients with pericardial effusion (online supplementary table S1). Interestingly, the 2019 SLE EULAR/ACR classification score was higher in SLE patients (median: 30 (11–45)) as compared with non-SLE AID (median: 8 (6–12), $p=0.0006$) and idiopathic pericarditis patients (median: 6 (5–12), $p<0.00001$). Moreover, the 2019 classification set score strongly correlated with the Systemic Lupus Erythematosus Disease Activity Index activity score⁶ as shown online supplementary figure S1 ($R^2=0.8105$, $p<0.00001$). Setting the 2019 SLE EULAR/ACR classification threshold score >12 (out of a theoretical maximum of 51) instead of ≥ 10 increased the specificity of 2019 SLE EULAR/ACR criteria from 84.38% to 100%. Overall, in patients with pericardial effusion and positive ANA, the diagnosis of SLE could be ruled out when 2019 SLE EULAR/ACR criteria score was <10 and confirmed when the score was >12 .

Table 1 Patients clinical and biological characteristics

	SLE n=17	Non-SLE AID n=6	Idiopathic n=26	P value*
General features				
Median age at diagnosis, years (range)	32.4 (18.4–46.7)	47.2 (30.5–61.1)	51.4 (24.5–79.9)	0.028
Female, n (%)	17 (100)	6 (100)	11 (42.3)	0.0001
SLEDAI, median (range)	15 (6–38)	–	–	–
Clinical features, n (%)				
Fever	5 (29.4)	1 (16.7)	7 (26.9)	1.000
Pericardial effusion†	17 (100)	6 (100)	26 (100)	1.000
Acute pericarditis‡	8 (47.1)	5 (83.3)	21 (80.8)	0.044
Cardiac tamponade§	0 (0)	1 (16.7)	15 (57.7)	0.0001
Pleural effusion	10 (58.8)	5 (83.3)	19 (73.1)	0.507
Non-scarring alopecia	0 (0)	0 (0)	0 (0)	1.000
Oral ulcers	2 (11.8)	0 (0)	0 (0)	0.151
Subacute cutaneous lupus	1 (5.9)	0 (0)	0 (0)	0.395
Acute cutaneous lupus	2 (11.8)	0 (0)	0 (0)	0.151
Delirium	1 (5.9)	0 (0)	0 (0)	0.395
Psychosis	0 (0)	0 (0)	0 (0)	1.000
Seizure	2 (11.8)	0 (0)	0 (0)	0.151
Joint involvement	11 (64.7)	2 (33.3)	0 (0)	<0.00001
Biological features, n (%)				
Leucopenia	6 (35.3)	0 (0)	0 (0)	0.002
Thrombocytopenia	5 (29.4)	0 (0)	0 (0)	0.006
Autoimmune haemolysis	2 (11.8)	0 (0)	0 (0)	0.151
Proteinuria >0.5 g/24	11 (64.7)	0 (0)	1 (3.8)	0.006
Histological features¶, n (%)				
Class II or V lupus nephritis	3 (17.6)	0 (0)	0 (0)	0.055
Class III or IV lupus nephritis	6 (35.3)	0 (0)	0 (0)	0.002
Immunological features, n (%)				
ANA** $\geq 1/80$	17 (100)	60 (100)	26 (100)	1.000
ANA $\geq 1/160$	17 (100)	60 (100)	13 (50)	0.0004
ANA $\geq 1/320$	17 (100)	60 (100)	6 (23.1)	<0.00001
ANA $\geq 1/640$	16 (94.1)	5 (83.3)	4 (15.4)	<0.00001
ANA $\geq 1/1280$	12 (70.6)	4 (66.7)	1 (3.8)	<0.00001
Anti-dsDNA antibodies	13 (76.5)	0 (0)	2 (7.7)	<0.00001
Anti-Sm antibodies	3 (17.6)	0 (0)	0 (0)	0.055
aPL antibodies††	9 (52.9)	0	5 (19.2)	0.044
Low C3	12 (70.6)	0 (0)	0 (0)	<0.00001
Low C4	12 (70.6)	1 (16.7)	0 (0)	<0.00001
Sets of criteria, n (%)				
SLE ACR-1997	16 (94.1)	0 (0)	0 (0)	<0.00001
SLE SLICC	16 (94.1)	0 (0)	0 (0)	<0.00001
2019 SLE EULAR/ACR	17 (100)	2 (33.3)	3 (11.5)	<0.00001
Score, median (range)	30 (11–45)	8 (6–12)	6 (5–12)	<0.00001

*As compared between SLE and idiopathic and determined using Mann-Whitney test for continuous variables and Fisher's test for categorical variables.

†Pericardial effusion defined as ultrasound evidence for pericardial effusion.

‡Acute pericarditis defined as pericardial chest pain associated with pericardial effusion on ultrasound.

§Cardiac tamponade defined as a life-threatening compression of the heart requiring surgical drainage.

¶Histological features on renal biopsy according to ISN/RPS 2003 classification.

**Antinuclear antibodies (ANA) titer measurement on Hep-2 cells.

††aPL antibodies included anticardiolipin antibodies (IgG or IgM) at medium or high titer (>40 GPL or MPL units) and/or positive anti- $\beta 2$ GP1 antibodies (IgG or IgM) and/or positive lupus anticoagulant. ACR, American College of Rheumatology; AID, autoimmune disease; ANA, antinuclear antibodies on Hep-2 cells; aPL, antiphospholipid; C3 and C4, serum complement components C3 and C4; dsDNA, double-stranded DNA; SLE, systemic lupus erythematosus; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; SLICC, Systemic Lupus International Collaborating Clinics; Sm, Smith.

Comparative analysis showed that SLE patients were younger, more frequently female and had higher titers of ANA while cardiac tamponade was more frequent in idiopathic pericarditis. Interestingly, non-SLE AID features appeared to belong to a spectrum between SLE and idiopathic pericarditis.

In conclusion, this study shows that the new 2019 SLE EULAR/ACR criteria for SLE are helpful in clinical practice for the diagnosis of SLE in patients admitted for pericardial effusion.

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