Proposal and validation of new activity states definitions according severity in SLE on the basis of RELESSER-PROS register database

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OBJECTIVE: To propose a definition for moderate disease activity state (MODAS) and severe disease activity state (SEDAS) in SLE and using the RELESSER-PROS cohort to describe the prevalence of both states of activity and to analyse the impact of this categorization on different outcomes.

METHODS: The study population belongs to the RELESSER-PROS prospective cohort with data from patients followed annually for 4 years. Definitions:

- **MODAS** the presence of at least one of the following conditions: <4 cSLEDAI ≤ 8 or $1< PGA \leq 2$ (without severe clinical manifestations)
- **SEDAS:** SLEDAIc >8 or PGA > 2 or the presence of severe SLEDAI and Non-SLEDAI manifestations.
- **Low disease activity (No MODAS nor SEDAS):** $1 \leq SLEDAIc \leq 4$ or $0 < PGA \leq 1$.

Subsequently, an internal validation was carried out, analysing the impact of belonging to one of the predefined groups in several robust outcomes overtime. A descriptive analysis was conducted for the variables based on the presence of MODAS or SEDAS in at least 1 of the 5 visits and according to the number of visits with MODAS or SEDAS. The significance level for all tests was set at 0.05.

RESULTS: A total of 1463 patients (90% women) were included, with a mean age (±SD) of 56 (±13.5) years. The mean disease duration of SLE (±SD) at V1 was 14 (±8.5) years.

Criteria for MODAS was met by 207 (14.1%) patients at V1, 110 patients (8.1%) at V2, 90 patients (7.2 %) at V3, 75 patients (6.8%) at V4 and 61 patients (5.8 %) at V5. On the other hand, 217 patients (14.8 %) at V1, 103 patients (7.6 %) at V2, 90 patients (7.2 %) at V3, 53 patients (4.8 %) at V4 and 62 patients (5.9%) at V5 met the Criteria for SEDAS.

Patients with at least 1 visit in MODAS or in SEDAS had significantly most damage accrual higher number of flares, more hospital admissions, and worse quality of life (p<0.001). Damage accrual and hospital admissions were significantly higher in SEDAS than in MODAS. This is also the case for all the outcomes, except for mortality, when comparing being in MODAS or SEDAS with not being in these states. **Figure 1**. Besides, the more visits in MODAS or in SEDAS, greater damage, more admissions, more flares and worse quality of life. The SEDAS entails the greater risk of all the defined activity states. Table 1 and 2.

Table 1. Outcomes taking into account the number of visits in SEDAS.

|	Number of visits in SEDAS				p-value 0 vs 1	p-value 1 vs 2	p-value 2 vs 3
	0 (n=1103)	1 (n=249)	2 (n=76)	3 (n=24)			
Deaths; n (%)	36 (3.26%)	5 (2.01%)	2 (2.63%)	0 (0%)	NS	NS	NS
Admissions; mean (SD)	0.72 (1.55)	1.31 (1.90)	2.09 (3.32)	3.63 (4.00)	<0.001*	1.000	0.281
Δ SDI (V5-V1); mean (SD)	0.41 (0.76)	0.69 (1.03)	1.30 (1.38)	1.57 (1.83)	0.003*	0.006*	1.000
Number of flares; mean (SD)	1.17 (1.92)	2.02 (2.53)	2.83 (2.80)	3.71 (2.20)	<0.001*	0.189	0.512
Quality of life (mean LIT); mean (SD)	28.2 (20.6)	33.3 (19.6)	37.2 (22.5)	38.3 (16.0)	0.001*	1.000	1.000
Quality of life (Highest LIT); mean (SD)	38.1 (24.2)	45.2 (22.9)	50.2 (26.4)	53.3 (19.7)	0.001*	1.000	1.000

NS: not significant. *p<0.05

Table 2. Outcomes taking into account the number of visits in MODAS.

	Number of visits in MODAS				p-value 0 vs 1	p-value 1 vs 2	p-value 2 vs 3
	0 (n=1103)	1 (n=249)	2 (n=76)	3 (n=24)			
Deaths; n (%)	26 (3.26%)	7 (3.27%)	3 (5.17%)	0 (0%)	NS	NS	NS
Admissions; mean (SD)	0.58 (1.35)	1.00 (1.73)	1.03 (1.83)	2.14 (3.94)	0.002*	1.000	1.000
Δ SDI (V5-V1); mean (SD)	0.33 (0.68)	0.56 (0.80)	0.61 (1.18)	0.85 (0.94)	0.001*	1.000	1.000
Number of flares; mean (SD)	0.79 (1.51)	1.77 (2.14)	3.26 (2.91)	3.57 (3.61)	<0.001*	<0.001*	1.000
Quality of life (mean LIT); mean (SD)	25.8 (20.2)	33.1 (20.6)	39.2 (18.0)	37.8 (21.2)	<0.001*	0.333	1.000
Quality of life (Highest LIT); mean (SD)	34.9 (23.5)	44.6 (24.1)	51.6 (21.6)	54.3 (27.0)	<0.001*	0.7118	1.000

Δ SDI: SLICC/ACR damage index in V5 minus SDI in V1; LIT: lupus impact tracker. NS: not significant. *p<0.05

Figure 1. Comparison of risk admissions, damage and quality of life between different states of activity

A Admissions
B Δ SDI (V5-V1)
C Number of flares
D Quality of life (Highest LIT)
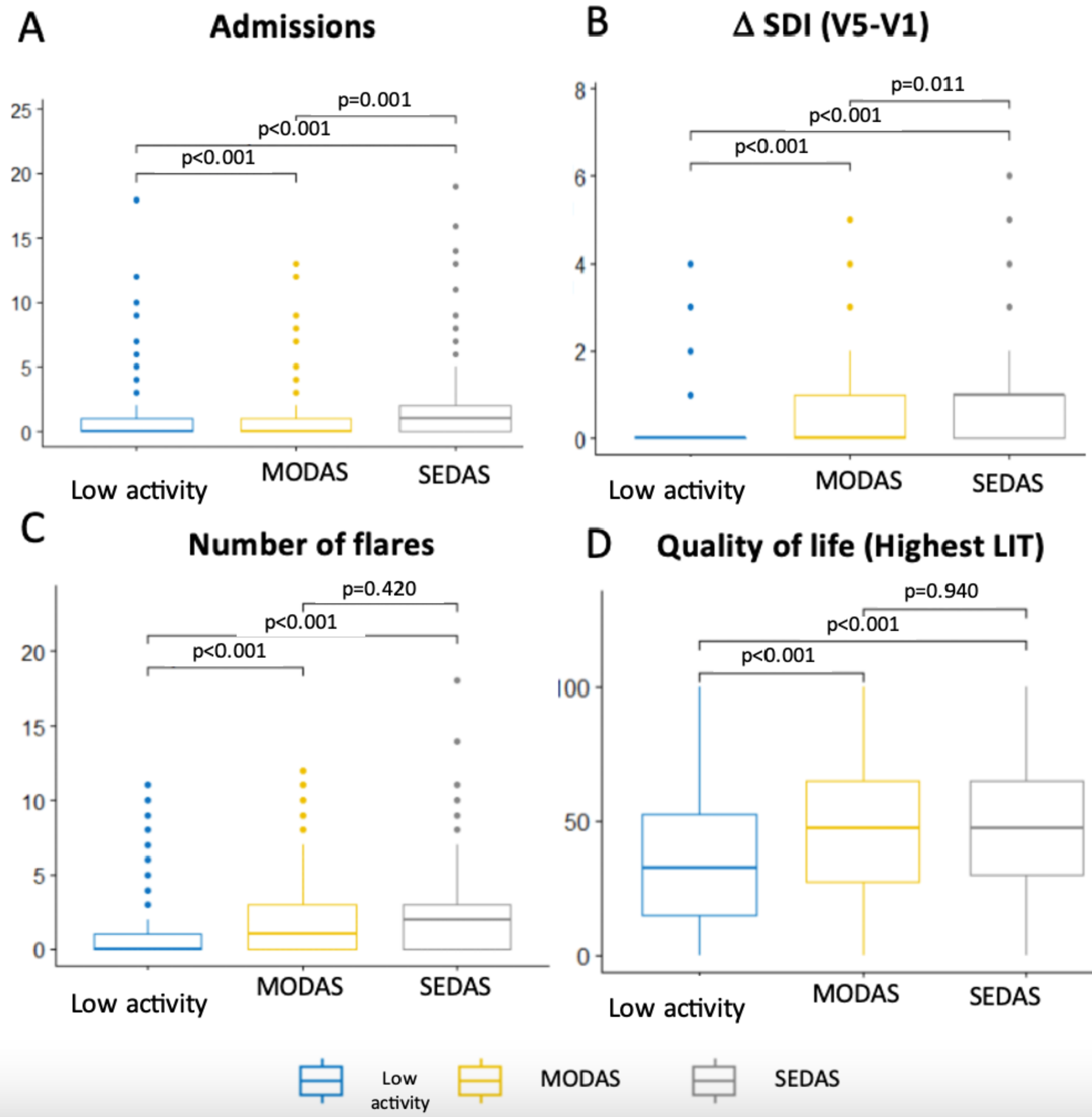
CONCLUSION: Patients who were in a state of moderate or severe activity at least one time had worse outcomes at the end of follow-up in terms of damage accrual, hospital admissions, number of flares and deterioration in HRQoL. Furthermore, more visits in these states entail a greater risk. The SEDAS is the one that is related to the worst outcomes. These results emphasize the importance of an adequate stratification of disease activity in SLE patients.

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