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Severe flares are associated with a poorer health-related quality of life (HRQoL) in patients with SLE: data from the Almenara Lupus Cohort

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ABSTRACT

Background Flares in patients with SLE, regardless of their severity, have been associated with damage accrual. However, their impact on health-related quality of life (HRQoL) has not been fully evaluated. In fact, disease activity is only minimally associated with HRQoL.

Objective To determine the association between flares and HRQoL.

Methods Patients from the Almenara Lupus Cohort were included. Visits occurring between December 2015 and February 2020 were evaluated. Flares were defined as an increase on the SLE Disease Activity Index 2000 (SLEDAI-2K) of at least 4 points; severe flares were those with a final SLEDAI-2K ≥12 and mild-moderate flares all the others. HRQoL was measured using the LupusQoL. Univariable and multivariable generalised estimating regression equations were performed, adjusting for possible confounders. Confounders were determined at one visit, whereas the outcome was determined on the subsequent visit; flares were determined based on the variation of the SLEDAI-2K between these visits.

Results Two hundred and seventy-seven patients were included; 256 (92.4%) were female, mean age at diagnosis was 36.0 (SD: 13.3) years and mean disease duration at baseline was 9.1 (SD: 7.1) years. Patients had mean of 4.8 (SD: 1.9) visits and a mean follow-up of 2.7 (1.1) years. Out of 1098 visits, 115 (10.5%) flares were defined, 17 were severe and 98 mild-moderate. After adjustment for possible confounders, only severe flares were associated with a poorer HRQoL in planning, pain, emotional health and fatigue.

Conclusions Severe flares, but not mild-moderate, flares are associated with poorer HRQoL.

Key messages

What is already known about this subject?

- Flares have been associated with damage, but their impact on health-related quality of life (HRQoL) has not been fully evaluated.

What does this study add?

- This study evaluates the impact of flares (mild-moderate or severe) on HRQoL.
- Severe flares are associated with poorer HRQoL.

How might this impact on clinical practice or future developments?

- This study reinforces the need to develop effective strategies that allow us to prevent flares.

INTRODUCTION

The management of SLE has improved during the last several decades, improving patients' survival; however, these patients still have an impaired health-related quality of life (HRQoL).[1]

Several sociodemographic factors have been associated with an impaired HRQoL like age, ethnicity, poverty, lower educational level and inadequate social support.[2–7] The impact of disease activity[2 8–11] or damage[12–14] on HRQoL is still controversial. Flares have been associated with poorer HRQoL in France,[15] Thailand[16] and in the USA.[17] These studies did not differentiate flares based on their severity, and the US study was based on patient-reported flares. HRQoL is one of the indicators that should be measured in the monitoring of patients with SLE in routine clinical practice.[18]

Based on international consensus, flares are defined as: 'a measurable increase in disease activity in one or more organ systems involving new or worse clinical findings, laboratory measurements. It is a temporary event and must be considered clinically significant by the assessor and usually there would be at least consideration of a change or an increase in treatment'.[19] Flares have been associated

with a higher damage accrual,[20–22] higher direct and indirect cost.[23 24]

The aim of this study was to evaluate the impact of flares categorising them into mild-moderate and severe on HRQoL.

METHODS

The Almenara Lupus Cohort has been previously described.[25] In short, this cohort was started in 2012 at the Rheumatology Department of the Hospital Guillermo Almenara Irigoyen in Lima, Peru. Patients included in the Almenara Lupus Cohort were managed by physicians from our Rheumatology Department who participated in the study. These visits took place in the ambulatory setting. Patients who signed the informed consent were recruited and followed every 6 months. Evaluations included an interview, medical records review, physical examination and laboratory tests. For these analyses, we have included those patients with at least two visits between December 2015 and February 2020.

SLE was defined using the 1997 revised American College of Rheumatology (ACR) criteria.[26] Demographic data included sex, age at diagnosis, socioeconomic status according to the Graffar method[11] and educational level, defined as years of formal education. Disease activity was ascertained using the SLE Disease Activity Index 2000 (SLEDAI-2K).[27] Damage was ascertained with the Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI).[28] HRQoL was ascertained using the LupusQoL.[29] Therapeutic variables included current prednisone dose, antimalarials and immunosuppressive drug use (including methotrexate, azathioprine, leflunomide, mycophenolate mofetil, calcineurin inhibitors, cyclophosphamide and rituximab); the latter were recorded as current, past or never administered.

Flare was defined as an increase of the SLEDAI-2K of at least 4 points. Severe flares were those with a final SLEDAI-2K ≥12 and mild-moderate flares all the others.[30 31] Minimum clinically important differences (MCIDs) were defined using the cut-off proposed by McElhone *et al*.[32]

Statistical analyses

Categorical variables are reported as numbers and percentages, numerical variables as mean and SD. The mean values for each LupusQoL domain at the index visit and at the subsequent visit as a function of the absence of flare or the presence of mild-moderate or severe flares were compared using analysis of variance.

Univariable and multivariable generalised estimating regression equations were performed for each domain of the LupusQoL, adjusting for possible confounders. Possible confounders included in the multivariable analyses were sex, age at diagnosis, socioeconomic status, educational level, disease duration, SDI, prednisone daily dose, antimalarial use, immunosuppressive drug use and the same domain of the LupusQoL. Confounders were determined at one visit, whereas the outcome was determined at the subsequent visit; flares were determined based on the variation of the SLEDAI-2K between these visits.

A p<0.05 was considered significant in all analyses. All analyses were performed using SPSS V.27.0 (IBM).

Table 1 Characteristics of the patients at baseline

Characteristics	N (%) or mean (SD)
Female sex	256 (92.4)
Age at diagnosis, years	36.0 (13.3)
Disease duration, years	9.0 (7.0)
SLEDAI-2K	1.3 (2.5)
SDI ≥1	164 (58.4)
SDI	1.3 (1.5)
Prednisone daily dose, mg/day	2.1 (3.4)
Antimalarial use	
Never	10 (3.6)
Past	19 (6.9)
Current	248 (89.5)
Immunosuppressive drug use	
Never	61 (22.0)
Past	68 (24.5)
Current	148 (53.4)
LupusQoL domain	
Physical health	66.1 (23.5)
Pain	68.0 (27.3)
Planning	68.6 (29.2)
Intimate relationship	59.1 (35.9)
Burden to others	53.3 (31.3)
Emotional health	64.5 (25.4)
Body image	60.0 (30.2)
Fatigue	61.8 (27.4)

N, number; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SLEDAI-2K, SLE Disease Activity Index 2000.

RESULTS

Two hundred and seventy-seven patients were included; 256 (92.4%) were female, mean age at diagnosis was 36.0 (SD: 13.3) years and mean disease duration at baseline was 9.1 (SD: 7.1) years. Patients had mean of 4.8 (SD: 1.9) visits and a mean follow-up of 2.7 (1.1) years. Most patients in this cohort are Mestizo, that is of European and Amerindian ancestral background. General characteristics of these patients are depicted in table 1. The most affected domains of the LupusQoL at baseline were burden to others, intimate relationship and body image.

The proportion of patients who achieved an MCID is depicted in table 2.

Table 2 Change in HRQoL between two consecutive visits

	Improved	Same	Worse
Physical health	285 (26.0%)	536 (48.8%)	277 (25.2%)
Pain	390 (35.5%)	337 (30.7%)	371 (33.8%)
Planning	370 (33.7%)	361 (32.9%)	367 (33.4%)
Intimate relationship	316 (28.8%)	448 (40.8%)	334 (30.4%)
Burden to others	298 (27.1%)	381 (34.7%)	419 (38.2%)
Emotional health	352 (32.1%)	424 (38.6%)	322 (29.3%)
Body image	349 (31.8%)	283 (25.8%)	466 (42.4%)
Fatigue	269 (24.5%)	394 (35.9%)	435 (39.6%)

HRQoL, health-related quality of life.

When we evaluated the HRQoL at the index visit, only emotional health was lower in those patients who will subsequently present severe flares. However, these patients had lower HRQoL in the pain, planning and emotional health domains at the subsequent visits. In contrast, patients with mild-moderate flares had similar values in all HRQoL domains than those without flares at the index visit (table 3).

Out of 1098 visits, 115 (10.5%) flares were defined, 17 were severe and 98 mild-moderate. The incidence of flares was 15.3 per 100 patient-years; this corresponded to 2.3 per 100 patient-years for severe flare and to 13.1 per 100 patient-years for mild-moderate flares. Univariable associations between variables and the domains of the LupusQoL are depicted in table 4. Of importance, severe flares were associated with a poorer HRQoL in planning, pain, emotional health and fatigue. After adjustment for possible confounders, severe flares remained associated with a poorer HRQoL in the same domains (table 5).

DISCUSSION

In this primarily Mestizo-prevalent lupus cohort, severe, but not mild-moderate, flares were associated with a lower HRQoL, independently of other well-known risk factors for this endpoint.

The mean HRQoL domain scores in our study were similar to those reported in other Latin America studies[33–35] including two from Peru which included the current cohort but also patients from other centres,[36 37]

Table 3 LupusQoL domains before and after each visit as a function of the presence or absence of flares

	No flare	Mild-moderate flares	Severe flares	
	Mean (SD)	Mean (SD)	Mean (SD)	P value
At the index visit				
Physical health	68.0 (23.2)	64.1 (23.3)	63.5 (25.6)	0.192
Pain	70.7 (25.3)	67.3 (27.7)	58.3 (30.7)	0.058
Planning	71.0 (27.3)	70.0 (26.5)	65.3 (28.5)	0.638
Intimate relationship	59.4 (34.5)	53.1 (34.0)	68.8 (30.8)	0.265
Burden to others	55.1 (31.1)	55.5 (30.9)	55.6 (31.3)	0.990
Emotional health	65.8 (25.9)	66.4 (24.9)	50.8 (30.4)	0.032
Body image	61.6 (31.9)	62.0 (27.9)	54.7 (35.9)	0.691
Fatigue	63.2 (26.0)	64.6 (25.5)	54.2 (27.4)	0.287
At the subsequent visit				
Physical health	68.3 (23.0)	67.7 (22.4)	57.0 (25.5)	0.133
Pain	71.8 (24.5)	67.1 (27.6)	50.5 (30.7)	0.001
Planning	72.3 (26.1)	68.6 (27.4)	57.4 (28.5)	0.032
Intimate relationship	60.2 (34.1)	55.0 (33.7)	61.3 (37.5)	0.517
Burden to others	56.2 (31.1)	53.2 (31.4)	45.1 (36.1)	0.247
Emotional health	66.3 (25.8)	69.2 (25.7)	45.3 (27.0)	0.002
Body image	61.1 (32.2)	64.1 (31.1)	47.0 (30.9)	0.157
Fatigue	64.0 (25.5)	63.6 (25.7)	50.7 (25.9)	0.103

LupusQoL, Lupus Quality of Life.

Table 4 Association between flares and health-related quality of life; univariable models

	Physical health		Pain		Planning		Intimate relationship		Burden to others		Emotional health		Body image		Fatigue	
	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value
Flares																
Severe	−11.3 (6.5)	0.084	**−21.3 (7.7)**	**0.006**	**−14.9 (7.0)**	**0.032**	1.0 (12.5)	0.939	−11.0 (8.4)	0.190	**−20.9 (6.4)**	**0.001**	−14.0 (7.8)	0.075	**−13.3 (6.1)**	**0.029**
Mild-moderate	−0.6 (2.3)	0.797	−4.7 (2.8)	0.095	−3.7 (2.9)	0.208	−5.3 (4.4)	0.232	−2.9 (3.3)	0.384	2.9 (2.7)	0.269	3.2 (3.3)	0.341	−0.4 (2.7)	0.876
No flares	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Male sex	6.8 (4.4)	0.124	6.7 (4.4)	0.130	3.5 (5.1)	0.489	12.1 (8.6)	0.157	0.4 (6.7)	0.951	2.5 (6.4)	0.703	3.2 (6.1)	0.604	3.6 (6.1)	0.549
Age at diagnosis, years	**−0.4 (0.1)**	**<0.001**	**−0.4 (0.1=**	**<0.001**	**−0.4 (0.1)**	**<0.001**	**−0.9 (0.2)**	**<0.001**	−0.1 (0.1)	0.303	**−0.3 (0.1)**	**0.002**	**−0.3 (0.1)**	**0.037**	**−0.3 (0.1)**	**0.013**
Socioeconomic status																
High	**11.7 (3.9)**	**0.003**	**11.0 (3.9)**	**0.005**	**12.0 (3.8)**	**0.002**	**19.5 (5.4)**	**<0.001**	2.0 (4.8)	0.682	**10.0 (4.3)**	**0.019**	8.1 (4.4)	0.063	**8.3 (4.2)**	**0.047**
Medium	5.7 (3.9)	0.146	5.0 (4.0)	0.208	0.4 (4.1)	0.915	3.8 (5.9)	0.594	2.7 (5.0)	0.599	1.3 (4.5)	0.773	1.1 (4.6)	0.814	2.8 (4.1)	0.498
Low	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Educational level, years	**1.1 (0.5)**	**0.012**	**1.1 (0.5)**	**0.034**	**1.3 (0.4)**	**0.002**	**2.7 (0.7)**	**<0.001**	0.2 (0.5)	0.603	**1.3 (0.5)**	**0.004**	**1.3 (0.5)**	**0.008**	**1.1 (0.5)**	**0.019**
Disease duration	0.1 (0.1)	0.561	0.2 (0.2)	0.232	**0.4 (0.2)**	**0.009**	0.4 (0.3)	0.164	**0.6 (0.2)**	**0.002**	**0.3 (0.2)**	**0.033**	0.2 (0.2)	0.417	**0.3 (0.2)**	**0.034**
SDI	**−3.9 (0.8)**	**<0.001**	**−2.8 (0.9)**	**0.002**	−2.6 (0.9)	0.004	−2.4 (1.4)	0.082	−1.6 (1.0)	0.102	−0.9 (0.9)	0.315	**−2.1 (1.0)**	**0.036**	−1.1 (0.9)	0.197
Prednisone, mg/day	−0.5 (0.3)	0.138	−0.3 (0.3)	0.377	−0.6 (0.3)	0.088	0.7 (0.5)	0.181	−0.7 (0.4)	0.112	−0.3 (0.4)	0.355	0.2 (0.4)	0.568	−0.6 (0.4)	0.114
Antimalarial use																
Current	−5.9 (8.0)	0.464	−4.5 (7.4)	0.541	−11.3 (6.2)	0.070	−19.1 (10.9)	0.080	**−19.6 (6.3)**	**0.002**	−10.1 (7.5)	0.178	0.2 (13.7)	0.987	**−11.1 (4.9)**	**0.022**
Past	−5.9 (8.9)	0.509	−3.3 (8.4)	0.693	−6.2 (7.3)	0.391	−14.0 (12.2)	0.253	**−18.1 (7.8)**	**0.021**	−5.4 (8.6)	0.531	−1.0 (14.5)	0.947	−10.0 (6.3)	0.117
Never	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Immunosuppressive drug use																
Current	−3.6 (3.1)	0.235	−4.9 (2.9)	0.093	−4.0 (3.6)	0.257	−4–6 (5.1)	0.372	−3.0 (4.5)	0.405	1.3 (3.4)	0.709	−0.6 (4.1)	0.878	2.0 (3.7)	0.598
Past	2.4 (3.3)	0.463	3.0 (3.3)	0.367	1.4 (4.0)	0.726	−1.5 (5.9)	0.801	−2.2 (5.0)	0.657	4.9 (3.9)	0.210	−0.4 (4.8)	0.936	**8.3 (4.1)**	**0.043**
Never	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Same domain of LupusQoL	0.7 (0.0)	**<0.001**	**0.6 (0.0)**	**<0.001**	**0.7 (0.0)**	**<0.001**	**0.6 (0.0)**	**<0.001**	**0.6 (0.0)**	**<0.001**	**0.7 (0.0)**	**<0.001**	**0.5 (0.0)**	**<0.001**	**0.7 (0.0)**	**<0.001**

Bolded entries are those with a p-value <0.05.
LupusQoL, Lupus Quality of Life; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SE, SE of the estimate.

Table 5 Association between flares and health-related quality of life. Multivariable models

	Physical health		Pain		Planning		Intimate relationship		Burden to others		Emotional health		Body image		Fatigue	
	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value
Flares																
Severe	−7.4 (4.6)	0.105	**−12.0 (5.1)**	**0.020**	**−10.1 (4.4)**	**0.023**	−6.3 (10.1)	0.538	−10.9 (6.9)	0.116	**−9.5 (4.3)**	**0.028**	−10.4 (6.6)	0.113	**−6.7 (2.9)**	**0.023**
Mild-moderate	2.2 (1.7)	0.202	−1.9 (2.0)	0.343	−1.8 (1.8)	0.334	−2.6 (2.8)	0.357	−2.4 (2.6)	0.354	3.2 (1.8)	0.080	3.9 (2.7)	0.159	−0.3 (1.8)	0.868
No flares	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Male sex	**4.1 (2.0)**	**0.043**	**5.4 (2.3)**	**0.021**	3.8 (2.4)	0.106	**10.6 (4.6)**	**0.022**	1.9 (3.1)	0.543	1.9 (2.5)	0.435	2.7 (3.6)	0.448	4.0 (2.3)	0.076
Age at diagnosis, years	**−0.2 (0.0)**	**<0.001**	**−0.1 (0.1)**	**0.005**	−0.1 (0.0)	0.068	**−0.4 (0.1)**	**<0.001**	0.0 (0.1)	0.657	0.0 (0.0)	0.372	0.0 (0.1)	0.782	0.0 (0.0)	0.695
Socioeconomic status																
High	3.3 (2.0)	0.110	4.3 (2.4)	0.081	4.0 (2.2)	0.068	6.1 (4.4)	0.162	−1.5 (2.8)	0.576	1.5 (2.0)	0.443	1.1 (3.2)	0.728	−0.5 (2.2)	0.836
Medium	2.2 (1.7)	0.196	2.4 (2.1)	0.259	0.5 (1.8)	0.765	1.6 (3.7)	0.677	0.7 (2.3)	0.765	−0.1 (1.8)	0.942	−1.4 (2.9)	0.633	−0.5 (1.8)	0.763
Low	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Educational level, years	−0.1 (0.2)	0.647	−0.1 (0.3)	0.626	−0.1 (0.2)	0.787	0.0 (0.6)	0.936	0.2 (0.3)	0.556	0.2 (0.2)	0.409	0.6 (0.4)	0.097	0.4 (0.3)	0.185
Disease duration	−0.1 (0.1)	0.417	0.0 (0.1)	0.962	0.1 (0.1)	0.252	0.0 (0.1)	0.996	**0.3 (0.1)**	**0.015**	0.1 (0.1)	0.495	0.2 (0.1)	0.222	0.1 (0.1)	0.167
SDI	**−1.1 (0.4)**	**0.004**	**−1.0 (0.4)**	**0.016**	−0.8 (0.4)	0.050	−0.1 (0.8)	0.904	−0.8 (0.5)	0.084	−0.5 (0.4)	0.222	−1.1 (0.7)	0.087	−0.5 (0.4)	0.152
Prednisone, mg/day	−0.3 (0.2)	0.058	−0.1 (0.2)	0.676	−0.3 (0.2)	0.149	−0.4 (0.3)	0.191	−0.4 (0.2)	0.124	−0.3 (0.2)	0.153	0.0 (0.2)	0.872	**−0.3 (0.2)**	**0.034**
Antimalarial use																
Current	−1.4 (2.4)	0.559	1.2 (4.0)	0.761	−1.6 (2.4)	0.509	−6.0 (3.6)	0.090	**−6.7 (2.4)**	**0.009**	−2.1 (3.3)	0.528	4.7 (7.1)	0.507	−1.5 (2.1)	0.477
Past	−1.0 (2.8)	0.727	2.2 (4.3)	0.616	−0.1 (2.8)	0.960	−2.9 (5.1)	0.568	**−7.0 (3.1)**	**0.029**	0.1 (3.7)	0.981	2.1 (7.6)	0.785	−1.3 (2.6)	0.599
Never	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Immunosuppressive drug use																
Current	−0.9 (1.2)	0.436	−1.6 (1.4)	0.161	−1.4 (1.5)	0.332	−1.3 (2.8)	0.648	−0.9 (2.0)	0.965	2.2 (1.4)	0.105	0.2 (2.5)	0.927	2.0 (1.4)	0.161
Past	0.9 (1.4)	0.519	0.6 (16)	0.709	0.5 (1.6)	0.763	−1.9 (3.4)	0.573	−1.5 (2.3)	0.508	2.6 (1.6)	0.096	1.0 (2.8)	0.712	**4.3 (1.6)**	**0.008**
Never	Ref		Ref		Ref		Ref		Ref		Ref		Ref		Ref	
Same domain of LupusQoL	**0.7 (0.0)**	**<0.001**	**0.6 (0.0)**	**<0.001**	**0.6 (0.0)**	**<0.001**	**0.5 (0.0)**	**<0.001**	**0.6 (0.0)**	**<0.001**	**0.7 (0.0)**	**<0.001**	**0.5 (0.0)**	**<0.001**	**0.7 (0.0)**	**<0.001**

Bolded entries are those with a p-value <0.05.
LupusQoL, Lupus Quality of Life; SDI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; SE, SE of the estimate.

UK[38] and Canada[39] ; overall these scores are higher than the original study from the USA[40] but not according with a more recent study from New York City.[41] These scores were lower than those reported from China.[42]

Our incidence of flares (15 per 100 patient-years) was slightly lower than the one reported in a study from Hong Kong (24 per 100 patient-years)[23 43] but similar to the one reported in China (12 per 100 patient-years),[44] Latin America (17 per 100 patient-years)[20] and in Padova, Italy (19 per 100 patient-years)[45] but higher than the one reported in Rome, Italy (7 per 100 patient-years).[46]

In a study from Hong Kong, investigators evaluated the cross-sectional association between flares in the preceding year and HRQoL, finding that those patients experiencing flares in the preceding year had a lower HRQoL in some domains (role limitation due to physical problems, general health, social function, role limitation due to emotional problems and the physical component summary (PCS) of the Short-Form 36 (SF-36)); however, in the multivariable model, the number of flares was only associated with role limitation due to physical problems. Severe flares were not associated with HRQoL.[43] In a study from Thailand, flares were associated with a lower PCS of the SF-36 and the global SLEQOL but not with the mental component summary of the SF-36.[16] In a post-hoc analysis of the BLISS 52 trial, patients who had flares had a worsening on their HRQoL in almost all the domains of the SF-36 (the only exception being role emotional).[47] In a study from France, authors examined the impact of flares (categorised based on the organ involved) and found that the physical domains of HRQoL were most affected by musculoskeletal and cutaneous flares, but also by renal and neurological flares; however, these authors did not take into account the severity of the flares.[15] In the Toronto cohort, using the same definition of flare, LupusQoL domain scores were lower in those who flared, but, they only had 14 visits (out of 376) defined as flare and they were not able to adjust the model for possible confounders.[39] However, in a study from the UK, worsening of disease activity [as measured using the British Lupus Isles Assessment Group (BILAG) index] was not associated with changes in the LupusQoL or the SF-36.[32]

Disease activity has been associated with HRQoL in previous reports,[34 36 38 40 48 49] but these studies evaluated this association cross-sectionally. A better control of disease activity, defined as the achievement of remission or low disease activity, has been associated with a better HRQoL in several cohorts[16 50–55] which is consistent with the data from our report.

When flares are reported by the patients, they tend to be associated with a poorer HRQoL as noted by Katz *et al* in a study from the USA[17]; furthermore, it is important to point out that patient-reported disease activity has been shown to be associated with worse HRQoL.[56]

Lower emotional health before the occurrence of severe flares could be a reflection of a more severe disease, but it could also reflect the presence of some manifestations otherwise not recognised in the physician-assessed disease activity indices, but which are perceived by the patients. Further studies are needed to determine these associations.

Other variables associated with HRQoL in the multivariable models were male sex, age at diagnosis, disease duration, SDI, prednisone dose, antimalarial and immunosuppressive drug use. The association between male sex and age at diagnosis has been previously reported by other groups reinforcing the importance of sociodemographic factors on HRQoL.[36 38 40] The association between damage and treatment and HRQoL may reflect the impact of the severity of the disease on HRQoL which is consistent with has been reported by others.[34 36 38 40 48 49]

Our study has some limitations: first, as this is a prevalent cohort, we cannot exclude the impact of disease characteristics before the baseline visit. Second, due to the relatively small sample size, we were not able to evaluate the impact of specific types of flares on HRQoL. Third, due to the relatively low prevalence of some comorbidities, specifically of fibromyalgia and depression, we were not able to evaluate their impact on the patients' HRQoL. The main strength of this study is to evaluate the impact of flares (and its severity) in a primarily Mestizo Latin American population.

In conclusion, severe flares, but not mild-moderate, flares are associated with poorer HRQoL, mainly on planning, pain, emotional health and fatigue domains.

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Patient and public involvement The Almenara Lupus Cohort used focus groups, interviews and questionnaires to determine the patients' priorities and preferences including which outcomes are relevant to them, and if there are any problems with the instruments used or the length of the visits. Patients are involved in recruitment

for the study, as they inform their relatives and friends about the cohort, and invite them to participate in the educational activities; if these contacts have SLE, they are invited into the cohort if they are affiliated with the Peruvian social security system. The results of our studies are reported to our patients during our different educational activities.

Patient consent for publication Not required.

Ethics approval This study involves human participants and has been approved by the Hospital Guillermo Almenara Irigoyen Institutional Review Board (3474-OCID-G-RAA-ESSALUD-11, 271-CEI-CIDG-RAA-ESSALUD-13, 302-CEI-ICD-G-RAA-14, 3027-OCID-G-RAA-ESSALUD-15 and 4072-OCID-G-HNGAI-ESSALUD-2017). Participants gave informed consent to participate in the study before taking part.

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