Rheumatology 2004;43:1580–1586 doi:10.1093/rheumatology/keh392
Advance Access publication 14 September 2004

Health-related quality of life in Italian patients with systemic lupus erythematosus. II. Role of clinical, immunological and psychological determinants

A. Doria, S. Rinaldi, M. Ermani[1], F. Salaffi[2], L. Iaccarino, A. Ghirardello, S. Zampieri, S. Della Libera, G. Perini[1] and S. Todesco

***Objective*. To investigate the role of clinical, immunological and psychological variables in influencing the health-related quality of life (HRQOL) of Italian patients with systemic lupus erythematosus (SLE).**

***Methods*. The Medical Outcomes Study Short Form-36 was applied in a cohort of 126 SLE patients. At the time of HRQOL testing all patients underwent a clinical and laboratory evaluation, together with the measure of disease activity, severity and damage. In addition, a battery of psychological tests including the Hamilton Anxiety Scale (HAS) and the Hamilton Depression Rating scale (HAM-D) was applied.**

***Results*. The parameters which seemed to greatly influence the impairment of HRQOL were older age, arthralgia–arthritis and higher HAS scores as well as HAM-D. In multivariate analysis (adjusted for age), arthralgia–arthritis and a higher HAM-D score were associated with HRQOL impairment. No relationship between HRQOL and SLE activity, severity or damage were found. However, a relationship between HAS or HAM-D scores and damage or arthralgia–arthritis was noted.**

***Conclusion*. Anxiety, depression and joint pain seem to be the major determinants of HRQOL impairment in SLE patients. Damage seems to influence HRQOL mostly through depression.**

KEY WORDS: SF-36, Health-related quality of life, Systemic lupus erythematosus, Anxiety, Depression.

In recent years interest in the assessment of outcome of chronic diseases through measurements of functional status, health status and health-related quality of life (HRQOL) has been increasing [1].

Systemic lupus erythematosus (SLE) is a chronic inflammatory disease, characterized by alternate phases of remission and exacerbation of the clinical symptoms. During the disease course all the organs and tissues can be potentially involved, sometimes irreversibly. For these reasons, SLE can affect different aspects of the patient's life, leading to an impairment of HRQOL.

The term 'quality of life' or 'HRQOL' [1] refers to the physical, psychological, mental and social aspects of the concept of health, which are in turn influenced by life experiences and expectations of the patient.

As the concept of health and the capacity of coping with possible limitations and disabilities can vary from subject to subject, the same type of physical damage may influence the HRQOL of different persons in a different way. For this reason it is important to be able to integrate the objective evaluation of the patient's health, which is up to the clinician, with the subjective perception which the patient has of his/her own health state [2].

Moreover, during the course of SLE, psychological distress is a common event: depression, anxiety and psychosis are the most commonly reported symptoms [3, 4]. Their prevalence ranges between 17 and 75% as reported in different studies [3, 4]. This wide range can be due to the different tests used to detect psychological distress and to the characteristics of the populations studied. Psychological distress could be a contributing factor to impairment of HRQOL in SLE patients.

The aim of our study was to evaluate the relationship between HRQOL and the clinical as well as immunological aspects of the disease in Italian patients with SLE. Moreover, we wanted to evaluate the possible influence of psychological factors such as depression and anxiety both on HRQOL and disease course.

Patients and methods

Subjects

We considered a sample size of 126 consecutive out-patients affected with SLE (110 females, 16 males; mean age 38.9 ± 11.9 yr, range 18–65; mean disease duration 9.9 ± 6.3 yr, range 1–32). At the time of HRQOL assessment, patients underwent complete clinical and immunological evaluations. Moreover, HRQOL assessment was performed in a group of 96 age- and sex-matched healthy subjects, as controls.

The study was approved by the relevant medical ethics committee and all patients gave written consent.

The methods used for disease classification, definition of organ involvement, nuclear and antiphospholipid antibody detection, disease activity, damage and quality of life assessment have been detailed elsewhere [5]. Briefly, disease was classified according to the American College of Rheumatology (ACR) Classification Criteria for SLE [6], disease activity was measured by the European Consensus Lupus Activity Measure (ECLAM) score [7], cumulative damage using the Systemic Lupus International Collaborating Clinic/American College of Rheumatology (SLICC/ACR) damage

Division of Rheumatology, Department of Medical and Surgical Sciences, [1]Department of Neuroscience, University of Padua and [2]Department of Rheumatology, University of Ancona, Italy.

Submitted 7 May 2004; revised version accepted 4 August 2004.

Correspondence to: A. Doria, Cattedra e Divisione di Reumatologia, Dipartimento di Scienze Mediche e Chirurgiche, Via Giustiniani, 2, 35128 Padova, Italy. E-mail: adoria@unipd.it

index [8], and quality of life using the Medical Outcomes Study Short Form-36 (SF-36) [9, 10]. An ECLAM score of >2 was considered indicative of active disease.

Moreover, patients were split into two groups: mild and severe SLE [11]. Patients with skin, joint and haematological involvement (apart from haemolytic anaemia) and serositis were subclassified as mild SLE, whereas those with central nervous system (CNS) and renal involvement, lung and heart parenchymal manifestations and haemolytic anaemia were subclassified as severe SLE. As specified elsewhere [5], for term definition of SLE-specific features we used those included in the ACR criteria [6]. However, for the purpose of this study, we considered arthralgia–arthritis as variable, including arthritis defined according to the ACR criteria and/or persistent arthralgia.

SLE relapse was defined as an event characterized by the appearance of clinical and/or haematological abnormalities or by the worsening of pre-existing manifestations which requested an increment of corticosteroid dosage and/or the introduction of an immunosuppressive agent.

In addition, we applied a battery of tests for the evaluation of psychological performance (that included anxiety and depression). The same examiner evaluated all the patients during a 30-min session and calculated the test score.

Evaluation of anxiety and depression

The Hamilton Anxiety Scale (HAS) includes 14 items, each scoring from 0 to 4. The evaluation of the presence and intensity of different items is based on the patient's condition in the last 3–7 days. The total score ranges between 0 and 56. A score $\leq$5 indicates lack of anxiety, between 6 and 14 mild anxiety and $\geq$15 a clinically significant level of anxiety [12].

The Hamilton Depression Rating scale (HAM-D) is a scale for recording and measuring the prevalence and the intensity of specific symptoms of depression. It includes 21 items; the first 17 are considered for the score calculation. The cut-off scores, established on the basis of many clinical studies, are as follows: 0–7 no depression, 8–15 mild depression, $\geq$16 moderate to severe depression. The scale has been validated and has shown good correlation with the other main indices for measuring the intensity of depressive symptoms [13].

Statistical analysis

Scores are variables measured by an ordinal scale and their distributions showed a significant deviation from normality (Kolmogorov–Smirnov test for normal distribution): consequently a non-parametric statistic was used. The Mann–Whitney *U*-test was used for independent samples. Linear correlation between variables was checked using Spearman's ρ coefficient. Dichotomous variables were analysed using Pearson's χ^2 or the Fisher exact test. Significance of age was evaluated using the Student's *t*-test for independent samples. Multivariate analysis was performed using the logistic regression model. Statistical significance was set at $P < 0.05$. All analysis was performed using the statistical software package 'Statistica' (Statsoft Inc.).

Results

Clinical and laboratory findings

The prominent clinical and serological features of our out-patients as well as the mean ECLAM score and the mean SLICC/ACR damage index have been reported elsewhere [5]. The SLICC/ACR damage index was not correlated to disease duration or to ECLAM score.

Thirty-one patients (24.6%) were affected with severe SLE and 95 (75.4%) with mild SLE. Patients with severe SLE were younger than those with mild SLE: mean age (± S.D.) 31.4 ± 7.7 *vs* 41.5 ± 12 yr ($P < 0.0001$), whereas the mean disease duration (± S.D.) was not significantly different in the two groups 94.8 ± 54.7 *vs* 126.7 ± 79.5 months.

Anxiety and depression

The mean values (± S.D.) of HAS and HAM-D scores observed in 126 patients were 10.2 ± 5.8 (median 11; range 0–25) and 6.7 ± 4.5 (median 6; range 0–22), respectively. A weak linear relationship between HAS or HAM-D scores and SLICC damage index score ($\rho = 0.26$, $P < 0.004$ and $\rho = 0.30$, $P < 0.001$, respectively) was found. The mean HAM-D score was higher in patients with arthralgia–arthritis then in those without such manifestation: 8.7 ± 4.7 *vs* 6.04 ± 4.2, $P < 0.005$.

HAS and HAM-D were converted into ordinal type scales, using the following clinical score: anxiety (absent $\leq$5, mild = 6–14, clinically significant $\geq$15), depression (absent $\leq$7, mild = 8–15, clinically significant $\geq$16). According to these clinical definitions (Table 1), 94 patients (74.6%) demonstrated mild or clinically significant anxiety and 51 patients (40.5%) mild or clinically significant depression. All depressed patients were also anxious.

Arthralgia–arthritis was observed in 14 patients (18.7%) without depression, in 17 (35.4%) with mild depression and in 2 (66.7%) with significant depression ($P < 0.03$). We did not find any other significant relationship between anxiety or depression categories and clinical variables.

Quality of life

The scores of HRQOL, including overall score as well as the Physical Component Summary (PCS) and Mental Component Summary (MCS), were lower in SLE patients than in controls ($P < 0.00001$, $P < 0.00001$ and $P < 0.0001$, respectively). The scores of all SF-36 subscales but two, role—physical (RP) and social function (SF), were also lower in patients than in controls. All HRQOL scores are detailed elsewhere [5].

The mean (μ) and standard deviation (σ) subscale values of the control group were used in order to subdivide SLE population into two groups of subjects with respect to each scale: patients with high or low HRQOL score. Patients with values of less than $\mu - 3\sigma$ with respect to the specific subscale were considered to have a low score. It is worth noting that 'high' and 'low' scores do not correspond to 'normal' or 'pathological' values, since they represent ordinal variables. According to this definition, among the 126 SLE patients 58 (46%) had a low overall score, 42 (33.3%) by MCS and 55 (43.7%) by PCS.

The sub-classification of the patients according to the established cut-off for each HRQOL subscale and the relationships between HRQOL categories and major disease parameters are reported in Tables 2 and 3.

Table 1. Number of patients subdivided according to the anxiety (HAS) and depression (HAM-D) scales

	HAS scale			
HAM-D scale	Absent	Mild	Significant	Total
Absent	32	38	5	75
Mild	0	22	26	48
Significant	0	0	3	3
Total	32	60	34	126

HAM-D: Hamilton Depression Rating scale; HAS: Hamilton Anxiety Scale. See section on Patients and methods for details.

TABLE 2. Univariate analysis: relationship between MCS or MCS subscale categories and major SLE parameters

Test	Variables (value expression)	MCS			VT			SF			RE			MH		
		High	*P*	Low	High	*P*	Low	High	*P*	Low	High	*P*	Low	High	*P*	Low
	No. of patients		84		42	109		17	91		35	92		34	99	
χ^2	Female (%)	86		90	85		100	89		83	87		88	86		93
t	Age (mean ± S.D.)	36 ± 11	<0.0001	45 ± 12	38 ± 12	<0.002	48 ± 10	37 ± 11	<0.05	44 ± 12	38 ± 11		42 ± 13	37 ± 11	<0.002	45 ± 12
U	Disease duration (mean ± S.D.)	119 ± 77		117 ± 73	120 ± 76		109 ± 70	121 ± 79		112 ± 66	120 ± 73		115 ± 82	117 ± 79		124 ± 60
χ^2	Skin rash (%)	9		2	7		0	7		6	10		0	9		0
χ^2	Arthralgia–arthritis (%)	14	<0.0001	50	20	<0.0001	65	18	<0.002	49	21	<0.05	41	21	<0.05	44
χ^2	Raynaud's phenomenon (%)	19		26	22		18	22		20	22		21	20		26
χ^2	Renal involvement (%)	26		12	24		6	23		17	23		18	24		11
χ^2	CNS involvement (%)	4		2	3		6	3		3	3		3	3		4
χ^2	Anti-dsDNA (%)	51		50	52		41	49		54	53		44	54		41
χ^2	Anti-U1RNP (%)	26		36	31		18	31		26	29		29	26		41
χ^2	Anti-Ro/SSA (%)	27		33	29		29	30		29	28		32	26		41
χ^2	Anti-La/SSB (%)	7		7	6		12	7		9	7		9	7		7
χ^2	aCL (%)	37		40	39		29	36		43	36		44	36		44
χ^2	LAC (%)	19		10	17		6	19		9	17		12	20	<0.05	0
χ^2	Severe SLE (%)	30		14	27		12	26		20	26		21	27		15
χ^2	Active SLE (%)	49		60	51		59	51		57	50		59	49		63
U	ECLAM (mean ± S.D.)	1.7 ± 1.2		1.6 ± 0.9	1.7 ± 1.2		1.6 ± 0.7	1.7 ± 1.2		1.7 ± 0.9	1.7 ± 1.1		1.7 ± 1.2	1.7 ± 1.2		1.7 ± 0.9
U	SLICC/ACR DI (mean ± S.D.)	0.30 ± 0.9		0.38 ± 0.7	0.31 ± 0.8		0.47 ± 0.9	0.29 ± 0.9	<0.05	0.46 ± 0.8	0.33 ± 0.9		0.35 ± 0.7	0.34 ± 0.9		0.30 ± 0.7
U	No. of flares (mean ± S.D.)	1.9 ± 2.7		2.1 ± 3.2	2.0 ± 2.9		1.7 ± 2.6	1.8 ± 2.7		2.3 ± 3.2	1.9 ± 2.7		2.3 ± 3.2	1.9 ± 2.8		2.1 ± 3.3
U	Time to the last flare (mean ± S.D.)	54 ± 60		58 ± 60	54 ± 58		62 ± 69	56 ± 61		52 ± 58	56 ± 60		54 ± 60	52 ± 58		66 ± 66
U	HAS (mean ± S.D.)	8.1 ± 5.3	<0.0001	14.3 ± 4.6	9.4 ± 5.7	<0.0001	15.5 ± 3.8	8.9 ± 5.5	<0.0001	13.6 ± 5.4	8.7 ± 5.6	<0.0001	14.3 ± 5.3	8.7 ± 5.4	<0.0001	15.6 ± 4.1
U	HAM-D (mean ± S.D.)	4.9 ± 3.5	<0.0001	10.3 ± 4.1	6.2 ± 4.4	<0.002	10.1 ± 3.5	5.5 ± 3.7	<0.0001	10.0 ± 4.7	5.6 ± 4.1	<0.0001	9.7 ± 4.1	5.7 ± 3.9	<0.0001	10.6 ± 4.3

Key: MCS, Mental Component Summary; VT, vitality; SF, social function; RE, role—emotional; MH, mental health. High: high HRQOL score (see text for definition). Low: low HRQOL score (see text for definition). χ^2 = Pearson χ^2. *U* = Mann–Whitney *U*-test. *t* = Student's *t* for independent measures. CNS, central nervous system; dsDNA, double-stranded DNA; aCL, anticardiolipin antibodies; LAC, lupus anticoagulant. SLE was considered severe in patients with CNS and renal involvement, lung and heart parenchymal manifestations and haemolytic anaemia. ECLAM, European Consensus Lupus Activity Measure. ECLAM scores >2 are considered indicative of active disease. SLICC/ACR DI, Systemic Lupus International Collaborating Clinic/American College of Rheumatology Damage Index. HAS, Hamilton Anxiety Scale. HAM-D, Hamilton Depression Rating Scale.

TABLE 3. Univariate analysis: relationship between PCS or PCS subscale categories and major SLE parameters

Test	Variables (value expression)	PCS			GH			PF			RP			BP			
		High	*P*	Low	High	*P*	Low	High	*P*	Low	High	*P*	Low	High	*P*	Low	
	No. of patients		71			55	48		78	109		17	85		41	97		29
χ^2	Female (%)	89		85	83		90	88		82	89		83	89		83		
t	Age (mean ± S.D.)	36 ± 10	<0.002	43 ± 13	37 ± 10		40 ± 13	38 ± 12	<0.05	46 ± 11	37 ± 11	<0.05	43 ± 13	38 ± 12	<0.05	43 ± 12		
U	Disease duration (mean ± S.D.)	114 ± 76		124 ± 74	122 ± 84		117 ± 70	116 ± 72		134 ± 95	117 ± 72		121 ± 81	117 ± 72		124 ± 86		
χ^2	Skin rash (%)	11		2	6		8	8		0	8		5	8		3		
χ^2	Arthralgia–arthritis (%)	6	<0.0001	53	4	<0.0001	40	19	<0.0001	71	13	<0.0001	54	17	<0.0001	55		
χ^2	Raynaud's phenomenon (%)	21		22	15		26	22		18	21		22	21		24		
χ^2	Renal involvement (%)	25		16	21		22	23		12	25		15	26	<0.05	7		
χ^2	CNS involvement (%)	3		3	2		4	4		0	2		5	3		3		
χ^2	Anti-dsDNA (%)	51		51	44		55	50		53	53		46	53		45		
χ^2	Anti-U1RNP (%)	32		25	23		33	30		24	33		22	29		31		
χ^2	Anti-Ro/SSA (%)	24		36	21		35	29		29	26		37	27		38		
χ^2	Anti-La/SSB (%)	4		11	4		9	6		12	6		10	4	<0.05	17		
χ^2	aCL (%)	35		42	35		40	37		47	35		44	35		48		
χ^2	LAC (%)	14		18	15		17	16		18	15		17	13		24		
χ^2	Severe SLE (%)	28		20	23		26	27		12	27		20	29	<0.05	10		
χ^2	Active SLE (%)	46		60	40	<0.05	60	50		65	46	<0.05	66	51		59		
U	ECLAM (mean ± S.D.)	1.5 ± 1		1.9 ± 1.1	1.5 ± 1.2		1.8 ± 1.0	1.6 ± 1.1		2.0 ± 1.0	1.5 ± 1.1	<0.05	2.0 ± 1.2	1.6 ± 1.2		1.7 ± 0.9		
U	SLICC/ACR DI (mean ± S.D.)	0.21 ± 0.7		0.49 ± 0.9	0.21 ± 0.8		0.41 ± 0.8	0.31 ± 0.8		0.47 ± 0.9	0.29 ± 0.9	<0.05	0.41 ± 0.7	0.31 ± 0.9		0.41 ± 0.8		
U	No. of flares (mean ± S.D.)	1.7 ± 2.6		2.4 ± 3.1	1.4 ± 2.8	<0.05	2.3 ± 2.9	1.7 ± 2.6	<0.05	4.0 ± 3.6	1.9 ± 2.9		2.1 ± 2.7	1.7 ± 2.6		2.8 ± 3.6		
U	Time to the last flare (mean ± S.D.)	60 ± 60		48 ± 59	72 ± 69	<0.05	44 ± 50	57 ± 59		43 ± 64	57 ± 58		50 ± 63	56 ± 60		51 ± 58		
U	HAS (mean ± S.D.)	8.5 ± 5.6	<0.0001	12.4 ± 5.5	7 ± 5	<0.0001	12.2 ± 5.5	10 ± 5		11.9 ± 4.4	9.0 ± 5.8	<0.002	12.6 ± 5.3	9.4 ± 5.6	<0.002	12.9 ± 5.9		
U	HAM-D (mean ± S.D.)	5.1 ± 3.7	<0.0001	8.8 ± 4.6	4.2 ± 3.5	<0.0001	8.3 ± 4.3	6.4 ± 4.5		8.5 ± 4.5	5.7 ± 4.2	<0.002	8.8 ± 4.3	6.0 ± 3.9	<0.0001	9.2 ± 5.4		

PCS: physical component summary, GH: general health, PF: physical function, RP: role–physical, BP: bodily pain. High: high HRQOL score (see text for definition), Low: low HRQOL score (see text for definition). Other terms/abbreviations as Table 2.

In SLE patients, the parameters which seem to greatly influence the reduction of SF-36 scores were: older age, presence of arthralgia–arthritis and higher scores of HAS as well as HAM-D. Moreover, active disease was associated with reduced general health (GH) ($P = 0.021$) and RP ($P = 0.036$), severe disease with reduced mental health (MH) ($P < 0.05$), anti-La/SSB antibody with reduced bodily pain (BP) ($P = 0.02$), a higher number of disease relapses with reduced GH ($P = 0.03$) and physical function (PF) ($P = 0.006$), a shorter interval between the last relapse and HRQOL assessment with reduced GH ($P < 0.05$) and higher ECLAM and SLICC/ACR damage index scores with reduced RP ($P = 0.04$ for both).

The negative correlations between HRQOL scales and HAM-D or HAS scores (Table 4) further confirm the great impact of anxiety and depression on HRQOL in SLE patients. The coefficients are negative since, differently from HRQOL score, HAM-D and HAS worsen with increasing score.

Multivariate models

We applied the logistic regression model to identify the independent variables significantly correlated with the low score of total SF-36, MCS and PCS (Table 5). We considered only those variables significant in univariate analysis. After adjusting for age, arthralgia–arthritis and HAM-D were found independent variables significantly associated ($P < 0.00001$) with the low SF-36 overall score, MCS and PCS.

Table 4. Linear correlation between SF-36 scales or dimensions and HAM-D or HAS scores (Spearman ρ coefficient)

	HAM-D		HAS	
	ρ	$P <$	ρ	$P <$
Overall score	−0.59	0.00001	−0.55	0.00001
PCS	−0.48	0.00001	−0.44	0.00001
MCS	−0.62	0.00001	−0.59	0.00001
GH	−0.49	0.00001	−0.46	0.00001
PF	−0.34	0.00008	−0.33	0.0002
RP	−0.35	0.00005	−0.31	0.0004
BP	−0.36	0.00004	−0.33	0.0002
VT	−0.46	0.00001	−0.45	0.00001
SF	−0.57	0.00001	−0.48	0.00001
RE	−0.50	0.00001	−0.49	0.00001
MH	−0.45	0.00001	−0.50	0.00001

Key: PCS, Physical Component Summary; MCS, Mental Component Summary; GH, general health; PF, physical function; RP, role—physical; BP, bodily pain; VT, vitality; SF, social function; RE, role—emotional; MH, mental health.

Discussion

Our cohort of SLE patients is similar in terms of clinical and immunological features to other cohorts of SLE patients with a mean disease duration of approximately 10 yr [14].

Only 20% of our patients had permanent damage, a percentage lower than that observed in other studies [15–20]. This difference could probably be due to the fact that our patients were all Caucasians and that the majority of them (25%) had mild disease. However, other studies observed a low prevalence of damage in Caucasian patients [19].

In our patients, permanent damage was not correlated with disease duration or disease activity, in keeping with other authors [16, 19, 20]. The lack of correlation between damage and disease duration could be due to the low extent of damage as well as to the relatively short duration of disease in our patients.

However, the characteristics of our cohort exactly represent the subjects to whom we want to address our study, i.e. a group of out-patients, thus excluding in-patients with high disease activity and/or severity, whose lifestyle is certainly modified.

In this cohort of SLE patients, we observed a compromise of HRQOL, as reported in many other studies [16, 18, 21–25]. It is worth noting that a previous study [5] showed that in SLE both PCS and MCS contribute to the decrease of HRQOL and that, different from the case in healthy subjects, in SLE there is a close mutual interaction between these two scales. Moreover, a greater than expected worsening of HRQOL related to the increase of age classes has been observed.

In agreement with data reported elsewhere [5], age was one of the major determinants of HRQOL reduction in our cohort. Interestingly, HRQOL was not influenced by moderate damage nor by disease severity in our patients. The relationship between HRQOL and disease activity was more conflicting. We did not find any correlations between SF-36 overall score, MCS or PCS and disease activity. This could be due to the fact that disease activity was substantially low in our patients. In fact, in keeping with some authors [18, 21, 22, 24], it is expected that patients with a more active disease have an impairment of daily life activities which leads, in turn, to a reduction of HRQOL. We found a correlation between GH and disease activity or the number of disease relapses experienced by the patients (Table 3). We also noted a positive

Table 5. Multiple logistic regression analysis (best model) of factors associated with SF-36 low score in the 126 SLE patients (adjusted for age)

	Odds ratio	95% CI	$P <$
(a) Dependent variable: low SF-36 overall score			
Independent variables			
Arthralgia–arthritis	11.8	4.1–33.5	
HAM-D (score)	10.1	4.5–23	
Model	22.2	8.8–56	0.00001
(b) Dependent variable: low MCS score			
Independent variables			
Arthralgia–arthritis	4.5	1.9–10.9	
HAM-D (score)	24.5	8.9–67.6	
Model	12.0	4.9–29.8	0.00001
(c) Dependent variable: low PCS score			
Independent variables			
Arthralgia–arthritis	18.7	5.9–58.4	
HAM-D (score)	6.5	3.0–14.3	
Model	16.0	6.2–41.5	0.00001

Key: MOS SF-36, Medical Outcomes Study Short Form-36; MCS, Mental Component Summary; PCS, Physical Component Summary; HAM-D, Hamilton Depression Rating Scale.

correlation between GH and the time elapsed from the last disease flare and the HRQOL assessment. As expected, RP was also related to disease activity (Table 3). Therefore it is possible that SLE activity could influence some HRQOL subscales, but in patients with low disease activity the effect on the overall HRQOL scores could be masked by other determinants.

GH is the subscale which shows the patient's perception of his/her own general health status. It is worth noting that GH is one of the most compromised subscales in SLE patients compared with healthy subjects, as we have shown elsewhere [5]. Therefore, one could wonder why this subscale is compromised in patients with active disease but not in patients with permanent damage or severe disease. Our results, particularly the relationships between GH and the number of SLE flares or the time to the last relapse, suggest that disease activity, more than disease severity or damage, represents a rapid change in the health status of patients. In addition, changes in SLE activity are often unpredictable in terms of flare duration as well as of possible future consequences.

It is also worth noting that arthralgia–arthritis was the unique clinical manifestation able to influence the HRQOL of our patients. Joint pain, with or without a true arthritis, worsens HRQOL either because of the large amount of energy and attention required by the patient to cope with it or because it represents a persistent signal of the disease itself.

In the light of these results we can assume that many SLE outpatients with mild disease manifestations, including arthralgia–arthritis, low disease activity and limited extent of damage—and who are therefore able to live quite a 'normal' life—have a compromised HRQOL, comparable to that found in severe chronic obstructive pulmonary disease (COPD) and in cardiovascular disease [9, 17], i.e. in patients who are much more compromised on a physical level.

Thus, the parameters which allow us to define the level of physical health of the patient, including disease severity, activity and permanent damage, supply us with an incomplete representation of the well-being of the patient. It therefore becomes necessary to evaluate other aspects [17]. For this reason we submitted our patients to a psychopathological investigation in order to find out about the prevalence of complaints related to depression and anxiety. Our results, in agreement with those reported by others [26, 27], showed a high prevalence of anxious and depressive manifestations in SLE patients. The overall score of SF-36 was inversely correlated to both HAS and HAM-D scores (Table 4). These results are similar to those obtained by other authors [2, 28–30].

HAS and HAM-D scores did not correlate with disease duration or with disease activity, in keeping with other reports [31], whereas both were correlated with permanent damage. Moreover, in keeping with other authors [32], we found a relationship between arthralgia–arthritis and depression. It has been shown that pain, especially chronic pain, can lead to the development of depressive symptoms which, in turn, can worsen the pain itself [33]. It is interesting that in our sample arthralgia–arthritis worsens the majority of psychosocial indices, indicating a crucial role for pain in modulating mood and well-being. However, in our sample depression and arthralgia–arthritis were independent variables in modulating HRQOL, suggesting the presence of a more complex model in which pain and depression, when present concurrently, have a magnifying effect on HRQOL, but they also contribute significantly to lowering HRQOL when present separately.

We can therefore put forward the hypothesis that permanent physical damage and/or chronic joint pain could lead, in some people, to the development of anxious and/or depressive symptoms (mostly depressive) which, in turn, could influence the person's perception of HRQOL, determining a worsening of it.

In conclusion, the compromising of HRQOL does not seem to depend directly on SLE activity, severity or permanent damage due to the disease itself, but it is probably mostly related to joint pain and depression, which are influenced, at least in part, by progressive cumulative damage. Whether depression simply reveals a psychological reaction to the disease or represents a neurobiological phenomenon still remains to be addressed.

Rheumatology	Key messages
	• In SLE, the HRQOL impairment does not seem to depend directly on disease severity or permanent damage. • Physical damage and/or chronic joint pain could lead to the development of anxious and/or depressive symptoms. • Anxiety, depression and joint pain could, in turn, influence the person perception of HRQOL, determining a worsening of it.

The authors have declared no conflicts of interest.

References

1. Testa MA, Simonson DC. Assessment of quality of life outcomes. N Eng J Med 1996;334:835–40.
2. Gordon C, Clarke AE. Quality of life and economic evaluation in SLE clinical trials. Lupus 1999;8:645–54.
3. Purandare KN, Wagle AC, Parker SR. Psychiatric morbidity in patients with systemic lupus erythematosus. Q J Med 1999;92:283–6.
4. Iverson GL, Sawyer DC, McCracken LM, Kozora E. Assessing depression in systemic lupus erythematosus: determining reliable change. Lupus 2001;10:266–71.
5. Rinaldi S, Doria A, Salaffi F *et al*. Health-related quality of life in Italian patients with systemic lupus erythematosus. I. Relationship between physical and mental dimension and impact of age. Rheumatology Advance Access published September 7, 2004, 10.1093/rheumatology/keh397.
6. Tan EM, Cohen AS, Fries JF, Masi AT, McShane DJ, Rothfield NF. The 1982 revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum 1982;25:1271–7.
7. Vitali C, Bencivelli W, Isenberg DA *et al*. Disease activity in systemic lupus erythematosus: report of the Consensus Study Group of the European Workshop for Rheumatology Research. II. Identification of the variables indicative of disease activity and their use in the development of an activity score. The European Consensus Study Group for Disease Activity in SLE. Clin Exp Rheumatol 1992;10:541–7.
8. Gladman D, Ginzler E, Goldsmith C *et al*. The development and initial validation of the Systemic Lupus International Collaborating Clinics/American College of Rheumatology damage index for systemic lupus erythematosus. Arthritis Rheum 1996;39:363–9.
9. Ware JE Jr, Sherbourne CD. The MOS 36-item short form health survey (SF-36). 1. Conceptual frame-work and item selection. Med Care 1992;30:473–81.
10. Apolone G, Mosconi P. The Italian SF-36 Health Survey: translation, validation and norming. J Clin Epidemiol 1998;51:1025–36.
11. American College of Rheumatology Ad Hoc Committee on Systemic Lupus Erythematosus Guidelines. Guidelines for Referral and Management of Systemic Lupus Erythematosus in Adults. Arthritis Rheum 1999;42:1785–96.
12. Maier W, Buller R, Philipp M, Heuser I. The Hamilton Anxiety Scale: reliability, validity and sensitivity to change in anxiety and depressive disorders. J Affect Disord 1988;14:61–8.
13. Fava GA, Kellner R, Munari F, Pavan L. The Hamilton Depression Rating Scale in normal and depressives. Acta Psychiatr Scand 1992; 1:26–32.

14. Cervera R, Khamashta MA, Font J *et al*. Morbidity and mortality in systemic lupus erythematosus during a 10-year period: a comparison of early and late manifestations in a cohort of 1,000 patients. Medicine 2003;82:299–308.
15. Isenberg D, Ramsey-Goldman R. Assessing patients with lupus: towards a drug responder index. Rheumatology 1999;38:1045–9.
16. Gorgos L, Goldman D, Petri M. The ACR/SLICC damage index in systemic lupus erythematosus (SLE). Arthritis Rheum 1993;36:S68.
17. Fortin PR, Abrahamowicz M, Neville C *et al*. Impact of disease activity and cumulative damage on the health of lupus patients. Lupus 1998;7:101–7.
18. Stoll T, Gordon C, Seifert B *et al*. Consistency and validity of patient administered assessment of quality of life by the MOS SF-36; its association with disease activity and damage in patients with systemic lupus erythematosus. J Rheumatol 1997;24:1608–14.
19. Gladman D, Urowitz MB, Ong A, Gough J, MacKinnon A. Lack of correlation among the 3 outcomes describing SLE: disease activity, damage and quality of life. Clin Exp Rheumatol 1996;14:305–8.
20. Gladman DD, Urowitz MB. The SLICC/ACR damage index: progress report and experience in the field. Lupus 1999;8:632–7.
21. Sutcliffe N, Clarke AE, Levinton C, Frost C, Gordon C, Isenberg DA. Associates of health status in patients with systemic lupus erythematosus. J Rheumatol 1999;26:2352–6.
22. Thumboo J, Fong KY, Chan SP *et al*. A prospective study of factors affecting quality of life in systemic lupus erythematosus. J Rheumatol 2000;27:1414–20.
23. Dobkin PL, Da Costa D, Dritsa M *et al*. Quality of life in systemic lupus erythematosus patients during more and less active disease states: differential contributors to mental and physical health. Arthritis Care Res 1999;12:401–10.
24. Wang C, Mayo NE, Fortin PR. The relationship between health related quality of life and disease activity and damage in systemic lupus erythematosus. J Rheumatol 2001;28:25–32.
25. Rinaldi S, Doria A, Vescovi F *et al*. Quality of life in systemic lupus erythematosus. Reumatismo 2001;53:108–15.
26. Hay EM, Black D, Huddy A *et al*. Psychiatric disorder and cognitive impairment in systemic lupus erythematosus. Arthritis Rheum 1992;35:411–6.
27. McCracken LM, Semenchuk EM, Goetsch VL. Cross-sectional and longitudinal analyses of coping responses and health status in persons with SLE. Behav Med 1995;20:179–87.
28. Dobkin PL, Fortin PR, Joseph L, Esdaile JM, Danoff DS, Clarke AE. Psychosocial contributors to mental and physical health in patients with systemic lupus erythematosus. Arthritis Care Res 1998;11:23–31.
29. Da Costa D, Dobkin PL, Pinard L *et al*. The role of stress in functional disability among women with systemic lupus erythematosus: a prospective study. Arthritis Care Res 1999;12:112–9.
30. Sutcliffe N, Clarke AE, Levinton C, Frost C, Gordon C, Isenberg DA. Associates of health status in patients with SLE. J Rheumatol 1999;26:2352–6.
31. Shortall E, Isenberg D, Newman SP. Factors associated with mood and mood disorders in SLE. Lupus 1995;4:272–9.
32. Vines SW, Gupta S, Whiteside T, Dostal-Johnson D, Hummler-Davis A. The relationship between chronic pain, immune function, depression, and health behaviors. Biol Res Nurs 2003;5:18–29.
33. Fishbain DA, Cutler R, Rosomoff HL, Rosomoff RS. Chronic pain-associated depression: antecedent or consequence of chronic pain? A review. Clin J Pain 1997;143:116–37.