

HEALTH-RELATED QUALITY OF LIFE IN PORTUGUESE SLE PATIENTS: AN OUTCOME MEASURE INDEPENDENT OF DISEASE ACTIVITY AND CUMULATIVE DAMAGE

Cátia Duarte*, Pedro Abreu*, Maura Couto*, Cláudia Vaz*, Armando Malcata*, Luís Inês***

Abstract

Purpose: To evaluate quality of life in Portuguese patients with Systemic Lupus Erythematosus (SLE) and its correlation with disease activity and cumulative damage.

Methods: We included consecutive SLE patients, fulfilling the 1997 ACR Classification Criteria for SLE and followed at the Rheumatology Department of the University Hospital of Coimbra, Portugal at time of visit to the outpatient clinic. Quality of life was evaluated using the patient self-assessment questionnaire Medical Outcomes Survey Short Form-36 (SF-36) (validated Portuguese version). The consulting rheumatologist fulfilled the SLE associated indexes for cumulative damage (Systemic Lupus International Collaborating Clinics- Damage Index: SLICC/ACR-DI) and disease activity (Systemic Lupus Erythematosus Disease Activity Index: SLEDAI 2000). Correlation between SLEDAI and SLICC and SF-36 was tested with the Spearman Coefficient. Significant level considered was 0.05.

Results: The study included 133 SLE patients (90.2% female, mean age – 40.7 years, mean disease duration – 8.7 years). Most patients presented low disease activity (mean SLEDAI = 4.23) and limited cumulative damage (mean SLICC = 0.76). Despite that, SF-36 mean scores were below 70% in all eight domains of the index. Physical function domains showed lower scores than mental function domains. The QoL in this group of patients is significantly impaired when compared with the reference Portuguese population ($p < 0.05$ in all domains). There was no correlation between clinical activity or cumulative damage and quality of life.

Conclusion: QoL is significantly compromised in

this group of SLE patients, but not related with disease activity or damage. These findings suggest that disease activity, cumulative damage and QoL are independent outcome measures and should all be used to assess the full impact of disease in SLE patients.

Keywords: Systemic Lupus Erythematosus; Quality of Life; MOS Sf-36; SLEDAI; SLICC/ACR-DI; Coimbra Lupus Cohort.

Introduction

Systemic Lupus Erythematosus (SLE) is a multi-system rheumatic autoimmune disease, with a chronic course characterized by alternate episodes of remission and exacerbation that may involve almost any organ or system, with high variability among patients and in the same patient over time.

Over the last decades, the advances in diagnosis and management of SLE improved significantly the survival of SLE patients, from an acute disease with a high rate of short-term mortality in the 1950's to a chronic condition with five year survival rates now approaching 95%¹⁻⁴ and 10-year survival rates above 85%¹⁻³, at least for those patients managed at specialized centers. Consequently, outcome measures in SLE must go much beyond mortality data.

At present, optimal care for SLE patients aims to provide a long-term health status as close to that of the general population as possible. To guide quality clinical care there is a need to characterize and monitor the full spectrum of SLE effects, including disease activity (reversible), cumulative damage (irreversible) and health-related quality of life. A comprehensive assessment should consider these different domains, as recommended⁵⁻⁷.

Disease activity outcome measures include an evaluation of a variety of clinical and laboratorial findings, related to intrinsic disease mechanism,

* Rheumatology Department, University Hospital of Coimbra, Portugal

*** Health Sciences School, University of Beira Interior, Covilhã, Portugal

and are potentially reversible with treatment. Cumulative damage is irreversible, and could be due to the disease, its treatment or both, or co-morbidities. However these outcomes, based essentially in physical and laboratorial findings, do not directly capture the psychological and social impact of the disease or its treatment in patient's QoL. As a chronic disease, SLE has, apart from physical impact in terms of disease activity and irreversible and cumulative organ damage, a wide range of impacts in emotional, psychological and social aspects of patient's life⁵.

Health Related Quality of Life (HRQoL) has been defined as a multi-domain concept that represents the patient's overall perception of the impact of an illness and its treatments⁸ and the degree to which persons perceive themselves able to function physically, emotionally and socially⁹. Assessing the QoL is thus an important measure to appraise how much the disease and its treatment is affecting an individual¹⁰ and his or her physical, mental and social domains of life.

There are several instruments validated to evaluate QoL in healthy and disease populations. The most commonly used worldwide is the Medical Outcomes Short Form Survey 36 (SF-36). Several studies in general healthy populations demonstrated that normal values vary greatly between different countries¹¹⁻¹³.

Previous studies in other countries showed a significant compromise of QoL in SLE patients, with lower QoL when compared with healthy controls or population norms¹⁴⁻¹⁹. Mean QoL of SLE patients was found to be worst than in patients with hypertension, myocardial infarction or diabetes²⁰. Studies comparing SLE with RA show a higher impact among RA patients in the physical components but with similar results for mental components^{15, 21}. There are no previous studies characterising QoL in a representative SLE population in Portugal.

The relationship between QoL with disease activity and cumulative damage has been researched in previous studies with conflicting results^{10, 18, 22-25}.

It is also possible that the potential contribution of disease activity and cumulative damage to QoL varies in SLE populations in different countries. We hypothesise that the QoL of SLE patients in Portugal correlates with disease activity and damage. Alternatively QoL may depend upon the patient's overall perception of the impact of the illness and its treatments, more related to psychosocial and

cultural context than to objective disease outcome measures.

The objectives of this study were: 1) to characterise QoL in a representative SLE population in Portugal; 2) to evaluate correlation of QoL in this population with disease activity and cumulative damage measures.

Materials and Methods

Patients

One hundred and thirty three consecutive patients attending the Lupus Clinic of the Rheumatology Department at Coimbra University Hospital were enrolled in this cross sectional study, between 2006 and 2008. All patients met ≥ 4 of the American College of Rheumatology (ACR) Criteria for Classification of SLE²⁶. Patients unable to understand or to answer the self-questionnaire were excluded.

Study Evaluation

Study evaluation was cross-sectional and data collected at time of programmed visit to the Outpatient Clinic. Disease activity and cumulative damage measures were evaluated by the physician and the patient fulfilled the self-questionnaire of QoL at time of inclusion.

Assessment of QoL

QoL was assessed with the Portuguese validated version of the self-administered SF-36 questionnaire^{27, 28}. This is a general, non disease-specific, validated instrument for QoL assessment of general population as well as patients with chronic illnesses as SLE. This instrument consists of 36 items covering eight domains: Physical Function (PF), Physical role (PR), Bodily pain (BP), Vitality (V), General Health (GH), Emotional Role (ER), Mental Health (MH) and Social Functioning (SF). The global score and the ones for each domain ranges from 0 to 100 with higher scores indicating better QoL²⁹.

Measure of Disease activity:

Clinical activity of SLE was assessed using SLEDAI 2000³⁰. It is a physician-rated, valid and reliable index of lupus activity that reports on 24 descriptors with pre-assigned severity weights. The total SLEDAI score can range from 0 (no activity) to 105 (maximum activity).

Measure of Cumulative Damage

Clinical damage due to SLE was assessed using The Systemic Lupus International Collaborating Clinic/ American College of Rheumatology Damage Index (SLICC/ACR DI)³¹. Damage means irreversible impairment due to SLE or its treatment and is usually defined as a clinical feature that has to be continuously present for at least six months to score. The SLICC/ACR DI reports on 12 organs or systems which are ocular (ranges of score 0-2), neuropsychiatric (0-6), renal (0-3), pulmonary (0-5), cardiovascular (0-6), peripheral vascular (0-5), gastrointestinal (0-6), musculoskeletal (0-6), dermatological (0-3), gonadal (0-1), diabetes (0-1) and malignancy (0-2).

Statistical Analysis

All statistical analysis was performed by SPSS® version 15.0. Categorical variables were presented as percentage and continuous variables were presented as means and standard deviation (SD).

The normality for each variable was assessed using Shapiro Wilk Test. The Spearman rank correlation test was applied to correlate disease activity and damage with QoL in SLE patients. Comparison of SF-36 scores for each domain between SLE patients and previously available representative results for the general Portuguese population³² were performed using a one-sample test.

A statistical significance was considered when $p < 0,05$.

Results

133 patients comprised the study population, with 90.2 % ($n=120$) women, mean age of 40.69 ± 14.02 years and mean disease duration of 8.69 ± 7.13 years.

The mean disease activity, as assessed by SLEDAI in these patients is low (4.23 ± 4.27 ; range from 0 to 33). The majority of the patients (70.4%) are in remission or mildly active, with a SLEDAI score lower than six and only 4.3% of patients presented high disease activity with a score of 10 or higher (Table I).

The cumulative damage is low, with a mean of score of 0.76 (0.76 ± 1.09 , range from 0 to 5). The majority of patients (54.6%) do not present any irreversible damage due to SLE or its treatment

(SLICC/DI= 0) (Table I).

QoL assessed by SF-36 is low in this group of SLE patients. Mean scores are lower than 70% in all domains, with lower scores in the General Health domain (39,04%). The mean scores are lower for the four domains of the physical component than for the domains of mental component (Table I).

Due the non-normality of data (Shapiro Wilk Test, $p < 0,05$), Spearman rank correlation was used to test correlations between QoL and disease activity (SLEDAI), cumulative damage (SLICC), disease duration and age. Except for Physical Function and Physical Role, all domains varied inversely with SLEDAI, although none achieved statistical significance.

No correlation is observed between cumulative damage assessed by SLICC/DI and SF-36 domains (Table II).

No correlation exists also between disease duration and any scores of SF-36. There is a weak negative correlation between age and all domains included in SF-36 (r varies between -0,2 to -0,4, $p < 0,01$ for all domains).

When comparing the SF-36 in SLE patients, with results previously published from a large sample representative of the general Portuguese population³², the scores are statistically lower in the SLE population. Despite being statistically significantly lower, Mental Health was the domain with scores closer to those observed in the general Portuguese population (59.22 vs 64.04%; $p=0.03$). All the other domains present a higher mean difference (between 8 and 23%; $p < 0.001$ for all of them). The difference to the Portuguese Population is higher for the domains of the physical component.

Table I.

	Mean $\pm$ SD (%)
SLEDAI	4,23 $\pm$ 4,27
SLICC/DI	0,76 $\pm$ 1,09
Physical Function	57,01 $\pm$ 26,38
Physical Role	47,39 $\pm$ 41,71
Bodily Pain	53,3 $\pm$ 26,64
General Health	39,07 $\pm$ 17,03
Vitality	48,11 $\pm$ 22,02
Emotional Role	60,09 $\pm$ 41,72
Social Function	66,76 $\pm$ 27,66
Mental Health	59,0 $\pm$ 25,36

Table II. Correlation of Quality of Life (MOS SF-36) and Disease Activity (SLEDAI) and damage (SLICC/DI)

	Disease Activity (SLEDAI)		Cumulative Damage (SLICC/DI)	
	r	p	r	p
Physical Function	0,048	0,607	0,073	0,411
Physical Role	0,035	0,706	-0,002	0,979
Bodily Pain	-0,08	0,936	0,072	0,415
General Health	-0,053	0,574	0,002	0,979
Vitality	-0,086	0,357	0,008	0,925
Emotional Role	-0,046	0,623	0,035	0,699
Social Function	-0,134	0,151	0,055	0,534
Mental Health	-0,027	0,776	0,063	0,478

Discussion

QoL is becoming an important focus on clinical research during the last years, mainly in chronic diseases as SLE. Studies have been conducted in other countries but to our knowledge no published studies exist in Portugal, regarding SLE.

In our study, QoL in this sample of SLE patients, assessed by SF-36, is low. The major impact is observed in the domains of the physical component. When compared with the reference values from a large Portuguese sample³², all scores are significantly lower.

Patients present a mean low disease activity, with the majority of the patients in remission or inactive disease. The damage is also low in this cohort of patients, with more than half of the patients without any organ damage due the disease or its treatment. We did not find a statistically correlation between QoL and disease activity or damage in this group of patients.

Our results are consistent with other published studies. All the studies conducted show lower quality of life in SLE patients when compared with what is expected for the reference general population^{14,17,18} or when compared with healthy controls^{15,16,19,33-35}.

The absence of correlation between disease activity and QoL found in our study is also reported in other studies. Most studies using SLEDAI^{14,24,36,37} to assess disease activity showed no correlation with QoL. However, other studies reported an association. Two studies, from South Africa and USA, report a weak negative correlation of SLEDAI with

physical component but not with mental components of SF-36^{16,22}. One study from China found a negative association between disease activity and both components of SF-36³⁵, another study with Mexican women reported a negative weak correlation between SLEDAI and some domains of SF-36²⁵. When BILAG is used as a measure of disease activity, a weak correlation is reported in 3 studies^{14,38,39}. Interestingly, when SLAM is used, a negative correlation with QoL is shown in most studies^{18,24,36}. In two of them^{18,36}, both SLAM and SLEDAI were used and a correlation of QoL with SLAM was found but not with SLEDAI. This discrepancy could be due to a higher sensitivity of SLAM to patient's SLE related subjective complaints that are not scored in the SLEDAI or BILAG.

Similar to ours, some studies from Canada, Singapore and Brazil, report no association between damage and QoL^{37,38,40-42}. Other studies found that damage was correlated with QoL^{14,15,18,22,39} but this correlation was usually weak and only for physical domains of SF-36.

A recent comprehensive review of literature of QoL in SLE patients shows the discrepancy between studies in this field and the tendency of no correlation with disease activity or damage⁴³.

Important caveats should be referred in our study. This is a cross sectional study, without a comparison group. We made an indirect comparison, using data reporting SF-36 scores from a representative sample from the Portuguese general population. This carries some limitations. Socio-demographic and clinical factors, known as potential predictors of QoL, could not be adjusted for

this comparison, such as gender, age, level of education, type of work, income, labour activity status, social support, residence area, depression, anxiety or fibromyalgia. For example, our SLE population included more women (90.2% vs 58.1%) and studies of QoL show that women tend to have lower scores. This study was conducted in one single centre in the central region of the country. The generalizability of these results should be made carefully. However, according with previous publications, our cohort is similar with other Portuguese Cohorts^{44, 45}, and, in our understanding, be representative of Portuguese SLE Patients.

Future studies, comparing with healthy controls and adjusting for these variables, are necessary to confirm and validate our results and better characterize SLE impact on QoL.

In conclusion, this study characterised QoL in a large Portuguese SLE population. This provides previously unavailable data for SLE patients in this country. The indirect comparison with the Portuguese general population suggests a significant impact of SLE in the patient's QoL. The low QoL presented by these patients could not be explained by SLE disease activity and cumulative damage. This corroborates similar results from most studies in other countries.

These results support the concept of QoL as an independent outcome measure that should be incorporated in the quality care management of SLE patients. Assessing QoL is thus an important measure to appraise how much the disease process and its treatment is affecting an individual, to identify potential factors of poor QoL and to program adequate interventions.

Correspondence to

Cátia Duarte
Serviço de Reumatologia
Hospitais da Universidade de Coimbra
Praceta Mota Pinto
3030-300 Coimbra
E-mail: catiacmduarte@gmail.com

References

1. Cervera R, Kamashta MA, Font J et al. Morbidity and mortality in systemic lupus erythematosus during 10-year period: a comparison of early and late manifestation in a cohort of 1000 patients. *Medicine*, 2003; 82: 299-308
2. Kasitanon N, Madger LS, Petri M. Predictors of survival on systemic lupus erythematosus. *Medicine* 2006; 85: 147-156
3. Funauchi M, Shimadzu H, Tamaki C et al. Survival study by organ damage in 346 Japanese with systemic lupus erythematosus: results from a single center. *Rheumatol Int* 2007; 27: 243-249
4. Pons-Estel BA, Catoggio LJ, Cardiel MH et al. The GLADEL multinational Latin American prospective inception cohort of 1,214 patients with systemic lupus erythematosus: Ethnic and disease heterogeneity among "Hispanics". *Medicine* 2004; 83:1-18
5. Panopalis P, Clarke AE. Quality of life in systemic lupus erythematosus. *Clin Develop Immunol* 2006; 13:321-324
6. Gladman D, Urowitz M, Fortin P et al. Systemic Lupus International Collaborating Clinics conference on assessment of lupus flare and quality of life measures. *J Rheumatol* 1996;23: 1953-1955
7. Smolen JS, Strand V, Cardiel M et al. Randomized Clinical trials and longitudinal observational studies in systemic lupus erythematosus: consensus on a preliminary core set of outcome domains. *J Rheumatol* 1999; 26:504-507
8. Food and Drug Administration. Guidance for Industry Patient-Reported outcome Measures: Use in Medical Product development to support labeling claims. Available at: <http://www.fda.gov/CDER/GUIDANCE/5460dft.htm>
9. Last JM, editor. A dictionary of Epidemiology. New York: Oxford University Press, 1995
10. Khana S, Pal H, Pandey RM, Handa R. The relationship between disease activity and quality of life in systemic lupus erythematosus. *Rheumatology* 2004; 43:1536-1540
11. Apolone G, Mosconi P. The Italian SF-36 Health Survey: translation, validation and norming. *Journal of Clinical Epidemiology* 1998. 51;11:1025-1036.
12. Ware JE et al. - SF-36 health survey manual and interpretation guide. Boston, MA : New England Medical Center, 1993.
13. Leplège A, Ecosse E, Verdier A, Perneger TV. The French SF-36 health survey: translation, cultural adaptation and preliminary psychometric evaluation. *Journal of Clinical Epidemiology* 1998;51:1013-1023.
14. Stoll T, Gordon C, Seifert B, Richardson K, Bacon PA, Isenberg DA. Consistency and validity of patient administered assessment of quality of life by the Mc, OS SF-36; its association with disease activity and damage in patients with systemic lupus erythematosus. *J Rheumatol* 1997; 24:1608-1614
15. Gilboe IM, Kvien TK, Husby G. Health status in systemic lupus erythematosus compared to rheumatoid arthritis and healthy controls. *J Rheumatol* 1999;26: 1694-1700
16. Benitha R, Tikly M. Functional disability and health related quality of life in South Africans with rheumatoid arthritis and systemic lupus erythematosus. *Clin Rheumatol* 2007; 26: 24-29
17. Thumboo J, Fong KY, Ng TP, Leong KW, Feng PH, Boey ML. Initial construct cross-cultural validation of the short form 36 for quality of life assessment of sys-

- temic lupus erythematosus patients in Singapore. *Ann Acad Med Singapore*, 1997;26:282-84
18. 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: 525-532
 19. Stuchiffe N, Clarke A, Levington C, Frost C, Gordon C, Isenberg D. Associates of health status in patients with systemic lupus erythematosus. *J Rheumatol* 1999;26:2352-2356
 20. Jolly M. How Does Quality of Life of patients with Systemic Lupus Erythematosus compare with that of other common chronic illnesses? *J Rheumatol* 2005; 32:1706-1708
 21. Burckhardt CS, Archenholtz B, Bjelle A. Quality of life of women with systemic lupus erythematosus: a comparison with women with rheumatoid arthritis. *J Rheumatol* 1993; 20: 977-981
 22. Jolly M, Utset TO. Can Disease specific measures for systemic measures for systemic lupus erythematosus predict patients health related quality of life? *Lupus* 2004;13:924-926.
 23. Gladman DD, Urowitz MB, Ong A, Gough J, Mackinnon. Lack of correlation among 3 outcomes describing SLE: disease activity, damage and quality of life. *Clin Exp Rheumatol* 1996;14:305-308
 24. Saba J, Quinet RJ, Davis WE et al. Inverse correlation of each functional status scale of the SF-36 with degree of disease activity in systemic lupus erythematosus (m-SLAM). *Joint Bone Spine* 2003;70:348-351
 25. Pérez-Cuevas JB, Formiga F, Garcia-Carrasco M, Ramos M, Lara C, Rojas-Rodriguez J. A quality of life study in women with systemic lupus erythematosus and its relation to disease activity. *An Med Interna* 1999; 16:457-460
 26. Hochberg C. Updating the American College Rheumatology revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1997 40:1725
 27. Ferreira Lopes P. Criação da Versão Portuguesa do MOS-SF36, Parte I-Adaptação cultural e linguística. *Acta Médica Portuguesa* 2000; 13:55-66
 28. Ferreira Lopes P. Criação da Versão Portuguesa do MOS-SF36. Parte II-Testes de validação. *Acta Médica Portuguesa* 2000; 13: 119-127
 29. <http://www.sf-36.org/tools/SF36.shtml>
 30. Gladman CC, Ibanez D, Urowitz. Systemic Lupus Erythematosus disease activity index 2000. *J Rheumatology* 2002;29:288-291
 31. Gladman DD, Ginzler E, Goldsmith C et al. The development and initial validation of the Systemic Lupus International Collaborating Clinics/ American College of Rheumatology Damage Index in patients with systemic lupus erythematosus. *Arthritis Rheum* 1996; 39:363-369
 32. Ferreira Lopes P, Santana P. Percepção do estado de saúde e da qualidade de vida da população portuguesa active: contributo para a definição de normas portuguesas. *Revista Portuguesa de Saúde Pública* 2003; 21:15-30
 33. Abu-shakra M, Mader R, Langevitz P et al. Quality of life in systemic lupus erythematosus: a controlled study. *J Rheumatol* 1999;26:306-309
 34. 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 (Oxford)*. 2004;43:1574-1579
 35. Zheng Y, Ye DQ, Pan HF et al. Influence of social support on health-related quality of life in patients with systemic lupus erythematosus. *Clin Rheumatol* 2009; 28:265-269
 36. Fortin PR, Abrahamowicz M, Neville C et al. Impact of disease activity and cumulative damage on the health of lupus patients. *Lupus* 1998; 7:101-107
 37. Gladman DD, Urowitz MB, Ong A, Gough J, MacKinnon A. A comparison of five health status instruments in patients with systemic lupus erythematosus (SLE). *Lupus* 1996; 5:190-195
 38. Thumboo J, Fong KY, Ng TP et al. Validation of the MOS SF-36 for quality of life assessment of patients with systemic lupus erythematosus in Singapore. *J Rheumatol* 1999;26:97-102
 39. Thumboo J, Feng PH, Boey ML, Soh CH, Thio S, Fong KY. Validation of the Chinese SF-36 for quality of life assessment in patients with systemic lupus erythematosus. *Lupus* 2000;9:708-712
 40. Freire EA, Maia IO, Nepomuceno JC, Ciconelli RM. Damage index assessment and quality of life in systemic lupus erythematosus patients (with long-term disease) in Northeastern Brazil. *Clin Rheumatol* 2007;26:423-428
 41. Kuriya B, Gladman DD, Ibañez D, Urowitz MB. Quality of life over time in patients with systemic lupus erythematosus. *Arthritis Rheum* 2008; 15:59:181-185
 42. Hanly JG. Disease activity, cumulative damage and quality of life in systemic lupus erythematosus: results of a cross-sectional study. *Lupus* 1997;6:243-247
 43. McElhone K, Abbott J and The LS. A review of health related quality of life in systemic lupus erythematosus. *Lupus* 2006;15:633-643
 44. Santos MJ, Capela S, Figueira R et al. Characterization of a Portuguese population with systemic lupus erythematosus. *Acta Reumatol Port* 2007; 32:153-161
 45. Vasconcelos C, Farinha F, Barbosa P et al. 125 different Clinical patterns in a cohort of 451 SLE patients. *Lupus* 2008; 17: 489