

Factors predictive of overall health over the course of the disease in patients with systemic lupus erythematosus from the LUMINA cohort (LXII): use of the SF-6D

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Abstract

Objective

Health related quality of life (HRQOL) over course of the disease was ascertained in SLE patients from LUMINA, a multiethnic US cohort, using the SF-36-derived utility measure, the SF-6D.

Methods

All available visits were examined to predict HRQOL using either variables from the baseline or enrollment visits or from the preceding visits. The physical and mental component summary (PCS and MCS, respectively) measures of the SF-36 were also examined. A total of 2662 visits from 588 SLE patients were included; 90% of the patients were women, 19% Hispanic-Texans, 17% Hispanic-Puerto Ricans, 35% African Americans and 29% Caucasians. The patients' mean (SD) SF-6D was 0.6 (0.1).

Results

In multivariable analyses, Hispanic-Texan ethnicity and higher levels of social support were predictors of HRQOL whereas older age, poverty, greater disease activity and damage and higher levels of fatigue, helplessness and abnormal illness-related behaviors were negative predictors. Prior SF-6D was the strongest variable predictive of subsequent HRQOL, when included. The analyses in which the PCS and MCS were examined as end-points were, overall, consistent with the SF-6D results.

Conclusion

We conclude that the SF-6D index provides an adequate measure of self-perceived HRQOL and that patients' self-perception of HRQOL is influenced by disease and non-disease related factors.

Key words

SF-36, SF-6D, quality of life, lupus.

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Introduction

Self-reported health-related quality of life (HRQOL) is an important construct in healthy and disease populations but particularly in those suffering from chronic ailments (1-3); this is the case in systemic lupus erythematosus (SLE). Moreover, the OMERACT group (for Outcome Measures in Rheumatology) (4) has recommended that a measure of HRQOL be included when examining outcomes in patients with SLE. Several instruments have been developed to ascertain HRQOL in a standardized manner; one of them, the Short Form-36 (SF-36), is now widely used in clinical and research settings and in different diseases, SLE included (5-8).

The SF-6D index is a preference-based measure of HRQOL which includes six dimensions derived from the SF-36 (9, 10). Even though the SF-6D was originally derived as a utility measure for economic evaluations in health care, it has been used to assess HRQOL in different diseases and conditions such as asthma, diabetes mellitus, coronary artery disease, rheumatoid arthritis and hip fractures (11-16). As compared to the SF-36 which is reported as two summary measures (physical and mental, PCS and MCS), the SF-6D index is a single numerical value which represents different states of health (from very poor, 0.296 to perfect health, 1.0) and thus it is easy to grasp by clinicians and researchers alike.

Utilizing the SF-36, we and others have previously shown that SLE patients function at levels lower than individuals from the general population; that is the case for both the PCS and MCS measures of the SF-36 (17-19). Furthermore, in our initial cross-sectional analyses we showed that variables from the psychological and behavioral domains appear to be more important determinants of poor levels of self-reported functioning than disease-related variables (7). Moreover, poor baseline HRQOL predicted subsequent poor HRQOL in our patients (20).

More recently, we have examined whether poor self-reported HRQOL assessed early in the course of the disease using the SF-6D index may have an impact in the accrual of damage in

patients from the LUMINA cohort (21). Indeed, we found that lower SF-6D values early in the course of the disease predicted damage accrual at last visit; however, the SF-6D did not appear to exert an independent effect on mortality in these patients.

We have now expanded our investigations by examining variables from the initial and subsequent study visits predictive of HRQOL over the course of the disease utilizing the SF-6D and a time-dependent approach. We hypothesized that disease and non-disease related factors will account for the levels of HRQOL in our patients. Moreover, we hypothesized that disease-related factors may be more important predictors at disease onset but that non-disease related factors may be more relevant subsequently. For completion, we have also examined the summary measures of the SF-36 as predictors of subsequent HRQOL as more patients and years of observation have been accrued in the cohort since our original observations were published a few years ago (7, 20).

Patients and methods

Patients

LUMINA is a multiethnic cohort of patients with SLE; the constitution of this cohort has been previously reported (7, 20, 22) and it is now briefly described. LUMINA is a collaborative research effort between the University of Alabama at Birmingham (UAB), the University of Texas Health Science Center at Houston (UTH) and the University of Puerto Rico Medical Sciences Campus (UPR). The cohort is constituted by patients of Hispanic (from Texas and Puerto Rico), African American and Caucasian ethnicities. Patients meeting the American College of Rheumatology (ACR) criteria for SLE (23), with ≤ 5 years of disease duration at enrollment, ≥ 16 years of age and of defined ethnicity (four grandparents of the same ethnic background) were eligible to be enrolled in the study. Visits are conducted every six months during the first year and yearly thereafter. The study visits consist of a review of all available medical records, questionnaires, interviews, physical examination and phlebotomy (24).

Competing interests: none declared.

Variables

The LUMINA database includes variables from the socioeconomic-demographic, clinical, immunological, genetic, psychological and behavioral domains. All variables are obtained at each study visit; only those included in these analyses will be described in detail.

Socioeconomic-demographic variables included are age, gender, ethnicity, marital status, education, poverty (as defined by the US Federal government adjusted for the number of members in the household) (25) and unhealthy-related behaviors (lack of exercising, cigarette smoking, alcohol drinking and recreational drug use).

Clinical variables included are disease duration defined as the interval between the time at which patients met the ACR criteria (TD, herein) and the time of enrollment (T0, herein), number of ACR criteria at T0, disease activity (ascertained with the Systemic Lupus Activity Measure-Revised or SLAM-R) (26), disease damage [ascertained with the Systemic Lupus International Collaborating Clinics (SLICC) Damage Index (SDI)] (27), fatigue ascertained with the Fatigue Severity Scale (FSS) (28), fibromyalgia (defined per the ACR criteria) (29) and depression (defined per the U.S. Preventive Services Task Force questionnaire) (30). These last two variables, however, could not be included in the multivariable analyses since they were added to the study years after it had started and thus were unavailable at the baseline and earlier visits in a significant proportion of patients (*vide infra*).

Psychosocial and behavioral domain variables included are social support ascertained with the Interpersonal Support Evaluation List (ISEL) where higher scores indicate better social support (31), learned helplessness assessed with the Rheumatology Attitudes Index (32, 33) and abnormal illness-related behaviors ascertained with the Illness Behavior Questionnaire (IBQ) (34); higher scores indicate either greater degree of helplessness or of abnormal illness-related behaviors, respectively. The SF-6D index was derived from the SF-36 according with the algorithm described by Brazier *et al.* (9, 35) based on Standard Gamble methodology; it

constitutes the dependent variable in these analyses. As compared with the SF-36 (eight dimensions or subscales and two summary measures, PCS and MCS) (36), the SF-6D has six dimensions as the general health dimension has been omitted and the role physical and emotional dimensions have been combined into one. These dimensions and the number of items in each are as follow: physical functioning (3 items), role limitation (2 items), social functioning (1 item), bodily pain (2 items), mental health (1 item) and vitality (1 item); a single numeric value ranging from 0.296 (poorest health, worse than being dead) to 1.0 (perfect health) is then generated to constitute the SF-6D index.

Statistical analyses

In order to examine the variables predictive of HRQOL over the course of the disease using the SF-6D from all study visits as the dependent variable, two sets of analyses were performed. In the first set, only T0 variables were examined and in the second set, variables from the visits preceding the ones being assessed were included. In both sets of analyses, mixed model regressions were performed. Variables with a *p*-value ≤ 0.10 in the univariable analyses were entered in the multivariable analyses; age, gender and ethnicity were included regardless of their level of significance in the univariable analyses. In the second set of analyses, two separate models were examined; one model included the prior SF-6D score and the other model did not. In these analyses all patients' visits (*n*=2662) in which the SF-36 had been ascertained and the SF-6D therefore could be derived were included. For patients for whom the SF-36 was not available at T0 (*n*=40), the SF-6D index was derived at the subsequent visit. In an alternative model, the PCS and MCS measures of the SF-36 were the dependent variables. Since the SF-6D is a mathematical derivation of the SF-36, the PCS and MCS and the SF-6D index could not be included in the same model. Statistical significance was defined as a *p*-value ≤ 0.05 . All statistical analyses were performed using SAS, version 9.1 (SAS Institute, Cary, NC, USA).

Results

A total of 2662 visits from 588 patients (range 2-10 visits per patient) were included in these analyses. Baseline characteristics of the patients studied are shown in Table I. Ninety percent of the patients were women; their mean (SD) age, number of years of education and disease duration were 36.6 (12.4), 13.0 (3.1) and 1.6 (1.4) years, respectively. The ethnic groups were represented as follows: 110 (19%) Hispanic-Texans, 102 (17%) Hispanic-Puerto Ricans, 206 (35%) African Americans and 170 (29%) Caucasians. Fifty-two percent of the patients were married/living together and 33% were below the poverty line. The patients' mean (SD) SF-6D

Table I. Baseline characteristics of LUMINA* patients studied.

| Variable | n=588 |
|--|-------------|
| Gender, female, % | 90 |
| Age, years, mean (SD) | 36.6 (12.4) |
| Ethnicity, % | |
| Hispanic-Texan | 19 |
| Hispanic-Puerto Rican | 17 |
| African American | 35 |
| Caucasian | 29 |
| Marital status, married/together, % | 52 |
| Education, years, mean (SD) | 13.0 (3.1) |
| Lack of exercise, % | 59 |
| Smoking, % | 13 |
| Drinking, % | 9 |
| Poverty [†] , % | 33 |
| Disease duration, years, mean (SD) | 1.6 (1.4) |
| ACR [‡] criteria number at diagnosis, mean (SD) | 5.3 (1.6) |
| SLAM-R [§] score at T0, mean (SD) | 9.2 (5.6) |
| SDI [§] score at T0, mean (SD) | 0.7 (1.2) |
| Pain, mean (SD) | 3.8 (3.1) |
| Fatigue, mean (SD) | 4.9 (1.3) |
| Depression [§] , % | 42 |
| Fibromyalgia, % | 6 |
| Social support ^{**} score, mean (SD) | 7.8 (1.8) |
| Helplessness ^{**} score, mean (SD) | 39.8 (6.7) |
| Abnormal illness-related behaviors* score, mean (SD) | 18.6 (6.7) |
| SF-6D, mean (SD) | 0.6 (0.1) |

*Lupus in Minorities: NAture vs. Nurture Depression (*n*=138) and fibromyalgia (*n*=349) were not ascertained in all patients as these variables were added to the protocol later; [†]as defined by the US Federal government guidelines; [‡]American College of Rheumatology; [§]Systemic Lupus Activity Measure-Revised; [§]Systemic Lupus International Collaborating Clinics (SLICC) Damage Index; ^{**}Ascertained with the Interpersonal Support Evaluation List, the Rheumatology Attitudes Index and the Illness Behaviors Questionnaire, respectively.

and number of ACR criteria were 0.6 (0.1) and 5.3 (1.6), respectively. The mean (SD) SLAM-R and SDI scores were 9.2 (5.6) and 0.7 (1.2), respectively; these scores indicate moderate levels of disease activity and limited damage accrual, respectively (26, 27). Overall, patients exhibited moderate levels of pain and fatigue; they also exhibited low levels of social support [7.8 (1.8)], high levels of helplessness [39.8 (6.7)] and of abnormal illness-related behaviors [18.6 (6.7)], respectively. In over 40% of the patients in whom depression had been ascertained at T0 (n=108) it was present; 7% of 288 patients in whom fibromyalgia had been ascertained at T0, exhibited it.

T0 variables predicting SF-6D over the course of the disease

In the multivariable analyses, Hispanic-Texan ethnicity (Caucasian being the reference group) and higher levels of social support were independently and positively predictive of HRQOL whereas older age, poverty, greater disease activity, increasing fatigue and higher levels of helplessness and of abnormal illness-related behaviors were negatively and independently predictive of HRQOL. Of note, depression could not be included in this model given that this parameter had not been ascertained at T0 in all patients as it was added to the visits at a later time point (data not available at T0 in 480 patients). The corresponding univariable analyses and the z- and p-values for both univariable and multivariable analyses are depicted in Table II.

Variables from the preceding visit predicting SF-6D over the course of the disease

In the multivariable analyses, higher levels of social support and a higher prior SF-6D were independently and positively predictive of HRQOL whereas older age, poverty, greater damage accrual, increasing fatigue ($p<0.0001$), and higher levels of helplessness ($p=0.0192$) and of abnormal illness-related behaviors ($p<0.0001$) were negatively and independently predictive of HRQOL over the course of the disease. Fibromyalgia and depression were not entered into

Table II. Baseline variables predicting SF-6D over the disease course in LUMINA patients.

| Variable | Univariable | | Multivariable | |
|--|-------------|----------|---------------|----------|
| | Z | p-value | Z | p-value |
| Gender, female | 0.31 | 0.7560 | | |
| Age | -3.12 | 0.0018 | -7.79 | < 0.0001 |
| Ethnicity* | | | | |
| Hispanic-Texan | 1.28 | 0.2021 | 3.55 | 0.0004 |
| Hispanic-Puerto Rican | 1.11 | 0.2660 | | |
| African American | -1.27 | 0.2053 | | |
| Marital status, married/together | 1.14 | 0.2556 | | |
| Education | 3.51 | 0.0004 | | |
| Lack of exercise | -3.39 | 0.0007 | | |
| Smoking | -1.89 | 0.0582 | | |
| Drinking | -2.25 | 0.0247 | | |
| Poverty [†] | -5.45 | < 0.0001 | -3.17 | 0.0015 |
| ACR criteria number | -8.70 | < 0.0001 | | |
| SLAM-R [‡] | -13.61 | < 0.0001 | -6.51 | < 0.0001 |
| SDI score [§] | -4.72 | < 0.0001 | | |
| Pain | -0.94 | 0.3479 | | |
| Fatigue | -20.91 | < 0.0001 | -13.40 | < 0.0001 |
| Depression [§] | -4.40 | < 0.0001 | | |
| Fibromyalgia [§] | 1.57 | 0.1162 | | |
| Social support score ^{**} | 13.50 | < 0.0001 | 4.62 | < 0.0001 |
| Helplessness score ^{**} | -21.87 | < 0.0001 | -9.57 | < 0.0001 |
| Abnormal illness-related behaviors score ^{**} | -18.75 | < 0.0001 | -9.97 | < 0.0001 |

*Caucasian is the reference group; [†]as defined by the US Federal government guidelines; [‡]Systemic Lupus Activity Measure-Revised; [§]Systemic Lupus International Collaborating Clinics (SLICC) Damage Index; [§]variables not entered in the multivariable analysis (see text); ** Ascertained with the Interpersonal Support Evaluation List, the Rheumatology Attitudes Index and the Illness Behaviors Questionnaire, respectively.

Table III. Variables from the preceding visit predicting SF-6D over the disease course in LUMINA patients.

| Variable | Univariable | | Multivariable | |
|--|-------------|----------|---------------|----------|
| | Z | p-value | Z | p-value |
| Gender, female | 0.26 | 0.7954 | | |
| Age | -3.44 | 0.0006 | -5.81 | < 0.0001 |
| Ethnicity* | | | | |
| Hispanic-Texan | 0.53 | 0.5960 | | |
| African American | -1.95 | 0.0507 | | |
| Caucasian | -0.98 | 0.3260 | | |
| Marital status, married/together | 1.46 | 0.1439 | | |
| Education | 3.29 | 0.0010 | | |
| Lack of exercise | -3.31 | 0.0009 | | |
| Smoking | -1.7 | 0.0882 | | |
| Drinking | -2.00 | 0.0459 | | |
| Poverty [†] | -4.70 | < 0.0001 | -2.80 | 0.0051 |
| SLAM-R [‡] | -8.36 | < 0.0001 | | |
| SDI score [§] | -4.10 | < 0.0001 | -2.05 | 0.0407 |
| Fatigue | -15.22 | < 0.0001 | -4.40 | < 0.0001 |
| Depression [§] | -8.69 | < 0.0001 | | |
| Fibromyalgia [§] | -6.47 | < 0.0001 | | |
| Social support score ^{**} | 10.01 | < 0.0001 | 2.16 | 0.0305 |
| Helplessness score ^{**} | -15.17 | < 0.0001 | -2.34 | 0.0192 |
| Abnormal illness-related behaviors score ^{**} | -12.87 | < 0.0001 | -4.22 | < 0.0001 |
| Prior SF-6D | 35.13 | < 0.0001 | 16.36 | < 0.0001 |

*Hispanic-Puerto Rican is the reference group; [†]as defined by the US Federal government guidelines; [‡]Systemic Lupus Activity Measure-Revised; [§]Systemic Lupus International Collaborating Clinics (SLICC) Damage Index; [§]variables not entered in the multivariable analysis (see text); ** Ascertained with the Interpersonal Support Evaluation List, the Rheumatology Attitudes Index and the Illness Behaviors Questionnaire, respectively.

this model because these variables were not available in a large proportion of patients' visits [nearly two-thirds (n=1824) of patients' visits for depression and one third for fibromyalgia (n=1075)]. The corresponding univariable analyses and the z- and p-values for both univariable and multivariable analyses are depicted in Table III.

When the SF-6D index from the preceding visits was removed from the model, the results were overall consistent although some differences were

observed. Hispanic-Texan ethnicity became a positive predictor of HRQOL, disease activity became a negative predictor and damage accrual lost its statistical significance (data not shown).

Alternative model

When instead of the SF-6D, the PCS and MCS measures of the SF-36 were examined as the dependent variables, the results were overall consistent with those described above in both models for the SF-6D (T0 variables and vari-

ables from the preceding visit), with some exceptions. Tables IV and V depict the comparisons between the results of these models.

Discussion

Life expectancy in SLE has improved over the last few decades, making it now a chronic disease; unfortunately, these patients' quality of life may be impaired. In fact, HRQOL is considered one of the outcome measures agreed upon to assess lupus patients enrolled in

Table IV. Comparison of the baseline variables independently associated with HRQOL when the PCS and MCS measures of the SF-36 or SF-6D are the dependent variables.

| T0 variables | PCS | | MCS | | SF-6D | |
|---|--------------------------|----------|--------------------------|----------|--------------------------|----------|
| | Direction of association | p-value | Direction of association | p-value | Direction of association | p-value |
| Age | – | < 0.0001 | | | – | < 0.0001 |
| Ethnicity* | | | | | | |
| Hispanic-Texan | + | 0.0002 | + | 0.0322 | + | 0.0004 |
| Hispanic-Puerto Rican | + | < 0.0001 | + | 0.0037 | | |
| African American | | | | | | |
| Lack of exercise | – | 0.0094 | | | | |
| Smoking | – | 0.0276 | | | | |
| Poverty [†] | – | < 0.0001 | | | – | 0.0015 |
| ACR criteria number | – | 0.0047 | + | 0.0054 | | |
| SLAM-R [‡] | – | < 0.0001 | – | 0.0028 | – | < 0.0001 |
| SDI score [§] | – | 0.0059 | | | | |
| Fatigue | – | < 0.0001 | – | < 0.0001 | – | < 0.0001 |
| Social support score [§] | | | + | < 0.0001 | + | < 0.0001 |
| Helplessness score [§] | – | < 0.0001 | – | < 0.0001 | – | < 0.0001 |
| Abnormal illness-related behaviors [§] score | – | 0.0050 | – | < 0.0001 | – | < 0.0001 |

*Caucasian is the reference group; [†]as defined by the US Federal government guidelines; [‡]Systemic Lupus Activity Measure-Revised; [§]Systemic Lupus International Collaborating Clinics (SLICC) Damage Index; [§]Ascertained with the Interpersonal Support Evaluation List, the Rheumatology Attitudes Index, and the Illness Behaviors Questionnaire, respectively.

Table V. Comparison of the variables from the preceding visit independently associated with HRQOL when the PCS and MCS measures of the SF-36 or SF-6D are the dependent variables.

| Variables from preceding visit | PCS | | MCS | | SF-6D | |
|---|--------------------------|----------|--------------------------|----------|--------------------------|----------|
| | Direction of association | p-value | Direction of association | p-value | Direction of association | p-value |
| Age | – | < 0.0001 | | | – | < 0.0001 |
| Ethnicity* | | | | | | |
| Hispanic-Texan | – | 0.0128 | | | | |
| African American | – | < 0.0001 | | | | |
| Caucasian | – | < 0.0001 | | | | |
| Lack of exercise | – | 0.0089 | | | | |
| Poverty [†] | – | < 0.0001 | | | – | 0.0051 |
| SDI score [§] | – | 0.0261 | | | – | 0.0407 |
| Fatigue | – | 0.0003 | – | 0.0002 | – | < 0.0001 |
| Social support score [§] | | | + | 0.0244 | + | 0.0305 |
| Helplessness score [§] | – | 0.0111 | – | 0.0333 | – | 0.0192 |
| Abnormal illness-related behaviors score [§] | – | 0.0471 | – | < 0.0001 | – | < 0.0001 |
| Prior SF-6D/PCS/MCS, respectively | + | < 0.0001 | + | < 0.0001 | + | < 0.0001 |

*Hispanic-Puerto Rican is the reference group; [†]as defined by the US Federal government guidelines; [‡]Systemic Lupus Activity Measure-Revised; [§]Systemic Lupus International Collaborating Clinics (SLICC) Damage Index; [§]Ascertained with the Interpersonal Support Evaluation List, the Rheumatology Attitudes Index, and the Illness Behaviors Questionnaire, respectively.

clinical trials (4). For the most part, the SF-36 has been used to ascertain this construct (1, 7).

To our knowledge, we are the first to use the SF-6D index to ascertain HRQOL in patients with lupus. In our initial report we examined if self-reported HRQOL, as assessed early in the course of the disease, could be an independent predictor of damage accrual, which indeed was the case (21). We have now taken an additional step, that is, to examine the factors predictive of HRQOL over the disease course. We have also compared and contrasted the SF-6D with the SF-36 from which it is derived. Whether T0 variables or variables preceding the visit under scrutiny were included, we have now shown that HRQOL over the course of the disease is influenced not only by disease-related factors (disease activity, damage accrual and fatigue) but also by socioeconomic-demographic (age, Hispanic-Texan ethnicity and poverty) and psychological and behavioral factors (social support, helplessness and abnormal illness-related behaviors). Furthermore, we have also shown that HRQOL over time is significantly influenced by prior HRQOL. Although some differences were observed in the analyses performed (SF-6D or SF-36 and the timing of the variables), the overall results are supportive of our initial hypothesis, that is of the multiplicity of factors affecting overall HRQOL in lupus patients. Although it is very likely that fibromyalgia and depression also exert an important impact on self-reported HRQOL (37), these constructs could not be included in the models examined because these data were not available in all study visits as they were added to the protocol a few years into the study.

Although we have previously examined the predictors of HRQOL utilizing the SF-36 in our cohort (7, 20), we believe the SF-6D, which was developed primarily as a utility measure to be used in economic evaluations, offers certain advantages over the SF-36. As opposed to the SF-36 which provides two summary measures and eight subscales values, the SF-6D provides a single numeric value which may vary from 0.296 in patients failing

in all six dimensions of the index to 1 for those in perfect health; this single score is equally easy to understand by outcome researches as well as by clinicians working in the discipline. Not surprisingly, however, our results are consistent with the analyses previously reported, and with the ones also reported now using the SF-36. Furthermore, whether the SF-6D or the summary measures of the SF-36 are examined, our results emphasize the importance HRQOL early in the disease course exerts in HRQOL subsequently; that is poor HRQOL is usually followed by poor HRQOL and viceversa. These observations are consistent with those made by Kuriya *et al.* in patients from the Toronto Lupus cohort (37).

Among the socioeconomic-demographic factors, HRQOL tended to be negatively influenced by age and poverty. The negative impact of aging and poverty in HRQOL has been described not only in lupus (17), but in most other chronic diseases (38-40). Of interest, when the summary measures of the SF-36 were the end-points in our analyses, poverty was a negative predictor of PCS but not of MCS; this probably reflects the fact that poverty is more strongly associated with the subscales of the SF-36 that are used to derive the PCS (and the SF-6D) than those used to derive the MCS. It is also of interest that even though patients of Hispanic-Texan and African American ethnicities tend to experience more severe disease and accrue more damage, no negative association between either ethnic group and HRQOL was demonstrated; in fact, when we included the T0 variables to predict HRQOL, whether the dependent variable was the SF-6D or the SF-36 measures (PCS and MCS), being of Hispanic-Texan but not of African American ethnicity was positively predictive of overall HRQOL; we hypothesized that this may reflect a better social network and coping styles as well as lower levels of helplessness in patients from this ethnic group as compared to those of African American ethnicity; however, our data failed to support this hypothesis as this group had better social support [7.7 (1.6) vs. 7.3 (1.7), $p=0.0426$] and coping skills

[18.6 (6.7) vs. 21.3 (6.2), $p=0.0011$] and lower levels of helplessness [39.7 (6.5) vs. 40.5 (6.6), $p=0.3253$] than the Hispanic-Texans.

We have previously reported that non-disease related factors appear to be more important determinants of self-reported HRQOL as measured by the SF-36 than disease related factors. In the corresponding analyses presented now (T0 variables predicting subsequent HRQOL), in addition to the psychosocial variables, disease activity was now strongly associated with HRQOL for both the SF-6D and the SF-36 measures. However this relationship was not evident when the variables preceding the visit being examined were considered. In our previous longitudinal analyses, we could not demonstrate, damage being a negative predictor of overall HRQOL (20); however, we have now found damage to negatively predict PCS (but not the MCS); this association is, however, not as strong as the one between the SF-6D and damage (21). Given that disease activity and damage accrual are strongly associated, these findings are not unexpected.

Among the psychological and behavioral factors, adequate social support has been shown to be positively associated with HRQOL in cross sectional studies (41-43). In fact, in all the models that we examined, social support was a positive predictor while helplessness and abnormal illness-related behaviors were negative predictors of HRQOL. These findings emphasize the importance of an adequate social network and healthy coping behaviors in affecting the patients' self-perception of HRQOL.

Our study, however, is not without some limitations. Firstly, patients in our cohort are followed yearly which may not be frequent enough to clearly depict their HRQOL over time; for example, we may have missed episodes of high disease activity impacting the patients overall HRQOL. Secondly, because depression and fibromyalgia had not been systematically ascertained in our patients at cohort initiation, we were unable to include these variables in our multivariable models. We suspect, however, based on the strength of the univariable associations (depression at

baseline and over time and fibromyalgia over time) that both constructs are also very important predictors of overall HRQOL. Thirdly, given that we have not examined any of the currently available lupus specific instruments, we can not make any comment about which of them may better reflect these patients' overall HRQOL. Undoubtedly, the SF-36 or its derivation, the SF-6D do not measure body image, self-esteem and other important patient-related constructs (18, 44), which in patients with lupus can be significantly affected either by the disease (integument involvement) or its therapies (Cushingoid features). Finally, although other variables or disease features may be important determinants of HRQOL, we only included in the study the ones we hypothesized *a priori* would have an impact on the HRQOL.

In summary, the data we have presented show that HRQOL over the course of SLE is influenced by disease and non-disease related factors; age, poverty, fatigue, the degree of disease activity, damage, helplessness and abnormal illness-related behaviors are negative predictors whereas Hispanic-Texan ethnicity and adequate social support are positive predictors of overall HRQOL. Importantly, the patient's level of self-reported overall HRQOL appears to be a very strong predictor of subsequent HRQOL; moreover, our data suggest that the SF-6D is at least as good to assess HRQOL as the SF-36, from which it is derived; furthermore, it offers certain advantages given that it is easily interpretable by both, clinicians and researchers. Our data, as well as data from others (1, 17, 41-43) suggest that in patients with lupus, attention should be given not only to the management of their disease but also to the associated psychosocial factors. Such an approach should almost certainly yield better overall outcomes for these patients.

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