Time in remission and low disease activity state (LDAS) are associated with a better quality of life in patients with systemic lupus erythematosus: results from LUMINA (LXXIX), a multiethnic, multicentre US cohort

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ABSTRACT

AIMS To determine whether the proportion of time systemic lupus erythematosus patients achieve remission/low disease activity state (LDAS) is associated with a better quality of life (QoL).

PATIENTS AND METHODS Patients from a well-established multiethnic, multicentre US cohort were included: remission: Systemic Lupus Activity Measure (SLAM) score=0, prednisone≤5 mg/day and no immunosuppressants; LDAS not in remission, SLAM score<3, prednisone≤7.5 mg/day, no immunosuppressants; the combined proportion of time patients were in these states was the independent variable. The endpoints were the Physical and Mental Components Summary measures (PCS and MCS, respectively) and the individual subscales of the Short Form (SF)-36 at the last visit. Linear regression was used to estimate the association between the proportion of follow-up time in remission/LDAS and the SF-36 measures with and without adjustment for possible confounders.

RESULTS Four hundred and eighty-three patients were included. The per cent of time on remission/LDAS was associated with better QoL after adjusting for potential confounders; for the PCS the parameter estimate was 9.47 (p<0.0001), for the MCS 5.89 (p=0.0027), and for the subscales they ranged between 7.51 (p=0.0495) for mental health and 31.79 (p<0.0001) for role physical.

CONCLUSIONS The per cent of time lupus patients stay on remission/LDAS is associated with a better QoL as measured by SF-36.

INTRODUCTION

Over the last few years, remission and low disease activity state (LDAS) have proved to reduce damage in patients with systemic lupus erythematosus (SLE) from several cohorts across the world.1-10 However, patient-reported outcomes, including health-related quality of life (HRQoL), are not strongly associated with disease activity or treatment, so, the impact of these states on HRQoL needs to be evaluated. The importance of HRQoL in the management of SLE has been proposed several times, including quality indicators for the management of patients with SLE11 which have been embraced by the European League Against Rheumatism.12 The association of these states with a better HRQoL has been evaluated only in a few studies.3 13-15 We have now aimed at determining the beneficial effects of achieving these states in the HRQoL in patients with lupus from a multiethnic, multicentre lupus cohort (LUMINA for Lupus in Minorities: Nature vs Nurture).
PATIENTS AND METHODS

The LUMINA cohort has been previously described. In short, this cohort was started in 1995 and up to 2009 had recruited over 600 patients with SLE according to the American College of Rheumatology (ACR) criteria; these patients were of either Caucasian (28%), African (37%) or Hispanic (35%) ancestry and were recruited at three US academic institutions in Alabama, Texas and Puerto Rico. A baseline visit was followed by visits performed every 6 months for the first year and yearly thereafter. Socioeconomic, demographic and clinical data were obtained at all visits. Disease activity was ascertained with the Systemic Lupus Activity Measure (SLAM), disease damage with the Systemic Lupus International Collaborating Clinics/ACR Damage Index (SDI) and HRQoL with the summary measures (Physical and Mental Components Summary scores (PCS and MCS, respectively)) and subscales (Physical functioning, Role Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role Emotional, Mental Health) of the Short-Form 36 (SF-36). The definitions of remission and LDAS were based on a previous study; in short, visits were classified as corresponding to remission (SLAM score = 0 and prednisone $\leq$ 5 mg/day and no immunosuppressants), LDAS ((not in remission), SLAM score $\leq$ 3, prednisone $\leq$ 7.5 mg/day, no immunosuppressants) or neither: active. Antimalarials were allowed in all patients. Patients were assumed to remain in the same state until their subsequent visit. Because of the relatively small number of visits corresponding to remission, remission and LDAS visits were examined as a single variable. In order to determine the per cent of time on remission/LDAS, the SLAM was recorded in all visits.

The association between the SF-36 scores (summary measures and subscales) at the time of last follow-up and the per cent of time on remission/LDAS was modelled using a linear regression with and without adjustment for the following baseline variables: age, gender, racial/ethnic group, education, poverty, social support, abnormal illness behaviours, fibromyalgia, disease activity, damage and the baseline scores of the corresponding SF-36 summary measures and subscales. The definitions for these confounding variables have been previously described. All statistical analyses were performed using SAS V.9.4 (SAS Institute).

RESULTS

Visits for 483 LUMINA patients were included; 157 (24.5%) patients could not be included because they either had only one visit or were lacking some of the variables needed to classify their visits. Excluded patients were more frequently Hispanic or African-American, a larger proportion of them were below the poverty line, their interpersonal support, illness behaviour questionnaire and HRQoL scores were lower but had higher baseline SLAM and SDI scores. Among the patients included, the majority of them were women 433 (89.6%) and their mean (SD) age and disease duration at the baseline visit were 36.9 (12.6) years and 1.4 (1.3) years, respectively. Two hundred and ninety-two patients (60.5%) were using antimalarials at baseline. The mean baseline PCS and MCS scores of the SF-36 were 34.9 (9.9) and 40.1 (10.2). The total number of visits for these patients was 2423, the median number of visits per patient was 4 and the IQR 4. From a total follow-up of 2004 patient/years, 23 (1.1%) were on remission, 314 (15.7%) were on LDAS and 1667 (83.2%) were active. The mean follow-up PCS and MCS scores of the SF-36 were 35.5 (9.7) and 40.5 (10.3). The longer patients were on remission/LDAS, the higher the score of SF-36 (summary measures and subscales); per each increase of 10% of the time on remission/LDAS the PCS increase 0.95 and the MCS 0.59 and the subcomponents increase between 0.75 (Mental Health) and 3.18 (Role Physical). These data are depicted in table 1.

DISCUSSION

This study shows that the longer patients with SLE remain on remission/LDAS, the better their HRQoL, even after adjusting for age, gender, racial/ethnic group, education, poverty, social support, abnormal illness behaviours, fibromyalgia, disease activity, damage and the baseline scores of the corresponding SF-36 summary measures and subscales.

HRQoL does not seem to be strongly associated with disease activity in patients with SLE, in particular if non-specific questionnaires are used, and it has been reported to be influenced but treatments used, probably due to their adverse events; taking together this information could explain why remission or LDAS would impact on HRQoL. The impact of remission and LDAS on HRQoL has been evaluated in a few cross-sectional studies and in two longitudinal. For LDAS, using the SF-36, the Asia Pacific Lupus Collaboration (APLC) cohort reported an association between being on LDAS, defined as low LDAS, and a better HRQoL in the two main component summary measures and seven out of the eight domains of this instrument. And, in a Chinese cohort, being on remission for at least 5 years was associated with a better HRQoL, that was the case for the two main component summary measures and six out of the eight domains of the SF-36 and in the global and five out of the eight domains of the LupusPRO. The longitudinal data examining this matter comes from two studies. One, from a Peruvian lupus cohort in which patients on LDAS or remission for more than 75% of their follow-up experienced better QoL as measured by the LupusQoL (in four out of eight domains), and, those who were on LDAS or remission for 50–75% of their follow-up presented also a better QoL in the physical health domain, compared with those who were on LDAS or remission for less than 25%. The second study comes from a Dutch cohort in which patients on remission (on or off therapy) had a better HRQoL in the PCS of the SF-36, but not in the MCS; among those on remission, those patients with...
remission off therapy had a better HRQoL in the PCS than those on therapy. Even though LLDAS and LDAS are not exactly the same, they measure a very similar construct.

This study has some limitations. First, we could not use the original definitions of remission and LDAS because the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) was used on them which was not recorded in our cohort; rather, we used the SLAM for defining these states, fact which has not been validated in other cohorts. Second, as we examined time on LDAS/remission as the percentage of the total follow-up time, we were unable to determine the minimum time needed to be on remission/LDAS to achieve a better HRQoL. Third, due to the relative short time on LDAS and remission, we could not determine independently the impact of LDAS and remission on HRQoL. The main strength of this study is that is the first study that evaluates longitudinally the impact of the percentage of time on LDAS/remission on the HRQoL in patients with lupus from a multiethnic lupus cohort.

In conclusion, the per cent of time lupus patients stay on remission or LDAS is associated with a better QoL as measured by summary measures and subscales of the SF-36. These data have important implications for the management of patients with lupus.

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### Contributors
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### Table 1 Multivariable regression analysis of time in remission and LDAS and quality of life as measured by the summary measures and subscales of the SF-36

<table>
<thead>
<tr>
<th>SF-36</th>
<th>Number of patients</th>
<th>Estimate</th>
<th>SE</th>
<th>T value</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical Component Summary Score</td>
<td>456</td>
<td>9.47</td>
<td>1.86</td>
<td>5.10</td>
<td>&lt;0.0001</td>
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<tr>
<td>Physical functioning</td>
<td>472</td>
<td>18.14</td>
<td>4.85</td>
<td>3.74</td>
<td>0.0002</td>
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<tr>
<td>Role physical</td>
<td>466</td>
<td>31.79</td>
<td>6.28</td>
<td>5.06</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Bodily pain</td>
<td>469</td>
<td>19.97</td>
<td>4.91</td>
<td>4.07</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>General health</td>
<td>469</td>
<td>23.15</td>
<td>3.95</td>
<td>5.86</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Mental Component Summary Score</td>
<td>456</td>
<td>5.89</td>
<td>1.96</td>
<td>3.01</td>
<td>0.0027</td>
</tr>
<tr>
<td>Social functioning</td>
<td>468</td>
<td>19.03</td>
<td>4.78</td>
<td>3.98</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Role emotional</td>
<td>463</td>
<td>26.28</td>
<td>6.37</td>
<td>4.13</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Vitality</td>
<td>472</td>
<td>13.39</td>
<td>4.03</td>
<td>3.32</td>
<td>0.0010</td>
</tr>
<tr>
<td>Mental health</td>
<td>472</td>
<td>7.51</td>
<td>3.81</td>
<td>1.97</td>
<td>0.0495</td>
</tr>
</tbody>
</table>

Possible confounders were: age, gender, racial/ethnic group, education, poverty, social support, abnormal illness behaviours, fibromyalgia, disease activity, damage and the baseline scores of the corresponding SF-36 summary measures and subscales.

LDAS, low disease activity state; SF-36, Short Form-36.

### REFERENCES


