Association of systemic lupus erythematosus and hypermobility

M Gumà, A Olivé, J Roca, J Forcada, J C Duró, S Holgado, E Casado, X Mezquiriz, X Tena

**Objective:** To investigate joint laxity in patients with systemic lupus erythematosus (SLE).

**Setting:** University Hospital.

**Methods:** 81 patients with SLE (1999 American College of Rheumatology criteria; 72 (89%) women and nine (11%) men, mean age 42.9 (SD 16.1) years), who regularly attended a specialist SLE clinic were examined. The control group comprised 280 patients attending a general practitioner (193 (69%) women and 87 (31%) men, mean age 44.7 (SD 11.2) years). Joint laxity was measured according to the criteria of Beighton et al (total score 4 or more). A regression analysis was performed.

**Results:** Thirty nine (48%) patients with SLE and 42 (15%) of the control group were hypermobile. A logistic regression model was developed. The odds ratio of the association between laxity and SLE after adjustment for age and sex was 2.31 in the group younger than 49 years, and 1.99 in the group aged 49 years or older. Neither the clinical and analytical profile nor the use of corticosteroids was related to joint laxity.

**Conclusion:** Patients with SLE showed more hypermobility than controls. Hypermobility was more profound in older patients with SLE (≥49 years). Joint laxity was not associated with any clinical or analytical pattern. Treatment with corticosteroids was not related to joint laxity.

Patients with SLE and hypermobility syndrome share some clinical features in common—namely, arthralgies and myalgias. To recognise that patients with SLE are hypermobile is important for the management of the disease.

The first report of an association between joint laxity and rheumatological symptoms was published in 1947. Thereafter, joint laxity was recognised as a common disorder characterised by the ability to perform certain passive movements of the joints. In 1967 the hypermobility syndrome was described in a group of patients with joint laxity and musculoskeletal complaints in the absence of any other demonstrable disease.

It has been shown that mobility varies according to sex, age, and ethnic background. Hypermobile joints are more prevalent in younger women of Afro-American or Asian origin. Diagnosing joint laxity requires measurement of the amplitude of joint movements. The nine point scale of Beighton et al is that most often used.

Recent reports have focused on specific rheumatological complaints encountered in adult patients with joint laxity. Frequent diagnoses for hypermobile patients were arthralgies and soft tissue rheumatism. However, one report found an association with inflammatory arthropathies, especially with SLE. Other authors found that 10 of 59 (17%) patients with SLE were hypermobile.

The association of joint laxity and SLE seems to be related to the occurrence of two entities which are common in young women.

The aim of this paper was to determine if patients with SLE were more hypermobile than a control population.

**PATIENTS AND METHODS**

Eighty one patients (72 women and nine men, mean age 42.9 (SD 16.1) years with SLE (American College of Rheumatology (ACR) revised criteria) were studied. Patients were consecutively enrolled between January 1999 and July 1999 in an SLE clinic. The clinical and analytical features retrospectively assessed in the SLE group were (a) cutaneous lesions; (b) vasculitis; (c) lung and heart involvement; (d) musculoskeletal involvement; (e) neurological disorders; (f) renal disorder; (g) haematological disorder; (h) autoantibodies; (i) total doses (mg) of corticosteroids; and (j) treatment with other drugs.

As a control group, 280 new patients (193 women and 87 men, mean age 44.7 (SD 11.2) years, who were visited in a primary care centre were selected (period of enrolment January 1999–July 1999). To avoid information bias general practitioners were trained to evaluate joint laxity using the criteria of Beighton et al. Patients were excluded if they suspected of having Marfan or Ehler-Danlos syndromes—namely, the presence of a marfanoid habitus, dermal extensibility, and cutaneous scarring. Patients with renal failure and on haemodialysis were excluded.

Hypermobility was determined prospectively according to the criteria of Beighton et al. Patients were given a score of 0–9, one point being allocated for the ability to perform each of the tests: (a) passive dorsiflexion of the little finger beyond 90º; (b) passive apposition of the thumb to the flexor aspects of the forearm; (c) hyperextension of the elbow beyond 10º; (d) hyperextension of the knee beyond 10º; and (e) forward flexion of the trunk, with the knees straight, so the palms of the hands rested easily on the floor. Patients were considered hypermobile if they scored 4 or more out of 9. Hypermobility was measured without blinding.

**Statistical analysis**

The outcome of interest was joint laxity. Independent variables were age, sex, and SLE status. Age was reduced to two categories with the cut off point at the median. Subjects less than 49 years old were the reference category. Male subjects were the reference category for sex; for SLE status it was subjects without SLE.

Student’s t tests and χ² tests were used to evaluate differences in age, sex, and laxity in the two groups according to SLE status.

Abbreviations: ACR, American College of Rheumatology; CI, confidence interval; OR, odds ratio; SLE, systemic lupus erythematosus
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RESULTS

Joint laxity was present in 39 of the 81 patients with SLE (48%). Women were the majority in both the hypermobile subgroup (36; 92%) and in the non-hypermobile subgroup (34; 81%). The mean age of hypermobile patients was 37 (SD 10.4) years. Non-hypermobile patients were older (48 (SD 15.8) years). Patients with joint laxity had a mean score of 7, whereas patients with SLE but without joint laxity had a score of 1. The duration of SLE was 7.34 (SD 4.58) years (range 1–22 years). There were no differences between mobile and non-mobile patients with SLE. Joint laxity in the control group was present in 15% of patients (42/280). There were 39 (93%) women in the hypermobile subgroup and 154 (65%) in the non-hypermobile subgroup. The mean age of hypermobile patients was 28 (SD 11) years and that of the non-hypermobile group was 47 (SD 18) years. Patients with joint laxity had a mean score of 6 whereas patients without joint laxity had a mean score of 0.5.

There were significantly more women in the group with SLE (p=0.001). This group was younger but the difference was not significant. Prevalence of joint laxity was significantly higher in the group with SLE than in the control group (p=0.001).

Forty five per cent of patients with SLE were taking corticosteroids (cumulative dose 3366 (SD 6242) mg, range 0–32 000 mg). The total dose of corticosteroids between the patients with joint laxity (3430 (SD 7780) mg) and the patients without joint laxity (3484 (SD 4719) mg) was not significantly different. The univariate study also showed no relation between hypermobility and glucocorticosteroid treatment in the SLE group. There were no significant associations between hypermobility and any immunological, clinical, or analytical features of SLE.

To further investigate the association of SLE and joint laxity and the possible role of sex and age as confounding factors or effect modifiers, we performed a univariate analysis of the association between joint laxity and the covariates. Joint laxity was strongly associated with female sex and SLE (odds ratio (OR)=7.8, p<0.001). The OR for laxity in patients with SLE was 5.39-fold higher than in patients without SLE. Age was inversely associated with joint laxity (OR=0.26, p<0.001).

Because joint laxity decreases as age increases, we analysed the association between joint laxity and SLE status stratified by age. We used the median age (49 years) of the study population to divide it into two groups (table 1). There seems to be an interaction between age and SLE because the OR for SLE status was modified by age. The OR for joint laxity in subjects who did not have SLE, compared with those who did, was 3.24 for those younger than 49, but it increased to 21.03 for those 49 years old or older. The increase was not random. This was suggested by the lack of overlap of the confidence intervals of the ORs. The same analysis was performed with sex as the variable. Sex was strongly associated with joint laxity but there was no interaction between sex and SLE status.

Finally, to estimate the independent association between joint laxity and SLE status, a logistic regression model was developed. This included three dummy variables for sex, age, and SLE status and an interaction term for the interaction between age and SLE status. An interaction term was created for combinations of the dummy variables age and SLE status. The OR of the association between laxity and SLE for both age groups was adjusted for sex. Although both ORs decreased compared with the univariate analysis, a strong association between SLE and joint laxity remained (OR=5.39, 95% CI 3118–9520, p<0.001).

DISCUSSION

Patients with SLE tend to have a generalised tendinous condition, especially those who present with Jaccoud’s arthropathy, atlantoaxial subluxation, and tendinitis. Bleifeld and Inglis described a localised hand hypermobility in half of their patients with SLE. Distal interphalangeal joint laxity and wrist instability were the most frequent clinical manifestations.

Babini et al have reported several studies about joint laxity in patients with SLE. They proposed that both Jaccoud’s syndrome and atlantoaxial subluxation in patients were the expression of a generalised tendinous condition, partially attributable to a secondary hyperparathyroidism related to chronic renal failure. Parathyroid hormone may affect ligaments and tendons either by a direct effect on collagen or by increasing collagenase activity. These factors may account for the laxity of capsular and ligamentous structures seen in this disorder.13–15

However, Bridges et al found joint laxity in three patients with SLE. As their patients had neither renal failure nor hyperparathyroidism, they pointed out that it would be a new association. They suggested, however, that this association was more likely to be related to the occurrence of two entities which were common in young women. Interestingly enough, no association was found in a controlled study of patients with SLE who had a severe disease requiring long term treatment with corticosteroids.16 In this study, joint laxity was not associated with either age at onset of disease, disease duration, or corticosteroid treatment. The differences from the present work might be related to methodological differences.

Our study showed that a group of patients with SLE had more hypermobility than in a control population. It is worth emphasising that the association between SLE and joint laxity

Table 1 Association between systemic lupus erythematosus (SLE) status and joint laxity according to age

<table>
<thead>
<tr>
<th>Age group</th>
<th>Unadjusted</th>
<th>Adjusted by sex*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Odds ratio (95% CI)</td>
<td>p Value</td>
</tr>
<tr>
<td>&lt;49</td>
<td>3.24 (1.584 to 6.624)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>≥49</td>
<td>21.03 (6.971 to 63.463)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The p value is that for the method used for testing the hypothesis that the value of the underlying odds ratio is equal to one.

*The multiple logistic model was –2.45+1.92 (female) – 2.50 (age ≥49 years) + 0.84 (SLE) + 2.05 (age ≥49 years)SLE. The p value of the interaction term was 0.0029. Goodness of fit statistic=0.0381 with 1df (p=0.845). Area under the ROC curve: 0.81.
was more profound as age increased (≥49 years). Furthermore, SLE prevented the loss of joint laxity acquired during youth. 

Joint laxity was not related to the use of corticosteroids, as suggested in previous studies. Neither renal failure nor hyperparathyroidism were related. There was no statistical association between hypermobility and any immunological, clinical, or analytical features of SLE.

More than 80% of the patients with SLE developed musculoskeletal symptoms—namely, arthritis, arthralgies, and myalgies. Although most of these symptoms are related to SLE activity, some might be related to hypermobility syndrome. Further studies are required to determine the frequency of hypermobility syndrome in patients with SLE.

Recognition of joint laxity may be useful for assessing patients with SLE. A diagnosis of hypermobility may be important for identifying aggravating factors and introducing preventive measures.

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