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PAPER

Health-related quality of life, fatigue and mood in patients with SLE and high levels of pain compared to controls and patients with low levels of pain

E Waldheim[1], A-C Elkan[2], S Pettersson[1], R van Vollenhoven[3], S Bergman[4], J Frostegård[5] and E Welin Henriksson[1]
[1]Unit of Rheumatology, Karolinska University Hospital, Sweden; Division of Nursing, Department of Neurobiology, Care Science and Society, Karolinska Institutet, Sweden; [2]Innovation and Development SRQ (Swedish Rheumatology Quality Register) Dept. of Rheumatology, Karolinska University Hospital, Sweden; Institute of Environmental Medicine, Karolinska Institutet, Sweden; [3]Unit of Rheumatology, Karolinska University Hospital, Sweden; Department of Medicine, Solna, Karolinska Institutet, Sweden; [4]Research and Development Centre, Spenshult Hospital, Sweden; Department of Rheumatology, Clinical Sciences, Lund University, Sweden; and [5]Institute of Environmental Medicine, Unit of Immunology and Chronic Disease, Karolinska Institutet, Sweden

Objective: The objective of this paper is to investigate health-related quality of life (HRQoL), fatigue, anxiety and depression in patients with systemic lupus erythematosus (SLE) and higher levels of pain and to compare them to patients with lower levels of pain and controls. **Method:** Patients were dichotomized into two groups based on SLE-related pain score on the visual analog scale (VAS): low-pain group (76%, $n = 64$, VAS 0–39 mm) and high-pain group (24%, $n = 20$, VAS 40–100 mm). Sex- and age-matched controls were randomly selected from the general population. Participants were asked to complete questionnaires regarding self-reported pain, HRQoL, fatigue, anxiety and depression. Medical assessments also were recorded. **Result:** Fatigue score in the high-pain group (median, 36.5; interquartile range (IQR), 32.5–39.7) was significantly higher ($p < 0.001$) compared to the low-pain group (median, 23; IQR, 14.6–34.1), as well as scores for anxiety (median, 9; IQR, 6.5–11.5) and depression (median, 7.5; IQR, 5.5–9) ($p < 0.001$). The high-pain group had significantly lower scores compared to the low-pain group in all dimensions in the SF-36 ($p \leq 0.001$–0.007). No statistical differences were detected between the low-pain group and controls in any measurement except for the dimensions physical function, general health, vitality and social function in SF-36. **Conclusion:** Patients with SLE scoring higher degrees of pain were burdened with more fatigue, anxiety and depression and lower levels of HRQoL compared to patients with lower levels of pain who did not differ significantly from the general population in most dimensions. These results elucidate the importance of identifying patients with higher degrees of pain who are probably in need of more extensive multidimensional interventions to decrease symptom burden. *Lupus* (2013) **22,** 1118–1127.

Key words: Systemic lupus erythematosus; pain; health-related quality of life; fatigue; depression; anxiety

Introduction

Systemic lupus erythematosus (SLE) is a chronic, systemic, autoimmune rheumatic disease potentially affecting most organ systems, and is characterized by a wide array of associated medical problems, including side effects of pharmacotherapy.[1]

Although the survival rate of patients with SLE has improved, the mortality rate is still higher compared to the general population.[2]

Approximately 50–90% of patients with SLE report pain in different locations, mainly in the musculoskeletal system.[3–9] and patients with SLE have also been reported to have higher scores regarding pain compared to healthy controls.[10] Pain in SLE is reported to be a serious problem affecting health.[4,11,12]

SLE-related pain has also been reported to be associated with more fatigue,[13] with psychological distress[14] and impaired health-related quality of life (HRQoL),[6,14] as well as a predictor for fatigue.[15]

Correspondence to: Eva Waldheim, Karolinska University Hospital Huddinge, R72, Stockholm, 14186, Sweden
Email: eva.waldheim@karolinska.se
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In addition, Danoff-Burg and Friedberg (2009)[16] assessed the unmet needs of patients with SLE concerning fatigue, pain, depression and anxiety.

In summary, there are previous reports of pain as a common symptom of SLE as well as associations between pain and impaired HRQoL, more fatigue, anxiety and depression. However, considering the varying degree of pain in SLE; the heterogeneous nature of SLE; and the multifactorial nature of HRQoL, fatigue, anxiety and depression, it is of interest to explore whether a higher degree of pain is associated with a greater symptom burden compared to a lower degree of pain. To the best of our knowledge, few studies have focused on the pain-related variations in HRQoL, fatigue, anxiety and depression in patients with SLE. In the current study, we aimed to investigate and compare HRQoL, fatigue, anxiety and depression in patients who reported higher levels of SLE-related pain with patients who reported lower levels of SLE-related pain and with sex- and age-matched controls from the general population. We hoped that a deeper insight into the variations in SLE symptoms with respect to lower and higher levels of pain can be used to guide planning of targeted interventions that can reduce the symptom burden in patients with SLE.

Study participants and methods

This cross-sectional study is a part of the SLE Vascular Impact Cohort (SLEVIC) study,[17] which included 18- to 70-year-old patients with SLE, according to the 1982 revised American College of Rheumatology (ACR) criteria.[18] Of these, 84 patients were recruited for the present study. For the controls, 91 sex- and age-matched subjects from the same greater urban area were recruited as a random general population sample from the Swedish population registry. The Stockholm Regional Ethical Review Board approved this study, and all participants gave written informed consent.

In order to perform comparative statistical analysis we used previously obtained results[19] wherein the patients were dichotomized into two groups according to self-reported SLE-related pain scores on the visual analog scale (VAS). Because of the distribution of self-reported SLE-related pain scores on the VAS (Figure 1(a)), the cut-off value 40 mm was chosen because the values above 40 mm were beyond Q3 (>Q3), and this quartile constituted the group of patients with the most severe pain in this cohort. This cut-off value also coincides with the cut-off value that commonly counts for moderate pain intensity.[20] The use of 40 mm as a cut-off value allowed for two distinctly separate groups that did not overlap (Figure 1(b)). The group of patients who scored SLE-related pain 0–39 mm on the VAS was termed the "low-pain group" and the group with a VAS score of 40–100 mm was termed the "high-pain group." Overall, there were 72 (86%) females and 12 (14%) males. The low-pain group consisted of 54 (84%) females and 10 (16%) males, and the high-pain group of 18 (90%) females and two (10%) males. The control group consisted of 91 participants: 78 (86%) females and 13(14%) males (Table 1).

For consistent comparison regarding pain between patients and controls, measures of "overall pain" were used. Only the dichotomizing of the patients into the low- and high-pain group is based on SLE-related pain.

All study participants, patients and controls, were asked to complete the following questionnaires during the inclusion visit of the SLEVIC study.

The pain VAS

The VAS has long been used to measure self-reported pain.[21–23] The scale range is 0–100 mm, and was connected to the questions "How much pain have you experienced in average the last week?" and for the patients only "How much pain due to SLE have you experienced in average the last week?"

The Medical Outcomes Survey-Short Form 36 (SF-36) standard Swedish version 1.0

The SF-36 is commonly used to measure HRQoL.[24–26] The questionnaire is generic but has previously been validated and used in patients with SLE.[27] The SF-36 measures physical and mental health and consists of questions divided into the following eight dimensions: physical function (PF), role physical (RP), bodily pain (BP), vitality (fatigue) (VT), general health (GH), social function (SF), role emotional (RE) and mental health (MH). The score range is 0–100, and a higher score indicates better health.

The Multidimensional Assessment of Fatigue (MAF)

The MAF is a 16-item instrument used to measure self-reported fatigue over the past week.[28]

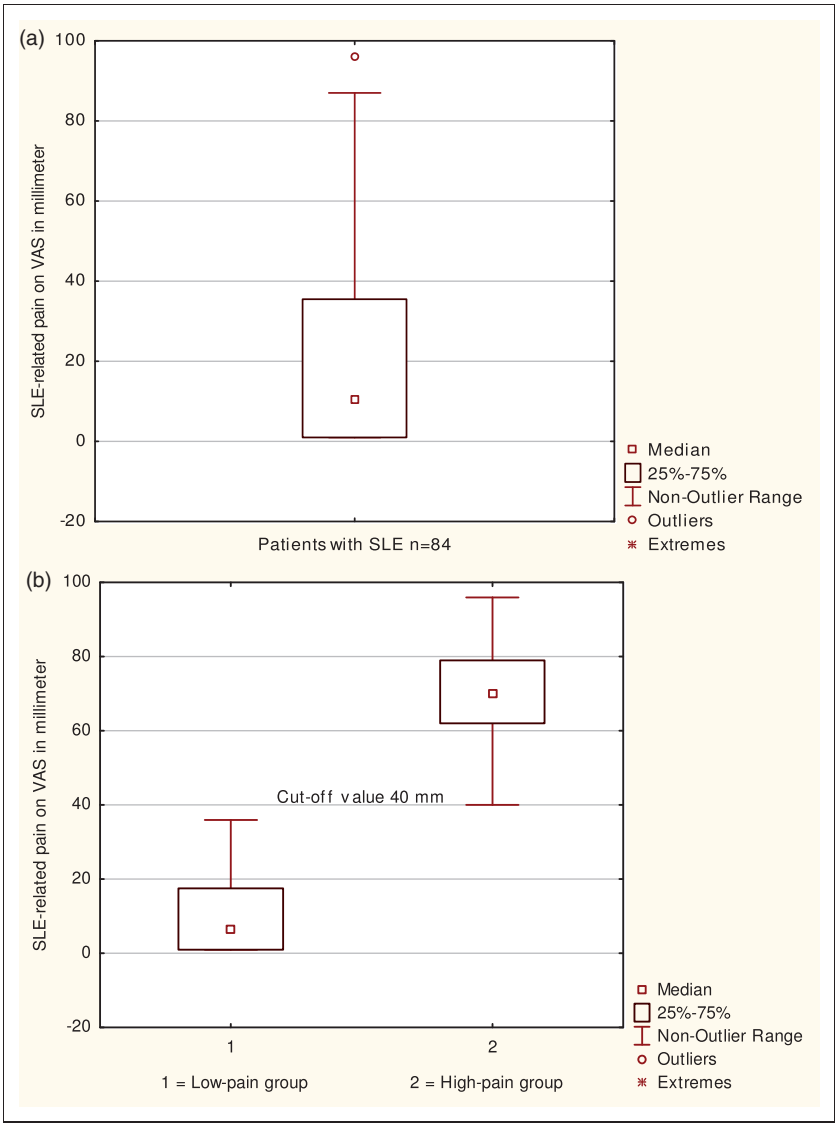

Figure 1 (a). Distribution of self-reported SLE-related pain on VAS in the patient group, $n = 84$. (b). Distribution of self-reported SLE-related pain on VAS in the low-pain group and in the high-pain group.
SLE: systemic lupus erythematosus; VAS: visual analog scale.

Table 1 Characteristics of the study population

	Controls n = *91*	*LPG* n = *64*	*HPG* n = *20*	*Difference LPG and HPG* p *value*
Females *n*/%	78/86%	54/84%	18/90%	0.53
Males *n*/%	13/14%	10/16%	2/10%	NA
Age, years, median, (IQR)	48.1 (34.1–59.7)	45.9 (32.3–56.95)	45.95 (37.05–58)	0.71
BMI, (IQR)	24.8 (21.79–27.39)	24.69 (22.88–27.46)	24.39 (19.54–27.33)	0.78
Current dose of glucocorticoids, mg/day, median, (IQR)	NA	3.44 (0–6.25)	5.63 (0–10)	0.14
Disease duration, years, median, (IQR)	NA	10 (5–17.5)	5.5 (3–9.5)	*0.008*
Disease damage SLICC, median, (IQR)	NA	1 (0–2)	1 (0–3)	0.21
Disease activity SLAM, median, (IQR)	NA	5.5 (4–8)	10.5 (8–14)	*0.001*
Disease activity SLEDAI, median, (IQR)	NA	2 (0–4)	4.5 (2.5–9.5)	*0.01*
ESR, mm, median, (IQR)	7 (5–13)	17 (12–26)	27 (13.5–43)	*0.04*

LPG: low-pain group; HPG: high-pain group; IQR: interquartile range; BMI: body mass index; SLICC: Systemic Lupus International Collaborating Clinics Damage Index; SLAM: Systemic Lupus Activity Measure; SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; ESR: erythrocyte sedimentation rate.

It consists of four dimensions: severity (items 1 and 2), distress (item 3), degree of interference in activities of daily living (items 4–14) and timing (items 15 and 16). In items 1–14, the study participants graded the effect of fatigue from 1 to 10. Items 15 and 16 consist of multiple-choice responses. Items 1–15 are used to calculate the Global Fatigue Index (GFI); its score range is 1–50, where 50 denotes severe fatigue. The reliability and validity of the MAF questionnaire was originally established in patients with rheumatoid arthritis[29] but has also been used in a pilot study in Swedish patients with systemic sclerosis.[30]

The Hospital Anxiety and Depression Scale (HADS)

The HADS is used to assess self-reported symptoms of depression and anxiety.[31,32] It consists of 14 questions divided into the subscales of depression and anxiety: seven pertain to depression and the other seven to anxiety. The points are summarized for each subscale, and can be compared with cut-off values for mild to moderate symptom states and for clinically significant states. The score range is 0–21 for depression as well as anxiety.

A score of eight to 10 denotes a symptom of mild to moderate inconvenience both in the anxiety and depression subscales of HADS in different contexts, and scores above 10 denote a clinically significant state.[33]

All of the questionnaires showed acceptable to excellent internal consistency (Cronbach's alpha 0.79–0.93).

In addition, demographics and the following medical measurements (for the patients with SLE only) were used to characterize the study population.

Disease activity (Systemic Lupus Activity Measure (SLAM), Systemic Lupus Erythematosus Disease Activity Index (SLEDAI), erythrocyte sedimentation rate (ESR)) and disease damage (Systemic Lupus International Collaborating Clinics Damage Index (SLICC))

The SLAM and SLEDAI were used to measure disease activity in different organ systems and the SLICC/ACR to measure disease damage.[34] The SLAM is an objective as well as a subjective measure of 11 organ systems and eight laboratory manifestations that occurred during the last month. The score range is 0–84, where a score $\geq$7 is considered clinically significant.

The SLEDAI includes 24 weighted objective clinical and laboratory variables covering the last 10 days. The score range is 0–105 : 0, no activity; 1–5, mild activity; 6–10, moderate activity; 11–19, high activity; and $\geq$20, very high activity.

The ESR, measured according to Westergren's method,[35] was also used as a measure of disease activity. SLICC capture manifestations persisting continuously over six months after onset of SLE as damage. Score range is 0–47.[34,36]

Statistical analysis

Descriptive statistical analysis was performed using nonparametric methods, and data were presented as medians and interquartile ranges (IQR) due to non-normally distributed and ordinal data. The differences between patient groups and controls were assessed using nonparametric methods, such as the Sign Test and the Mann-Whitney U Test, because of the non-normal distribution of the analyzed variable. The level of significance was set at <0.05. Power analysis was calculated between the entire patient group and the controls, between the low-pain group and the high-pain group, and between the controls and the low- and high-pain groups (Table 2). Power calculation for the nonparametric and parametric tests were performed using the nQuery Advisor 4.0 (Statistical Solutions, USA) software and the STATISTICA 10 (Stat Soft Scandinavia AB, Uppsala, Sweden) software, respectively. Statistical analyses were performed using STATISTICA 10.

Results

As reported previously,[19] the low-pain group and the high-pain group did not differ significantly from one another in proportion of women, age, treatment with glucocorticoids and disease damage. But the two groups differed significantly from each other in disease duration and disease activity measured by the SLAM, SLEDAI and ESR (Table 1), with higher disease activity and shorter disease duration in the high-pain group. However, the SLEDAI and SLAM indicated only mild to moderate disease activity.

Pain

The median for overall pain and for SLE-related pain in the low-pain group was 11 mm (IQR, 2–22 mm) and 6.5 mm (IQR, 1–17.5 mm), respectively. In the high-pain group, the median for overall pain and for SLE-related pain was 72 mm

Table 2 Power calculation

	Patients versus controls		*Low-pain group versus controls*		*High-pain group versus controls*		*Low-pain group versus high-pain group*	
Sample size (*n*)	74	91	56	91	18	91	56	18
Power	0.63	0.72	0.08	0.10	0.99	0.99	0.99	0.99

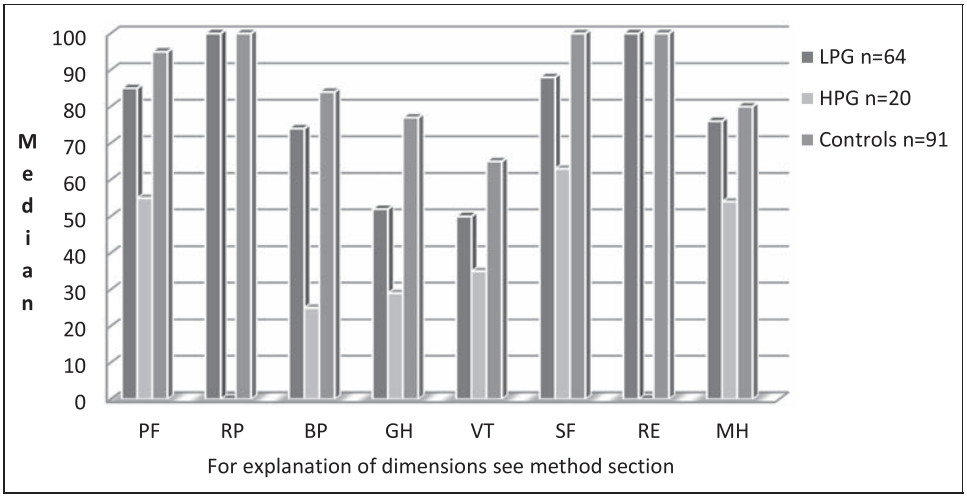

Figure 2 Health-related quality of life (dimensions in SF-36) for the low-pain group (LPG), the high-pain group (HPG) and the controls.
SF-36: Medical Outcomes Survey-Short Form 36 (SF-36) standard Swedish version 1.0; PF: physical function; RP: role physical; BP: bodily pain; VT: vitality (fatigue); GH: general health; SF: social function; RE: role emotional; MH: mental health.

(IQR, 64–80 mm) and 70 mm (IQR, 62–79 mm), respectively.

When comparing overall pain to SLE-related pain, no significant difference was found in the high-pain group ($p = 0.06$) or in the low-pain group ($p = 0.15$). The differences in overall pain as well as in SLE-related pain between the low-pain and high-pain groups were significant ($p < 0.001$).

The median score for overall pain in the control group ($n = 91$) was 5 mm (IQR, 0–36 mm).

No statistical difference was found between overall pain and SLE-related pain in the patient group and as planned (see Study participants and methods section) we used overall pain for appropriate comparisons between the patient group and the control group. No significant difference in overall pain was found between the low-pain group and the control group ($p = 0.65$), but a significant difference did exist between the high-pain group and the control group ($p < 0.001$).

HRQoL

The SF-36 scores of the low- and high-pain group and the control group are presented in Figure 2. The high-pain group was found to have SF-36 scores significantly lower than those of the low-pain group ($p \leq 0.001$–0.007) as well as for the controls ($p \leq 0.001$) for all dimensions (Figure 2). No significant difference was found in the scores for *role physical*, *bodily pain*, *role emotional* and *mental health* between the control group and the low-pain group (Figure 2).

Fatigue

The high-pain group had a significantly higher MAF/GFI (median, 36.5; IQR, 32.5–39.7) than did the low-pain group (median, 23; IQR, 14.6–34.1; $p < 0.001$; Figure 3). The most affected activities of daily life in the high-pain group were *household chores*, *work* and *visit or socialize with friends and family*. The least affected activities were *engage in sexual activity* and *exercise other than walking* (Figure 4). No significant difference was found in *engage in sexual activity, engage in leisure and recreational activities*, *walk* and *exercise, other than walking* between the low-pain group and the high-pain group (Figure 4).

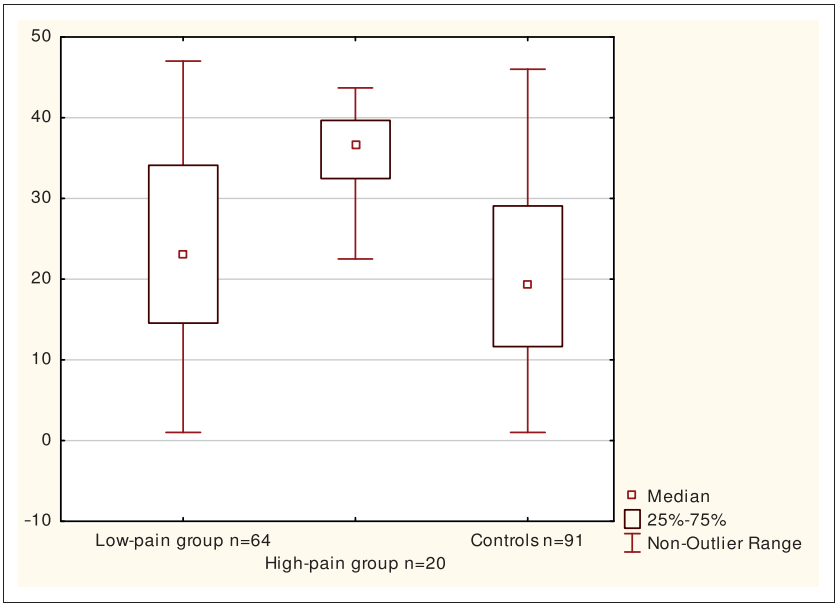

Figure 3 Global Fatigue Index (GFI) in MAF.
MAF: Multidimensional Assessment of Fatigue.

The median MAF/GFI for the control group was 19.4 (IQR, 11.63–29.05). The activities of daily life most affected by fatigue in the control group were *household chores* and *shopping*. The least affected activities were *hygiene*, *dress* and *engage in sexual activity* (Figure 4).

The MAF/GFI score of the low-pain group was higher compared to the control group but the difference was not significant ($p = 0.09$). In addition, no significant differences were found in the activities of daily life between the low-pain group and control group (Figure 4). The differences between the high-pain group and control group were significant for all items in the MAF ($p \leq 0.001$–0.04), except for *engage in sexual activity* and *exercise other than walking* (Figure 4).

In the high-pain group, 50% of the patients had experienced fatigue every day compared with 33% in the low-pain group and 24% in the control group (Table 3). The high-pain group represented the largest population of patients with increased fatigue (Table 3).

Anxiety and depression

The anxiety index of the high-pain group indicated symptoms of mild to moderate inconvenience (median, 9; IQR, 6.5–11.5), but not the depression index (median, 7.5; IQR, 5.5–9). The HADS scores in the low-pain group indicated no symptoms regarding anxiety (median, 4; IQR, 3–8) or depression (median, 3; IQR, 1–5). The high-pain group showed significantly higher values for both depression and anxiety than did the low-pain group ($p < 0.001$, Figure 5).

In the control group, the median values for anxiety and depression index were 4 (IQR, 2–7) and 2 (IQR, 1–4), respectively, indicating the absence of symptoms regarding anxiety or depression (Figure 5).

No significant difference was found between the low-pain group and the control group regarding anxiety ($p = 0.81$) and depression ($p = 0.19$) (Figure 5). The difference between the high-pain group and the control group was significant both for anxiety and depression ($p < 0.001$; Figure 5).

Discussion

By performing subgroup analysis in the present study, we demonstrated that as much as one-fourth of the SLE cohort reported moderate to severe pain and in addition lower scores of HRQoL and greater levels of fatigue, anxiety and depression. These individuals may have different needs compared to the majority of patients in this cohort, who did not report more pain, fatigue, anxiety and depression or worse HRQoL compared to controls from the general population. The intervention approach for these individuals should

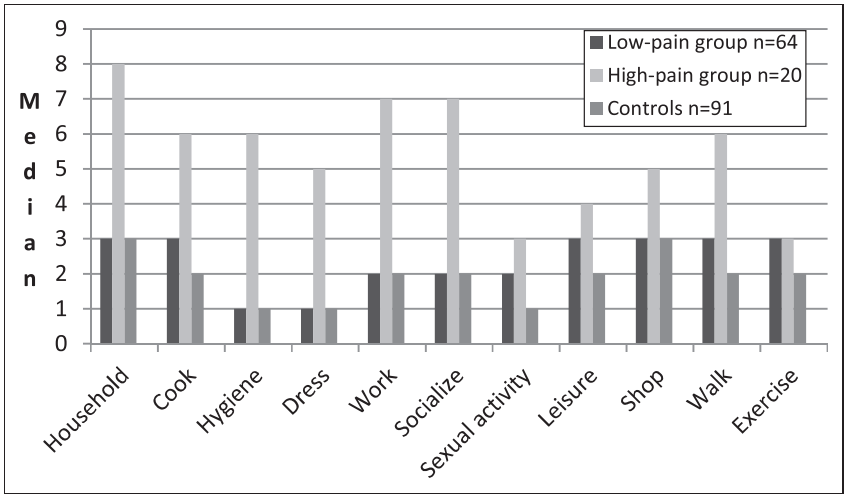

Figure 4 MAF. Interference (scale 1–10) of fatigue in activities of daily living (items 4–14) in the low-pain group, the high-pain group and in controls.
MAF: Multidimensional Assessment of Fatigue.

Table 3 Questions regarding fatigue (MAF)

	Low-pain group n/%	*High-pain group* n/%	*Controls* n/%
Item 15: "Over the past week, how often have you been fatigued?"			
Hardly any days	9/14%	0/0	10/11%
Occasionally, but not most days	11/17%	1/5%	23/25%
Most, but not all days	16/25%	9/45%	24/26%
Every day	21/33%	10/50%	22/24%
Item 16: "To what degree has your fatigue changed during the past week?"			
Decreased	6/9%	0/0%	10/11%
Stayed the same	26/41%	3/15%	35/38%
Fatigue has gone up and down	24/38%	15/75%	33/36%
Increased	1/2%	2/10%	1/1%

MAF: Multidimensional Assessment of Fatigue.

probably be more intense than that of the majority of patients in this cohort. Even from an ethical as well as a health-economic perspective, prioritization of individuals with greater care needs is important. The results of this study indicate that SLE-related pain may be an important marker for more extensive multidimensional nursing interventions.

Several results of this study are broadly consistent with previous studies in terms of higher scores of pain,[10] impaired HRQoL,[17,18,19,20,21,22] more fatigue,[10,13] anxiety and depression[10,14] in patients with SLE compared to controls. However, this study provides deeper insights into the symptoms associated with pain as the patient group is divided into the low- and high-pain groups. To the best of our knowledge, no other study has investigated HRQoL, fatigue, anxiety and depression from this perspective, except for Burgos et al. (2009).[13] They used the median of pain scores on the VAS as a reference point and showed that patients with higher levels of pain also had worse values of fatigue; this result is also in line with the results of this present study. However, this study provides a more detailed understanding by studying patients with the highest level of pain (>Q3) and by not using the median as a reference point. None of the patients in the high-pain group had a known diagnosis of fibromyalgia. This does not preclude the presence of fibromyalgia because the patients in this study were not investigated regarding fibromyalgia. Staud (2006)[37] showed in a review that up to 47% of patients with SLE are affected with concomitant fibromyalgia. These patients were also highly

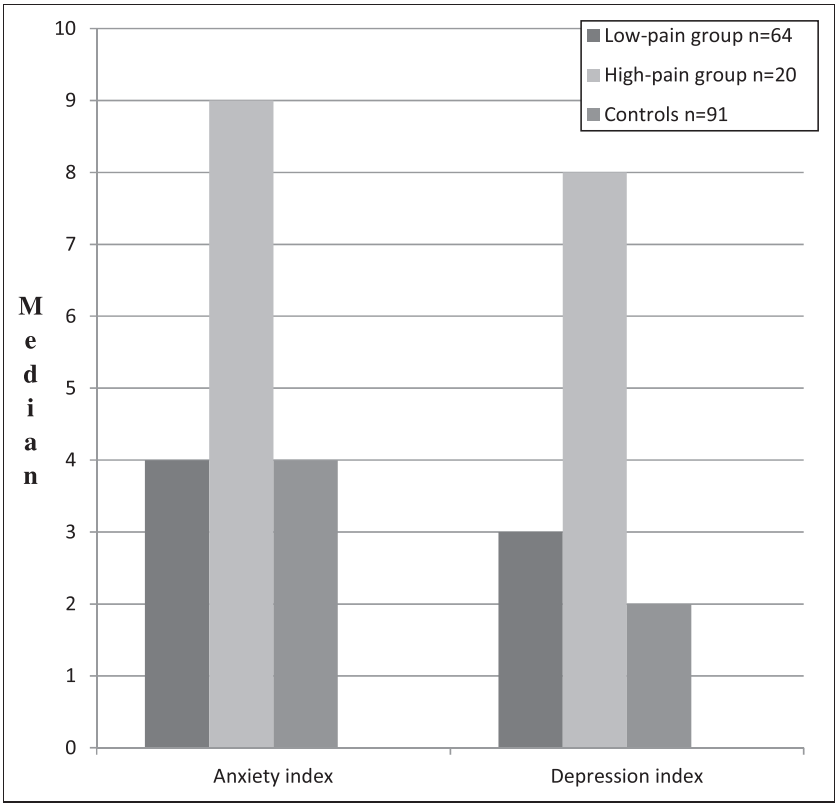

Figure 5 Anxiety and depression (HADS) in the low-pain group, the high-pain group and in controls. HADS: Hospital Anxiety and Depression Scale.

symptomatic with severe fatigue, depressed mood and impaired HRQoL besides widespread pain and joint pain. Staud (2006)[37] also suggests common central pain mechanisms in SLE and fibromyalgia. Fatigue is commonly present in SLE and fibromyalgia[38] and the higher levels of fatigue in the high-pain group may reinforce the suspicion of concomitant fibromyalgia in this group.

The cut-off value on the VAS for SLE-related pain (40 mm) used in this study was based on discussions and the distribution of VAS scores reported by the patients in the study. The VAS scores reported by patients in the high-pain group also constituted values beyond Q3 (>Q3). Although few previous studies have validated a cut-off value on the VAS for patients with nonmalignant long-standing pain, the score of 40 mm used to divide our study population appeared to have been useful in detecting differences between the two patient groups. The aim for separating disease-related pain from other types of pain was the focus of SLE and an effort to avoid influence of other painful conditions that may affect all humans. It is probably a challenge for the patients with SLE to separate disease-related pain from other types of pain as has been performed in this study. But the questions connected to the VAS are intended to display the experience of the patients and do not claim the absolute truth.

The high-pain group had significant higher disease activity as measured by the SLAM and SLEDAI, but despite that, the disease activity in the high-pain group indicated only mild (SLEDAI) to moderate (SLAM) disease activity. This indicated that disease activity may have some significance regarding pain in SLE but pain in SLE may also be present in the case of low disease activity. Therefore, these results suggest that disease activity measured not only by the SLAM and SLEDAI, but rather pain, can be regarded as a marker for greater symptom burden. Morand et al. (1994)[39] also concluded that the presence of fibromyalgia in SLE interferes with rating of disease activity measured by the SLAM.

Only scores of the high-pain group indicated symptoms of mild to moderate inconvenience for anxiety, which could be interpreted as overall good mental health in this SLE cohort. However, the higher score of anxiety in the high-pain group leads to the question of what patients in this

group concerns. Phillips et al. (2009)[40] showed that patients having little understanding of lupus exhibited higher levels of depression. Maybe poor understanding of SLE also might cause anxiety. Support and patient education about SLE and how to manage SLE-related symptoms within nurse-led clinics may alleviate anxiety and depression.[41,42] In our study, the patient group and the control group were recruited from the same geographic area, and no significant differences were found in the characteristics of the groups, except for the ESRs. Therefore, we believe that the comparisons between the patients and controls in our study were appropriate. Since SLE is much more common among woman, comparison between sexes was considered inappropriate. One limitation of this study is its cross-sectional design, which does not allow for following up the progress of the examined variables during the course of the disease. Despite the small sample size, several significant findings indicate pain in SLE to be an important topic for further investigation, and our study provides a good foundation for future studies.

This current study does not answer questions about causality, but highlights the symptom burden in patients with high levels of pain as well as the need for health care providers to meet the requirements of patients with greater symptom burden. Therefore, further studies designed to determine causality and to identify patients' needs are recommended for appropriate targeted interventions in rheumatology care. Nurse-led clinics,[40,41] which impart support and education, individually or in a group, may be appropriate for the patients to obtain knowledge about SLE, its treatment and its medicines. Systematic monitoring of pain treatment seems essential.

Conclusions

Patients with SLE are a heterogeneous group regarding pain. Most patients in this SLE cohort did not seem to be burdened with more pain nor did they display lower levels of HRQoL or greater fatigue, anxiety and depression compared to the general population. However, as much as one-fourth of the patients in this SLE cohort reported moderate to severe disease-related pain and were also burdened with lower levels of HRQoL, and higher degree of fatigue, anxiety, and depression. Disease-related pain may therefore serve as a marker for greater symptom burden, independent of disease activity, and identifying patients with higher degrees of pain appears important for extended pain management.

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Conflict of interest

The authors have no conflicts of interest to declare.

References

1 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 (Baltimore)* 2003; 82: 299–308.
2 Rahman A, Isenberg D. Systemic lupus erythematosus. *N Engl J Med* 2008; 358: 929–939.
3 Askanase A, Shum K, Mitnick H. Systemic lupus erythematosus: An overview. *Soc Work Health Care* 2012; 51: 576–586.
4 Greco C, Rudy T, Manzi S. Adaption to chronic pain in systemic lupus erythematosus: Applicability of the multidimensional pain inventory. *Pain Med* 2003; 4: 39–50.
5 Lessa B, Santana A, Lima I, *et al*. Prevalence and classification of headache in patients with systemic lupus erythematosus. *Clin Rheumatol* 2006; 25: 850–853.
6 McElhone K, Abbott J, Shelmerdine J, *et al*. Development and validation of a disease-specific health-related quality of life measure: The LupusQoL, for adults with systemic lupus erythematosus. *Arthritis Care Res* 2007; 57: 972–979.
7 Ozbek S, Sert M, Paydas S, Soy M. Delay in diagnosis of SLE: The importance of arthritis/arthralgia as the initial symptom. *Acta Med Okayama* 2003; 57: 1–4.
8 Pettersson S, Lövgren M, Eriksson LE, *et al*. An exploration of patient-reported symptoms in systemic lupus erythematosus and the relationship to health-related quality of life. *Scand J Rheumatol* 2012; 41: 383–390.
9 Weder-Cisneros ND, Téllez-Zenteno JF, Cardiel MH, *et al*. Prevalence and factors associated with headache in patients with systemic lupus erythematosus. *Cephalalgia* 2004; 24: 1031–1044.

10 Kozora E, Ellison MC, West S. Depression and pain in systemic lupus erythematosus (SLE): Relationship to the American College of Rheumatology SLE neuropsychological battery. *Arthritis Care Res* 2006; 55: 628–635.
11 Robinson Jr D, Aguilar D, Schoenwetter M, *et al*. Impact of systemic lupus erythematosus on health, family and work: The patient perspective. *Arthritis Care Res* 2010; 62: 266–273.
12 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.
13 Burgos PI, Alarcón GS, McGwin Jr G, Crews KQ, Reveille JD, Vilá LM. Disease activity and damage are not associated with increased levels of fatigue in systemic lupus erythematosus patients from a multiethnic cohort: LXVII. *Arthritis Care Res* 2009; 61: 1179–1186.
14 Doria A, Rinaldi S, Ermani M, *et al*. Health-related quality of life in Italian patients with systemic lupus erythematosus: II. Role of clinical, immunological and psychological determinants. *Rheumatology (Oxford)* 2004; 43: 1580–1586.
15 Jump RL, Robinson ME, Armstrong AE, Barnes EV, Kilbourn KM, Richards HB. Fatigue in systemic lupus erythematosus: Contributions of disease activity, pain, depression and perceived social support. *J Rheumatol* 2005; 32: 1699–1705.
16 Danoff-Burg S, Friedberg F. Unmet needs of patients with systemic lupus erythematosus. *Behav Med* 2009; 35: 5–13.
17 Anania C, Gustavsson T, Hua X, *et al*. Increased prevalence of vulnerable atherosclerotic plaques and low levels of natural IgM antibodies against phosphorylcholine in patients with systemic lupus erythematosus. *Arthritis Res Ther* 2010; 12: R214.
18 Tan EM, Cohen AS, Fries JF, *et al*. The 1982 revised criteria for the classification of systemic lupus erythematosus. *Arthritis Rheum* 1982; 25: 1271–1277.
19 Waldheim E, Elkan AC, Bergman S, *et al*. Extent and characteristics of self-reported pain in patients with systemic lupus erythematosus. *Lupus* 2013; 22: 136–143.
20 Breivik H, Borchgrevink PC, Allen SM, *et al*. Assessment of pain. *Br J Anaesth* 2008; 101: 17–24.
21 Price D, McGrath P, Rafii A, Buckingham B. The validation of visual analogue scales as ratio scale measures for chronic and experimental pain. *Pain* 1983; 17: 45–56.
22 Price D, Bush F, Long S, Harkins SW. A comparison of pain measurement characteristics of mechanical visual analogue and simple numerical rating scale. *Pain* 1994; 56: 217–226.
23 Clark P, Lavielle P, Martínez H. Learning from pain scales: Patient perspective. *J Rheumatol* 2003; 30: 1584–1588.
24 Sullivan M, Karlsson J, Ware Jr JE. The Swedish SF-36 Health Survey-1. Evaluation of data quality, scaling assumptions, reliability and construct validity across general populations in Sweden. *Soc Sci Med* 1995; 41: 1349–1358.
25 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: 1608–1614.
26 Sullivan M, Karlsson J. The Swedish SF-36 Health Survey III. Evaluation of criterion-based validity: Results from normative population. *J Clin Epidemiol* 1998; 51: 1105–1113.
27 Thumboo J, Strand V. Health-related quality of life in patients with systemic lupus erythematosus: An update. *Ann Acad Med Singapore* 2007; 40: 67–73.
28 Belza BL. Comparison of self-reported fatigue in rheumatoid arthritis. *J Rheumatol* 1995; 22: 639–643.
29 Belza LB, Henke CJ, Yelin EH, Epstein WV, Gilliss CL. Correlates of fatigue in older adults with rheumatoid arthritis. *Nurs Res* 1993; 42: 93–99.
30 Sandqvist G, Archenholtz B, Scheja A, Hesselstrand R. The Swedish version of the Multidimensional Assessment of Fatigue (MAF) in systemic sclerosis: Reproducibility and correlations to other fatigue instruments. *Scand J Rheumatol* 2011; 40: 493–494.
31 Lisspers J, Nygren A, Söderman E. Hospital anxiety and depression scale (HAD): Some psychometric data for a Swedish sample. *Acta Psychiatr Scand* 1997; 96: 281–286.
32 Zigmond AS, Snaith RP. The hospital anxiety and depression scale. *Acta Psychiatr Scand* 1983; 67: 361–370.
33 Bjelland I, Dahl AA, Haug TT, Neckelmann D. The validity of the Hospital Anxiety and Depression Scale. An updated literature review. *J Psychosom Res* 2002; 52: 69–77.
34 Griffiths B, Mosca M, Gordon C. Assessment of patients with systemic lupus erythematosus and the use of lupus activity indices (review). *Best Pract Res Cl Rh* 2005; 19: 685–708.
35 Bridgen M. Clinical utility of the erythrocyte sedimentation rate. *Am Fam Physician* 1999; 60: 1443–1450.
36 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: 363–369.
37 Staud R. Are patients with systemic lupus erythematosus at increased risk for fibromyalgia? *Curr Rheumatol Rep* 2006; 8: 430–435.
38 Staud R. Peripheral and central mechanisms of fatigue in inflammatory and noninflammatory rheumatic disease. *Curr Rheumatol Rep* 2012; 14: 539–548.
39 Morand E, Miller M, Littlejohn G. Fibromyalgia syndrome and disease activity in systemic lupus erythematosus. *Lupus* 1994; 3: 187–191.
40 Phillip EJ, Lindner H, Lederman L. Relationship with illness perceptions with depression among individuals diagnosed with lupus. *Depress Anxiety* 2009; 26: 575–582.
41 Bala SV, Samuelsson K, Hagell P, Svensson B, Fridlund B, Hesselgard K. The experience of care at nurse-led rheumatology clinics. *Musculoskeletal Care* 2012; 10: 202–211.
42 Ryan S, Hassell AB, Lewis M, Farrell A. Impact of a rheumatology expert nurse on the wellbeing of patients attending a drug monitoring clinic. *J Adv Nurs* 2006; 53: 277–286.