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Prediction of depression in systemic lupus erythematosus patients using SF-36 Mental Health scores

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Abstract

Objective. As depression is common in systemic lupus erythematosus (SLE) patients, we investigated whether and how the Medical Outcome Survey Short Form 36 (SF-36) scores, routinely used in the assessment of SLE patients, would indicate the absence or presence of depression.

Methods. The Depression subscale of the Hospital Anxiety and Depression Scale (HADS-D) and the SF-36 were applied in a cross-sectional cohort of 60 SLE patients [mean age 45 (S.D. 15) yr, disease duration 11 (9) yr, 90% female, 100% Caucasians]. The SF-36 domain score with the closest association with HADS-D was used for further analysis. On the basis of HADS-D scores, the patients were split into two groups: one without depression (score < 8) and the other with possible depression (score $\geqslant 8$).

Results. The SF-36 Mental Health score was most closely correlated to the depression score ($\rho = -0.69$, $P < 0.0005$). The calculated Mental Health score cut-off value which significantly differentiated possibly depressed from non-depressed SLE patients was 61. Its sensitivity for the detection of possible depression was 89%, its specificity 77% and its negative predictive value 97%.

Conclusions. The present study contributes to knowledge of means of excluding depression and the prevention of underdiagnosis and undertreatment of depression in SLE patients.

KEY WORDS: SLE, SF-36, HADS, Depression.

Systemic lupus erythematosus (SLE) is an autoimmune rheumatic disease characterized by periods of active disease and remission and has a heterogeneous clinical pattern, as organ/system involvement varies widely in extent and severity. In extreme cases, episodes of active disease can be lethal but are usually controlled by appropriate therapy. A significant number of patients with SLE suffer from depression. Factors leading to depression in SLE include direct brain damage, constitutional symptoms, patients' responses to the burden of disease, and the social consequences of the disease. Most episodes of depression in SLE patients appear to be caused by non-organic factors [1].

There is broad agreement about the assessment of SLE patients. Optimally, this should encompass a disease activity measure [2] and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index [3–6]. Assessment is not considered to be complete without information about the patient's view of her/his health status as assessed, for example, by the Medical Outcomes Survey Short Form 36 (SF-36) [7, 8].

However, despite the prevalence of depression in SLE [9], no formal assessment of depression is performed routinely in SLE patients. Depression is commonly underdiagnosed in other physical illnesses [10], and it is therefore likely that this also applies in SLE.

Given that the SF-36 is used in the routine assessment of people with SLE, the overall aim of the present study was to determine whether the SF-36 could be helpful in screening for depression. In a previous study, the Mental Health domain of the SF-36 correlated significantly with depression scores derived from the Centre for Epidemiological Studies Depression Scale (CES-D) [11].

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However, in common with many other depression scales, the CES-D has not been validated for use in people with physical symptoms. The somatic items included in it might be scored positively by people with SLE regardless of the presence of depression, thus potentially overestimating the prevalence of depression [12]. By contrast, the Hospital Anxiety and Depression Scale (HADS) was developed and validated specifically for use in the physically ill and does not rely on somatic symptoms of depression [13]. The specific aims of this study were therefore to confirm that, of the domains of the SF-36, the Mental Health subscale would correlate most strongly with the depression subscale of the HADS (HADS-D) and to determine the extent to which the SF-36 Mental Health subscale could match the HADS-D as a screening instrument for depression in people with SLE.

Patients and methods

Patient sample

A convenience sample of German-speaking Swiss SLE patients was recruited via local rheumatologists, nephrologists, dermatologists and general practitioners. In addition, a letter was sent to each member of the regional SLE patients' organization asking him or her to participate in the study. To be eligible, patients had to fulfil the American Rheumatism Association (ARA) classification criteria [14]. The duration of the disease was measured from the time when the patient first met the fourth ARA criterion.

Measures

SLICC/ACR Damage Index. Damage, i.e. irreversible impairment since the onset of SLE, is usually defined as a clinical feature that has to be present continuously for at least 6 months in order to score [3–6]. Briefly, damage is defined for 11 organ systems (ocular, neuropsychiatric, renal, pulmonary, cardiovascular, peripheral vascular, gastrointestinal, musculoskeletal, skin, gonadal and endocrine) and the occurrence of malignancy. Theoretically, damage can either be stable or increase over time, to a maximum of 47 points.

British Isles Lupus Assessment Group Disease Activity Index. The British Isles Lupus Assessment Group Disease Activity Index (BILAG) measures SLE-related disease activity in eight organ-based components (general, mucocutaneous, neurological, musculoskeletal, cardiovascular/respiratory, vasculitis, renal and haematological) [2, 15, 16] and is based upon the principle of the physician's intention to treat. To obtain a global score, BILAG component scores can be assigned numerical values: A = 9 (most active disease), B = 3 (intermediate activity), C = 1 (mild and stable disease activity), D = 0 (inactive disease) and E = 0 (no activity ever), resulting in a potential global score ranging from 0 to 72. This numerical score has been shown to be valid [16] by its significant associations with the patient's and doctor's global assessments and with six of seven domains of SF-20+ (Medical Outcomes Survey Short Form 20 with an additional question about fatigue).

SF-36. The SF-36 is the most widely used generic instrument to assess health-related quality of life [7]. It consists of eight domains (Physical Function, Role Function Physical, Role Function Emotional, Social Function, Mental Health, General Health, Vitality, and Pain). The domain scores are rated so that higher values indicate better health (range 0–100). SF-36 has been shown to be valid in SLE patients [8] as it strongly discriminates SLE patients from controls and is significantly associated with disease activity. The validity of the German version of SF-36 has been demonstrated for patients with rheumatic diseases [17].

HADS. This is a 14-item, self-administered rating scale designed to measure anxiety and depression in physically ill individuals [13]. In the present study, only the seven-item Depression subscale (HADS-D) was used. The maximum score is 21. Scores of $\geqslant 8$ represent possible depression [13]. The German version of HADS has been validated in 6200 patients and control persons and found to be equivalent to the English original [13, 18].

Statistical analyses

The associations between disease measures were investigated using Spearman's rank correlation. Because of multiple comparisons [12; Table 1] Bonferroni's correction was performed. Thus, only differences with $P < 0.004$ (0.05/12) were considered statistically significant. The domain of SF-36 with the closest correlation to HADS-D (which was found to be the SF-36 Mental Health score) was used for further analysis. To compare the SF-36 Mental Health scores between the depressed (HADS-D score $\geqslant 8$) and non-depressed SLE patients, Student's two-tailed *t*-test was used. To calculate the threshold value for the Mental Health score to distinguish depressed from non-depressed patients, the procedure described by Jacobson *et al.* [19] was applied: cut-off (SF-36 Mental Health score) = (S.D. in depressed subjects × mean in non-depressed subjects) ± (S.D. in non-depressed subjects × mean in depressed subjects)/(S.D. in depressed subjects + S.D. in non-depressed subjects).

Results

Of the 78 people who applied to participate in the study, 18 did not fulfil the ARA criteria for SLE. All the remaining 60 SLE patients were Caucasians and 90% of them were female. All patients were positive for antinuclear antibodies and 85% were positive for antibodies against double-stranded DNA (as measured by immunofluorescence or enzyme immunosorbent assay). Table 1 shows the characteristics of the SLE patients.

Table 2 shows the correlations between the domains of SF-36 and the HADS-D. Because three patients had

TABLE 1. Characteristics of the SLE patients ($n=60$)

Variable	Mean	Standard deviation and/or range
Age (yr)	44.5	15.4
Disease duration (yr)	11.4	9, 1–37
HADS-D score	3.0	3.5
SF-36 General Health	49.7	19.7
SF-36 Physical Function	64.6	24.5
SF-36 Role Function Physical	49.6	24.8
SF-36 Pain	54.9	28.7
SF-36 Vitality	47.9	20.7
SF-36 Social Function	65.1	22.6
SF-36 Role Function Emotional	74.7	19.2
SF-36 Mental Health	69.4	19.1
BILAG total score	4.8	1–11
SLICC/ACR damage index total score	0.8	0–5

Higher scores mean worse health except for SF-36.

TABLE 2. Spearman's rank correlation coefficients between HADS-D and SF-36 scores (P value)

Score	HADS-D
SF-36 General Health	−0.48 (<0.0005)
SF-36 Physical Function	−0.51 (<0.0005)
SF-36 Role Function Physical	−0.66 (<0.0005)
SF-36 Pain	−0.51 (<0.0005)
SF-36 Vitality	−0.65 (<0.0005)
SF-36 Social Function	−0.59 (<0.0005)
SF-36 Role Function Emotional	−0.47 (<0.0005)
SF-36 Mental Health	−0.69 (<0.0005)

not completed the SF-36 or HADS-D questionnaires fully, only 57 patients were available for the analyses. As hypothesized, the HADS-D score correlated most closely with the SF-36 Mental Health domain score. Although some other SF-36 domain scores or the mental component scale (Spearman's $\rho = -0.57$) were nearly as closely correlated to HADS-D, further analysis was based solely upon the SF-36 Mental Health domain score. Nine patients (16%) scored as depressed on the HADS-D. The mean SF-36 Mental Health score in these nine depressed SLE patients was 46.2 (S.D. 15.5) compared with 74.6 (15.5) in the 48 non-depressed patients ($P < 0.0005$). The calculated Mental Health score cut-off value which significantly differentiated depressed from non-depressed SLE patients was 61. Nineteen patients (33% of the sample) had SF-36 Mental Health scores below 61. With this cut-off, the sensitivity of the Mental Health score in detecting possible depression was 89% (8/9), its specificity 77% (37/48), its positive predictive value 42% (8/19) and its negative predictive value 97% (1/38).

No significant bivariate correlations were found between HADS-D or SF-36 Mental Health scores and age, disease duration, total BILAG or SLICC/ACR damage scores. The correlations with neurological disease activity or neuropsychiatric damage, although stronger than those with the total BILAG or damage scores, were still weak (Spearman's ρ between 0.24 and −0.14) and not significant ($P > 0.07$).

Discussion

We found a prevalence of 16% (9/57) for depression in our SLE sample, which is in good agreement with the literature [20]. As expected [11], the Mental Health score was the domain of SF-36 most closely related to the Depression scores. The calculated Mental Health score cut-off value optimally distinguishing depressed from non-depressed SLE patients was 61. The high negative predictive value of this cut-off score (97%), together with its high sensitivity (89%), indicates that where people with SLE score above 61 on the SF-36 Mental Health subscale, depression would be extremely unusual. In general, a negative result from a highly sensitive test usually rules out this diagnosis (i.e. depression).

Among the 19 patients who had SF-36 Mental Health scores of $\leqslant 61$, 42% were possibly depressed. While this represents a substantial rate of false-positives, using the SF-36 Mental Health score to screen for depression in this way raises the odds of a patient having depression from approximately 1 : 5 (in the overall sample) to nearly 1 : 1. This subgroup warrants further assessment for depression and possibly even specialist psychiatric assessment. Focusing further attention on this subgroup requires less time and fewer resources than assessing the entire sample more thoroughly for depression. The lack of correlation between depression scores and total or neurological/neuropsychiatric disease activity/damage scores suggests that depression in our patients is more likely to be due to non-organic causes than to the disease process of SLE itself, as others have found [20]. Depending on the cause of the depression, the appropriate treatment may be started. This may be a treatment targeted to the disease process of SLE itself or a broad spectrum of therapeutic possibilities, including psychotherapy and antidepressants, as recently outlined in a comprehensive editorial [21].

Although the present sample was a convenience one, it was comparable in all disease and health status measures to other samples known to be representative of out-patients with SLE. For instance, the mean total damage score of the present study (0.8) was only slightly lower than that of the Bloomsbury (1.2) or Montreal cohorts (1.3) with a similar mean disease duration (10 and 15 yr) [22, 23]. Our study population also compared well with the Bloomsbury SLE patient cohort [16] with respect to the measured disease activity (total BILAG index 4.8 and 5.2 respectively). Finally, the SF-36 scores of our cohort were very close to those of other studies [8, 23]. Thus, it is likely that our results will apply generally to out-patients with SLE. Nevertheless, before our results can be considered definitive, the study must be replicated in an independent sample. It would be helpful to conduct the same study using larger samples, with a wider range of sociodemographic and clinical variables, e.g. with higher disease activity, more damage, different

ethnic backgrounds, etc. Further studies could also focus on the risk factors for depression in SLE patients which were not the subject of the present study.

Depression in SLE may remain undiagnosed for a variety of reasons, not least the fact that it can present with symptoms found in SLE itself, such as lethargy and increased pain. Given that the SF-36 is used routinely in assessing patients with SLE, the results of our study suggest that data gathered in routine practice could contribute significantly to improving the detection of depression in people with SLE. This is very worthwhile because accurate diagnosis is a prerequisite for effective treatment, and this in turn is likely to improve patients' quality of life substantially.

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