The Relationship Between Neuropsychiatric, Clinical, and Laboratory Variables and Quality of Life of Chinese Patients with Systemic Lupus Erythematosus

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ABSTRACT. ***Objective.*** To investigate the role of neuropsychiatric (NP), clinical, and laboratory variables in influencing the health related quality of life (HRQOL) of Chinese patients with systemic lupus erythematosus (SLE).

Methods. The Medical Outcomes Study Short Form-36 was applied in a cohort of 291 patients with SLE. At the time of HRQOL testing all patients underwent a clinical and laboratory evaluation together with measures of disease activity and damage. Patients also submitted to a battery of NP tests.

Results. Using multivariate analysis, NP involvement-ever was associated with impairment of the general health subscale. Cerebrovascular disease and mononeuropathy were associated with impairment of the physical function subscale, while the latter was also associated with impairment of the role-emotional subscale. Cognitive impairment was associated with impairment of the mental health subscale. The Hospital Anxiety and Depression (HAD) depression score was associated with impairment of all the 8 subscales, physical, and mental summary scores. The HAD anxiety score was associated with impairment of predominantly mental function. Active arthritis, lower education level, and serum albumin levels were associated with impairment of predominantly physical function. Advancing age and damage were associated with impairment of both physical and mental function. Low hemoglobin level and female sex were associated with impairment of predominantly mental function.

Conclusion. NP involvement and low-grade inflammation as reflected by low serum albumin and hemoglobin concentrations were associated with impaired HRQOL in patients with SLE, independent of other sociodemographic and clinical variables. (First Release May 1 2008; J Rheumatol 2008;35:1038–45)

Key Indexing Terms:
SYSTEMIC LUPUS ERYTHEMATOSUS
NEUROPSYCHIATRIC
CHINESE
HEALTH RELATED QUALITY OF LIFE

Systemic lupus erythematosus (SLE) is a chronic multisystem disease that primarily affects young women. Longterm survival of Chinese patients with SLE is comparable to that reported for Caucasian patients[1]. With improvement in survival in SLE, attention has focused on the reductions in health related quality of life (HRQOL) in these patients. The majority of studies assessing important domains of HRQOL in SLE have been performed in Western sociocultural contexts[2]. Studies pertaining to quality of life in Chinese patients with SLE have been limited[3,4].

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It is well known that HRQOL is significantly influenced by SLE[5]. The reason for this is uncertain. Studies have identified older age[6-10], shorter disease duration[9], joint pain/arthritis[6,11], endstage renal failure[12], socioeconomic status[7,8], psychosocial factors[3,7-9,11,13], fatigue[9,14], pain[9], fibromyalgia[10,15], and knowledge of lupus[1] as factors associated with impaired HRQOL in patients with SLE. Devins and Edworthy found that educational attainment emerged as an independent mediator for the race-related difference in the HRQOL in 3 ethnic groups (Whites, Blacks, Asians), but the numbers of Asians were small[2]. The association between disease activity or damage and HRQOL in SLE patients remains controversial[3-16].

Relatively little is known regarding whether neuropsychiatric (NP) disease in lupus was associated with a significant reduction in quality of life[17]. Neurocognitive dysfunction has been shown to be associated with impaired physical functioning, independent of other risk factors[16]. However, the instrument used for diagnosing the condition was not specified[16]. Anxiety and depression[13,15] consistently have

been shown to be associated with impaired HRQOL. Thumboo, *et al* studied HRQOL in 3 groups of patients comprising predominately Chinese (85%)[18]. However, no validated instrument for anxiety and depression was used in that study.

The aim of our study was to ascertain the possible influence of NP manifestations on HRQOL in Chinese patients with SLE using validated instruments. Moreover, we wished to evaluate the effect of laboratory markers of disease activity and clinical variables on HRQOL in SLE.

MATERIALS AND METHODS

Two hundred ninety-one consecutive patients were recruited from the Rheumatology Clinic of the Prince of Wales Hospital, Hong Kong. All patients fulfilled the 1997 American College of Rheumatology (ACR) revised criteria for the classification of SLE[19]. The Ethics Committee of the Chinese University of Hong Kong approved this study, and all patients provided written informed consent.

SLE activity and complications. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)[20] and the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index (SDI)[21] were used to indicate disease activity and damage, respectively. The occurrence of NP disease was determined using the ACR nomenclature and standard definitions for NP-SLE[22]. Evaluations of current levels of anxiety, depression, and cognitive dysfunction are listed below. Laboratory studies included complete blood counts, renal and liver function tests, C3, C4, and anti-ds-DNA (ELISA, Diastat; Axis-Shield Diagnostics, Dundee, UK). The current steroid dosage was obtained by chart review. Concomitant use of hydroxychloroquine and immunosuppressants was noted.

Evaluation of anxiety, depression, cognitive dysfunction. Research assistants administered the following questionnaires and tests: the Hospital Anxiety and Depression Scale (HAD)[23], Chinese Mini-Mental State Examination (MMSE) score[24], and the Chinese version of the Mattis Dementia Rating Scale – Initiation/Perseveration (CDRS-IP) subscale[25].

The HAD[23] was used to assess anxiety and depressive symptoms; it is a validated and reliable psychological measure widely used in medically ill populations, particularly in hospital settings. This 14-item self-report questionnaire has two 7-item subscales for anxiety (HAD-A) and depression (HAD-D). Scores range from 0 to 21 for each subscale, and a score $\geq$ 8 on either subscale is conventionally used to define anxiety and depression. At this cutoff, the HAD has shown high sensitivity (80%) and specificity (90%)[26] in depressed Chinese patients.

The Hong Kong Chinese version of the MMSE is a validated, brief, general cognitive test that examines orientation, memory, attention, language, and construction skills, and it has been validated. Out of the maximum score of 30, the optimal cutoff points for dementia vary from 18 in illiterate subjects to 22 for those with more than 2 years of schooling[24]. The MMSE was administered to identify overt intellectual impairment.

Alhough the MMSE was shown to be useful in screening for cognitive impairment in Chinese individuals, its brevity limits the ability to provide detailed assessment of different cognitive abilities. The MMSE is known to have substantial false-negative rates in previous studies on NPSLE, does not cover all domains of cognitive functioning, fails to detect early or milder forms of cognitive impairment, is relatively insensitive to detect changes over time, and is influenced by the subject's sociodemographic features[27]. In addition, it is biased toward detection of memory and language disturbance and is insensitive to executive cognitive dysfunction[28]. Executive cognitive dysfunction is one of the commonly reported areas of impairment in SLE[29]. Therefore, the CDRS-IP subscale (CDRS), a validated executive measure[30], was incorporated along with the MMSE to provide a more comprehensive coverage of cognitive functions. This subscale included tests of verbal fluency and cognitive and motor programming. The highest score of the CDRS-IP subscale is 37. A cutoff score of 26 has a sensitivity of 85% and specificity of 94% to discriminate Chinese patients with Alzheimer's disease and healthy individuals[25].

Quality of life assessment. HRQOL was assessed using the SF-36 questionnaire. The SF-36 is a generic instrument with scores that are based on responses to individual questions, which are summarized into 8 scales, each of which measures a health concept[31]. These 8 scales, weighted according to normative data, are scored from 0 to 100, higher scores reflecting better HRQOL[31]. The SF-36 has been validated for use in Chinese[32], and it can be completed within 10 minutes by most people. The originators of the SF-36 have developed algorithms to calculate 2 psychometrically based summary measures: the physical component summary (PCS) score and the mental component summary (MCS) score[33]. The PCS and MCS provide greater precision, reduce the number of statistical comparisons needed, and eliminate the floor and ceiling effects noted in several of the subscales[34]. Normative values of the SF-36 survey of the Chinese adult population in Hong Kong have been published[35,36], including age- and sex-specific values for the 8 SF-36 subscales[35].

Explanatory variables. The explanatory variables considered for association with impaired HRQOL were social and demographic characteristics including age, sex, and education level. SLE related variables included age at diagnosis of SLE, disease duration, and the presence of ACR criteria ever. In addition, we investigated whether there had been any NP manifestations ever; NP events attributed to SLE alone, recent NP events (within 5 years from the interview), current level of psychological distress (anxiety and depression); and whether the presence of cognitive dysfunction would affect the functional outcome. We also assessed whether disease damage (by SDI), current active arthritis, and disease activity using the SLEDAI and current blood test results (serum hemoglobin and albumin levels) could be associated with impaired HRQOL.

Statistical analyses. Results are expressed as mean ± SD for normally distributed data. Non-normally distributed data are expressed as median (interquartile range). Comparisons between the SLE patients with HRQOL assessment and the rest of the total cohort of SLE patients for demographic and clinical characteristics were performed using descriptive statistics and parametric and nonparametric tests, as appropriate. Comparisons between the HRQOL of SLE patients and healthy controls[35,36] were performed using parametric and nonparametric tests, as appropriate. Association between the explanatory variables and 8 SF-36 scales, the PCS, and MCS were tested using chi-square tests for categorical variables, and Pearson and Spearman correlations for continuous variables with normal and skewed distribution, respectively. Comparisons for continuous variables between 3 groups were analyzed using one-way ANOVA with Bonferroni adjustment. Variables with p values < 0.1 in the univariate analysis were entered into linear regression analysis (backward, stepwise selection). Variables that were skewed were logarithmically transformed before entering the regression analysis. All hypotheses were 2-tailed, and p values < 0.05 were considered significant. Analyses were performed using SPSS for Windows, version 13.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Demographic, clinical, and laboratory characteristics. Two hundred ninety-one Chinese patients with SLE were recruited, with a male to female ratio of 1:23. The mean age at the time of the survey was 42 ± 12 years. The mean age at diagnosis was 32 ± 13 years and the median disease duration was 9.7 years (range 6.2–15.8). One-third (32%) were single and 68% were married/widowed/divorced. The mean level of education was 10 ± 4 years. One hundred ninety-three (66%) patients were currently taking prednisolone, with a

median daily dose of 5.0 mg (range 5.0–7.5). Eighty-seven (30%) patients were currently taking immunosuppressants, including azathioprine (n = 57, 19.6%), cyclophosphamide (n = 7, 2.4%), mycophenolate mofetil (n = 12, 4.1%), cyclosporin A (n = 5, 1.7%), leflunomide (n = 3, 1.0%), and methotrexate (n = 3, 1.0%) and 108 were taking hydroxychloroquine (37%). The clinical and immunological profile (ever) of patients recruited in this study was similar to the rest of the patients in the cohort (Table 1).

At the time of the assessment, 189 (65%) patients had inactive disease with a SLEDAI of 0. The remaining 102 patients had mild to moderate disease activity, with a median SLEDAI of 4 (range 2–4). Fifteen (5.2%) patients had active arthritis. The serum hemoglobin and albumin levels were 12.0 ± 1.7 g/dl and 39.7 ± 4.2 g/l, respectively.

Seventy-three (25%) patients had damage in at least one of the organ systems, with a median SDI of 1 (range 1–2).

Neuropsychiatric assessment. Seventy-seven (26.4%) patients had a total of 96 episodes of NP events ever. Nineteen patients (25%) had 2 NP events. The last NP events occurred at 6.4 (range 2.8–9.7) years from the date of assessment. In 31/77 (40%) of these patients, the last NP events occurred within the past 5 years. Sixty-seven (69.6%) events were attributed to SLE only, 2 (2.2%) were attributed to non-SLE causes, and 27 (28.2%) were attributed to both. The most common manifestations included seizures (21/77, 27.3%), psychosis (15/77, 19.4%), cerebrovascular disease (15/77, 19.4%), headache (13/77, 16.9%), mononeuropathy (9/77, 11.7%), and mood disorder (9/77, 11.7%). Other less common manifestations included anxiety disorder (4/77 5.2%), cognitive dysfunction (3/77, 3.9%), acute confusional state (2/77, 2.6%), aseptic meningitis (2/77, 2.6%), myasthenia gravis (2/77, 2.6%), and cranial neuropathy (1/77, 1.3%). Fifty patients (65%) had all the NP events attributed to SLE only, and 27 patients (35%) had at least one NP event attributed to non-SLE causes or both.

Table 1. The clinical and immunological profile (ever) of SLE patients recruited in this study were similar to the rest of the patients in the cohort.

	SF-36 Results (n = 291) n (%)	SF-36 Not Done (n = 440) n (%)	p
Female	279 (95.9)	410 (93.2)	0.15
Malar	104 (35.7)	140 (31.8)	0.23
Discoid	32 (11.0)	41 (9.3)	0.45
Photosensitivity	79 (27.1)	93 (21.1)	0.05
Oral ulcer	76 (26.1)	89 (20.2)	0.05
Arthritis	213 (73.1)	307 (69.8)	0.24
Serositis	86 (29.6)	141 (32.0)	0.62
Renal	156 (53.6)	263 (59.8)	0.19
Neuropsychiatric	77 (26.4)	132 (30.0)	0.35
Hematologic	253 (86.9)	376 (85.5)	0.21
Anti-ds-DNA	205 (70.4)	296 (67.3)	0.21
Anti-Smith	52 (17.9)	71 (16.1)	0.48
Anti-Ro	150 (51.5)	233 (53.0)	0.94
Anti-La	43 (14.8)	68 (15.5)	0.92
Anti-cardiolipin	104 (35.7)	154 (35.0)	0.69
Lupus anticoagulant	18 (6.2)	27 (6.1)	1.0

At the time of assessment, the median values of the HAD anxiety score and depression score were 4 (range 2–7) and 3 (1–6), respectively. According to the suggested cutoff scores, anxiety disorder was present in 64/291 (22%) patients, and 61/291 (18.2%) had depression. The median MMSE score was 29 (range 26–30), and the CDRS-IP subscale score was 35.2 ± 4.2. According to the suggested cutoff scores, dementia and cognitive impairment was present in 13/291 (4.5%) and 19/291 (6.5%) patients, respectively.

The HAD depression score correlated with the age at diagnosis of SLE (rho = 0.12, $p < 0.05$) and the MMSE score (rho = –0.17, $p < 0.01$). No other significant relationship between anxiety or depression was found between other demographic or clinical variables.

Quality of life. The scores for HRQOL, including all the 8 scales and the PCS and MCS scores, were significantly lower in the SLE patients compared with healthy controls (Figure 1). When the data were compared with the female controls, female patients with SLE had significantly lower scores in all the 8 SF-36 subscales. In male patients with SLE, physical function (PF), role-physical (RP), and bodily pain (BP) were significantly lower compared to sex-matched controls (data not shown).

Table 2 summarizes the variables associated with the 8 scales and PCS and MCS scores in the univariate analysis with a p value < 0.1. Variables including disease duration, the presence of other ACR criteria ever, history of psychosis, mood disorder, anxiety disorder or other less common NP manifestations, and the SLEDAI score were not associated with impaired HRQOL (data not shown).

NP event duration and HRQOL. Patients were subdivided into 3 groups based on whether the last NP event occurred within the past 5 years (group 1, n = 31), more than 5 years previously (Group 2, n = 46), or never had NP events (Group 3, n = 214). Group 1 patients had significantly impaired RP subscale (38.9 ± 26.7) compared to Group 2 (63.4 ± 40.2; p = 0.001) and Group 3 (52.1 ± 41.7; p = 0.006). Group 1 patients also had significantly impaired social function (SF) subscale (60.3 ± 22.9) compared to Group 2 (75.0 ± 24.4; p = 0.02) and Group 3 (73.9 ± 22.6; p = 0.009). The PCS score for Group 1 was significantly impaired (40.6 ± 7.2) compared to Group 3 (45.1 ± 9.2; p = 0.04). No differences were noted between Groups 1 and 2 in the PCS scores. The 2 subscales RP and SF and the PCS scores between Groups 2 and 3 were similar. No differences were found between these 3 groups of patients in the other 6 subscales or the MCS scores (data not shown).

NP event attribution and HRQOL. Patients were subdivided into 3 groups based on whether they had NP events attributed to SLE only (Group 1, n = 50) or events attributed to non-SLE causes or both (Group 2, n = 27), and patients who never had NP events (Group 3, n = 214). Group 2 patients

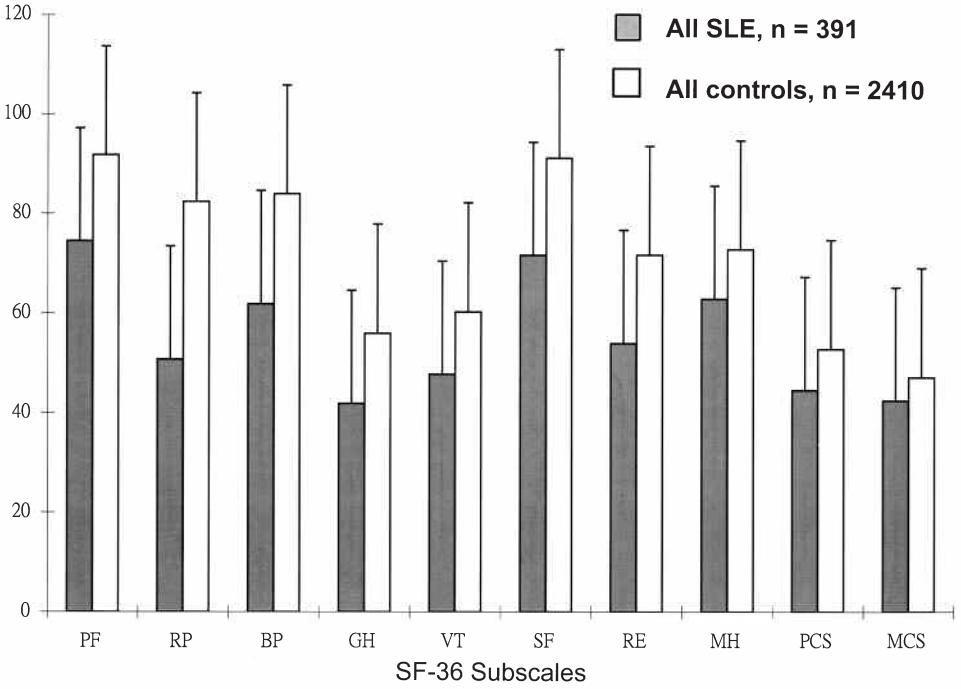

Figure 1. SF-36 subscales and PCS and MCS scores in patients with SLE and controls[35,36] PF: physical function, RP: role-physical, BP: bodily pain, VT: vitality, RE: role-emotional, MH: mental health, SF: social function, GH: general health, PCS: physical component summary, MCS: mental component summary. $p < 0.0001$ in all the 8 SF-36 subscales and PCS and MCS scores, SLE compared to control.

Table 2A. Univariate analysis: Pearson or Spearman correlation between SF-36 subscales and clinical demographic variables (continuous variables).

Variables	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS
Age	–0.33*	–0.21*	–0.17*	–0.06	–0.10	–0.02	–0.18*	–0.05	–0.23*	–0.10
Years of education	0.23*	0.25*	0.20*	0.09	0.12*	0.02	0.17*	0.10	0.24*	0.09
Age at diagnosis	–0.31*	–0.18*	–0.13*	–0.07	–0.14*	–0.04	–0.14*	–0.08	–0.22*	–0.06
SDI	–0.18*	–0.07	–0.07	–0.10	–0.045	–0.12	–0.09	0.04	–0.14*	–0.01
Hemoglobin level	0.12*	0.17*	0.03	0.15*	0.18*	0.12•	0.14*	0.04	0.15*	0.11*
Serum albumin	0.16*	0.10	0.07	0.14*	0.12*	0.12*	0.05	–0.00	0.17*	0.02
CDRS-IP	0.15*	0.11	0.07	0.02	0.07	–0.05	0.08	0.12*	0.11	0.05
MMSE score	0.24*	0.27*	0.17*	0.07	0.13*	0.15*	0.21*	0.14*	0.23*	0.15*
HAD anxiety score	–0.33*	–0.40*	–0.35*	–0.48*	–0.48*	–0.43*	–0.48*	–0.70*	–0.29*	–0.66*
HAD depression score	–0.50*	–0.52*	–0.45*	–0.47*	–0.52*	–0.59*	–0.48*	–0.61*	–0.47*	–0.59*

PF: physical function, RP: role-physical, BP: bodily pain, VT: vitality, RE: role-emotional, MH: mental health, SF: social function, GH: general health, PCS: physical component summary, MCS: mental component summary. NP event duration: duration of last NP event from date of study, years. SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) damage index; CDRS-IP: Chinese version of the Mattis Dementia Rating Scale Initiation/Perseveration subscale; MMSE: Chinese Mini-Mental State Examination. HAD: Hospital Anxiety and Depression Scale. * $p < 0.1$.

had slightly impaired BP subscale scores (50.4 ± 23.9) compared to Group 1 (63.3 ± 23.9; $p = 0.09$), and they were significantly impaired compared to Group 3 (63.4 ± 24.5; $p = 0.03$). No differences were noted between Groups 1 and 3 in this subscale. No differences were found between these 3 groups of patients in the other 7 scales or the PCS and MCS scores (data not shown).

Independent explanatory variables associated with impairment of the 8 scales and the PCS and MCS scores in the multivariate analysis are summarized in Table 3. NP involvement-ever was one of the independent explanatory variables associated with impairment of the general health (GH) subscale. Cerebrovascular disease and mononeuropathy were independent explanatory variables associated with impairment of the PF subscale, while the latter was also one of the independent explanatory variables associated with impairment of the role emotional (RE) subscale. Cognitive impairment as indicated by the CDRS-IP score was one of

Table 2B. Univariate analysis: the relationship between SF-36 physical component subscales, physical component summary score, and clinical and demographic variables (categorical variables).

	Physical Function		Role Physical		Bodily Pain		General Health		PCS	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Female	74.8 ± 22.1	72.1 ± 26.0	51.4 ± 42.1	37.5 ± 39.2	61.9 ± 24.3	64.3 ± 31.8	42.2 ± 21.6	45.5 ± 20.6	64.4 ± 8.9	40.7 ± 10.9
ACR features ever										
Arthritis	74.5 ± 22.3	75.5 ± 22.4	50.5 ± 42.1	54.7 ± 41.3	60.3 ± 23.4*	68.4 ± 26.6	41.6 ± 21.5	44.8 ± 21.8	44.2 ± 8.9	46.1 ± 9.0
Renal	76.4 ± 21.6	72.4 ± 23.0	55.8 ± 41.4*	46.7 ± 42.1	64.4 ± 25.3	60.2 ± 23.4	42.7 ± 21.3	41.9 ± 21.7	45.4 ± 8.8	43.8 ± 9.2
Neuropsychiatric	70.8 ± 23.8*	75.8 ± 21.7	46.1 ± 43.3	53.0 ± 41.5	58.1 ± 24.5*	63.7 ± 24.5	39.0 ± 22.2	43.4 ± 21.1	42.9 ± 8.3*	45.2 ± 9.2
Headache	88.1 ± 10.5*	74.0 ± 22.4	63.5 ± 42.8	50.3 ± 41.9	52.5 ± 13.8*	62.4 ± 24.9	42.0 ± 15.7	42.3 ± 21.8	45.8 ± 5.2	44.5 ± 9.1
Seizure disorder	74.1 ± 25.4	74.6 ± 22.1	56.0 ± 41.0	51.2 ± 42.0	65.3 ± 29.7	62.3 ± 24.2	42.0 ± 23.0	42.4 ± 21.4	44.1 ± 9.0	44.7 ± 9.0
CVD	58.7 ± 30.1*	75.5 ± 21.6	30.0 ± 41.4*	52.7 ± 41.6	56.9 ± 31.0	62.8 ± 24.2	41.0 ± 26.8	42.5 ± 21.2	39.2 ± 10.3*	45.0 ± 8.9
Mononeuropathy	55.6 ± 20.1*	75.2 ± 22.2	33.3 ± 39.5	52.1 ± 41.9	55.9 ± 16.5	62.7 ± 24.8	29.3 ± 12.6*	42.8 ± 21.6	40.9 ± 6.7	44.8 ± 9.1
Current clinical features										
Anxiety	66.9 ± 20.9*	76.8 ± 22.1	30.9 ± 36.4*	56.5 ± 41.8	50.3 ± 19.7*	65.3 ± 24.9	29.3 ± 15.3*	46.0 ± 21.6	41.8 ± 7.5*	45.4 ± 9.2
Depression	55.5 ± 22.0*	78.9 ± 20.0	18.4 ± 31.5*	58.1 ± 40.6	44.3 ± 20.4*	65.9 ± 23.7	28.2 ± 15.2*	45.5 ± 21.5	37.8 ± 8.8*	46.1 ± 8.3
Cognitive impairment	61.8 ± 26.4*	75.5 ± 21.7	32.9 ± 32.3*	52.1 ± 42.3	51.1 ± 20.8*	62.7 ± 24.7	40.5 ± 21.4	42.5 ± 21.6	41.0 ± 6.9	44.9 ± 9.1
Active arthritis (n = 15)	62.7 ± 28.0	75.3 ± 21.8	21.7 ± 35.2*	53.7 ± 41.4	37.9 ± 19.6*	63.4 ± 23.8	30.8 ± 16.2*	42.8 ± 20.8	36.5 ± 8.1*	45.2 ± 8.8

PCS: physical component summary; CVD: cerebrovascular disease. * $p < 0.1$.

Table 2C. Univariate analysis: the relationship between SF-36 mental component subscales, mental component summary score, and clinical and demographic variables (categorical variables).

	Social Function		Vitality		Role-Emotional		Mental Health		MCS	
	Yes	No	Yes	No	Yes	No	Yes	No	Yes	No
Female	48.0 ± 19.9	52.1 ± 19.9	72.3 ± 23.1	77.1 ± 25.5	52.9 ± 45.0*	83.3 ± 33.3	63.2 ± 17.5	72.3 ± 16.1	42.5 ± 10.7*	50.8 ± 7.0
ACR features ever										
Arthritis	37.3 ± 22.5*	48.6 ± 19.5	50.0 ± 21.7*	74.0 ± 22.3	40.0 ± 45.8	55.1 ± 44.9	57.3 ± 23.0	63.8 ± 17.3	38.6 ± 14.0	43.0 ± 10.4
Renal	46.7 ± 20.2	49.4 ± 19.7	74.3 ± 23.5	71.3 ± 21.7	59.2 ± 43.1	49.3 ± 46.5	64.1 ± 17.7	63.3 ± 17.7	43.3 ± 10.8	42.5 ± 10.8
Neuropsychiatric	48.1 ± 19.7	47.9 ± 20.1	68.7 ± 24.5*	74.0 ± 22.4	50.2 ± 45.8	55.7 ± 44.7	62.2 ± 17.5	64.2 ± 17.7	42.2 ± 11.4	43.1 ± 10.6
Headache	78.8 ± 18.7	72.2 ± 23.3	55.4 ± 13.3	47.8 ± 20.0	64.1 ± 44.0	53.7 ± 45.1	68.3 ± 14.8	63.3 ± 17.6	45.7 ± 9.3	42.7 ± 10.8
Seizure disorder	51.9 ± 20.8	47.6 ± 20.0	73.8 ± 22.0	72.7 ± 22.8	71.4 ± 36.9*	53.3 ± 45.2	66.3 ± 15.2	63.5 ± 17.9	46.3 ± 9.3	42.6 ± 10.8
CVD	48.3 ± 21.1	47.9 ± 20.0	65.0 ± 25.5	73.3 ± 22.5	46.7 ± 46.8	55.1 ± 44.8	64.5 ± 17.6	63.7 ± 17.7	43.7 ± 12.6	42.9 ± 10.7
Mononeuropathy	46.7 ± 15.6	47.9 ± 20.2	59.7 ± 19.5	73.3 ± 22.7	18.5 ± 37.7*	55.8 ± 44.6	51.1 ± 16.0*	64.1 ± 17.6	35.6 ± 9.7*	43.1 ± 10.7
Current clinical features										
Anxiety current	36.2 ± 19.1*	51.5 ± 18.7	57.2 ± 20.6*	76.8 ± 22.0	25.5 ± 36.0*	62.3 ± 44.0	47.1 ± 15.0*	68.2 ± 15.3	33.3 ± 8.2*	45.5 ± 9.8
Depression	32.8 ± 17.6*	51.5 ± 18.7	51.9 ± 18.9*	77.1 ± 21.5	20.1 ± 35.4*	61.8 ± 43.4	47.6 ± 14.3*	67.1 ± 16.2	33.5 ± 8.7*	44.9 ± 10.0
Cognitive impairment	39.7 ± 20.0	48.7 ± 19.7	69.1 ± 22.6	72.7 ± 23.2	40.4 ± 46.6	55.2 ± 44.8	52.4 ± 15.4*	64.3 ± 17.4	38.9 ± 10.7	43.1 ± 10.7
Active arthritis (n = 15)	37.3 ± 22.5*	48.6 ± 19.5	50.0 ± 21.7*	74.0 ± 22.3	40.0 ± 45.8	55.1 ± 44.9	57.3 ± 23.0	63.8 ± 17.3	38.6 ± 14.0	43.0 ± 10.4

MCS: mental component summary; CVD: cerebrovascular disease. * $p < 0.1$.

the 3 independent explanatory variables associated with impairment of the mental health (MH) subscale.

The HAD depression score was the only independent explanatory variable associated with impairment of all the 8 subscales and PCS and MCS scores, while the HAD anxiety score was associated with impairment of all the 4 MH subscales [vitality (VT), SF, RE, MH], the MCS score, and the GH subscale.

Active arthritis, damage (by SDI), and low serum albumin levels were associated with impairment of the PCS score and the SF subscale. In addition, active arthritis was also associated with impairment of 3 out of 4 physical health subscales (PF, RP, BP), while low serum albumin levels were associated with impairment of the GH subscale.

Low hemoglobin level and advancing age were associated with impairment of the PF, VT, and RE subscales; the former was associated with impairment of the MCS score, while the latter was associated with impairment of the PCS score. Low education level was associated with impairment of the RP and BP subscales; and female sex was associated with impairment of the RE subscale and the MCS score.

DISCUSSION

It is obvious that the domains of HRQOL affected by SLE

Table 3. Final regression models showing p values for independent variables associated with the 8 SF-36 subscales and physical and mental component summary scores.

Variables	Physical Components of SF-36					Mental Components of SF-36				
	PF	RP	BP	GH	PCS	SF	VT	RE	MH	MCS
Age	< 0.001						0.002	0.003		
Female								0.039		0.014
Years of education		< 0.001	< 0.004		< 0.001					
Active arthritis	0.02	0.002	< 0.001		< 0.001	< 0.001				
Hemoglobin level	0.01						0.01	0.02		0.04
Serum albumin				0.002	0.02	0.03				
SDI					0.045					
Neuropsychiatric ever				< 0.05						
Mononeuropathy ever	< 0.05							< 0.05		
Cerebrovascular disease ever	< 0.04									
CDRS-IP									0.006	
HAD anxiety score				< 0.001		0.003	< 0.001	< 0.001	< 0.001	< 0.001
HAD depression score	< 0.001	< 0.001	< 0.001	< 0.004	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Adjusted R^2	0.383	0.359	0.275	0.296	0.331	0.433	0.354	0.313	0.558	0.486

For definitions, see Table 2A.

may vary in different sociocultural contexts because HRQOL is affected by culture, highlighting the need for such studies in Chinese patients. This is one of the largest studies on HRQOL in patients with SLE, and is the largest study on Chinese with SLE. Our cohort of patients was similar to other SLE cohorts in terms of clinical and immunological features[3,7,11,14,37,38]. All the 8 scales of the SF-36 survey as well as the PCS and MCS scores were significantly lower in this group of SLE patients with mild disease, compared to the healthy controls, similar to studies in other parts of the world[3,10,37,39]. The differences between most of the 8 SF-36 subscales remained significant in the female patients (age < 65 yrs) compared with age- and sex-matched controls. In the male SLE and the older female SLE (age ≥ 65 yrs) groups, the interpretation would be difficult due to the small sample size.

The overall prevalence of NP disease in our group (26.4%) was similar to an earlier study done in Chinese (19%)[40], which is lower than that in Caucasians (37% to 95%)[41]. The most common NP manifestations in our cohort, headache, cerebrovascular disease, seizures, psychosis, depression, and anxiety, were similar to those reported previously[40,41]. Only one previous study specifically looked at the association of NP manifestations and HRQOL[17]. However, other potential confounding variables that may be associated with impaired HRQOL, and the patterns of HRQOL deficit associated with different NP manifestations, were not addressed. In our study, NP involvement was shown to be an independent variable associated with impairment of both physical and mental function in SLE, after adjusting for other sociodemographic and clinical variables. NP manifestations, cerebrovascular disease, and mononeuropathy-ever were associated with predominantly impaired physical function, although the latter also affected the mental function. Using logistic regression analysis, recent NP events (occurred within 5 yrs) and NP events attributed to SLE alone were not associated with impaired HRQOL. However, these results would need to be confirmed by future large-scale prospective studies.

Cognitive dysfunction, assessed using neuropsychologic assessment techniques, has been reported in up to 80% of patients with SLE[42], although most studies have found prevalence between 17% and 66%[43,44]. Subtle cognitive deficits detected by formal neuropsychologic testing have not been associated with a negative influence on quality of life[45]. Moreover, these tests are cumbersome and time-consuming. In our study, executive cognitive dysfunction as reflected by the low CDRS-IP score was found to be an independent explanatory variable associated with impairment of the MH subscale. Future studies should focus on the course of cognitive dysfunction over time.

In agreement with previous studies[15,38], we observed a high prevalence of depression and anxiety. The HAD depression score, in particular, was the most important independent explanatory variable associated with impairment of all the 8 SF-36 subscales and PCS and MCS scores. Other investigators also found that the psychological variable strongly predicted QOL[10,15,46]. In our SLE group, HAD depression score correlated weakly with the age at diagnosis of SLE and the MMSE score. We noted no association between history of arthritis or current active arthritis and depression, in contrast to a previous study[15]. No other significant relationship between anxiety or depression was found between other demographic or clinical variables, in keeping with another report[15]. Our results emphasize that not only physical but also psychological well-being can greatly influence QOL.

We found no association between HRQOL and disease activity as reflected by the SLEDAI score, similar to previous studies[4,6,16]. However, we found that low serum hemo-

globin and albumin levels were independent explanatory variables for impaired physical and mental function, which has not been studied previously. Some of these patients with low-grade inflammatory activity may have had slightly low serum albumin and hemoglobin levels that were not revealed by the SLEDAI. Indeed, prospective studies have found that change in disease activity over time was associated with change in QOL[18]. Whether treating this low-grade activity with low-dose prednisone or hydroxychloroquine may improve HRQOL in these patients would need to be addressed in future studies.

One potential limitation of our study is in the variety of constructs measured. It was designed to focus on neuropsychiatric, laboratory, and clinical variables and HRQOL. Socioeconomic status indicators such as income and psychosocial factors, and other variables including fatigue, pain, fibromyalgia, and knowledge about lupus were not included. These parameters might have explained the rest of the variance in the QOL in these patients. However, it would be too burdensome for patients to complete such a large battery of tests at any one time. As QOL is dependent on sociocultural factors, our results may not be generalizable to other countries with different sociocultural backgrounds. The third limitation would be the cross-sectional design. Prospective studies would be required to confirm any causal relationship between these variables and QOL.

Our study attempts to raise awareness about the influence of neuropsychiatric factors on HRQOL of patients with SLE. Our findings suggest that both the physical and mental components of the HRQOL are severely affected by the NP manifestations in this group of Chinese patients with SLE. Although physical variables such as older age, inflammation (low serum hemoglobin and albumin levels and arthritis), and disease damage are clearly associated with impaired function, psychological factors are critical to understanding the disease experience of persons with SLE. Routine psychological assessment in addition to clinical assessment should be considered in order to optimize HRQOL.

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