Subscale analysis of quality of life in patients with systemic lupus erythematosus: association with depression, fatigue, disease activity and damage

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Abstract

Objectives

The quality of life (QoL) in systemic lupus erythematosus (SLE) patients may be affected by psychological features and disease status. We evaluated the QoL of SLE patients according to four subscales of QoL compared to healthy controls, and the association with affecting factors.

Methods

108 patients with SLE and 52 healthy controls completed a psychological questionnaire. Depression, fatigue, and QoL were assessed with the Centre for Epidemiologic Studies Depression Scale, the Profile of Mood States Fatigue-Inertia Scale, and Functional Assessment Chronic Illness Therapy. Disease activity and damage index were measured by the SLE Disease Activity Index and SLE Collaborating Clinics/American College of Rheumatology.

Results

SLE patients showed higher degrees of depression ($p=0.005$) and a lower total QoL score than the controls ($p=0.003$). In the subscale analysis, physical well-being (PWB) and emotional well-being (EWB) were lower in the SLE group than the control group ($p<0.001$ for both). Multivariate analysis identified correlations between the following factors: total QoL with depression and daily glucocorticoid dose; PWB with depression, fatigue, and daily glucocorticoid; EWB with depression and functional well-being (FWB) with depression.

Conclusion

The QoL of SLE patients was lower than that of healthy controls. QoL subscales of the SLE patients were associated with daily glucocorticoid dose, depression, and fatigue rather than disease activity or damage. Comprehensive evaluation of psychological problems and appropriate management may improve the QoL of SLE patients, especially those using higher doses of glucocorticoids, even if disease activity and damage are not severe.

Key words

quality of life, SLE, glucocorticoid, disease activity, damage

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Introduction

Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that affects multiple organs and systems. Over the past 50 years, the survival rate of SLE patients has improved dramatically with the 10-year survival rate approaching 90% (1). As a result, disease management has focused not only on survival, disease activity control, or minimising organ damage, but also on the health-related quality of life (QoL). This has become increasingly important for patients with SLE.

A diagnosis of SLE has physical, psychological, and socio-economic implications for the individual. Patients with SLE have concerns about persistent pain, loss of function, work disability, and the potential toxic effects of long-term treatment; these concerns can result in psychological problems such as depression and fatigue. In turn the QoL of the patients can be affected. However, there were different reports regarding whether or not disease activity and/or drugs can affect psychological symptoms (2-6). Moreover, there is little information about how psychological symptoms, disease activity, damage, and drugs are related to the QoL of patients with SLE (7-9).

The Functional Assessment of Chronic Illness Therapy (FACIT) measurement is a collection of health-related QoL questionnaires targeted to the evaluating management of chronic illness (10). It is composed of four primary QoL domains, physical well-being (PWB), social/family well-being (SWB), emotional well-being (EWB), and functional well-being (FWB), which are useful for the analytical assessment of QoL. FACIT is widely used to study patients with different types of cancer, or various chronic diseases such as viral infections, multiple sclerosis, and rheumatoid arthritis as well as the general population (10, 11).

An analytic assessment and understanding of the QoL of SLE patients is important in order to enhance the QoL of these individuals. Thus, this study first compared the QoL subscale scores and psychological factors, including depression and fatigue, of patients with SLE and healthy controls using the FACIT questionnaires. We also investigated these parameters according to SLE disease activity, severity of damage, organ involvement, and daily dosage of glucocorticoids, in particular, measured QoL based upon psychological problems. Finally, associations between each of the QoL subscale scores of the patients with SLE and the above parameters were also investigated.

Patients and methods

Patients

This study included 108 patients with SLE and 52 healthy controls. Subjects were selected from the inpatient and outpatient rheumatology clinics at Severance Hospital, Yonsei University College of Medicine in Seoul, South Korea from January 1, 2007 to July 31, 2007. This centre is a specialised tertiary care hospital. Inclusion criteria were ages greater than 18 years and a diagnosis of SLE according to the revised American College of Rheumatology (ACR) criteria (12). Exclusion criteria were the presence of cognitive deficits such as mental retardation or an acute state of confusion which prevented the patients from completing the questionnaires. Among the 120 patients with SLE visiting our rheumatology clinic during this period, 108 patients participated in this study except for 4 patients who had cognitive deficits, 5 patients who refused our study, and 3 patients who did not complete the questionnaires. A total number of 52 voluntary healthy subjects were included in this study. All of them satisfied the following inclusion criteria; ages over 18 years, no evidence of autoimmune diseases and chronic inflammatory diseases, no past history and evidence of autoimmune diseases or chronic inflammatory diseases, and volunteers. These controls were age- and sex-matched to the subject group for this study. This study was approved by the institutional ethics committee, and all of the patients provided written informed consent prior to their participation. Participants completed the self-questionnaires measuring QoL, depression, and fatigue. Basic characteristics of the participants are shown in Table I. The groups did not significantly differ in age, gender distri-

Table I. Basic characteristics of the study participants. Patients with SLE did not significantly differ in age, gender distribution, or education levels compared to the healthy controls.

	SLE (n=108)	Control (n=52)	*p*-value
Age (years)	37.4 ± 11.1	33.6 ± 11.6	NS
Gender (female, %)	92.5	76.9	NS
Education (years)	14.2 ± 3.2	15.1 ± 2.7	NS
Disease duration (years)	7.2 ± 5.9		
SLEDAI	3.8 ± 3.3		
SLIACC/ACR	1.4 ± 1.3		
Neuropsychiatric disease (%)	13.9		
Renal disease (%)	37.0		
Pulmonary disease (%)	10.2		
Cardiovascular disease (%)	14.8		
Gastrointestinal disease (%)	3.7		
ESR (mm/hr)	36.3 ± 28.0		
CRP (mg/dL)	0.53 ± 1.96		
Prednisolone dose (mg/day)	7.1 ± 7.9		
Prednisolone use (%)	84.3		
Cyclophosphamide use (%)	0.9		
Azathioprine use (%)	10.2		
Mycophenolate mofetil use (%)	11.1		
Cyclosporine use (%)	3.7		

Values represent the mean ± SD. Clinical manifestations were defined by SLICC/ACR criteria. SLE: systemic lupus erythematosus; SLEDAI: SLE disease activity index; SLICC/ACR: SLE Collaborating Clinics/American College of Rheumatology; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein.

bution, or education levels. In the SLE group, there were 100 female patients. The mean age of the SLE group was 37.4±11.1 years with a mean disease duration of 7.2±5.9 years, and a mean education period of 14.2±3.2 years.

SLE disease activity and damage evaluation

We investigated SLE disease activity and damage index. SLE disease activity was measured with the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) (13). Patients with SLEDAI scores ≥8 were considered to be in the active disease group, while those with scores <8 were in the inactive group. To measure the cumulative irreversible damage due to the disease or therapy complications, which are defined as the continuous presence of any given item for at least 6 months, the Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index was used (14). We also measured the current daily glucocorticoid dose, serum erythrocyte sediment rate (ESR), and C-reactive protein (CRP) levels at the time of enrollment. Clinical manifestations were defined by SLICC/ACR criteria (14). As shown in Table I, the mean SLEDAI score was 3.8±3.3, the mean SLICC/ACR was 1.4±1.3, and the daily glucocorticoid dose was 7.1±7.9 mg.

Psychological features and quality of life measurements

Depression was evaluated using the Centre for Epidemiological Studies Depression Scale (CES-D) (15). The CES-D is a self-report, 20-item questionnaire that measures mood and vegetative motor functions during the preceding week. The CES-D total scores range from 0 to 60 and a score ≥16 indicates clinical depression (15). Fatigue was evaluated using the 7-item fatigue-inertia subscale of the Profile of Mood States Fatigue-Inertia Scale (POMS-F) (16). The POMS-F is a self-report questionnaire that measures fatigue during the preceding week with total scores ranging from 0 to 28.

We used the FACIT, version 4, for the evaluation of the QoL. The FACIT is a 27-item compilation of questions divided into 4 primary domains: PWB, SWB, EWB, and FWB (10). If individual questions were skipped, scores were prorated using the average scores from other answers measuring the same scale. If data were missing, prorating the subscale scores was acceptable as long as more than 50% of the items were answered; a total score was considered appropriate, if the overall item response rate was greater than 80%. All FACIT scales were scored so that a higher score corresponded to higher QoL. The total FACIT score was obtained by summing the individual subscale scores. In addition, we used the Trial Outcome Index (TOI), which was the sum of the PWB and FWB, because of its ability to detect changes in physical and functional outcomes, at times even more so than the total FACIT score (10).

Statistical analysis

Data were expressed as the mean of each group; all values in the patients with SLE were compared to those of the controls. All measurements were expressed as the mean ± standard deviation. Student's *t*-test and χ^2-test were used to compare baseline demographic and clinical data as well as differences in the mean of both groups. Associations between variable clinical and psychological values were analysed by Pearson's correlation test. To evaluate the relative contribution of QoL, a hierarchical multiple linear regression model was used. Candidate predictor variables were selected for possible inclusion in the model based on theoretical considerations such as psychological features, daily glucocorticoid dose, disease activity, and damage index. Statistical significance was set at $p<0.05$ for all statistical tests. All analyses were performed using SPSS version 12.0 (SPSS Inc., Chicago, Illinois, USA).

Results

Psychological features and QOL

We compared the measurements of depression, fatigue, and QoL in the SLE and control groups. The results are shown in Table II. The SLE group had a significantly higher degrees of depression symptoms than the control group ($p=0.005$). The number of patients with clinical depression, as noted by a CES-D total score ≥16, was larger in the SLE group (65/108) than in the control group (25/52). POMS-F scores, which represented fatigue, were significantly

Table II. Comparison of psychological features and quality of life (QoL) between the SLE and control groups. The SLE group had significantly higher degrees of depression and fatigue than the control group. Patients with SLE showed a decreased total QoL than the controls. PWB, EWB, and TOI scores were lower in the SLE group than in the control group.

	SLE (n=108)	Control (n=52)	*p*-value
CES-D	19.01 ± 11.1	14.45 ± 8.13	0.005*
POMS-F	9.45 ± 6.81	7.02 ± 5.72	0.020*
Total QoL	67.94 ± 15.50	75.50 ± 2.54	0.003*
PWB	20.50 ± 5.76	24.63 ± 2.82	<0.001*
SWB	15.21 ± 5.56	14.94 ± 5.29	0.770
EWB	14.01 ± 4.18	16.25 ± 2.16	<0.001*
FWB	18.22 ± 5.78	19.67 ± 6.38	0.153
TOI	38.72 ± 9.88	44.31 ± 7.24	<0.001*

Values represent the mean ± SD. SLE: systemic lupus erythematosus; CES-D: centre for epidemiologic studies depression scale; POMS-F: profile of mood states fatigue-inertia scale; QoL: quality of life; PWB: physical well-being; SWB: social well-being; EWB: emotional well-being; FWB: functional well-being; TOI: trial outcome index. *$p<0.05$.

higher in the SLE groups compared to the controls ($p=0.020$). Patients with SLE had significantly lower total QoL scores than the controls ($p=0.003$). When evaluated according to individual subscale scores, PWB, EWB, and TOI scores were lower in the SLE group than the control group ($p<0.001$), but there were no differences in SWB or FWB between these groups.

Subgroups analysis

Psychological features and QoL of the SLE patients were investigated according to the daily glucocorticoid dose and presence of depression (Table III). When comparing the patients who took more than 7.5 mg of glucocorticoid per day to those taking a daily glucocorticoid dose of less than or equal to 7.5 mg, the group using higher doses of glucocorticoids had significantly greater psychological symptoms such as depression and fatigue. With the exception of the SWB, overall QoL and all subscale scores measuring QoL were significantly lower in the group using higher doses of glucocorticoids. Patients with clinical depression (CES-D score ≥16) had significantly worse symptoms for all of psychological conditions and lower scores for all QoL parameters. When analysing the active and inactive groups according to the SLEDAI, the active group was found to have more severe depression and a lower PWB. However, there were no significant differences in any of the damage index analysis parameters. We also evaluated these parameters according to the presence of organ damage, as defined by the SLICC/ACR category; however, there were no significant differences between these groups.

Correlation of psychological features and QOL to other factors

In patients with SLE, we compared the psychological features and QoL to ESR, SLEDAI, SLICC/ACR, and daily glucocorticoid dose (Table IV). Depression was positively correlated with the SLEDAI and daily glucocorticoid dose. Total QoL was negatively correlated with the SLEDAI and daily glucocorticoid dose. In the subscale analysis, the following negative correlations were also found: PWB with ESR, SLEDAI and the daily glucocorticoid dose, EWB with the daily glucocorticoid dose, FWB with the daily glucocorticoid dose, and TOI with SLEDAI and the daily glucocorticoid dose. SLICC/ACR had no correlation to the psychological features, and total or subscale QoL scores. Comparing

Table III. Comparison of psychological parameters according to daily glucocorticoid dose, depression, and disease activity among the patients with SLE. The group using higher doses of glucocortoids had more severe symptoms of all psychological conditions such as depression, anxiety, anger, and fatigue. Total QoL and all QoL subscale scores, with the exception of SWB, were significantly lower in the group using higher doses of glucocorticoids. Patients with clinical depression had more severe symptoms of all psychological conditions and lower scores for all QoL parameters. When analysing the active and inactive groups according to the SLEDAI, the active group had more severe depression and a lower PWB.

	Glucocorticoid dose			Depression			Disease activity		
	PL ≤7.5 mg/d (n=76)	PL >7.5 mg/d (n=32)	*p*-value	CES-D<16 (n=43)	CES-D≥16 (n=65)	*p*-value	SLEDAI<8 (n=93)	SLEDAI≥8 (n=15)	*p*-value
SLEDAI	3.07 ± 2.86	5.41 ± 3.69	0.002*	2.84 ± 3.06	4.37 ± 3.32	0.017*	–	–	–
SLICC/ACR	1.13 ± 1.20	2.00 ± 1.19	0.001*	1.47 ± 1.47	1.34 ± 1.11	0.631	1.32 ± 1.24	1.80 ± 1.32	0.174
CES-D	17.10 ± 9.68	23.54 ± 9.80	0.002*	–	–	-	18.21 ± 9.25	23.96 ± 13.72	0.040*
POMS-F	8.37 ± 6.35	12.03 ± 7.28	0.010*	5.28 ± 4.48	12.21 ± 6.71	<0.001*	9.00 ± 6.31	12.28 ± 9.13	0.198
Total QoL	71.20 ± 1.59	60.22 ± 16.69	0.001*	78.86 ± 10.53	60.72 ± 13.99	<0.001*	69.47 ± 13.95	58.47 ± 21.10	0.069
PWB	22.01 ± 4.92	16.91 ± 6.10	<0.001*	22.21 ± 3.95	18.05 ± 5.47	<0.001*	21.19 ± 5.02	16.20 ± 8.06	0.034
SWB	15.12 ± 5.71	15.44 ± 5.27	0.787	17.00 ± 4.35	14.03 ± 5.97	0.006*	15.46 ± 5.16	13.67 ± 7.63	0.392
EWB	14.67 ± 3.71	12.43 ± 4.83	0.023*	16.26 ± 2.78	12.52 ± 4.30	<0.001*	14.19 ± 3.88	12.87 ± 5.74	0.400
FWB	19.39 ± 5.27	15.44 ± 6.06	0.001*	21.40 ± 5.09	16.12 ± 5.26	<0.001*	18.62 ± 5.48	15.73 ± 7.13	0.152
TOI	41.41 ± 8.44	32.34 ± 10.25	<0.001*	45.60 ± 7.36	34.17 ± 8.65	<0.001*	39.82 ± 9.02	31.93 ± 12.39	0.004*

Values represent the mean ± SD. PL: prednisolone; CES-D: centre for epidemiologic studies depression scale; SLEDAI: SLE disease activity index; SLICC/ACR: Collaborating Clinics/American College of Rheumatology; POMS-F: profile of mood states fatigue-inertia scale; QoL: quality of life; PWB: physical well-being; SWB: social well-being; EWB: emotional well-being; FWB: functional well-being; TOI: trial outcome index. *$p<0.05$.

QoL to age and education years, there was no significant correlation. However, longer disease duration was correlated with PWB (r=0.224, p=0.020) and EWB (r=0.223, p=0.020) as well as total QoL (r=0.231, p=0.016), but not with SWB and FWB.

Multiple linear regression analysis

Multiple linear regression analysis was conducted to examine the associations between QoL and other parameters including psychological features, daily glucocorticoid dose, disease duration, disease activity, and damage index. When several stratified analyses were performed according to these parameters, none of the QoL subscales were affected by disease duration, SLEDAI and SLICC/ACR in any multiple regression analysis models. Table V shows the results of a regression analysis model evaluating depression, fatigue, and daily glucocorticoid dose. Total QoL was affected by depression and daily glucocorticoid dose (p<0.001 and p=0.043, respectively; adjusted R^2=0.453). In the subscale analysis, PWB was associated with depression, fatigue, and daily glucocorticoid dose (p=0.032, p<0.001, and p=0.002, respectively; adjusted R^2=0.429). EWB was associated with depression and fatigue (p=0.001 and p=0.023, respectively; adjusted R^2=0.368), while FWB was associated with depression (p<0.001, adjusted R^2=0.265). The TOI, the sum of the PWB and FWB, was affected by depression and daily glucocorticoid dose (p<0.001 and p=0.008, respectively; adjusted R^2=0.423). However, SWB was not associated with any psychological feature.

Discussion

We evaluated the QoL of patients with SLE and examined the relationship of QoL with depression, fatigue, medication use, and disease activity and damage. Our findings showed that overall QoL, especially physical and emotional QoL, was lower in the SLE group than the control group. The SLE patients had more severe psychological conditions such as depression and fatigue than the controls. These features and concurrent higher glucocorticoid use

Table IV. Correlation of psychological features with background factors. Depression was correlated with SLEDAI and daily glucocorticoid dose. Total QoL was negatively correlated with SLEDAI and daily glucocorticoid dose. The following negative correlations were also identified: PWB with ESR, SLEDAI and daily glucocorticoid dose; EWB with daily glucocorticoid dose; FWB with daily glucocorticoid dose; TOI with SLEDAI and daily glucocorticoid dose.

	ESR (mm/hr)		SLEDAI		SLICC/ACR		PL (mg/d)	
	r-value	*p*-value	r-value	*p*-value	r-value	*p*-value	r-value	*p*-value
CES-D	0.062	0.521	0.231	0.016*	-0.007	0.940	0.259	0.007*
POMS-F	0.152	0.115	0.179	0.064	-0.094	0.331	0.178	0.065
Total QoL	-0.156	0.108	-0.250	0.009*	-0.024	0.803	-0.305	0.001*
PWB	-0.191	0.047*	-0.292	0.002*	-0.008	0.937	-0.369	<0.001*
SWB	-0.064	0.510	-0.123	0.205	0.064	0.509	-0.031	0.748
EWB	-0.076	0.434	-0.104	0.285	-0.043	0.656	-0.256	0.008*
FWB	-0.110	0.258	-0.187	0.052	-0.088	0.367	-0.235	0.014*
TOI	-0.176	0.069	-0.280	0.003*	-0.056	0.566	-0.353	<0.001*

ESR, erythrocyte sediment rate; SLEDAI: SLE disease activity index; SLICC/ACR: SLE Collaborating Clinics/American College of Rheumatology; PL: prednisolone; CES-D: centre for epidemiologic studies depression scale; POMS-F: profile of mood states fatigue-inertia scale; QoL: quality of life; PWB: physical well-being; SWB: social well-being; EWB: emotional well-being; FWB: functional well-being; TOI: trial outcome index.
*p<0.05.

Table V. Multiple linear regression analysis model including depression, fatigue, and daily glucocorticoid dose. Total QoL was affected by depression and daily glucocorticoid dose. In the subscale analysis, PWB was associated with fatigue and daily glucocorticoid dose, EWB was associated glucocorticoid dose, FWB was associated with depression, and TOI was associated with both depression and daily glucocorticoid dose.

	Variable	β	*p*-value	Adjusted R^2
Total QoL	Constant	88.164		0.453
	CES-D	-0.733	<0.001*	
	POMS-F	-0.449	0.052	
	Glucocorticoid dose	-0.287	0.049*	
PWB	Constant	27.308		0.429
	CES-D	-0.130	0.032*	
	POMS-F	-0.327	<0.001*	
	Glucocorticoid dose	-0.176	0.002*	
SWB	Constant	18.104		0.058
	CES-D	-0.142	0.057	
	POMS-F	-0.044	0.684	
	Glucocorticoid dose	0.032	0.642	
EWB	Constant	18.871		0.368
	CES-D	-0.158	0.001*	
	POMS-F	-0.153	0.023*	
	Glucocorticoid dose	-0.060	0.159	
FWB	Constant	23.880		0.265
	CES-D	-0.304	<0.001*	
	POMS-F	0.074	0.459	
	Glucocorticoid dose	-0.083	0.196	
TOI	Constant	51.188		0.423
	CES-D	-0.433	<0.001*	
	POMS-F	-0.253	0.094	
	Glucocorticoid dose	-0.259	0.008*	

CES-D: centre for epidemiologic studies depression scale; POMS-F: profile of mood states fatigue-inertia scale; QoL: quality of life; PWB: physical well-being; SWB: social well-being; EWB: emotional well-being; FWB: functional well-being; TOI: trial outcome index.
*p<0.05.

negatively affected the QoL of patients with SLE.

Higher levels of depression and fatigue were observed in the SLE group than the control group; these are consistent with prior studies (2, 6, 17-19). However, only severity of depression correlated with SLE disease activity. Depression severity was not associated with neuropsychiatric manifestations or damage index, but was associated with the daily dose of glucocorticoids. Previous studies reported various relationships between SLE disease activity and depression severity (3, 4, 20, 21). These different results might be due to various factors affecting depression, including the number of patients with neuropsychiatric conditions who participated in these studies, medication use, and chronic damage (2, 4, 20-22). Moreover, it was unclear whether depression was the cause or the result of active disease (20). The psychological problems of patients with SLE may be caused by neuropsychiatric conditions associated with the disease (2). However, none of the psychological problems observed in our study were significantly different between the patients with and without neuropsychiatric manifestations in the SLE group (data was not shown). This may be due to the exclusion of patients with severe current cognitive deficits such as mental retardation or who were in an acute state of confusion from this study to prevent bias from incomplete questionnaires. These findings suggest that the increased incidence of psychological problems among SLE patients was independent of mild and moderate neuropsychiatric manifestations of SLE.

The group with higher glucocorticoid use (>7.5 mg/day of prednisolone) had increased rates of depression as well as fatigue. Psychosis induced by glucocorticoids is uncommon among patients taking prednisolone at doses of <20 mg/day (23). However, moderate doses (>7.5 to ≤30 mg/day of prednisolone) of glucocorticoids are associated with genomic actions; various adverse reactions caused by glucocorticoids can indirectly affect psychological conditions such as depression, anxiety, and insomnia in the general population (24). In addition, the multiple linear analyses showed that the use of higher doses of glucocorticoids was an independent factor that negatively affected the QoL of patients with SLE. These findings indicate that physicians should closely monitor the patient's psychological health and QoL as well as disease activity when prescribing higher doses of glucocorticoids.

Total QoL scores were lower in the SLE group than the control group, similar to the results from other studies (7-9). In this study, it was found that the decreased total QoL negatively correlated with the SLEDAI and daily glucocorticoid dose. However, the correlation coefficients with SLEDAI were relatively small, and in the multiple linear analyses, total QoL was affected by depression and daily glucocorticoid dose (β=-0.733, p<0.001; and β=-0.287, p=0.043, respectively), but was not significantly affected by disease activity or damage index. Moreover, Table III showed that total QoL scores and all QoL subscales scores except TOI score were not different in both the higher and lower disease activity groups, but total QoL was decreased in patients with higher daily doses of glucocorticoids compared to those who with lower doses of glucocorticoids. These findings were different from previous reports stating that disease activity greatly affects the QoL of patients with SLE (7). Our finding showed that total QoL was more influenced by depression and glucocorticoid dose during the course of treatment than by disease activity or damage itself. Since people with depression tend to answer questions differently from people who are not depressed, the reporting bias for depression can be considered even after adjusting for depression. We cannot rule out the possibility of the association between QoL and SLE activity by this study, because generally active SLE leads to higher glucocorticoid treatment. So, these findings suggest that the physicians must comprehensively evaluate QoL and pay close attention to psychological problems in patients with SLE using high doses of glucocorticoids even when disease activity is well controlled.

QoL subscales such as physical, social, emotional, and functional QoL were evaluated for a deeper understanding. The subscale analysis showed somewhat different results from those seen for total QoL. Interestingly, patients with increased disease activity showed lower QoL for PWB compared to the patients with an inactive disease state. This could be because SLE patients with more active disease activity have less physical activity, and lower physical QoL was related to decreased physical activity. However, decreased physical QoL of SLE patients should be more associated with SLE itself rather than higher disease activity or damage. physical QoL was lower for patients with SLE than the controls (p<0.001) although overall disease activity of the patients enrolled in this study was not severe: mean SLEDAI was 3.8±3.3 and ESR was 36.3±28.0 mm/h. In addition, depression, fatigue, and daily glucocorticoid dose had greater effects on physical QoL than disease activity or damage index in the multiple linear analyses (Table V).

Multiple linear analyses also showed that EWB was affected by depression and fatigue. Considering the fact that emotional QoL is mostly affected by other psychological features and that emotional QoL is not as likely to change as quickly in response to physical health management such as pharmaceutical treatment (10), psychological intervention to treat depression or fatigue may be helpful for improving the emotional QoL of SLE patients. More data is needed to clarify the effects of psychological intervention on the emotional QoL of SLE patients.

There was a previous report showing that the functional ability of SLE patients was mostly affected by disability (8). However, the SLE group had lower FWB scores than the control group, and this difference was not statistically significant (p=0.153). When evaluating damage to organs such as musculoskeletal, renal, gastrointestinal, and pulmonary systems, there were no significant differences between these groups. We believe that one of the possible reasons for these results was due to the lower damage index scores of the enrolled

patients (mean SLICC/ACR, 1.4±1.3). Another reason may be that the severity of joint damage in SLE patients was relatively lower than that of patients with rheumatoid arthritis, indicating that functional ability is largely affected by musculoskeletal deformity.

Unlike other QoL subscales, the SWB of the SLE group and control group was not different and was not correlated with the psychological features, disease activity, damage index, or glucocorticoid dose in the multiple linear analysis. These findings imply that SLE patients might maintain social relationships with family and friends even if their social roles have changed over the course of the disease. A previous study also reported that patients with SLE can function well socially (25). However, we could not simply characterise the relationship between mental health and social QoL in SLE patients considering that another study has shown that depressed patients have impaired social functions and subjective social QoL (26). Our study was limited by the fact that we did not consider social support which can influence the mental health and disease activity in SLE patients (27). In addition, illness-related stigma and decreased self-esteem may affect social functions such as interpersonal relationships of SLE patients. Therefore, to define the social dimension of QoL in more detail for SLE patients, it will be necessary for social support, perceived stigma, and self-esteem to be considered as important factors.

TOI is composed of the PWB and FWB, and changes over time or in response to physical health intervention programs, at times even more so than total QoL (10). The similarities between the TOI scores with those indicating total QoL in this study suggest that the total QoLin patients with SLE can be improved by active evaluation and management.

In our study, age was not associated with total QoL and all QoL subscales, whereas disease duration was correlated with physical, emotional, and total QoL. There have been several studies on the relationship between age and physical QoL. However, their results are different depending on the research, *i.e.*, while some reported a negative correlation, others reported no correlation between age and physical QoL (28-34). These discrepancies may be due to several factors such as demographic differences between different cohorts. In some studies, it was found that a longer disease duration is associated with better physical health, QoL, mental health, and emotional health (28-31), whereas in other reports, it was shown that there was negative or no association of disease duration with physical health (32-24). It seems that the effect of disease duration on QoL is unclear, considering that the positive correlation was not shown in multiple regression analyses. There were some reports that higher education was associated with lower disease activity (35, 36). However, total QoL and all the QoL subscales were not correlated with educational years as well as disease activity in this study. Thus, we can say that the education years may not affect QoL in patients with SLE.

One of the limitations of our study is that it is a cross-sectional study. Although we analysed using multiple linear regression models to evaluate the relationship between disease activity itself and QoL, a longitudinal designed study needs to disentangle this relationship more exactly. Another limitation was in collecting study samples. SLE activity in this cohort is relatively low. CNS lupus shows comparatively high scores in the SLEDAI scoring system (13). In this study, patients who had cognitive deficits such as mental retardation or an acute state of confusion were excluded to avoid the reporting bias in fulfilling the questionnaires. In this process, some patients who had active disease were ruled out. However, 108 patients among 120 patients who visited our rheumatology clinic were enrolled in this study, which may represent the real world where lots of patients were followed with well-treated and generally mild or inactive disease status.

In conclusion, the QoL of the patients with SLE was lower than that of healthy controls irrespective of disease activity severity. The QoL subscale scores of the SLE patients were associated with the daily dose of glucocorticoids, depression, and fatigue rather than disease activity or damage index. These findings suggest that the comprehensive evaluation of psychological problems and appropriate management could be helpful for increasing QoL in patients with SLE, especially those using higher doses of glucocorticoids, even if disease activity and damage are not severe.

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