The quality of life in Chinese patients with systemic lupus erythematosus is associated with disease activity and psychiatric disorders: a path analysis

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Abstract

Objective

To identify the socioeconomic status, disease activity and psychiatric disorders that contribute to the health-related quality of life (HRQOL) in systemic lupus erythematosus (SLE) patients.

Methods

Data were collected from 170 SLE patients and 210 healthy individuals. All of the patients fulfilled the criteria for the classification of SLE and underwent disease activity assessment according to the SLE disease activity index (SLEDAI). Self-rated scales for anxiety (SAS) and depression (SDS) were used to evaluate the levels of anxiety and depression. The patients' general health status was measured using the Short Form (SF)-36 questionnaire. To provide greater clarity regarding the determinants of HRQOL, path analysis was used to explore the relationships between the various predictors and the health-related quality of life (HRQoL).

Results

SLE patients who have depression and anxiety are more likely to have a lower quality of life compared to those who are not depressed ($r=-0.735$, $p<0.01$; $r=-0.684$, $p<0.01$). All of the variables were significantly correlated with depression except age, gender and marital status. Education was negatively correlated with disease activity ($r=-0.272$, $p<0.05$) and anxiety ($r=-0.312$, $p<0.01$). Disease activity was positively correlated with anxiety ($r=0.198$, $p<0.05$). In addition, work status also correlated with anxiety ($r=-0.294$, $p<0.01$). A path-analytic models analysis suggested that the main influencing factors of HRQoL are the following: depression, anxiety, education level, income/family, disease activity, age, and work status. A χ^2 test ($\chi^2_{15=}17.71$, $p=0.28>0.05$) indicated that the path analysis model had an adequate goodness of fit value. Depression ($\beta=-0.616$, $p<0.05$) contributed the most to HRQOL. Depression, anxiety and disease activity contributed to HRQoL both directly and indirectly through other factors. Socioeconomic factors such as education, income/family and work status, however, did not contribute directly to HRQoL.

Conclusion

HRQoL in SLE is influenced by disease activity and psychiatric disorders. Socioeconomic status has no direct influence on the quality of life of lupus patients, while disease activity has a direct impact on the quality of life. Anxiety and depression were significant predictors of poor HRQoL. Understanding how these factors are inter-related may help clinicians focus their assessments and develop strategies to improve the HRQoL of lupus patients.

Key words

systemic lupus erythematosus, health-related quality of life, socioeconomic status, depression, anxiety,
SLE Disease Activity Index (SLEDAI), path analysis

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Introduction

Systemic lupus erythematosus (SLE) is a chronic inflammatory autoimmune disease that not only leads to multiple organ systems, but is also a significant risk factor for depression and anxiety (1-4). In addition, the disease exerts an unfavourable impact on the health-related quality of life (HRQoL), resulting in a high economic burden on society (5-7). The survival of patients with SLE has increased considerably over the past 2 decades, partly due to earlier diagnosis and better therapeutic approaches (8, 9). With improvements in SLE survival, increased attention has been focused on the reduction in HRQoL associated with this condition. Patients with SLE have reported scores on HRQoL measures that are 30–40% lower than those reported by age- and sex-matched peers. All domains of HRQoL appear to be affected by SLE (10). Capturing decrements and improvements in HRQoL has therefore become important in SLE clinical research, and these aims are advocated by both the US Food and Drug Administration, which provides guidance to SLE clinical researchers, and the Outcome Measures in Rheumatology Clinical Trials group (11, 12). The disease has profound effects on HRQoL that have been documented extensively in the literature (5). The magnitude of the HRQoL reduction in patients with SLE is as substantial as that observed in patients suffering from other severe chronic illnesses such as AIDS and RA (13, 14). Several factors, including socioeconomic status, disease activity and psychiatric disorders, can reportedly influence the quality of life in individuals with SLE. Other factors such as age and disease duration impact the quality of life in lupus patients in a complex manner (15-17). In addition, the chronic medication, damage, and loss of productivity hamper the quality of life in SLE patients (18). Research on the determinants of life quality in SLE patients showed that psychiatric disorders and disease activity are significant negative predictors (19, 20). Several studies used regression analysis to focus on the correlation between socioeconomic status, disease activity, psychiatric disorders and quality of life (2-3). However, analytical methods such as correlation cannot determine causal relationships between variables. Path analysis is a statistical technique for estimating the magnitude and significance (indirect and direct) of hypothetically causal relationships among sets of variables (21).

This study aims to identify which factors, including socioeconomic status, disease activity and psychiatric disorders, contribute to HRQol in patients with SLE and to explore the direct and indirect relationships that exist between the identified variables using path analysis.

Patients and methods

Participants

SLE patients were recruited from the Affiliated Hospital of Nantong University between January 2010 and July 2011. A total of 170 SLE patients and 210 healthy individuals were consecutively invited to participate in a single-center cross-sectional study. The healthy individuals were used as the control group. All of the patients fulfilled the 1997 American College of Rheumatology (ACR) revised criteria for the classification of SLE. Patients were excluded based on either of the following reasons: (1) they did not complete questionnaire; (2) they had comorbidities (*e.g.* serious infections or cardiac, respiratory, gastrointestinal, neurological, or endocrine disease) that could influence SLE activity. This study was approved by the Ethics Committee of the Affiliated Hospital of Nantong University, and written informed consent was obtained from all of the participants.

Measures of clinical variables

The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) was used to measure disease activity (22).

The Revised Self-Rating Anxiety Scale (SAS)

SAS (23) was used to evaluate the level of anxiety-related symptoms during the week prior to the survey. This self-administered test has 20 questions, with 15 items that reflect increasing anxiety levels and 5 questions that reflect decreasing anxiety levels. Each question was scored on a scale of 1 to 4 (rarely, sometimes, frequently, and always, respectively). The scores ranged between 20 and 80, where scores greater than 70 suggest severe anxious symptoms, scores between 60 and 69 indicate moderate to marked anxiety, scores between 50 and 59 suggest minimal to mild anxiety, and scores less than 50 indicate no anxious symptoms.

The Revised Self-Rating Depression Scale (SDS)
SDS (24) is a 20-item questionnaire designed to assess mood symptoms over the past week (*e.g.* 'I feel downhearted, blue and sad'). Each item is scored on a Likert scale ranging from 1 to 4. Scores greater than 70 suggest severe depressive symptoms, scores between 60 and 69 indicate moderate to marked depression, scores between 53 and 59 suggest minimal to mild depression, and scores less than 53 indicate no depressive symptoms.

Measure of the Quality of Life
The general health status of each patient was measured using the Short Form (SF)-36 questionnaire, which measures eight multi-item dimensions: physical functioning (PF, 10 items); role limitations due to physical problems (RP, four items); role limitations due to emotional problems (RE, three items); social functioning (SF, two items); mental health (MH, five items); energy/vitality (VT, four items); body pain (BP, two items); and general health perception (GH, five items). For each dimension, the item scores were coded, summed and transformed on a scale from 0 (worst possible health state measured by the questionnaire) to 100 (best possible health state).

Data analysis
SPSS version 17.0 and AMOS 17.0 (SPSS, Inc., Chicago, IL, USA) were used to perform the statistical analyses for this study. To provide an overview of the relationship between potential factors and HRQoL, correlation analyses were performed with the following variables: age, gender, marital status, work status education, income/ family, SLEDAI score, depression, anxiety and HRQoL. Next, we performed a path analysis to investigate and quantify the hypothesised association between demographic and socioeconomic factors (*i.e.* age, gender, marital status, education and family income), disease impairments and HRQoL. It was estimated and tested with a maximum likelihood algorithm. The chi-square statistic was used where a non-significant test indicated that the model and data were consistent. This test was chosen because it is sensitive to the number of variables included in a model and the sample size available (25). Additional measures of fit were also used to evaluate the model, such as goodness-of-fit index (GFI), adjusted goodness-of-fit index (AGFI), comparative fit index (CFI), and the root mean square error of approximation (RMSEA). The chi-square test assesses whether a significant amount of observed covariance between items remains unexplained by the model and should not be significant. A statistically significant chi-square result ($p<0.05$) indicates a bad model fit. The RMSEA takes into account the error of approximation of the model and should therefore be small (RMSEA<0.08) (26). The GFI and AGFI assess the extent to which the model provides a better fit compared to no model at all. These indices have a range between 0 and 1, where higher values (GFI>0.90, AGFI>0.85) indicate that the model closely fits the data (27). The CFI is an incremental fit index (28) that represents the proportionate improvements in a model fit by comparing the target model with a baseline model (usually a null model in which all of the observed variables are uncorrelated). The values range between 0 and 1, where values larger than 0.90 suggest a good model fit (29).

Table I. Demographic characteristics of SLE patients (n=158).

	Mean±SD	Frequency	Percentage
Age, years	32.9 ±10.2		
Gender			
Male		14	8.8
Female		144	91.2
SAS (≥50 score)		32	20.3
SDS (≥53 score)		52	32.9
SLEDAI score	11.8±9.5		
Marital status			
Single		32	20.3
Married		126	79.7
Education			
<9 years		86	54.4
≥9 years		72	45.6
Work status			
Working		30	19.0
Unemployed		128	81.0
Income/ family			
≤2000 Yuan		100	63.3
>2000 Yuan		58	36.7

Results

Participant characteristics
A total of 170 patients met the eligibility criteria. A small portion, 7.06% (n=12), did not complete the full questionnaire due to lack of interest, resulting in a total enrolment of 158 eligible SLE patients. Table I presents the baseline participant characteristics included in our analysis. Ages ranged from 13 to 60 with an average of approximately 32.9 years (SD=10.2). The majority of our study participants were female (91.2%) and married (79.7%), and the participants tended to have lower income (63.3%) and less than a high school-level education (54.4%). The SLEDAI score of the participants ranged from 2 to 55 (Mean=11.8, SD=9.5).

Correlation analysis
Table II shows the correlation values between each variable. In our study, we found that depressed and anxious

Table II. Correlations between HRQoL and the variables used in this study.

		Age	Gender	Marital status	Work status	Education	Income / family	SLEDAI score	SAS	SDS	HRQoL
Age	*r*	1									
	p	–									
Gender	*r*	-0.051	1								
	p	0.657	–								
Marital status	*r*	**0.546****	-0.037	1							
	p	<0.001	0.744	–							
Work status	*r*	-0.099	0.176	0.012	1						
	p	0.384	0.121	0.919	–						
Education	*r*	**-0.377****	0.106	**-0.250***	-0.140	1					
	p	0.001	0.351	0.026	0.218	–					
Income / family	*r*	-0.127	0.053	0.031	0.101	0.041	1				
	p	0.266	0.645	0.783	0.376	0.717	–				
SLEDAI score	*r*	-0.008	-0.022	0.124	0.103	**-0.272***	**-0.227***	1			
	p	0.946	0.847	0.275	0.364	0.015	0.044	–			
SAS	*r*	0.151	0.195	0.150	**0.294****	**-0.330****	-0.024	**0.198***	1		
	p	0.183	0.085	0.187	0.009	0.003	0.047	0.041	–		
SDS	*r*	0.067	0.119	0.143	**0.303****	**-0.312****	**-0.116***	**0.294****	**0.831****	1	
	p	0.559	0.295	0.209	0.007	0.005	0.835	0.009	0<0.001	–	
HRQoL	*r*	-0.178	-0.082	-0.098	-0.154	**0.307****	0.092	**-0.232***	**-0.684****	**-0.735****	1
	p	0.116	0.474	0.390	0.176	0.006	0.421	0.040	<0.001	<0.001	–

Spearman correlation was used to analyse the relation among gender, marital status, work status, education, income/ family, depression, anxiety and HRQoL. Pearson correlation was used to analyse the normal distribution variables such as age and disease activity and HRQoL.
Significant correlations are indicated (2-tailed): $^{*}p<0.05$, $^{**}p<0.01$.

SLE patients are more likely to have a lower quality of life compared with those who are not depressed (r=-0.735, $p<0.01$; r=-0.684, $p<0.01$). In addition, our results also showed that if the disease activity of patients is higher, their quality of life is lower (r=-0.232, $p<0.05$). However, those who had at least a 9-year education (*vs.* less than 9 years) are more likely to have a higher quality of life (r=0.307, $p<0.01$). All of the variables used in our study were significantly correlated with depression except age, gender and marital status. We also found that education was negatively correlated with disease activity (r=-0.272, $p<0.05$) and anxiety (r=-0.312, $p<0.01$). The disease activity of patients with a family income of more than 2000 Chinese Yuan per month (versus less than 2000 Yuan) is lower (r=-0.227, $p<0.05$), whilea family income is positively with anxiety (r=0.198, $p<0.05$). In addition, work status also correlated with anxiety (r=-0.294, $p<0.01$). Therefore, the above-mentioned demographics and disease characteristics were included in the final path analyses.

Path analysis

A path analysis model was developed to examine the relationship between socioeconomic factors and disease impairments with HRQoL. This model explained 76% of the variance in HRQoL in patients with SLE and indicated that our hypothetical model provides a reasonable explanation of the relationship between demographic factors, disease impairments and HRQoL. A χ^2 test was not significant ($\chi^2_{15=}17.71$, p=0.28>0.05), indicating that this model has an adequate goodness of fit val-

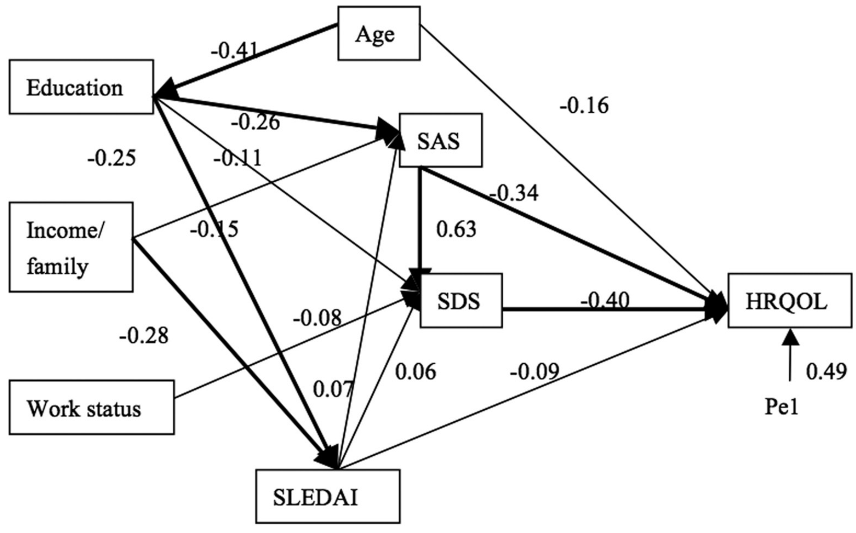

Fig. 1. Hypothetical causal path diagram for HRQoL of SLE patients. Path analysis results showing observed path among study variables. The arrows indicate the hypothetical cause-and-effect relationships between factors.

ue. Further support for the model was provided by an RMSEA value that was less than 0.05(RMSEA=0.048) and CFI, GFI and AGFI values that were all greater than 0.90. All of the hypothesised paths reached significance ($p<0.05$). The standardised path direct coefficients for the hypothetical model are presented in Figure 1. The direct, indirect, and total effects are displayed in Table III.

The results of this analysis suggest that HRQoL is mainly influenced by the following factors: depression, anxiety, level of education, income/family, disease activity, age, and work status. Among the variables explored in the path analyses, the strongest effect (-0.616) was found between depression and HRQoL; we also found that depression, anxiety and disease activity contributed both directly to HRQoL as well as indirectly through other factors. Socioeconomic factors such as education, income/family, age and work status, however, did not contribute directly to HRQoL. Instead, these factors contributed indirectly to HRQoL through other factors including depression, anxiety and disease activity. These findings highlight the benefit of using path analysis to examine the complex means by which socioeconomic factors and disease impairments interrelate with HRQoL.

Table III. Direct and indirect effect of variables in study model.

Variables	Direct effect	Indirect effect	Total effect	Total effect sorting
Age	–	-0.097	-0.097	6
Income / family	–	0.130	0.130	5
Education	–	0.238	0.238	3
Work status	–	0.031	0.031	7
SLEDAI score	-0.090	-0.065	-0.155	4
Anxiety	-0.338	-0.255	-0.593	2
Depression	-0.402	-0.214	-0.616	1

Discussion

Although socioeconomic status, disease activity and psychiatric disorders have been reported to affect quality of life, to our knowledge, no path analysis of quality of life prediction in SLE patients has been published. The strength of path analysis is that it provides an explicit theory of the relationships between variables, rather than simply testing a set of data from a linear association. In addition, path analysis produces clear results of the strength of the inherent mathematical relationships. Although regressions analysis provides information about the correlations of mathematical relationships, path analysis explicitly examines confirmatory relationships. Path analysis is also superior to regression analysis because it provides an explanation of both causal relations and the relative importance of the alternative path of influence (30). In the present study, we used a path analysis method to evaluate the interaction between variables and the quality of life in Chinese SLE patients. The models fit with the data reasonably well, indicating that it is possible to identify the key determinants of HRQoL in individuals with SLE using path analysis. The model coefficients and pathways show that a complex interaction exists between socioeconomic factors, disease impairments and HRQoL.

Several studies have focused on the importance of socioeconomic factors for the clinical outcome of SLE patients. It has been reported that SES, such as education and zip code-based annualised household income, are associated with HRQoL in SLE (31). Trupin and colleagues have reported that lower individual SES, as measured by education, household income, or poverty status, is associated with physical and mental health consequences in lupus patients (32). In our path-analytic models, we found that SES has no direct influence but correlates with HRQoL indirectly via depression, anxiety and SLEDAI. A previous study found that educational qualification had a significant association with anxiety and depression. The authors reported that monthly family income has no effect on the frequency of anxiety (33). Bultink and colleagues reported that unemployed lupus patients have a significantly higher frequency of neuropsychiatric organ damage (16). We have also found that work status directly impacts depression. It was unclear whether socioeconomic factors play an important role in lupus disease activity. It has been reported that private insurance or Medicare and higher education were also associated with less disease activity during SLE diagnosis (34). However, other groups found no relationship between socioeconomic status and disease outcome or organ damage (35, 36). In the current study, we have found that education level and family income affect disease activity.

Although HRQoL was found to be worse in SLE patients in all of the studies (37), associations between the measures of disease activity and HRQL have been examined with mixed findings. It has been reported that disease activity correlates with the SF-36 subscales. Vu *et al*. reported that higher disease activity on the SLEDAI correlates with lower scores in two SF-36 domains: bodily pain and general health (38). Fortin *et al*. found that an increase in disease activity over time led to worsening in all of the SF-36 domains (39). In contrast, other studies have failed to find a relationship between indices of disease activity and measures of HRQoL.

Gladman *et al*. reported that the total SF-36 score was not correlated with SLEDAI (40). A recent study reported that SLE patient QoL subscales are associated with daily glucocorticoid dose, depression, and fatigue rather than disease activity or damage (19). From our path analysis, we also showed that disease activity has both direct and indirect effects on the total SF-36 score.

A recent study reported that SLE patients with significantly poor health-related quality of life are also significantly more depressed and anxious compared to their healthy counterparts (41). Pettersson *et al*. reported that lupus patients with no present symptoms have a higher HRQoL and lower levels of depression and anxiety (42). A survey of Chinese SLE patients showed a significant correlation between anxiety and depression within all of the SF-36 domains (32). With our path analysis, we confirmed that both anxiety and depression are significant predictors of poor HRQoL.

Several studies have found that various other factors, such as age, may mediate HRQoL levels. A negative correlation has been reported between age and physical health (43). Goulia found that older patients with rheumatic diseases, including SLE, experience more impairment in HRQoL compared to younger patients (15). Our studies reveal that age has a direct correlation with HRQoL and contributes to it indirectly via a mediating factor (*e.g.* education).

The present study has several limitations. The first potential limitation is the failure to differentiate between men and women; gender differences in SLE patients require further analysis in a future study. Secondly, analysing psychological factors with self-report questionnaires implies that we have to take into account. Thirdly, the sample size was rather small and from a single hospital, and treatments such as daily glucocorticoid dose were not investigated. Fourth, we only used the measures of the SLEDAI to assess lupus activity. However, this index cannot reflect organ damage. Finally, comorbidities, which generally have a strong adverse impact on HRQoL in SLE, were not investigated.

In summary, our study confirms that socioeconomic status has no direct influence on the quality of life of lupus patients. Disease activity has a direct impact on quality of life. Anxiety and depression were significant predictors of poor HRQoL. To improve the quality of life in SLE patients, we should focus more attention on potential modifiable factors, including disease activity and psychosocial factors.

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