

The impact of disease activity and psychological status on quality of life for Chinese patients with primary Sjögren's syndrome

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Objective: The primary purpose of the present study was to survey the quality of life (QoL) in primary Sjögren's syndrome (pSS) and to analyze the relationships between disease activity, anxiety/depression, fatigue, pain, age, oral disorders, impaired swallowing, sicca symptoms, and QoL.

Patients and methods: A survey was conducted on 185 pSS patients and 168 healthy individuals using the Short Form 36 health survey for QoL. Disease activity was assessed using the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index. We examined these data using independent samples *t*-tests, Mann-Whitney U test, chi squared analysis, and linear regression.

Results: The result for each domain in Short Form 36 health survey was lower in pSS patients than in healthy controls, especially the score in the dimension of role physical function. In the bivariate analysis, age, pain, fatigue, disease activity, disease complication, anxiety/depression, oral disorders, and impaired swallowing correlated with QoL. Also, in the linear regression model, pain, fatigue, disease activity, impaired swallowing, and anxiety/depression remained the main predictors of QoL.

Conclusion: pSS patients had a considerably impaired QoL compared to the controls, and pSS could negatively affect the QoL of patients. Measuring QoL should be considered as a vital part of the comprehensive evaluation of the health status of pSS patients, which could contribute some valuable clues in improving the management of disease and treatment decisions.

Keywords: primary Sjögren's syndrome, quality of life, disease activity, depression

Background

Primary Sjögren's syndrome (pSS) is a systemic autoimmune disease characterized by chronic inflammation of exocrine glands such as the lachrymal and salivary glands, leading to dry eyes and dry mouth.¹ A majority of pSS patients also suffer from extraglandular symptoms including fatigue, mental disorders, musculoskeletal, and neurological symptoms.² In addition, pSS patients exhibit a 44 times higher relative risk for lymphoma development compared to the general population.³ This disease predominantly affects middle-aged women (women:men ratio 9:1), but can also be detected in children and the aged.⁴ pSS is a common autoimmune rheumatic condition, second only in frequency to rheumatoid arthritis, with a prevalence between 0.1% and 4.8% in various populations.⁵ pSS has a negative influence on health-related quality of life (HR-QoL)⁶ and is associated with high health care costs,⁷ pain,⁸ fatigue,⁹ work disability,¹⁰ and anxiety/depression.¹¹ Moreover, dry mouth in pSS may lead to oral

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uncomfortableness, trouble talking, impaired swallowing, tooth decay, and continual oral infections. Though these complications are not life-threatening, the complication and chronicity of symptoms can lead to heavy debility and a reduction in patient's quality of life (QoL).¹² Individuals with pSS also experience voice disturbances and specific voice-related manifestations that are related to decreased QoL.¹³

QoL is defined as the general well-being of individuals and societies, based on the individual's culture and life values with respect to that individual's objectives, expectation, and standards. HR-QoL is the impact of disease and its treatment of the individual's ability to function based on physical, mental, and social well-being.¹⁴ Variables that may affect the QoL of pSS patients include disease activity, fibromyalgia,¹⁵ comorbidity,² medical therapy,¹⁶ pain, fatigue, dryness, and anxiety/depression. In the literature, there are various studies investigating fatigue and discomfort, oral HR-QoL,¹⁷ employment and disability,¹⁸ and psychological status of pSS patients. However, to our best knowledge, there are a few previous studies focusing on how these variables might affect the HR-QoL in pSS, especially in China. The objective of the present study was to evaluate QoL in pSS and to explore the relationships between disease activity, fatigue, anxiety/depression, oral disorders, impaired swallowing, pain, age, dryness, and QoL.

Patients and methods

Participants

The study was carried out in the Affiliated Hospital of Nantong University from July 2016 to July 2017. pSS patients were outpatients or inpatients from the Department of Rheumatology; age- and sex-matched controls were randomly selected from the general population. The Ethics Committee of the Affiliated Hospital of Nantong University approved this study (approval number 2017-K003), and all participants met the American–European Consensus Group Criteria for pSS and gave written informed consent. All study participants were asked to complete the related questionnaires. Medical assessments also were recorded. There was no significant difference between the two groups in terms of age, sex, education level, occupation, and income/year.

Inclusion criteria and exclusion criteria

Inclusion criteria consisted of pSS diagnosis, age over 18 years, no known cognitive deficits, and Chinese speaking. Exclusion criteria consisted of secondary Sjögren syndrome, having serious systemic diseases lately (lymphoma, similar renal/pulmonary involvement, myositis, or vasculitis), and

participants with a physical or psychological problem (eg, cancer, psychiatric disorders) which may confound the outcome.

Methods

This study included 185 pSS patients according to the American–European Consensus Group criteria and 168 healthy controls. Sicca symptoms were assessed by the dryness domain of the European League Against Rheumatism Sjögren's Syndrome Patient-Reported Index.¹⁹ Disease activity was assessed using the European League Against Rheumatism Sjögren's Syndrome Disease Activity Index (ESSDAI).²⁰ Mental state was assessed through Hospital Anxiety and Depression Scale; it had acceptable internal consistency and test–retest reliability, with a Cronbach's alpha of 0.85 and intraclass correlation coefficient of 0.90.²¹ Independent samples *t*-tests, chi-squared analyses, Mann–Whitney U test, and linear regression modeling were used to analyze the data.

Demographics and clinical characteristics

Demographic characteristics and clinical variables were examined. Demographic variables included age, sex, education, marital status, and socioeconomic status. Next, differences in mean Hospital Anxiety and Depression Scale scores and QoL scores between pSS patients and control groups were analyzed. Clinical data such as disease duration and medication use were obtained by asking the patients or searching their electronic medical records.

The medical outcomes study, 36-item short-form health survey (SF-36)

The SF-36 instrument is aimed to rate HR-QoL within the previous 4 weeks. It includes 36 statements, with eight scales assessing two dimensions. The first dimension is physical health function and includes the following four specific scores: physical functioning (the extent to which health interferes with various activities), physical role functioning (the extent to which health interferes with usual daily activities), bodily pain, and general health. These physical scores are summarized by the physical composite score (PCS). The second dimension is the mental health function, which includes the following four specific scores: vitality, social functioning, emotional role functioning (limitations due to emotional problems), and mental health. These four mental scores are summarized by the mental composite score

(MCS). Each scale gives a standardized score that ranges from 0 to 100, with 0 illustrating the worst possible health state and 100 illustrating the best possible health state.^{22,23} In addition, this scale has been translated and validated for use in Hong Kong.^{24,25}

Convergent validity and discriminant validity were satisfactory for all except the social functioning scale. Cronbach's α coefficients ranged from 0.72 to 0.88 except 0.39 for the social functioning scale and 0.66 for the vitality scale. Two weeks test-retest reliability coefficients ranged from 0.66 to 0.94.²⁶

Fatigue severity scale

Fatigue was measured by using the fatigue severity scale. It is a self-reported instrument developed to explore the impact and severity of fatigue. It involves nine questions to assess the severity of fatigue, as it relates to daily activities such as physical functioning, exercise, work, and family/social life. The scores range from 1 to 7 for each item, with a lower score signifying less fatigue (the best condition is 9 points and the worst condition is 63 points). We used a cut-off score ≥ 4 to define fatigue.²⁷

Other related scales

Pain was investigated by the visual analog scale to identify pain severity. Patients were asked to estimate their experiences of pain during the last week, each on a visual analog scale of 0–10, with a higher score implying more severe pain.²⁸ The MD Anderson Dysphagia Inventory²⁹ measures patient's swallowing disorders symptoms (score ranges from 0 to 100, with higher scores indicating more severe symptoms), and the Oral Health Impact Profile 14³⁰ was used to measure oral distress.

Data analysis

Data were analyzed by IBM SPSS 22.0 package program. Continuous variables were expressed as mean \pm SD. Before the continuous variables were compared, it was checked whether the parametric test assumptions were met or not. Qualitative variables were presented as numbers and percentages. The distinction between independent groups in terms of the qualitative variables was evaluated by using chi-squared test. While conformity to normal distribution was evaluated by using Shapiro–Wilk test, the homogeneity of the variances was examined by using the Levene's test. The difference between independent groups in terms of numerical variables was investigated by using the independent samples

t-test in cases where the parametric test assumptions were met and by using the Mann–Whitney U test in cases where the said assumptions were not met. The presence of a correlation between the numerical variables was determined by Spearman's correlation coefficient. Multicollinearity between variables was checked by computing variance inflation factors before inclusion into the model. A backward procedure was used, removing variables with a *P*-value of >0.05 in the multivariable model in order of significance, until the best-fitting model was identified. While we regarded *P*-values <0.05 in each study as significant, we set stringent significant levels of *P*-values in the combined analysis based on Bonferroni's correction.

Written informed consent

Written informed consent was obtained from all individual participants included in the study.

Results

Patient characteristics

Of the 203 eligible cases, 185 patients fully completed the provided questionnaires, with a rough response rate of 91%. In pSS patients ($n=185$), the mean age was 50.12 ± 12.13 years, and 94.6% of the subjects were women. Demographic, clinical, and laboratory characteristics of the pSS patients and controls are presented in Table 1. Furthermore, the impact of disease-related variables on severity of depression and anxiety was assessed. Whether depression, anxiety, and disease-related variables can be determinants of QoL among affected individuals was also investigated. There was no significant difference in age, sex, education, occupation, and income/year between the pSS individuals and the controls ($P>0.05$). Tests of collinearity indicated good content validity.

QoL of pSS patients and controls

The scores of global SF-36, including PCS and MCS of pSS patients and the controls, are presented in Figure 1. Eight domains of SF-36 of the pSS patients and controls are shown in Table 2. The average global SF-36 score of pSS patients was 56.01 ± 18.13 , ranging from 13.94 to 98.13. Compared with the controls, all SF-36 domains and total scores were much lower in pSS patients ($P<0.01$).

Correlations between fatigue, disease activity etc, and QoL in pSS patients

As shown in Table 3, we found significant correlations between erythrocyte sedimentation rate, comorbidity,

Table 1 Demographic, clinical, and psychological characteristics of the pSS patients and controls

Clinical characteristics	pSS (n=185)	Controls (n=168)	$t/\chi^2/z$	P-value
Age, mean±SD, years	50.12±12.13	50.25±11.17	-0.105	0.916
Sex, female, n (%)	175 (94.6)	160 (95.2)	0.075	0.784
Marital status, n (%)			5.590	0.018
Married	172 (93)	165 (98.2)		
Single/divorced/bereaved	13 (7)	3 (1.8)		
Education, mean±SD, years	12.44±4.19	11.99±4.64	0.945	0.345
Employment status, n (%)			0.931	0.335
Employed	83 (44.9)	84 (50)		
Unemployed	102 (55.1)	84 (50)		
Income/person/year, yuan, n (%)			-0.671	0.502
<15,000 yuan	55 (29.7)	49 (29.2)		
15,000–33,000 yuan	55 (29.7)	61 (36.3)		
>33,000 yuan	75 (40.5)	58 (34.5)		
Type of medical insurance, n (%)			3.582	0.167
With basic medical insurance	170 (91.9)	164 (96.5)		
Self-pay	14 (7.6)	6 (3.6)		
Other	1 (0.5)	0 (0)		
HADS-A, mean±SD	6.43±3.99	3.04±2.78	9.315	0.000
HADS-D, mean±SD	6.63±4.16	3.89±2.8	7.318	0.000
Oral disorders, n (%)	165 (89.2)	101 (60.1)	8.246	0.000
Impaired swallowing, mean±SD	75.52±18.04	—		
Disease duration, mean±SD, years	4.34±5.24	—		
VAS pain (range 0–10), mean±SD	2.15±2.56	—		
ESR, mean±SD mm/h	29.16±23.99	—		
Hospitalization, yes, n (%)	124 (67)	—		
Comorbid conditions, yes, n (%)	112 (60.5)	—		
ESSDAI, mean±SD	9.56±7.3	—		
ESSPRI, mean±SD	4.18±1.89	—		
Impaired swallowing, n (%)	51 (27.57)	—		
Medicine use, n (%)	153 (82.7)	—		
Glucocorticoids, yes, n (%)	56 (30.3)	—		
Hydroxychloroquine, yes, n (%)	140 (75.7)	—		
Others, yes, n (%)	143 (77.3)	—		

Abbreviations: ESR, erythrocyte sedimentation rate; ESSPRI, European League Against Rheumatism Patient Reported Index; ESSDAI, European League Against Rheumatism Sjögren's Syndrome Disease Activity Index; HADS, Hospital Anxiety and Depression Scale; HADS-A, Hospital Anxiety Scale; HADS-D, Hospital Depression Scale; pSS, primary Sjögren's syndrome; VAS, visual analog scale.

hospitalization, and European League Against Rheumatism Sjögren's Syndrome Patient-Reported Index and QoL.

Stepwise linear regression analysis for the QoL

Stepwise linear regression analysis revealed depression, pain, and impaired swallowing were notably associated with the SF-36 PCS in pSS patients. Moreover, depression, anxiety, disease activity, fatigue, and impaired swallowing significantly accounted for the SF-36 MCS (Table 4). Finally, these variables explained 65.5% and 72.5% of the variance in PCS and MCS, respectively.

Discussion

pSS patients experience lower QoL compared to age- and sex-matched controls. Impaired QoL is associated with symptoms such as fatigue, pain, anxiety/depression, oral disorders, impaired swallowing, as well as disease activity, exemplifying the value of optimal management of all aspects of the disease. The underlying pathogenic process between depression and pSS remains unknown. Some studies attempted to explore depression in pSS patients; depression was reported as a relative factor of reduced QoL in Moroccan pSS patients.³¹ Segal et al³² stated that somatic fatigue was the main predictor of physical function and general health; additionally, depression was the key predictor of emotional

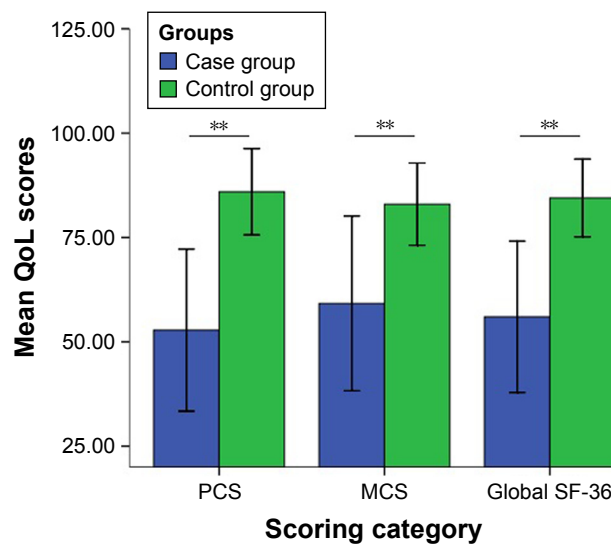


Figure 1 Global SF-36, PCS, and MCS among pSS patients and controls.

Note: ** $p < 0.01$.

Abbreviations: MCS, mental composite score; PCS, physical composite score; pSS, primary Sjögren's syndrome; QoL, quality of life; SF-36, Short Form 36 health survey.

well-being in the US. In agreement with the findings of previous studies, our study found that the strong correlation between MCS of the SF-36 and anxiety/depression in pSS patients emphasized the significance of the psychological dimension of SF-36. Consequently, recognition of determinants of depression and anxiety and their impact on QoL has noticeable clinical value, especially in China.

Fatigue is another essential symptom and has been reported to be associated with a reduction in HR-QoL in pSS.³³ A study from Germany reported that patients with pSS frequently suffer from fatigue that increases the risk of work disability and requires treatment by numerous health care specialists.³⁴ As expected, bivariate analysis showed that

fatigue correlated with all domains of the SF-36. Fatigue and pain are the most common extraglandular symptoms,³⁵ and pain severity explained 14% of the variance in disability of daily activities in Korean patients with pSS.³⁶ Our results were in line with previous studies reporting that pain is a major symptomatic problem related to low physical functioning and health outcomes. Therefore, systematic monitoring of pain treatment seems essential.

The results showed that pSS patients had a moderate level of disease activity, with a mean ESSDAI score of 9.56. Similarly, the mean ESSDAI score of pSS patients from multicenter clinics of France was 9.04.³⁷ The comparison to age- and sex-matched healthy controls suggests that the disease-related symptoms of pSS patients are not attributed to the natural process of aging, but age was truly thought to play a crucial role in dysregulation of the neuroendocrine system.³⁸ We found that patient-perceived swallowing disorders were relatively common in pSS and increased with disease severity, which was uniquely associated with reduced QoL. Since eating and drinking form an important part of social interaction, dysphagic pSS patients often eat in seclusion because of shame. Also, they worry choking on their food or develop aspiration pneumonia. Frequent worries can decrease the QoL even more and aggravate anxiety. Therefore, health care professionals need to pay more attention to pSS patients who manifest swallowing symptoms and to strengthen the assessment of swallowing function of the pSS patients in clinical practice.

Notably, a significant difference was found in the marital status between the groups. The possible explanation is that women with pSS often suffer from vaginal dryness. Many pSS patients were unable to continue regular marital relationship due to sexual difficulties. Disease severity and disease duration may cause an increase in the divorce rate.

There are several limitations of this study. First, this study is cross-sectional in design, which does not allow for following up the progress of the examined variables during the course of the disease, and thus, we are unable to comment on the causal relationships. Second, it fails to make a distinction between men and women because of the great sex disparity. Third, all subjects were from a single hospital and the scales were all self-administered, which might give rise to possible biases of the outcomes. Even so, we still consider that our results may provide important insights into this complex process by identifying the associations between variables and QoL in pSS patients.

Table 2 Eight domains in SF-36 of patients with pSS and the controls

	pSS (n=185)	Controls (n=168)	P-value
Physical function	76.51±23.10	92.97±11.28	<0.001
Role physical	32.56±38.62	92.56±19.83	<0.001
Body pain	74.51±23.55	88.34±15.79	<0.001
General health	41.19±19.67	69.95±16.05	<0.001
Vitality	55.16±15.35	74.08±10.99	<0.001
Social function	69.12±21.93	87.35±12.16	<0.001
Role emotional	42.88±45.43	92.06±21.96	<0.001
Mental health	66.98±13.26	78.43±8.53	<0.001
Physical composite score	52.80±19.41	85.96±10.33	<0.001
Mental composite score	59.21±20.92	82.98±9.85	<0.001

Note: Data are presented as mean±SD.

Abbreviations: pSS, primary Sjögren's syndrome; SF-36, Short Form 36 health survey.

Table 3 Correlations between disease activity, anxiety/depression, fatigue, pain, age, and QoL in pSS patients

Domains of SF-36	ESSDAI		VAS		HADS-A		HADS-D		FSS		Age	
	R	P-value	R	P-value	R	P-value	R	P-value	R	P-value	R	P-value
PF	-0.232	0.001**	-0.334	0.000**	-0.253	0.001**	-0.363	0.000**	-0.355	0.000**	-0.368	0.000**
RP	-0.354	0.000**	-0.251	0.001**	-0.415	0.000**	-0.403	0.003**	-0.453	0.000**	-0.308	0.000**
BP	-0.304	0.000**	-0.697	0.000**	-0.216	0.003**	-0.250	0.001**	-0.312	0.001**	-0.081	0.270
GH	-0.361	0.000**	-0.250	0.001**	-0.495	0.000**	-0.480	0.000**	-0.420	0.000**	-0.203	0.005**
VT	-0.274	0.000**	-0.274	0.000**	-0.463	0.000**	-0.497	0.000**	-0.542	0.000**	-0.271	0.000**
SF	-0.428	0.000**	-0.342	0.000**	-0.400	0.000**	-0.493	0.000**	-0.467	0.000**	-0.238	0.001**
RE	-0.299	0.000**	-0.230	0.002**	-0.475	0.000**	-0.463	0.000**	-0.404	0.000**	-0.166	0.000**
MH	-0.249	0.001**	-0.254	0.000**	-0.648	0.000**	-0.672	0.000**	-0.337	0.000**	-0.195	0.008**
PCS	-0.287	0.000**	-0.413	0.000**	-0.461	0.000**	-0.493	0.000**	-0.388	0.000**	-0.294	0.000**
MCS	-0.391	0.000**	-0.324	0.000**	-0.560	0.000**	-0.586	0.000**	-0.530	0.000**	-0.231	0.002**

Note: ** $P < 0.01$.

Abbreviations: BP, bodily pain; ESSDAI, European League Against Rheumatism Sjögren's Syndrome Disease Activity Index; FSS, Fatigue Severity Scale; GH, general health; HADS-A, Hospital Anxiety Scale; HADS-D, Hospital Depression Scale; MCS, mental composite score; MH, mental health; PCS, physical composite score; PF, physical functioning; pSS, primary Sjögren's syndrome; QoL, quality of life; RE, role emotional; RP, role physical; SF, social functioning; SF-36, Short Form 36 health survey; VAS, visual analog scale; VT, vitality.

Conclusion

Patients with pSS had a considerable impaired QoL in comparison with the healthy subjects. pSS could have an unfavorable influence on the QoL of patients. Measuring QoL should be considered as a vital part of the comprehensive evaluation of the health status of pSS patients, which could contribute some valuable clues to improving the management of disease and treatment decisions.

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Disclosure

The authors report no conflicts of interest in this work.

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Table 4 Result of analysis of forward stepwise ordered linear regression models in SF-36

Predictors	β	SE	P-value	B (95% CI)
MCS				
Depression	-0.260	0.392	0.001	-1.309 (-2.083, -0.535)
FSS	-0.251	0.725	0.000	-3.053 (-4.483, -1.623)
Impaired swallowing	0.171	0.068	0.004	0.198 (0.064, 0.332)
ESSDAI	-0.181	0.160	0.001	-0.525 (-0.916, -0.280)
Anxiety	-0.165	0.411	0.037	-0.866 (-1.677, -0.055)
PCS				
Impaired swallowing	0.322	0.065	0.000	0.346 (0.217, 0.475)
Depression	-0.327	0.282	0.000	-1.526 (-2.082, -0.970)
Pain	-0.260	0.444	0.000	-1.969 (-2.846, -1.093)

Abbreviations: ESSDAI, European League Against Rheumatism Sjögren's Syndrome Disease Activity Index; FSS, Fatigue Severity Scale; MCS, mental composite score; PCS, physical composite score; SE, standard error; SF-36, Short Form 36 health survey.

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