

Disease activity affects all domains of quality of life in patients with rheumatoid arthritis and is modified by disease duration

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Abstract

Objective

This study was conducted to determine how disease activity affects quality of life (QOL) and its interaction with functional impairments, and disease duration in patients with rheumatoid arthritis (RA).

Methods

This cross-sectional study enrolled 230 patients with RA from a rheumatology clinic in Taiwan and 227 healthy controls matched according to age, sex, marital status, and education. QOL was measured using the Taiwan version of the short form of the World Health Organisation Quality of Life (WHOQOL-BREF) questionnaire. Activity of RA was assessed by the Disease Activity Score in 28 joints using the erythrocyte sedimentation rate (DAS28). Functional disability was assessed by the Health Assessment Questionnaire (HAQ). Multiple regression analyses were performed to explore independent effects and interactions among DAS28, HAQ, and duration after controlling demographic factors.

Results

A higher HAQ score, longer duration of disease, and higher DAS28 score were independently associated with lower QOL scores. DAS28 score affected most items in all physical, psychological, environment, and social domains after controlling other factors. Besides, patients with longer disease duration showed aggravated scores on many facets of the physical and psychological domains, if their disease activity was elevated.

Conclusion

Disease activity affects QOL of RA patients in all domains. It also aggravates scores in physical and physiological domains among those with a longer duration.

Key words

rheumatoid arthritis, quality of life, disease activity, WHOQOL-BREF

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Introduction

Rheumatoid arthritis (RA) is a chronic inflammatory disease that has a considerable negative impact on the quality of life (QOL) (1). Individuals with RA typically suffer from chronic pain and joint inflammation, resulting in irreversible joint deformities, physical disability, functional impairment, depression, fear, and psychological distress (2). Additionally, some patients face social isolation and discrimination (3). Thus, RA may affect many aspects of individuals' lives, including those beyond "physical" or "psychological" domains (4). RA is not yet curable, and the major treatment goals are to control disease activity and to reduce the impact of RA on QOL. Therefore, identification of the major factors that affect QOL in RA patients may be useful for the continuous improvement of treatment strategies.

The three major determinants for clinical outcome in RA are disease activity, chronic damage to joints, and functional impairment (5). These factors have been identified as predictors of QOL in RA patients. However, since they are interrelated, one could confound others (6, 7). For example, as the duration of RA increases, joint damage and functional impairment also increase. Functional impairment is influenced primarily by disease activity ("reversible component") in the early phases of RA and resulted from accumulated joint damage ("irreversible component") in the later phases of RA (8). Therefore, the independent effect and interactions of these factors should be explored in one model simultaneously after control of other potential confounders. However, very few studies have conducted such analyses.

The EuroQOL-5 dimension (EQ-5D) and Short-Form-36 (SF-36) have been the two most frequently used generic instruments for assessment of the utility and psychometric characteristics of QOL in RA patients. However, SF-36 measures only physical and psychological components (9). Many studies reported that the social and environmental domains are important in QOL because they can restrict the role of RA patients in society (10-15). Hence, we

tried to determine how the above factors simultaneously affect physical, psychological, social, and environment domains. To achieve these objectives, the Taiwan version of the short form of the World Health Organisation Quality of Life (WHOQOL-BREF) questionnaire (16) was chosen to measure the QOL in this study. Disease activity was measured by the 28-joint Disease Activity (DAS28) score, and functional impairment by the Health Assessment Questionnaire (HAQ). We conducted this cross-sectional study because patients with a broad range of disease duration can provide fairly reliable estimates of health outcomes (17).

Patients and methods

RA population

The Ethics Review Board of Changhua Christian Hospital (Changhua, Taiwan) approved this study before commencement. All patients who came to the outpatient clinic of the Department of Allergy, Immunology and Rheumatology of Changhua Christian Hospital from May 2011 to December 2011 were invited to participate. All enrolled patients were over 16 years of age, fulfilled the diagnostic criteria of RA according to the 1987 American College of Rheumatology criteria (18), and provided written informed consent. The DAS28 score was calculated using the erythrocyte sedimentation rate. The duration of RA, educational level, marital status, employment status, and monthly income of each patient were recorded. A total of 230 patients were enrolled.

Reference (control) population

The control population comprised 227 healthy individuals of the general population of Taiwan matched with our RA patients in terms of sex, age, marital status, and education (Table I). These subjects were sampled randomly from a database of the 2001 National Health Interview Survey (NHIS), which was conducted by the National Health Research Institute and Bureau of Health Promotion, Department of Health of Taiwan (19).

The 2001 NHIS was designed to provide nationwide estimates of overall health status, health-related behav-

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iours, and usage of medical resources in the general population of Taiwan. The Taiwan version of the WHOQOL-BREF was one of the tools included in this national survey. A total of 27,160 eligible persons living in 7,357 households were selected by multistage sampling. The household size, age, sex, and urbanisation index of this sample matched those of the general population in January of 2001. The final 2001 NHIS data were collected from 25,464 persons living in 6,271 households, corresponding to a response of 93.8% by person and 91.4% by household (20). A total of 13,083 persons aged 20–65 years completed the WHOQOL-BREF. This cohort did not include elderly people so we added a community sample taken from metropolitan Taipei as a match for the 46 RA patients who were over 65 years of age.

QOL questionnaire

Investigations have suggested that the WHOQOL has good validity and reliability (15, 21). Only a few studies have assessed the QOL of RA patients using the WHOQOL-BREF (22, 23). Our version of the WHOQOL-BREF consisted of two global items (G1 for overall QOL and G2 for general health) and 26 items in the physical, psychological, social, and environment domains (21). There were two items specific to the Taiwanese WHOQOL-BREF. One item regarding “respect from others” was in the social domain and the other item regarding “eating what one likes to eat” was in the environment domain. The score of each item was 1 to 5, with a higher score indicating a better QOL. The different domains had different numbers of individual items. Each domain score was calculated as 4 × the mean score of all items. Thus, each of the four domains had a score from 4 to 20.

Statistical analyses

First, we conducted a descriptive analysis to compare the demographic characteristics of patients and control subjects. Then, we compared the QOL scores in the four domains of RA patients with those of healthy subjects. Multiple linear regression analyses were done to identify the major determinants (es-

Table I. Demographic and clinical characteristics of patients with rheumatoid arthritis (RA) and matched healthy subjects.

Characteristic	RA patients	Healthy subjects	<i>p</i> -value
Number of subjects	230	227	
Sex (% female)	80.0%	80.2%	0.962
Age (mean ± SD)	56.1±11.5	56.0±11.6	0.902
Marital status			0.755
Other	17.4%	16.3%	
Married	82.6%	83.7%	
Education (years)			0.472
≤12	86.5%	84.1%	
>12	13.5%	15.9%	
Employment			0.011
Other	70.0%	58.6%	
Full-time	30.0%	41.4%	
Monthly income			0.666
≤680 US dollars	70.9%	72.7%	
>680 US dollars	29.1%	27.3%	
DAS28 (mean ± SD)	3.98±1.51		
HAQ (mean ± SD)	0.50±0.63		
Disease duration (years)	6.53±6.72		

pecially demographic factors) in the four domains of the WHOQOL-BREF. These determinants were subsequently used to construct a linear regression model for RA patients. Additional clinical variables (DAS28, HAQ, disease duration) were used to assess the effects of each domain and of individual items. We also added the interaction terms of combined DAS28 and HAQ, HAQ and disease duration, and DAS28 and disease duration into this model to explore the interactive effects. Forward selection was used to select significant independent variables as the results are better in line with previous literature and clinical outcomes. $p < 0.05$ was used as the inclusion criterion. All data were collected and analysed using SAS ver9.2 (SAS, Cary, NC, USA).

Results

Basic characteristics of patients and controls

We recruited 230 RA patients and 227 control subjects who were matched for demographic and clinical characteristics. Enrolled patients and healthy subjects were comparable in sex, age, education, marital states, and monthly income, as summarised in Table I. Thirty percent of RA patients and 41.4% of controls were employed full-time. The mean duration of RA for enrolled patients was 6.53±6.72 years. The mean DAS28 score was 3.98±1.51 and mean HAQ score was 0.50±0.63, indicating

that our patients are mostly mild to moderate in severity.

Multiple linear regression analyses of QOL comparing RA patients and controls

Multiple linear regression analyses showed that age, education, and income level were significant determinants for different domains of the WHOQOL-BREF, indicating the necessity to adjust for these parameters (Table II). Model constructions for items and domains of WHOQOL-BREF with adjustment for demographic factors showed that RA patients had significantly lower scores in the physical ($p < 0.005$) and psychological ($p < 0.005$) domains than those of control subjects (Table II). In addition, the scores of both domains in RA patients worsened as disease duration increased ($p < 0.005$ for both domains). Interestingly, patients with RA tended to have higher scores in the environment domain as compared to the control subjects ($p < 0.005$).

Multiple linear regression analyses of QOL scores in individual domains and individual items in RA patients

Table III shows the results of multivariate regression analyses of the WHOQOL-BREF scores of RA patients in all four domains and of individual items in each domain. After controlling related risk factors, higher DAS28 scores were independently associated with lower

Table II. Multiple regression coefficients and standard errors (in parentheses) in patients with rheumatoid arthritis (RA) and healthy subjects.

WHOQOL Domains	Constant	RA (yes/no)	Disease duration (years)	Age (years)	Education (>12 years/≤12 years)	Monthly income (> vs. ≤680 US dollars)
Physical	14.40 (0.18)**	-1.25 (0.27)**	-0.10 (0.02)**	—	—	0.64 (0.26)**
Psychological	12.06 (0.62)**	—	-0.09 (0.02)**	—	0.71 (0.33)*	0.67 (0.27)*
Social	14.20 (0.10)**	—	—	—	—	—
Environment	11.14 (0.50)**	0.78 (0.19)**	—	0.04 (0.01)**	1.03 (0.27)**	—

* $p < 0.05$; ** $p < 0.005$. WHOQOL: World Health Organisation Quality of Life questionnaire.

Table III. Multiple regression coefficients and standard errors (in parentheses) for WHOQOL outcomes after adjustment for confounders[†].

Domains	Facets	DAS28	Disease duration (years)	HAQ	DAS28 duration*	DAS28 HAQ*	Duration HAQ*	Sex (female/male)	Age (years)
Physical	Overall QOL			-0.85 (0.32)*			0.03 (0.01)*		0.013(0.006)*
	General health	-0.17 (0.06)**	-0.04 (0.01)**	-0.81 (0.32)*			0.02 (0.01)*		0.015(0.006)*
		-0.46 (0.17)*		-3.64 (0.95)**		0.34 (0.16)*			0.037(0.015)*
	Pain					-0.1 (0.02)**			
	Medication			-1.51 (0.49)**	-0.009(0.004)*		0.04 (0.02)*		
	Energy			-0.72 (0.34)*	-0.006(0.003)*				0.015(0.005)**
	Mobility	-0.16 (0.06)*	-0.04 (0.01)**	-1.12 (0.3)*				0.43 (0.16)*	
	Sleep	-0.15 (0.06)*	-0.02 (0.01)*	-0.97 (0.33)**		0.15 (0.06)*			
	ADL	-0.14 (0.06)*		-1.05 (0.33)**				0.33 (0.14)*	
	Work	-0.14 (0.04)**					-0.03 (0.01)**	0.34 (0.14)*	0.011(0.005)*
Psychological		-0.36(0.16)*		-2.37 (0.82)**	-0.02 (0.01)*				0.049 (0.017)**
	Spirit	-0.25 (0.07)**		-0.73 (0.32)*					
	Concentration	-0.16 (0.06)*		-1.04 (0.36)**		0.15 (0.06)*			
	Appearance			-0.28 (0.11)*	-0.005(0.002)*				0.015(0.006)*
	Esteem				-0.02(0.01)*				0.03(0.006)**
Social	Negative feeling			-1.02 (0.41)*	-0.02(0.01)*				
	Relations						-0.02 (0.01)*		
	Sex	-0.1 (0.03)**							-0.019(0.005)**
Environment	Support	-0.08 (0.04)*					-0.02 (0.01)**		
		-0.45 (0.11)**	-0.17 (0.05)**		0.03 (0.01)*			0.77 (0.32)*	0.046 (0.012)**
	Safety	-0.22 (0.06)**		-0.69 (0.31)*		0.15 (0.06)*			0.017(0.006)*
	Finance	-0.17 (0.05)**							0.015(0.005)*
	Leisure		-0.03 (0.01)*						
	Home	-0.13 (0.04)**		-0.54 (0.22)*		0.12 (0.04)*			0.014(0.004)**
	Health care	-0.12 (0.03)**						0.28 (0.11)*	0.008(0.004)*
	Transportation	-0.11 (0.05)*	-0.04 (0.02)*	-0.71 (0.26)*		0.12 (0.04)**			
	Eating		-0.06 (0.02)*					0.37 (0.14)*	0.014(0.005)*

* $p < 0.05$, ** $p < 0.005$,[†]Confounders include income, marriage, employment, and education.

WHOQOL: World Health Organisation Quality of Life questionnaire; DAS28: Disease Activity Score in 28 joints using the erythrocyte sedimentation rate; HAQ: Health Assessment Questionnaire; ADL: activities of daily living.

QOL scores in all four domains. At the level of individual items, a higher DAS28 score was significantly associated with lower scores for four items in the physical domain (mobility, sleep, activities of daily living, and work), two items in the psychological domain (spirit and concentration), two items in the social domain (sexual life and social support), and five items in the environment domain (safety, finance, home, healthcare availability, and transportation).

A longer duration of disease was associated with lower scores on mobility and sleep in the physical domain, and leisure, transportation, and eating in the environment domain. Higher HAQ scores, or, more severe functional im-

pairment, were associated with lower QOL scores in the physical and psychological domains. At the level of individual items, higher HAQ scores were associated with lower scores on five items in the physical domain (medication, energy, mobility, sleep, and activities of daily living), four items in the psychological domain (spirit, concentration, appearance, and negative feelings), and three items in the environment domain (safety, home, and transportation).

In the analysis of the three interaction terms DAS28/disease duration, DAS28/HAQ, and disease duration/HAQ that were added into the model, only the term of DAS28 and disease duration had a significant influence to the WHOQOL outcomes. After a de-

tailed regression analysis with multiple interaction terms, higher DAS28 scores combined with longer duration of RA seemed to have additional negative impacts on facets of medication and energy in the physical domain, and facets of appearance, esteem, and negative feeling in the psychological domain, while DAS28 scores alone have no direct influence on these items. Interaction terms with positive coefficients in Table III, mostly on combined DAS28 and HAQ, reflect the over-adjustment effect from these two independent factors in multivariate regression analysis.

Discussion

To our limited knowledge, this study is the first to demonstrate unequivocally

that disease activity is an independent predictor of scores in all four domains of the WHOQOL, and the first to investigate the interactions between 3 major factors: DAS28, disease duration and HAQ (Tables III).

Disease activity and functional impairment provided different composite measurements of the clinical characteristics of RA patients. Therefore, improvement in disease activity would positively improve QOL scores independent of functional impairments, which corroborates with results from model constructions based on utility measures (24, 25) and psychometry using the SF-36 (26). Our study also demonstrates that disease activity and functional impairments both had impacts on physical and psychological domains, respectively, but functional impairment had no significant independent effect upon most items of the social and environmental QOL domains while disease activity did. In other words, RA activity is a major and important predictor for each domain in WHOQOL because patients might become accustomed to functional impairments measured by the HAQ. A similar situation has also been reported in patients with osteoarthritis (27).

Another key finding is that disease duration seems to intensify the effect of disease activity and this interaction plays a major role especially in the physical and psychological domains of WHOQOL. Therefore, we concluded that disease activity has the most significant impact on RA patients' QOL, and the longer these patients suffer from this disease, the worse their QOL can be.

Furthermore, it is interesting to see that age and disease duration had some opposite effects on QOL (Table II). In particular, our multivariate analyses suggested that increased age was associated with better scores on many individual items in the environment domain. Perhaps older RA patients in Taiwan are more resourceful to seek for a more intensive medical treatment, as they generally have more family members and/or friends available for assistance. In contrast, RA patients with a longer disease duration seemed to suffer from decreased scores in mobility and sleep in the physical domain, and

with leisure, transportation, and eating in the environment domain (Table III), which corroborate with the usual progressive nature of RA.

Results from this study also demonstrate that RA patients had significantly lower QOL scores in the physical and psychological domains than matched healthy controls did (Table II). This finding is consistent with those reported in previous studies which evaluated RA patients with the WHOQOL-BREF (15, 23). However, we also found that RA patients in Taiwan had significantly higher scores in the environment domain after correcting for potential confounders (28). The same trend seems to occur in Taiwanese patients who have epilepsy or who are undergoing dialysis (29, 30). These findings may be explained, at least in part, by the universal coverage provided by the National Health Insurance in Taiwan or by the public support for RA patients in Taiwan.

In a similar study conducted by Haroon *et al.*, QOL was also assessed using WHOQOL-BREF. However, only HAQ were found to independently affect QOL and functional disability was the most important factor affecting QOL in RA of that study (23). In addition, the present study enrolled more healthy subjects for the control group and had a much larger patient sample size, incorporated more demographics variable, and assessed individual items in different domains. Nevertheless, some limitations in this study should be mentioned. The present study only enrolled out patients from one medical center. As the outpatients are usually less severe than those who are hospitalised, it should be cautious that our results may be an underestimation to the hospitalised RA and generalisation to them. Another limitation is that significant determinants such as depression or cardiopulmonary disease which could have impact on the co-morbidity of QOL were not adjusted for.

Conclusion

Disease activity affects item scores in physical, psychological, social and environment domains independent of the HAQ score and disease duration in patients with RA, and the longer these pa-

tients suffer from this disease, the greater the impact of disease activity on RA patients' QOL would be. As we continuously improve the control of disease activity in RA patients, attention should be paid to those with a longer duration and follow-up QOL monitoring must also be obtained to corroborate our findings and hypothesis.

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