



## Structural Equation Modeling on Health-related Quality of Life of Patients with Ankylosing Spondylitis

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(Received 08 Aug 2016; accepted 18 Jan 2017)

### Abstract

**Background:** Ankylosing Spondylitis (AS) is a chronic, progressive, and inflammatory disease. The objective of this study was to construct a hypothetical model to determine factors affecting health-related quality of life (HRQOL) of AS patients (ASHRQOL).

**Methods:** A survey was conducted on 275 patients who visited Chonnam National University Bitgoeul Hospital. Data of different variables were collected over two months in 2015.

**Results:** A hypothetical model did not reach recommended level of fit verification. Therefore, health perception variable was eliminated on theoretical basis. Path between function and HRQOL was added after eliminating unimportant path before completing the final modified model.

**Conclusion:** The final revised model met recommended levels of fit test except AGFI. The model explained 57.6% of ASQOL. Further study is needed to develop efficient interventional strategy for improving ASHRQOL.

**Keywords:** Ankylosing spondylitis, Environmental support, Depression, Function

### Introduction

Ankylosing Spondylitis (AS) is a chronic, progressive, and inflammatory disease that can cause stiffness and pain on the back and peripheral joints. It can also cause inflammation of body parts (e.g., eyes, heart, lungs) and changes to body structure involving the axial skeleton (1). Morbidity of AS has been reported to be approximately 0.1-0.4% in the US (2). However, its actual rate could be higher since AS is easily misinterpreted as other diseases or simple back pain (3).

Factors affecting QOL include personal factors (4-8) such as smoking and sex, symptomatic factors (3,9,10) such as pain, stiffness, fatigue, quality of sleep (QOS), depression, and function (6,11,12), bio-physiological factors (13,14) such as hematological findings and BMI, non-pharmacological factors (15) such as exercise and

hot spring therapy, cognitive factors (16) including self-awareness, and environmental factors (17) including social support.

However, previous studies do not reflect symptomatic effects on AS patients' daily performance since they measure other parameters of QOL without theoretical basis. Instead, they predict HRQOL based on simple inter-factorial equations for each independent factor. Therefore, various factors need to be explored in order to improve AS patients' HRQOL based on relevant HRQOL model and validate each factor in a multi-dimensional and integral way.

All factors are verified mainly in chronic patients using Wilson & Cleary's HRQOL model (18-20). This model is very useful since it reflects general characteristics of AS patients. This model also includes personal and environmental factors that

reflect disease characteristics, symptoms, function, health awareness, and concept of HRQOL. This study was based on that structuring model to explain HRQOL of AS patients (ASHRQOL). Personal factors such as sex, smoking status, economic status, education, occupation, duration of illness, and duration of symptoms must be considered as factors of ASHRQOL (4-8,21-23). However, using categorically independent variable as a dummy variable is not recommended or practical (24). Thus, variables used in the structural model were limited to age, economic status, and smoking, the most powerful variables related to disease specificity. Smoking frequency (smoking) rather than smoking duration was validated as a key factor in this study because smoking intensity was more harmful than smoking duration (5).

C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and body mass index (BMI) are factors that affect QOL (14). In this study, CRP and ESR were validated as bio-physiological factors. Fatigue exerts negative effects on the quality of life of patients with ankylosing spondylitis (25). It also increases the limitation of their function (10). Nocturnal and general pain is strongly correlated with function, disease activity, and ASHRQOL (26). Morning stiffness also shows a significant correlation with HRQOL and the number of edematous joints of AS patients (27).

Anxiety and depression can significantly worsen disease activity and functional limitations (9,28). In this study, fatigue, pain, and morning stiffness were validated as symptomatic factors affecting QOL. Depression was parametrized based on results of many studies showing that depression and anxiety had direct impact on quality of life. Anxiety items were included in depression assessment tools (29).

Physical activity has shown positive effects on symptoms, functioning, and ASHRQOL (30-32). According to a meta-analysis of 10 papers, physical therapy can affect AS patients (33). Therefore, non-pharmaceutical factors were measured by physical activity.

The aim of this study was to construct a hypothetical model to determine factors affecting

health-related quality of life (HRQOL) of AS patients (ASHRQOL).

## Materials and Methods

### Samples

This study used a cross-sectional design. A minimum of > 250 cases were needed in this study considering the characteristic of AS being a rare incurable disease (24).

A total of 75 cases were used in our final analysis (282 questionnaires were distributed). All participants > 19 years old were diagnosed as AS. They were on drug therapy for at least four weeks. Patients provided informed consent before participating in this study. Of these, five cases dropped out and two cases were not analyzed because patients had > 10% missing values for each measured variable due to their insincere replies. These seven cases were excluded from analysis.

### Data Collection

All procedures performed in this study involving human participants were in accordance with ethical standards. All data were collected after obtaining approval from Chonnam National University Hospital Biomedical Research Ethics Committee (Approval number CNUH-2015-009).

This study was conducted at a rheumatology outpatient clinic in Chonnam University Hospital. Data were collected during a 2-month period in 2015. All researchers and trained data handlers were posted at the out-patient clinic after receiving approval before conducting this study.

In-body measurements for height, weight, and blood test for CRP and ESR were performed within two months after commencing this study. In each questionnaire, participants were required to answer all questions individually after reading each question (or after question were read to them and written by data handlers on request). Researchers recorded smoking, alcohol drinking, period after diagnosis, and medication through direct interviews or e-chats. If there were insufficient or omitted details, information was supplemented by direct contact between data handler and patient.

### Data analysis

IBM SPSS Statistics 20.0® (Chicago, IL, USA) and IBM SPSS AMOS 21.0® were used for data analysis. General characteristics and clinical characteristics of subjects were analyzed by descriptive statistics. Normality of descriptive statistics for observed variables was verified using median, mean, skewness, and kurtosis. Pearson's correlation coefficient was used to analyze relations between major key factors. Confirmatory factor analysis was used to identify the validity of latent variables. Structural equation modeling was used to verify the QOL model of ankylosing spondylitis patients and indirect/direct path coefficients of factors affecting ASHRQOL. Maximum likelihood that postulated multivariate normality was used to verify model structuring. To verify the fitness of the proposed model,  $\chi^2$  values, absolute fit index (GFI), modified fit index (AGFI), elemental mean square approximation error (RMSEA), suitable index (CFI), standard fit index (NFI), and Tucker-Lewis index suitable (TLI) were used.

### Validity, reliability, and rigor

In this study, Cronbach's  $\alpha$  value on environmental support was 0.972 using Medical Outcome Study Social Support Survey (34). Cronbach's  $\alpha$  on symptoms was 0.92 using the Korean version

Bath Ankylosing Spondylitis Disease Activity Index (35). Cronbach's  $\alpha$  value on depression was 0.923 using Korean Beck Depression Index-II (29). Cronbach's  $\alpha$  on function was 0.961 using Korean Bath Ankylosing Spondylitis Functional Index. Measure of health awareness was scored according to Status of Health using JH Oh's 1-point question tool adapted from the "Health Perception Questionnaire" sub-standard. Measure of physical activity was converted as successive score of MET (min/week) using Korean International Physical Activity Index. Cronbach's  $\alpha$  value on HRQOL was 0.799 using Korean ASAS-HI (36).

### Results

The mean age of study subjects was 40 years (range, 19 to 77 years). The skewness was below  $\pm 2.0$  and kurtosis was below 10.0 for all measured factors except CRP and physical activity, which satisfied the hypothesis of normal distribution. Skewness and kurtosis for CRP were 5.950 and 45.68, respectively. They were 3.67 and 17.71 for physical activity, respectively, which did not satisfy any hypothetical normal distribution. Thus, log-transformed statistical analysis was performed (Table 1).

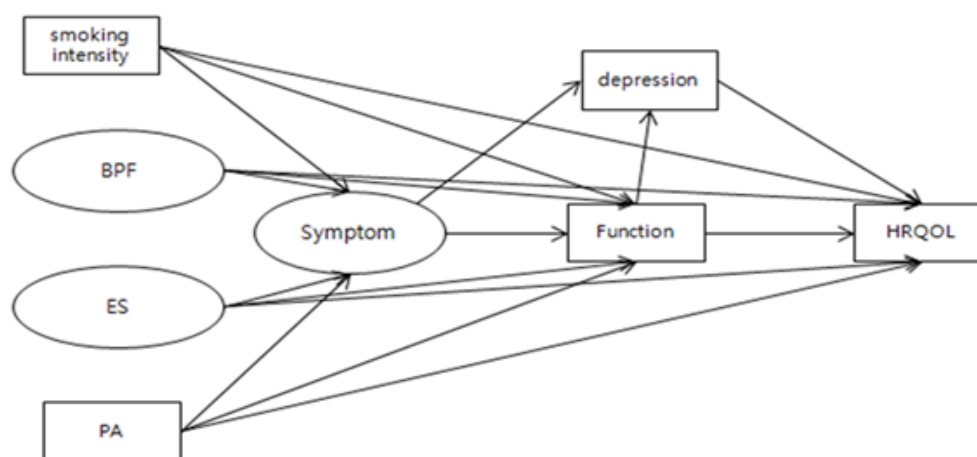


Fig. 1: Hypothetical model

BPF=Biological Physiological Factor, ES=Environmental Support, PA=Physical Activity, HRQOL=Health related Quality of Life

Factors that showed inter-factorial correlation coefficient  $> 0.75$  included material and affectionate support, positive social support, informational and emotional support, affectionate and positive social support, informational and emotional support, positive social and informational emotional support, and pain and stiffness. Affectionate and positive social support along with informational and emotional support was possibly related to latent variable of environmental support. Pain and stiffness were tied to latent variable of symptom. Results from this study indicated that there was no multicollinearity between independent factors.

Test results of the original hypothetical model (Fig. 1) were  $\chi^2 = 260.602$  ( $p < 0.001$ ,  $df = 70$ ), GFI = 0.895, AGFI = 0.821, RMSEA = 0.278, CFI = 0.920, NFI = 0.895. Results did not necessarily meet the recommended level of confidence of fitness index (FI). Thus, the original model was modified to achieve a simpler model with a sufficiently high FI. The index correction model met all satisfactory levels of FI confidence with the following results:  $\chi^2 = 164.634$  ( $p < 0.001$ ,  $df = 57$ ), GFI = 0.916, AGFI = 0.866, RMSEA = 0.083, CFI = 0.953, NFI = 0.930, and TLI = 0.936.

**Table 1:** Descriptive statistics of the measured variables (n=275)

<i>Variables</i>	<i>Mean<math>\pm</math>SD (Range)</i>	<i>Skewness</i>	<i>Kurtosis</i>
Smoking intensity	0.23 $\pm$ 0.41(0-2)	1.612	1.889
CRP <sup>a</sup>	0.56 $\pm$ 1.20(0-12)	5.95	45.68
ESR <sup>b</sup>	15.53 $\pm$ 14.82(0-80)	1.70	3.121
Material support	78.65 $\pm$ 17.35(20-100)	-0.90	0.71
Affectionate support	78.90 $\pm$ 17.88(20-100)	-0.94	0.80
Positive Social support	79.63 $\pm$ 18.18(20-100)	-0.86	0.40
Information Emotional support	75.64 $\pm$ 18.49(20-100)	-0.61	-0.03
Physical Activity	5172.56 $\pm$ 4405.91(0-32880)	3.67	17.71
Fatigue	4.65 $\pm$ 2.48(0-10)	-0.61	-0.84
Pain	9.73 $\pm$ 7.21(0-30)	0.59	-0.42
Stiffness	6.73 $\pm$ 5.38(0-20)	0.653	-0.57
Depression	13.59 $\pm$ 9.60(0-58)	1.14	2.13
Function	17.10 $\pm$ 22.72(0-96.60)	1.72	2.27
Health perception	2.67 $\pm$ 0.14(1-5)	0.14	-0.02
HRQOL <sup>c</sup>	5.70 $\pm$ 4.04(0-17)	0.58	-0.30

<sup>a</sup>CRP=C-reactive protein, <sup>b</sup>ESR=Erythrocyte sedimentation rate, <sup>c</sup>HRQOL=Health-related Quality of Life

Bootstrapping® program (IBM SPSS AMOS 21.0) was used for indirect-effect, direct-effect, and total-effect analysis of the final correction model. Results indicated that, among factors affecting AS HRQOL, physiological factors had direct effect of 0.192 ( $P < 0.01$ ), environmental support had negative direct effect of 0.303 ( $P <$

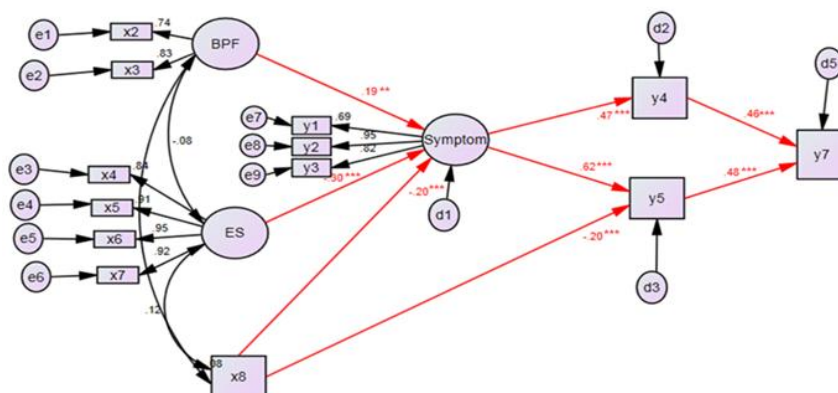
0.01), physical activity had negative direct effect of 0.197 ( $P < 0.01$ ) on symptoms, while symptoms had direct effect of 0.474 ( $P < 0.01$ ) on depression. Symptoms also showed direct effect of 0.625 on function. Physical activity showed negative direct effect of 0.204, negative indirect effect of 0.123, and negative total effect of 0.327 on

function. Depression showed direct effect of 0.459 while function showed direct effect of 0.475 on AS HRQOL with statistically satisfactory level of confidence. Among 20 hypotheses and hypothetical models, 13 were eliminated and one

was newly established. Eight hypotheses were verified to have statistically satisfactory levels of confidence (Fig. 2). Detailed results are shown in Table 2.

**Table 2:** Hypothesis of the final modified model

Endogenous variable	Hypothesis	Final Modified Model result
Symptom	H1 Smoking intensity could effect on symptom. (remove)	
	H2 Physiological factor could effect on symptom.	H1 support
	H3 Environmental support could effect on symptom.	H2 support
Depression	H4 Physical activity could effect on symptom.	H3 support
	H5 Symptom could effect on depression.	H4 support
	H6 Depression could effect on function. (remove)	
Function	H7 Smoking intensity could effect on function. (remove)	
	H8 Physiological facto could effect on function r. (remove)	
	H9 Symptom could effect on function.	H5 support
Health perception	H10 Environmental support could effect on function.	
	H11 Physical activity could effect on function.	H6 support
	H12 Depression could effect on health awareness. (remove)	
Health -related Quality of Life	H13 Smoking intensity could effect on health awareness. (remove)	
	H14 Function could effect on health awareness. (remove)	
	H15 Environmental support could effect on health awareness. (remove)	
	H16 Depression could effect on HRQOL.	H7 support
	H17 Smoking intensity could effect on HRQOL. (remove)	
	H18 Health awareness could effect on HRQOL. (remove)	
	H19 Environmental support could effect on HRQOL. (remove)	



**Fig. 2:** Hypothetical model

x2=C-reactive protein, x3=Erythrocyte sedimentation rate, x4=Material support, x5=Affectionate support, x6=Positive Social support, x7=Information Emotional support, x8=Physical Activity, y1=Fatigue, y2=Pain, y3=Stiffness, y4=Depression, y5=Function, y7=Health related quality of life, BPF=Biological Physical Factor, ES=Environmental Support, e1~e9=Measurement error, d1,2,3,5=Structural error.

\*\*\*:  $P < 0.001$ , \*\*:  $P < 0.01$ , \*:  $P < 0.05$



## Discussion

The final model proposed in this study was appropriate to explain AS HRQOL with 57.6% increase in explanation and adequate FI for confidence (except for AGI). Our results emphasize that depression should be a parameter since it significantly affects AS HRQOL. However, health awareness should be excluded because of poor evidence indicating its effect on AS HRQOL.

Pooling variables with different characteristics as a single latent variable is not justified. Aging can lower QOL and income while education can increase QOL. Personal characteristics should be considered in successive data because they have the same characteristics as other observed variables that measure a single latent variable. In this study, intensity of smoking was the most important key factor that could represent the characteristic of disease in "general characteristics", making it acceptable as an observed variable. Similar to our study, a narrative Turkish AS HRQOL study (12) has shown no significant relation between ESR and HRQOL or between CRP and HRQOL.

In a study on relationship among pain, family support, and HRQOL, Lim and Moon have reported that family support shows relevant correlation with pain and strong relevant correlation with QOL (3). Therefore, these four areas of social support are relevant to pain.

Spouse support has indirect effect via sense of loss while medical support has no indirect or direct effect on women's QOL after hysterectomy (37). In addition, social support has indirect effect on HRQOL via awareness and symptoms according to an obstructive sleep apnea study after substituting environmental with social support (38). Likewise, Oh and Lee have reported that environmental factors have significant indirect and direct effects on elderly QOL in patients with degenerative arthritis via symptom, function, and health awareness (39). Results of this study also showed no direct effect of environment support on HRQOL. However, it had significantly indirect effect on HRQOL through parameters of symptom, depression, and function.

Furthermore, there was a significant correlation ( $r = 0.619$ ,  $P = 0.028$ ) between fatigue and function, including significant correlation with physical role ( $r = -0.245$ ,  $P = 0.044$ ), vitality ( $r = -0.366$ ,  $P = 0.002$ ), general health ( $r = -0.390$ ,  $P = 0.010$ ), body pain ( $r = -0.436$ ,  $P < 0.001$ ), and mental health ( $r = -0.271$ ,  $P = 0.025$ ). Relevant co-relationship between quality of life and fatigue (co-relationship study between fatigue and other clinical factors) has been previously reported (16). This study also showed a significant correlation between fatigue and QOL ( $r = 0.37$ ,  $P < 0.05$ ).

Batmaz et al. have explained that QOL has a direct correlation with Quality of Sleep (QOS) ( $\beta = 0.265$ ,  $P = 0.017$ ) with 7% total change of effectiveness and a relevant co-relationship between subjective QOS and QOL (40). Although QOS is an influential factor indicating the need for objective measures and validation, it was excluded from our study as a bio-physiological factor. Nevertheless, QOS could be added as a parameter in future HRQOL studies of AS patients.

Our results showed that anxiety ( $r = 0.56$ ,  $P = 0.0001$ ) and depression ( $r = 0.60$ ,  $P = 0.001$ ) had correlation with QOL and function (anxiety:  $r = 0.40$ ,  $P = 0.0001$ ; depression:  $r = 0.39$ ,  $P = 0.001$ ). These results corroborated with an earlier report (28) showing a significant co-relationship between depression ( $r = 0.28$ ,  $P < 0.001$ ) and function. Depression ( $r = 0.48$ ,  $P < 0.001$ ) was correlated with HRQOL using the Korean Beck Depression Index-II (KBDI-II) method which included anxiety as a parameter.

Many previous studies have suggested a significant correlation between function and QOL. Therefore, function has sufficient theoretical basis as an influential factor for deciding ASHRQOL.

In a study on 75 AS patients, physical therapy has decreased disease activity from 38.7 to 26.7 points, functional limitation from 4.33 to 3.81 points, and pain level from 41.1 to 24.0 points (41). Another AS study has shown a 10.0-point decrease in disease activity and 7.3 points increase in health status a year later because of a 3-week rehab program (42). In this study, direct effect of physical activity on HRQOL through

mediating parameters of symptoms, depression, and function was insignificant. Meanwhile, a significant indirect effect ( $\beta = -0.167$ ,  $P = 0.007$ ) on QOL was observed. Research on physical activity among AS patients and inter-study differences in either pre- or post-therapy programs is limited.

## Limitations

The following three study limitations have to be carefully considered for this study. First, population representation was a limitation because all participants were out-patients from a rheumatology clinic in Chonnam University Hospital. Second, there might be data bias because self-reporting questionnaire was used. Third, generalization was difficult because other factors beyond our control were not addressed in this study.

## Conclusion

As a result of the final revised model fit test, the model met recommended levels except for AGFI. The model explained 57.6% of ASQOL. Based on our study, the following recommendations are made to promote AS HRQOL. First, function and depression were identified as important factors affecting QOL. Therefore, peer therapy (e.g., AS anonymous or group-activities) that can manage depression in local settings should be considered. Consultation with psychiatrists should also be considered when needed. Second, our results confirmed that symptoms and physical activity were important factors for improving function and depression. Therefore, program should be developed to improve physical activity of AS patients. Additionally, environmental support, physical activity, and bio-physical factors were confirmed to be able to improve AS symptoms. Environmental support was more important than bio-physical and physical activity factors. Development of social welfare system and family support program could improve environmental support. Finally, interventional nursing programs that can manage these integral factors

need to be developed to vigorously improve ASHRQOL.

## Ethical considerations

Ethical issues (Including plagiarism, informed consent, misconduct, data fabrication and/or falsification, double publication and/or submission, redundancy, etc.) have been completely observed by the authors.

## Acknowledgments

This study was supported by the Songwon University.

## Conflict of interest

Authors have no conflicts of interest to declare.

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