CE

1.5 ANCC Contact Hours

Causal Relationships Between Modifiable Risk Factors of Cognitive Impairment, Cognitive Function, Self-Management, and Quality of Life in Patients With Rheumatic Diseases

JiSuk Park ▼ HyunSoo Oh ▼ Won Park ▼ SeongRyul Kwon ▼ OkKyung Ham ▼ YeonOk Suh ▼ HyeSun Jeong ▼ WhaSook Seo

BACKGROUND: Rheumatic diseases are one of the most common types of chronic conditions that affect cognitive functions.

PURPOSE: To develop and verify a hypothetical model of causal relationships between modifiable risk factors for cognitive impairment, cognitive function, self-management, and quality of life in patients with rheumatic diseases.

METHODS: A hypothetical model was developed on the basis of empirical evidence. The fitness of the model was verified on 210 patients with rheumatic diseases.

RESULTS: The prevalence of cognitive impairment was 49.0%. Smoking, underlying diseases, pain, and fatigue had a significant direct effect on cognitive impairment. Only cognitive impairment had a significant direct effect on self-management. Fatigue, anxiety, depression, and cognitive function had a significant direct effect on quality of life.

CONCLUSIONS: The importance of proper management of symptoms and health habits should be emphasized to prevent and delay the progression of cognitive impairment and improve adherence to self-management regimens and quality of life.

Introduction

Rheumatic diseases are considered to be autoimmune diseases and are characterized by chronic inflammatory injury to multiple organs. There are more than 100 types of rheumatic diseases and the most common are rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), ankylosing spondylitis, fibromyalgia, Paget's disease, and Sjögren syndrome (De Melo & Da-Silva, 2012). Patients with rheumatic disease, in particular, may exhibit multidimensional problems associated with physical, psychosocial, and cognitive impairment (Bartolini et al., 2002; Shin, Katz, & Julian, 2013) that diminish quality of life (Rupp, Boshuizen, Dinant, Jacobi, & Van Den Bos, 2006). Rheumatic diseases frequently occur in young and middle-aged adulthood when cognitive decline is uncommon. Some degree of age-related cognitive decline is normal in healthy elderly adults, however, patients with rheumatic diseases may experience accelerated cognitive decline as they age.

Because the majority of chronic diseases are life-long conditions that can be managed but not cured, patients with a chronic disease need to learn how to manage their illness, that is, how to undertake self-management (Shin, Katz, et al., 2013). Although cognitive function is important for self-management and quality of life (Shin, Katz, et al., 2013), little is known of this issue in a background of rheumatic disease. The majority of previous studies regarding cognitive impairment in rheumatic diseases have focused on a few specific domains of cognitive functions, and thus, have only partially elucidated relationships among risk factors of cognitive impairment. Furthermore, findings regarding relationships between

JiSuk Park, PhD, RN, Head Nurse, Inha University Hospital, Incheon, Republic of Korea.

HyunSoo Oh, PhD, RN, Professor, Department of Nursing, Inha University, Incheon, Republic of Korea.

Won Park, PhD, MD, Professor, School of Medicine, Inha University, Incheon, Republic of Korea.

SeongRyul Kwon, PhD, MD, Professor, School of Medicine, Inha University, Incheon, Republic of Korea.

OkKyung Ham, PhD, RN, Professor, Department of Nursing, Inha University, Incheon, Republic of Korea.

YeonOk Suh, PhD, RN, Professor, Department of Nursing, Soonchunhyang University, Asan, Republic of Korea.

HyeSun Jeong, PhD, RN, Professor, Department of Nursing, Kongju National University, Gongju, Chungcheongnam Do, Republic of Korea.

WhaSook Seo, PhD, RN, Professor, Department of Nursing, Inha University, Incheon, Republic of Korea.

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cognitive impairment and associated risk factors vary to the extent that it is difficult to apply findings in clinical practice. Therefore, we considered that a comprehensive approach was required to identify the complicated and dynamic relationships between cognitive impairment, associated risk factors, self-management, and quality of life in patients with a rheumatic disease. In particular, we sought to clarify the strength and direction of causal relationships to enhance understanding and to predict the development of cognitive impairment in these patients.

Background

Rheumatic disease is one of the most common chronic conditions that affect cognitive functions, and accumulating evidence indicates meaningful cognitive impairment in patients with RA, SLE, and fibromyalgia (De Melo & Da-Silva, 2012; Glass, 2008). Previous reports indicate that the prevalence of cognitive impairment was 30% in RA, 27% in SLE, and 15% in fibromyalgia (Rodríguez-Andreu et al., 2009), which seem to be relatively high compared with 8% prevalence of age-related cognitive impairment in healthy individuals (Appenzeller, Bertolo, & Costallat, 2004). The most commonly affected cognitive domains in rheumatic diseases are visuospatial perception, executive function, memory, and attention (Roebuck-Spencer et al., 2006), and more than 90% of patients with a rheumatic disease have attention and memory deficits (Zachrisson, Regland, Jahreskog, Kron, & Gottfries, 2002).

The pathophysiological mechanisms underlying the development and progression of rheumatic disease-associated cognitive impairment are unclear, and it appears that multidimensional factors contribute. A review of the literature revealed that the following risk factors have been associated with cognitive impairment in rheumatic diseases: (1) demographic-related factors (age, gender, and education) (Abdul-Sattar, Goda, & Negm, 2013; Can & Gencay-Can, 2012; Fava et al., 2013); (2) health-threatening factors (smoking, alcohol consumption, and obesity) (Katz et al., 2012; Murray et al., 2012); (3) underlying diseases (cardiovascular diseases, hypertension, and diabetes mellitus) (Fava et al., 2013; Katz et al., 2012; Shin, Julian, & Katz, 2013); (4) steroid treatment (Katz et al., 2012; Shin, Julian, et al., 2013); and (5) psychosocial factors (anxiety, depression, and stress) (Can & Gencay-Can, 2012; Fava et al., 2013; Katz et al., 2012; Kim, 2012; Shin, Katz, et al., 2013).

Rheumatic diseases often cause diverse changes in daily life due to presenting symptoms and functional impairments, which sometimes lead to permanent disability. Therefore, self-management for patients with a rheumatic disease should involve more than simple adherence to treatment or symptom management guidelines, and include behavioral, psychological, and emotional management to promote psychosocial well-being and quality of life (Iversen, Hammond, & Betteridge, 2010). Accordingly, a complicated cognitive process incorporating attention, memory, reasoning, judgment, executive function, and problem solving ability is needed for self-management.

Aims

This study was conducted with the following three objectives: (1) to develop a hypothetical model that illustrates causal relationships between modifiable risk factors for cognitive impairment, cognitive function, self-management, and quality of life; (2) to verify the fitness of the derived hypothetical model by examining fit between its predictions and observed data; and (3) to elucidate direct and indirect causal relationships among variables in the derived model.

Methods

Study Design and Subjects

A nonexperimental, cross-sectional correlation design was adopted. Study subjects were 210 outpatients who were diagnosed with rheumatic disease (by a rheumatologist and based on diagnostic test results) and that were being treated at a rheumatology outpatient clinic at a university hospital in Incheon, South Korea. Potential candidates were nominated by physicians at the rheumatology outpatient clinic. However, only subjects who agreed to participate in the study after being informed of the study purposes and procedures and who satisfied the following criteria were recruited: (1) an age of $\geq$ 19 years; (2) able to read and comprehend the questionnaire; and (3) provided informed consent.

The rule of thumb regarding optimal sample size for maximum likelihood estimations during structural equation modeling and path analysis is that the study cohort should include more than 200 subjects to obtain stable parameter estimates (Bae, 2011). Actually, data were collected from 210 subjects based on expectations of missing or erratic responses. The missing data rule used in this study was that if more than 10% of data were missing, then the data for that subject were excluded from the study. However, none had to be excluded because of missing data in this study.

Construction of the Hypothetical Model

Studies have indicated that diverse risk factors affect cognitive impairment in rheumatic diseases, such as demographic characteristics, underlying diseases, and health-threatening, physiological, disease-related, drug-related, and psycho-emotional factors. However, only modifiable factors that can be potentially managed by treatment, education, intervention, or behavioral changes were included in the model.

With respect to health-threatening factors, obesity, smoking, and alcohol consumption have been shown to be significantly associated with cognitive impairment in stroke (Brainin et al., 2015) and rheumatic diseases (Katz et al., 2012). The presence of underlying diseases, such as hypertension, cardiovascular diseases, and diabetes mellitus, and disease-related factors, such as disease progression, disease activity, pain, and fatigue, have also been demonstrated to contribute to cognitive function decline (Can & Gencay-Can, 2012; Fava et al., 2013; Katz et al., 2012; Kim, 2012; Murray et al., 2012; Shin, Katz, et al., 2013; Shin, Juliaan, et al., 2013). Accordingly, these were included as extrinsic variables in the hypothetical

model. In addition, inflammatory indices (disease activity and C-reactive protein [CRP] level) and steroid use were included as extrinsic variables, because inflammatory response has been shown to negatively influence cognitive function (Abdul-Sattar et al., 2013; Can & Gencay-Can, 2012; El-Shafey, Abd-El-Geleel, & Soliman, 2012; Moraes-Fontes et al., 2012), and long-term steroid use has consistently been reported to increase the risk of cognitive impairment (Shin, Katz, et al., 2013). In addition, anxiety and depression were included as extrinsic variables as previous studies have demonstrated anxiety and depression have significant effects on cognitive functions (Julian, Merluzzi, & Mohr, 2007).

Close relationships between cognitive functions, self-management ability, and quality of life have been previously reported (Ovayolu, Ovayolu, & Karadag, 2011). Investigators have stressed that intact cognitive function is important for self-management, because cognitive impairment adversely affects ability to adopt and maintain self-management skills (Auyeung et al. 2008), and thus adversely influences quality of life (Ovayolu et al., 2011).

Several disease-related and psychological factors have been suggested to affect self-management ability and quality of life in patients with rheumatic diseases, and the most well-known disease-related and psychological risk factors of self-management are pain, fatigue, anxiety, and depression (De Cuyper, De Gucht, Maes, Van Camp, & De Clerck, 2016; Vermaak, Briffa, Langlands, Inderjeeth, & McQuade, 2015). In terms of quality of life, disease duration and activity (Gong & Mao, 2016; Hodkinson et al., 2012), pain (Hodkinson et al., 2012), fatigue (Gong & Mao, 2016), and anxiety/depression (Zhang et al., 2017) have been reported to have significant impact. On the basis of such empirical evidence, we developed a model that illustrates causal relationships between modifiable risk factors of cognitive impairment, cognitive function, self-management, and quality of life in patients with rheumatic diseases as shown in Figure 1.

Measurements

Regarding health-threatening behaviors, current cigarette smoking (yes/no) and consumption of any type of alcohol (yes/no) were assessed, and body mass index (BMI) was calculated as the body weight divided by the square of the body height (kg/m^2). To evaluate underlying disease status, we computed cardiovascular risk (CVR) score using a gender-specific algorithm based on age, sex, serum total cholesterol and high-density lipoprotein (HDL) levels, systolic blood pressure, smoking, and diabetes mellitus, that is used to estimate 10-year risk of developing heart disease (D'Agostino et al., 2008). Higher scores indicate higher risk of heart disease.

Disease progression and symptoms were examined with respect to cognitive impairment disease-related factors. The duration of rheumatic disease from diagnosis was evaluated as an index of disease progression, and pain and fatigue were assessed as symptom-related factors. Information regarding steroid use was collected from medical records. Because steroids are mostly administered orally in treating rheumatic diseases, steroid use was defined as receiving at least one prescription for oral steroids. On the other hand, steroid nonuse was defined as no mention of steroid use in the medical record.

Pain level was measured using a Numeric Rating Scale with responses ranging from *no pain* (scored as 0) to *maximum pain* (scored as 10). Despite its being a single-item scale, the Numeric Rating Scale has been widely used because of its high reliability (Krebs, Carey, & Weinberger, 2007). Fatigue level was measured using the Korean version of the 7-point, 9-item Fatigue Severity Scale (FSS), which was originally developed by Krupp, LaRocca, Muir-Nash, and Steinberg (1989) and translated into Korean by Chung and Song (2001). This scale evaluates the amount of fatigue felt during the previous week. Lower FSS scores indicate less fatigue. Construct validity of the FSS has been verified using known group methods and its reliability has also been confirmed (Cronbach's alpha = 0.93) (Chung & Song, 2001; Valko, Bassetti, Bloch, Held, & Baumann, 2008). Cronbach's alpha in the present study was 0.96.

Inflammatory status was measured using blood inflammatory indices, that is, rheumatic disease activity and CRP. Rheumatic disease activity was assessed using the Simplified Disease Activity Index (SDAI) (Smolen et al., 2003), which is the sum of five parameters, that is, number of tender and swollen joints (based on a 28-joint assessment), patient and physician assessment of disease activity on a 0–10 Numeric Rating Scale, and blood CRP level measured in mg/dl. The SDAI has been shown to have good construct, content, discriminant validity, and reliability (Aletaha & Smolen, 2005; Anderson, Zimmerman, Caplan, & Michaud, 2011). Construct validity of the SDAI can be verified by showing that it significantly correlated with other measures of empirically and conceptually relevant variables. Based on empirical evidence on the association between disease activity and quality of life in rheumatic disease, Aletaha and Smolen (2005) supported the construct validity of the SDAI by demonstrating a significant correlation with the Health Assessment Questionnaire (a measure of quality of life). They also showed a high degree of significant correlation between the SDAI with a previously validated measure of disease activity, the Disease Activity Score 28 (DAS 28), verifying criterion validity. Anderson et al. (2011) supported the reliability of the SDAI and reported good discriminant validity of the SDAI based on its ability to distinguish disease activity levels (low, moderate, and high) with a high degree of sensitivity.

Psychosocial symptoms, that is, anxiety and depression, were measured using the Korean version of the Hospital Anxiety and Depression Scale (HADS) developed by Zigmond and Snaith (1983) and translated into Korean by Oh, Min, and Park (1999). This scale is a 4-point, 14-item (7 for anxiety and 7 for depression) scale, where higher scores indicate higher levels of anxiety or depression. Construct validity of the Korean version of HADS has been verified by factor analysis and the known-group technique, and its reliability has also been supported (Cronbach's alpha values for anxiety and depression were 0.89 and 0.86, respectively) (Oh et al., 1999). Cronbach's alpha values in the present study were 0.85 for anxiety and 0.74 for depression.

Degrees of cognitive impairment were evaluated using the Mild Vascular Cognitive Impairment Assessment Tool developed by Oh, Kim, Shim, and Seo (2015). This tool was designed to assess degree of

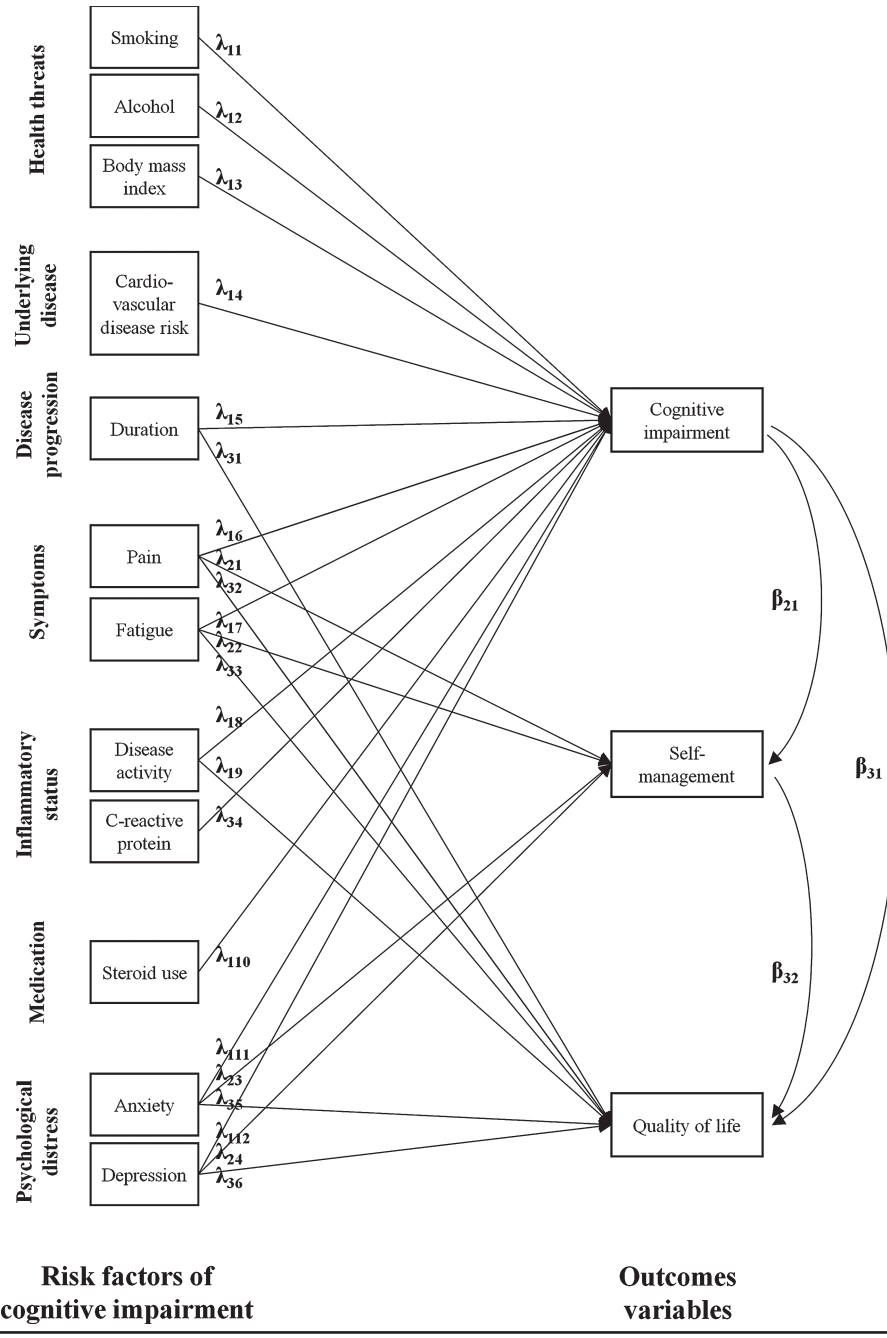

Figure 1. Hypothetical model.

vascular cognitive impairment regardless of cause, and contains 20 items that assess seven cognitive domains, namely, orientation, memory, language, attention, reasoning/abstraction, visuospatial perception, and executive function/problem solving. Total possible scores for the Mild Vascular Cognitive Impairment Assessment Tool range from 30 to 0, where lower scores indicate more severe cognitive impairment. Good content and face validities of the tool have been demonstrated. Its construct validity was verified by the original developers by receiver operating characteristic analysis. Internal consistency and inter-rater reliability were well supported: Cronbach's alpha (a coefficient of internal consistency) was high at 0.89, and inter-rater reliability was confirmed by a Spearman's rho value of 0.93 (Oh et al., 2015). Cronbach's alpha in the present study was 0.73.

Self-management was measured using the Korean version of the Partners in Health Scale, which was originally developed by Battersby, Ask, Reece, Markwick, and Collins (2003) and translated into Korean by Oh et al. (2015). This 8-point, 11-item scale was designed to evaluate self-management of chronic disease. The validity of this scale was confirmed with confirmatory factor analysis by the original developers and its reliability was also shown to be good (Cronbach's alpha = 0.86). The face, content, translation validity, and reliability of the Korean version of this scale were also well supported (CVI = 0.91, Cronbach's alpha = 0.93) by Oh et al. (2015). Cronbach's alpha in the present study was 0.85.

Quality of life was assessed using the Short Form-12 of the Health Survey Questionnaire (SF-12) developed by Ware, Kosinski, and Keller (1996) based on the MOS Short Form Health Survey (SF-36) (Ware & Sherbourne, 1992). The SF-12 was translated into Korean by Han, Lee, Iwaya, Kataoka, and Kohzuki (2004), who also verified its translation validity. Several studies have reported the validity and reliability of the Korean version of the SF-12 as a measure of health-related quality of life in the Korean population (Han et al., 2004; Kim et al., 2014). The scale consists of two subscales, which address physical and mental components, and contains 12 items (8 items with 3- to 5-point Likert-type scales and 4 dichotomous items with yes/no responses). Higher scores indicated higher quality of life. Cronbach's alpha for SF-12 in this study was relatively low (0.65), which we believe was due to the use of only eight Likert-type items for reliability testing.

Data Collection

Data collection was performed by the first author and one research assistant between August and December 2016. Prior to data collection, the research assistant was educated about the purposes of the study and the detailed procedure required for data collection. Data were obtained by medical record review and self-report using a questionnaire that was completed in a quiet conference room.

Most of clinical information was obtained from medical records. For data that could not be obtained from medical records, we used a self-reporting questionnaire in which study subjects read the question and selected a response. The questionnaire was written in Korean and consisted of 67 items organized into seven major scales (pain, fatigue, depression, anxiety, cognitive function, self-management ability, and quality of life), which were either originally developed in Korean or based upon Korean translation of English language as described earlier in detail. A pretest with 10 conveniently selected rheumatic disease patients (who met the inclusion criteria of this study) was conducted to ensure that the questionnaire was understandable and the time taken to complete the assessment was acceptable. Regardless of their educational levels (ranged from primary to college levels), no obvious problems with respect to understandability were found during the pretesting. The time required to complete the questionnaire ranged from 15 to 20 minutes.

For elderly individuals with reading difficulties due to presbyopia ($n = 20$), questionnaires were read by the data collectors, and more time was needed to complete the questionnaire (approximately 40 minutes). Because subjects responded directly to the questionnaire, we believe this process was not subject to bias.

A small gift (a nail care set worth 5 dollars) was rewarded to each study subject. Compensation was given after completing the questionnaire to avoid creating undue influence on a subject's decision to exercise his or her right to withdraw at any time.

Data Analysis

Descriptive analyses of subject general and health- and disease-related characteristics, major study variables, and reliability testing (Cronbach's alpha) were performed using SPSS version 23.0/PC (IBM-Data Solution, Seoul, South Korea). Path analysis was conducted using the Linear Structural Relationships (LISREL) 9.20 program (Scientific Software International, Skokie, Illinois) to verify the fitness of the devised hypothetical model. Path analysis is commonly used to assess causal relationships between a set of variables (Kellar & Kelvin, 2013). Because the present study examined direct and indirect correlations between cognitive function, multidimensional risk factors, self-management, and quality of life, path analysis appeared to suit our study purposes. Before examining direct and indirect correlations, goodness of fit of the hypothetical model was verified using several indicators of fit, namely, the chi-square value, root mean square of error of approximation (RMSEA), goodness-of-fit index (GFI), adjusted goodness of fit index (AGFI), normed fit index (NFI), non-normed fit index (NNFI), and compared fit index (CFI). Based on the literature, the following indicate a good model fit; chi-square test, GFI, AGFI, NFI, NNFI, CFI ≥ 0.90, and RMSEA ≤ 0.05. Table 1 provides an explanation for the statistics used in this study.

Ethical Consideration

This study was initiated after obtaining approval from the human research committee at the authors' university (institutional review board number: 160525-1A), the director of the Rheumatology Department and the president of the university hospital at which data were

Table 1. Summary of Statistics Used in the Study

Test	Reasoning	Details
Path analysis	To assess causal relationships between a set of variables	Path analysis was performed in two steps: (1) verification of the devised hypothetical model and (2) examination of statistical significance of parameters estimates
First step of path analysis	To verify the devised hypothetical model (the results are presented in Table 2).	Goodness-of-fit of the hypothetical model was verified using several indicators of fit, namely, the chi-square value, root mean square of error of approximation (RMSEA), goodness of fit index (GFI), adjusted goodness of fit index (AGFI), normed fit index (NFI), non-normed fit index (NNFI), and compared fit index (CFI).
Second step of path analysis	To examine statistical significance of parameter estimates of the hypothetical model (the results are presented in Table 3).	Direct and indirect correlations between cognitive function, multidimensional risk factors, self-management, and quality of life were examined.

collected. All study subjects were informed about study purposes and procedures and told that personal information would remain confidential and that data would be published as means and ranges. In addition, study subjects were assured they had the right not to participate and could withdraw from the study without prejudice at any stage. Written informed consent was obtained from all study subjects.

Results

A hypothetical model was developed on the basis of empirical evidence. The fitness of the model was verified on 210 patients with rheumatic diseases. In addition, direct and indirect causal relationships among variables in the derived model were examined.

Descriptive Statistics of Subject Characteristics and Major Variables

Mean study subject age was 53.20 (±12.34) years: 68 (32.4%) subjects <50 years, 80 (38.1%) between 50 and 59 years, and 62 (29.5%) ≥60 years. Of the 210 subjects, 161 (76.7%) were women, and 49 (23.3%) were men. Eighty-eight (41.9%) of subjects were employed. Regarding educational backgrounds, 23 (11.0%) were elementary school graduates, 55 (26.2%) were middle school graduates, 92 (43.8%) were high school graduates, and 40 (19.0%) were at least college graduates. The majority had a diagnosis of rheumatic arthritis (n = 179; 85.2%), and the remainder had a diagnosis of fibromyalgia (n = 28; 13.3%) or SLE (n = 3; 1.4%).

Thirty-two (15.2%) subjects were currently smokers and 46 (19.0%) consumed alcohol. Based on BMI (mean value: 23.66±4.09), 126 (60.6%) subjects had a normal weight, 68 (32.7%) were overweight, and 14 (6.7%) were underweight. Fifty-six (26.7%) subjects were hypertensive, 20 (9.5%) had diabetes mellitus, 6 (2.9%) had a cardiovascular disease, and 2 (1.0%) had a history of stroke. Mean overall CVR score was 9.45(±5.31), 153 (85.0%) were of low risk, 24 (13.3%) were of moderate risk, and 3 (1.7%) were of high risk.

Mean systolic blood pressure was 119.20 (±12.34) mmHg, and the majority (n = 197; 93.8%) had a systolic blood pressure of ≤140 mmHg. Mean blood cholesterol concentration was 169.48 (±34.71) mg/dl, and 171 (81.4%) subjects had a normal blood cholesterol level (≤200 mg/dl). Mean blood HDL concentration was 57.30 (±16.03) mg/dl, and 63 (35.2%) subjects had a normal blood cholesterol level (≥60 mg/dl).

Mean duration of rheumatic disease from diagnosis was 100.63 (±84.60) months, mean pain score was 2.77(±2.22)/10, which was relatively low, and mean fatigue score was 34.40(±14.5)/63, which indicated a medium level of fatigue. Mean blood CRP level was 0.35 (±0.77) mg/L and 143 (71.1%) subjects had a normal value (<0.3 mg/L). Regarding disease activity score (mean score: 9.33±8.88), 54 (28.0%) subjects were in remission, 79 (40.9%) had a low disease activity, 49 (25.4%) had a moderate disease activity, and 11 (5.7%) had a high disease activity state. Approximately half (n = 107; 51.0%) of the subjects were taking steroids for rheumatic disease.

Mean subject anxiety score was 6.41(±3.63)/21, and 70 (33.3%) subjects had a score of ≥8, indicating anxiety. Mean subject depression score was 7.36(±3.30)/21, and 100 (47.6%) subjects had a score of ≥8, indicating depression. Of the 210 subjects, 103 (49.0%) had a mild cognitive impairment and the remaining 107 (51.0%) had normal cognitive function. Mean cognitive function score was 23.01(±3.27)/30. Mean self-management score was 71.11(±11.26)/88, which was relatively high, and mean quality-of-life score was 62.94(±9.72)/100, which was a medium level.

Fitness of the Hypothetical Model

The majority of fit indicators were satisfactory (see Table 2): χ^2 test (χ^2= 15.36, p = .43), RMSEA < 0.01 (90% confidence interval: [0.0, 0.07]; optimal values: ≤0.06–0.08), NFI = 0.97 (optimal values: ≥0.80–0.90), NNFI = 0.99 (optimal values: ≥0.90), CFI = 0.99 (optimal values: ≥0.90), GFI = 0.99 (optimal values: ≥0.90), and AGFI = 0.93 (optimal values: ≥0.90). Accordingly, the model was not further modified.

Analysis of the Hypothetical Model

Using path analysis, direct and indirect correlations between cognitive function, multidimensional risk factors, self-management, and quality of life were examined.

Direct Effects on Cognitive Impairment

Of the cognitive impairment risk factors tested, smoking (β = −0.13, t = −2.02), CVR score (β = −0.36, t = −5.33), pain (β = −0.15, t = −1.79), and fatigue (β = −0.17, t = −2.29) were found to have a significant direct effect on cognitive impairment (see Figure 2) and their combined explicability was 21% (SMC=0.21). Of these factors, CVR score showed the largest value, which suggested that it was the most influential.

Table 2. Indices of Model Fit

	Hypothetical Model of the Study							
	Chi-square (p-value)	RMSEA (90% CI)[a]	NFI[b]	NNFI[c]	CFI[d]	GFI[e]	AGFI[f]	CN[g]
Fit indices	15.36 (.43)	0.01 (0.0, 0.07)	0.97	0.99	0.99	0.99	0.93	399.16

[a]Root mean square error of approximation (90% confidence interval).
[b]Normed fit index.
[c]Nonnormed fit index.
[d]Comparative fit index.
[e]Goodness of fit index.
[f]Adjusted goodness of fit index.
[g]Critical N.

Direct Effects on Self-Management

Of the self-management risk factors tested (pain, fatigue, anxiety, depression, and cognitive impairment), only cognitive impairment was found to have a significant direct effect on self-management ($\beta = 0.18$, $t = 2.60$; see Figure 2) and its explicability was 5% (see Table 3). The result indicates that self-management ability relies significantly on intact cognitive functions.

Direct Effects on Quality of Life

Of the quality of life risk factors tested (duration of disease from diagnosis, pain, fatigue, disease activity, anxiety, depression, cognitive function, and self-management), fatigue ($\beta = -0.24$, $t = -3.70$), anxiety ($\beta = -0.24$, $t = -2.93$), depression ($\beta = -0.16$, $t = -1.89$), and cognitive functions ($\beta = 0.22$, $t = 3.80$) were found to have significant direct effects on quality of life with a combined explicability of 40% (see Figure 2), which was relatively high (see Table 3). That is, patients with lower levels of fatigue, anxiety, or depression, or a higher cognitive function are more likely to have a higher quality of life. According to this analysis, these four significant factors had similar influences on quality of life.

Indirect Effects Between Variables

Of the indirect effects predicted, those between fatigue and self-management ($\beta = -0.03$, $t = -1.72$) and fatigue and quality of life ($\beta = -0.04$, $t = -1.97$) were significant (see Figure 2). However, it should be noted that although fatigue had a significant indirect effect, it had no total or direct effects on self-management. On the other hand, fatigue appeared to have a significant indirect effect on quality of life via two paths, that is, cognitive function and self-management. The overall indirect effect of fatigue, calculated by summing these two indirect effects, was significant (see Table 3).

Discussion

Rheumatic diseases are among the most prevalent systemic conditions worldwide. Because diagnosis and treatments of rheumatic diseases in Korea have largely been based on the American College of Rheumatology guidelines, there is unlikely to be any significant difference in clinical care for rheumatic disease patients in Korea versus other countries, including the United States. The prevalence and risk factors for cognitive impairment in Korean rheumatic disease appeared to be similar to those previously reported in other country.

In this study, approximately half (49.0%) of patients with a rheumatic disease were found to be cognitively impaired, which is comparable to reported incidence rates of 40%–70% for cognitive impairments after stroke (Rasquin et al., 2004). It should be noted that stroke is prevalent in the elderly, whereas rheumatic diseases are most common in young and middle-aged adults. Mean subject age in this study was 53.20 years and 32.4% of our study subjects were less than 50 years old. After taking the ages of our subjects into account, the proportion with cognitive impairment was markedly high.

Of the modifiable cognitive impairment risk factors included in the hypothetical model, smoking, CVR score, pain, and fatigue were found to have significant direct effects. Of the health-threatening factors, only smoking had a direct effect on cognitive impairment; alcohol consumption and obesity did not. Several other studies have demonstrated significant associations between smoking and cognitive impairment in patients with chronic diseases, including rheumatic diseases (Katz et al., 2012; Murray et al., 2012). However, published findings on relationships between BMI and cognitive impairment disagree. In one study, being overweight (BMI > 25) in midlife was associated with an increased risk of cognitive impairment, while being overweight in late life was associated with reduced cognitive risk (Park, Sung, Kim, & Lee, 2014). In the present study, no significant association was observed between BMI and cognitive impairment.

Diabetes mellitus and cardiovascular diseases, particularly hypertension, are well-known to be associated with cognitive impairment (Fava et al., 2013; Katz et al., 2012). Reitz, Tang, Manly, Mayeux, and Luchsinger (2007) found that patients with hypertension or diabetes mellitus are 1.4–1.5 times more likely to have cognitive impairment. In the present study, CVR scores exhibited a significant causal relationship with cognitive impairment. Because CVR scores were derived from age, sex, serum total cholesterol and HDL levels, systolic blood pressure, smoking, and diabetes mellitus, these scores may well have reflected underlying disease status.

Factors that contribute to cognitive impairment in rheumatic diseases may be dependent on disease type. In terms of SLE, cognitive impairment is known to be associated with neuropsychiatric syndrome, such as headache, mood disorders, and seizure (El-Shafey et al., 2012). In RA, cognitive impairment is reported to be associated with arthritis-related symptoms (Can & Gencay-Can, 2012). Considering that most of our subjects had RA, it was understandable that pain and fatigue (both common symptoms of RA) were found to be significant factors of cognitive impairment.

Rheumatic diseases are chronic inflammatory diseases characterized by cycles of relapse and remission. During relapse, active inflammatory processes cause complicated clinical symptoms in physical and/or psychological dimensions, which may contribute to the development of cognitive impairment (Anderson et al., 2011). In general, inflammatory status in rheumatic disease is evaluated using simple serologic inflammatory indices, such as CPR or ESR levels, or a more complex measure, such as disease activity (Murray et al., 2012). Disease activity was comprehensively assessed on the basis of symptoms (numbers of tender and swollen joints), blood ESR or CPR levels, radiological findings, and patient and physician global assessments of disease activity (Murray et al., 2012). Although previous studies have demonstrated that inflammatory response has a negative effect on cognitive impairment (Abdul-Sattar et al., 2013; Can & Gencay-Can, 2012; El-Shafey et al., 2012; Moraes-Fontes et al., 2012), in the present study, no significant direct effect was observed for CPR or disease activity.

Depression and anxiety are known to increase the risk of cognitive impairment. In particular, depression

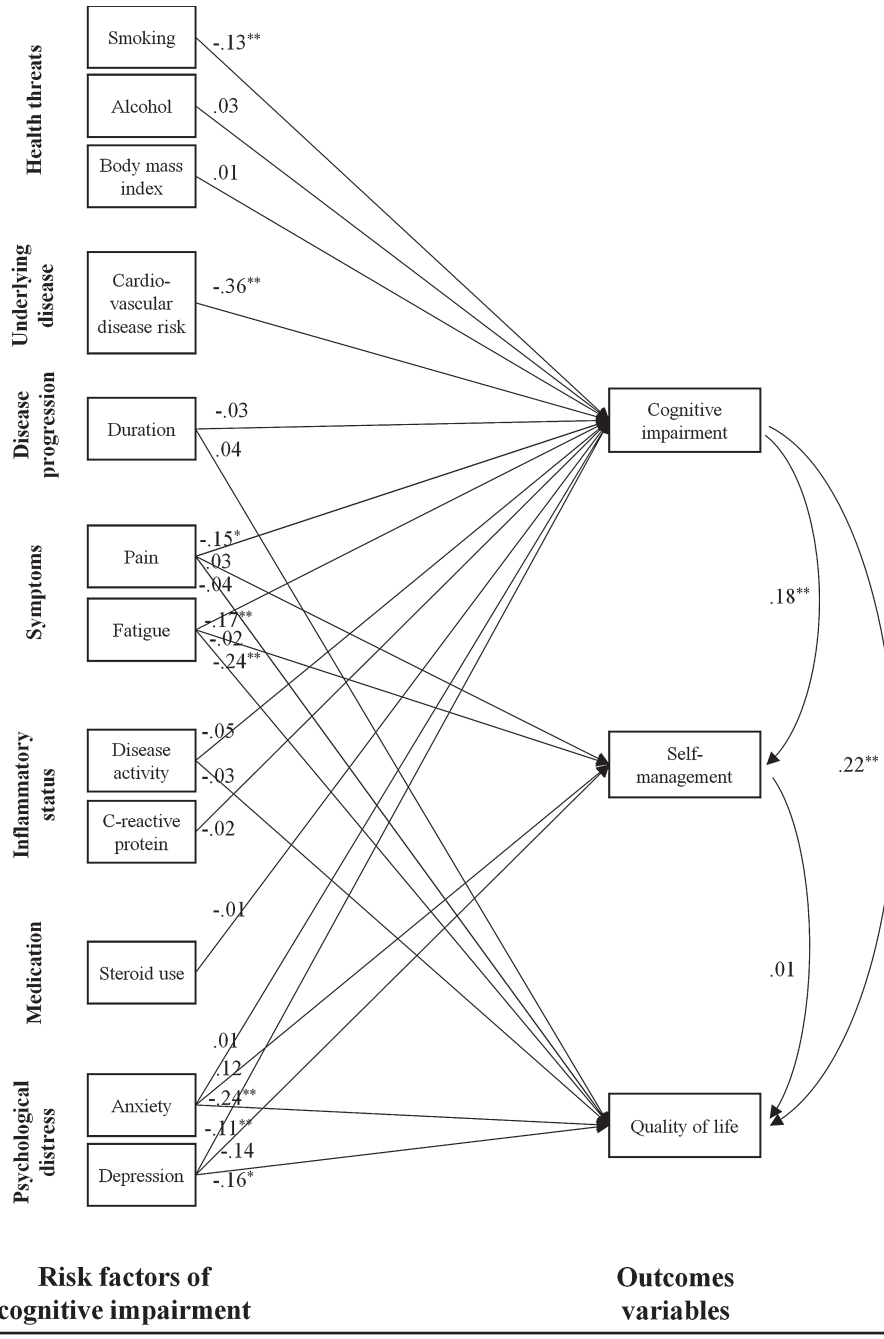

FIGURE 2. Results of model testing.

has been more frequently suggested to be associated with cognitive impairment than anxiety. Royall and Palmer (2013) reported depression had a significant effect on cognitive changes, and suggested that this effect was greater than that of an amyloid-related neuropathology. However, no significant causal (direct) relationship was observed between depression or anxiety and cognitive impairment in this study.

We speculate that such discrepancies in terms of disease activity, CRP, depression, and anxiety may have been due to the inclusion of different types of rheumatic disease and the use of different statistical tests. More specifically, the majority of previous studies on rheumatic disease cognitive impairment risk factors were conducted on SLE patients. In addition, previous studies commonly used univariate analysis, which cannot fully explain complex relationships between multiple variables, whereas we used path analysis to explore complicated causal relationships among multiple variables after adjusting for confounders.

In this study, cognitive function was found to have a direct positive effect on self-management. It has been stressed that self-management by patients with a rheumatic disease should be approached in a multidimensional manner to enable patients to manage symptoms properly, delay disease progression, and promote independence, quality of life, and psychological well-being (Iversen et al., 2010). This implies that self-management ability critically relies on intact cognitive functions, which is also strongly supported by the findings of this

Table 3. Causal Relationships Between Modifiable Risk Factors of Cognitive Impairment, Cognitive Function, Self-Management, and Quality of Life

Variables	Path Effect	Total β(*t*)	Direct β(*t*)	Indirect β(*t*)	SMC[a]
Cognitive function	Smoking	−0.13 (−2.02)[b]	−0.13 (−2.02)[b]	-	0.21
	Alcohol	0.03 (0.49)	0.03 (0.49)	-	
	Body mass index	0.01 (0.08)	0.01 (0.08)	-	
	Cardiovascular risk score	−0.36 (−5.33)[b]	−0.36 (−5.33)[b]	-	
	Disease duration	−0.03 (−0.51)	−0.03 (−0.51)	-	
	Pain	−0.15 (−1.79)[c]	−0.15 (−1.79)[c]	-	
	Fatigue	−0.17 (−2.29)[b]	−0.17 (−2.29)[b]	-	
	Disease activity	−0.05 (−0.72)	−0.05 (−0.72)	-	
	C-reactive protein	−0.02 (−0.32)	−0.02 (−0.32)	-	
	Steroid use	−0.01 (−0.22)	−0.01 (−0.22)	-	
	Anxiety	0.01 (0.05)	0.01 (0.05)	-	
	Depression	−0.11 (−1.14)	−0.11 (−1.14)	-	
Self-management	Pain	0.05 (0.76)	0.03 (0.48)	0.02 (1.30)	0.05
	Fatigue	−0.05 (−0.62)	−0.02 (−0.24)	−0.03 (−1.72)[c]	
	Anxiety	0.12 (1.15)	0.12 (1.16)	0.00 (0.05)	
	Depression	−0.16 (−1.53)	−0.14 (−1.34)	−0.02 (−1.05)	
	Cognitive function	0.18 (2.60)[b]	0.18 (2.60)[b]	-	
Quality of Life	Duration	0.03 (0.61)	0.04 (0.76)	−0.01 (−0.50)	0.40
	Pain	−0.02(−0.30)	−0.04 (−0.68)	0.02 (1.40)	
	Fatigue	−0.28 (−4.16)[b]	−0.24 (−3.70)[b]	−0.04 (−1.97)[b]	
	Disease activity	−0.04 (−0.58)	−0.03 (−0.41)	−0.01 (−0.71)	
	Anxiety	−0.24 (−2.83)[b]	−0.24 (−2.93)[b]	0.00 (0.08)	
	Depression	−0.18 (−2.13)[b]	−0.16 (−1.89)[c]	−0.02 (−1.07)	
	Cognitive function	0.22 (3.88)[b]	0.22 (3.80)[b]	0.00 (0.11)	
	Self-management	0.01 (0.11)	0.01 (0.11)	-	

[a]Squared multiple correlation.
[b]$t \geq 1.64$, $p \leq .050$ (one-tailed test).
[c]$t \geq 1.96$, $p \leq .010$ (one-tailed test).

study. On the other hand, our findings show that the direct effects of pain, depression, and anxiety on self-management were not significant.

In terms of quality of life, our findings indicated that cognitive function, fatigue, anxiety, and depression had a significant direct effect on quality of life, which suggests lower levels of fatigue, anxiety, or depression or a higher cognitive function may promote quality of life in patients with a rheumatic disease. In particular, fatigue was found to have direct and indirect effect (due to its relationships with cognitive function and self-management) on quality of life.

Study Limitations

Because data collection was limited to one university hospital, our findings should be further confirmed by larger, multicenter studies. As another study limitation, because the SF-12 (used to assess quality of life in this study) included several items assessing physical functioning, we did not employ independent measures of activities of daily living (ADL) and mobility despite their potential to affect self-management and cognitive function in rheumatic disease patients. Further studies are warranted to determine dynamic relationships between ADL and mobility levels, cognitive impairment, self-management, and quality of life in patients with a rheumatic disease.

Conclusions and Nursing Implications

After considering the ages of our study subjects, the prevalence (49.0%) of cognitive impairment appeared to be markedly high in patients with a rheumatic disease. Of the risk factors for cognitive impairment included in the hypothetical model, smoking, CVR score, pain, and fatigue were found to have a significant direct

effect on cognitive impairment. CVR score reflects underlying disease status, because it is calculated using serum total cholesterol and HDL levels, systolic blood pressure, smoking, and diabetes mellitus, and thus, the importance of proper management of underlying diseases and health-threatening factors should be emphasized to prevent the development of cognitive impairment and further cognitive deterioration in patients with a rheumatic disease.

Our findings also showed that cognitive impairment was directly affected by pain and fatigue, the most common symptoms of rheumatic disease, which indicates the need for symptom management to prevent such impairment. In addition, cognitive functions were found to affect self-management ability and quality of life directly, which indicates that those with better cognitive function may be more likely to engage in self-management and have a better quality of life.

Rheumatic disease is a quality-of-life concern because of its chronic, progressive nature and lack of a permanent cure, and therefore, one of the goals of nursing intervention for rheumatic disease should be to improve quality of life. In this study, quality of life was found to be directly affected by fatigue, anxiety, and depression, which emphasizes the importance of symptom management. Furthermore, because rheumatic diseases usually affect joints, patients and health professionals are more likely to focus on joint-related symptoms and functional disability, and easily disregard the presence of cognitive impairment. We advise patients, families, and orthopaedic nurses that cognitive impairment may begin relatively early during the course of rheumatic diseases, may affect daily activities and adherence to self-management regimens, and adversely affect quality of life. Therefore, we suggest that nursing assessment and management of cognitive function, symptoms, and inflammatory status should be conducted from initial diagnosis in patients with rheumatic diseases.

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