

Factors Associated with the Use of Complementary and Alternative Medicine for Korean Patients with Rheumatoid Arthritis

Minkyung Han, Yoon-Kyoung Sung, Soo-Kyung Cho, Dam Kim, Soyoun Won, Chan-Bum Choi, So-Young Bang, Hoon-Suk Cha, Jung-Yoon Choe, Won Tae Chung, Seung-Jae Hong, Jae-Bum Jun, Young Ok Jung, Seong-Kyu Kim, Tae-Hwan Kim, Eunmi Koh, Hye-Soon Lee, Jisoo Lee, Joo-Hyun Lee, Shin-Seok Lee, Seong-Su Nah, Seung-Cheol Shim, Dae-Hyun Yoo, Wan-Hee Yoo, Bo Young Yoon, Sun Ha Jee, and Sang-Cheol Bae

ABSTRACT. Objective. Rheumatoid arthritis (RA) is a chronic autoimmune disease that is often painful and debilitating. Patients with RA are increasingly receiving complementary and alternative medicine (CAM). We aimed to identify the patient characteristics and disease-specific factors associated with Korean patients with RA who decide to start treatment with CAM.

Methods. Among the total 5371 patients with RA in the KORean Observational study Network for Arthritis (KORONA), 2175 patients who had no experience with CAM were included in our study. In our study, we assessed the frequency of new incident CAM use, its patterns, and the predictive factors of new CAM use.

Results. Of the 2175 patients, 229 patients (10.5%) newly started receiving CAM within a year of enrolling in the cohort. Of those who started treatment with CAM, 17.0% received only herbal medicine, 54.6% only acupuncture treatments (7.0% used a combination of both), and 21.4% “Other” (e.g., physical therapy and placental extract injections). Women (OR 1.89, 95% CI 1.13–3.14) and patients with depression (OR 3.52, 95% CI 1.65–7.50) were significantly more likely to be treated with CAM. Regarding household types, patients who lived in an extended family (OR 1.78, 95% CI 1.08–2.95) or as part of a couple (OR 1.55, 95% CI 1.07–2.24) were more likely to be treated with CAM than patients living in a nuclear family.

Conclusion. Our study found, within a year, an incidence rate of 10.5% for new CAM use among patients with no previous experience with CAM. Sex, depression, and household type were significantly associated with new CAM use. (J Rheumatol First Release September 1 2015; doi:10.3899/jrheum.141447)

Key Indexing Terms:

RHEUMATOID ARTHRITIS
SEX

COMPLEMENTARY AND ALTERNATIVE MEDICINE
DEPRESSION
HOUSEHOLD

From the Clinical Research Center for Rheumatoid Arthritis, Seoul; Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul; Department of Rheumatology, Hanyang University Guri Hospital, Guri; Department of Rheumatology, Sungkyunkwan University School of Medicine, Samsung Medical Center, Seoul; Department of Rheumatology, Catholic University of Daegu School of Medicine, Daegu; Department of Rheumatology, Dong-A University Hospital, Busan; Department of Rheumatology, Kyung Hee University Hospital, Seoul; Department of Rheumatology, Hallym University Kangnam Sacred Heart Hospital, Seoul; Department of Rheumatology, Ewha Womans University Mokdong Hospital, Seoul; Department of Rheumatology, Inje University Ilsan Paik Hospital, Goyang; Department of Rheumatology, Chonnam National University Hospital, Gwangju; Department of Rheumatology, Soonchunhyang University Cheonan Hospital, Cheonan; Department of Rheumatology, Chungnam National University Hospital, Daejeon; Department of Rheumatology, Chonbuk National University Hospital, Jeonju; Department of Epidemiology and Health Promotion, Graduate School of Public Health Yonsei University, Seoul, Republic of Korea.

Supported by a grant of the Korea Healthcare Technology R&D Project, Ministry of Health and Welfare, Republic of Korea (H110C2020).

M. Han, MPH, Clinical Research Center for Rheumatoid Arthritis;
Y.K. Sung, MD, PhD, MPH, Clinical Research Center for Rheumatoid

Arthritis, and Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases; S.K. Cho, MD, PhD, Clinical Research Center for Rheumatoid Arthritis, and Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases; D. Kim, MD, PhD, Clinical Research Center for Rheumatoid Arthritis, and Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases; S. Won, MPH, PhD, Clinical Research Center for Rheumatoid Arthritis; C.B. Choi, MD, PhD, MPH, Clinical Research Center for Rheumatoid Arthritis, and Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases; S.Y. Bang, MD, PhD, Department of Rheumatology, Hanyang University Guri Hospital; H.S. Cha, MD, PhD, Department of Rheumatology, Sungkyunkwan University School of Medicine, Samsung Medical Center; J.Y. Choe, MD, PhD, Department of Rheumatology, Catholic University of Daegu School of Medicine; W.T. Chung, MD, PhD, Department of Rheumatology, Dong-A University Hospital; S.J. Hong, MD, PhD, Department of Rheumatology, Kyung Hee University Hospital; J.B. Jun, MD, PhD, Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases; Y.O. Jung, MD, PhD, Department of Rheumatology, Hallym University Kangnam Sacred Heart Hospital; S.K. Kim, MD, PhD, Department of Rheumatology, Catholic University of Daegu School of Medicine; T.H. Kim, MD, PhD, Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases; E. Koh, MD, PhD, Department of Rheumatology,

Sungkyunkwan University School of Medicine, Samsung Medical Center; H.S. Lee, MD, PhD, Department of Rheumatology, Hanyang University Guri Hospital; J. Lee, MD, PhD, Department of Rheumatology, Ewha Womans University Mokdong Hospital; J.H. Lee, MD, PhD, Department of Rheumatology, Inje University Ilsan Paik Hospital; S.S. Lee, MD, PhD, Department of Rheumatology, Chonnam National University Hospital; S.S. Nah, MD, PhD, Department of Rheumatology, Soonchunhyang University Cheonan Hospital; S.C. Shim, MD, PhD, Department of Rheumatology, Chungnam National University Hospital; D.H. Yoo, MD, PhD, Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases; W.H. Yoo, MD, PhD, Department of Rheumatology, Chonbuk National University Hospital; B.Y. Yoon, MD, PhD, Department of Rheumatology, Inje University Ilsan Paik Hospital; S.H. Jee, PhD, MPH, Department of Epidemiology and Health Promotion, Graduate School of Public Health Yonsei University; S.C. Bae, MD, PhD, MPH, Clinical Research Center for Rheumatoid Arthritis, and Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases.

Address correspondence to Dr. Sang-Cheol Bae, Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul 133-792, Republic of Korea. E-mail: scbae@hanyang.ac.kr

Accepted for publication July 9, 2015.

Rheumatoid arthritis (RA) is a common chronic autoimmune disease with a worldwide prevalence rate of 0.5–1%¹. It can be a debilitating and painful condition and may lead to substantial loss of function and mobility². The ultimate goal of RA treatment is to reduce pain by controlling inflammation, to prevent or delay joint damage, and to enhance quality of life^{2,3}. However, patients with RA report that conventional RA medicine often does not improve health, does not always alleviate pain, and produces undesirable side effects⁴.

Complementary and alternative medicine (CAM) has become popular with patients with rheumatic diseases and is widely used throughout the world, across different geographic and ethnic groups, and among people of different social and economic backgrounds^{5,6}. The most common reason given by patients for taking CAM is to treat pain^{7,8}. Many patients with RA have received CAM because of their dissatisfaction with conventional medicine, concern over the side effects of conventional medicine, or a need for personal control in their choice of healthcare. According to several studies, poorer health status and longer disease duration were associated with increased CAM use^{4,8,9}.

While there are some studies on the relationship between CAM use and RA^{10,11}, there is comparatively little research specifically on the risk factors associated with a patient deciding to start CAM use for the first time. Therefore, we aimed to identify patient characteristics and risk factors associated with new CAM use in Korean patients with RA.

MATERIALS AND METHODS

Study population. From July 2009 to December 2011, 5371 patients with RA who were over the age of 18 and who met the classification criteria suggested in 1987 by the American College of Rheumatology (ACR) were enrolled into the KOREAN Observational study Network for Arthritis (KORONA) database. Of these 5371 patients, 4190 followed up with the KORONA study 1 year after enrollment and continued to participate in regular annual followups. There have been 4 annual followups. Patients from 23 centers across South Korea were included in KORONA, covering a wide range of geographic, social, and economic backgrounds. These 23 centers account for about 38% of the tertiary academic hospital rheumatology

departments across Korea. All patients provided informed consent before enrolling in KORONA¹².

As shown in Figure 1, at the time of enrollment, 2564 patients had received or were receiving CAM, while 2807 patients had never received CAM. Patients who had no experience with CAM underwent a followup medical examination 1 year after enrollment. Of these 2807 patients, 2175 participated in the followup examination (630 patients did not follow up, and 2 lacked sufficient followup data). These 2175 patients were the subject group for our analysis of the factors associated with patients' decision to start treatment with CAM, as well as the patterns and frequency rate of this new CAM use.

Data collection: CAM. At the time of enrollment and at the 1-year followup, patients were given a questionnaire regarding CAM use. The questionnaires given at enrollment and at the followup were different. Each was completed through an interview with a practitioner who filled out the questionnaire according to the patient's response to each question. In the enrollment questionnaire, the first question was "Have you ever received treatment for rheumatoid arthritis outside of the treatment provided by hospitals?" In the followup questionnaire, the first question was "Have you received treatment for rheumatoid arthritis outside of the treatment provided by hospitals in the past year?" For both, patients responded either "yes" or "no." If patients responded "yes" on either questionnaire, the next question asked patients to choose from the options provided regarding which forms of CAM they had used. The options provided on the form were "Herbal medicine," "Chinese acupuncture," "Moxibustion/cupping," "Bee venom therapy," and "Other." If the patients responded with "Other," they were further asked to specify the treatment. This section of the survey excluded supplements that were independently dealt with in another section. Therefore, patients' response to this "Other" category did not include supplements.

Considering the various definitions of CAM provided by previous studies, the term generally means the diagnosis, treatment, and/or prevention of disease through various treatments, products, and/or medical procedures not included within the scope of modern medicine¹³. Chinese acupuncture and herbal medicines are the most widely known forms of CAM in Korea¹⁴. Many patients take dietary supplements. However, many patients take them after being suggested to do so or after receiving them as a gift, rather than taking them for a specific reason. Therefore, dietary supplements were excluded from our study. Thus, our study primarily defines CAM as use of any herbal medicines, acupuncture treatments, or other remedies not provided by standard hospital care (as described above).

Demographic and clinical features. Each patient was questioned on a variety of factors, including sex, age, age of disease onset, age of diagnosis, body mass index (BMI), education level, income, household type, comorbidities, prescribed drugs, history of CAM use, and drug side effects. Data on BMI was calculated after measuring patients' weight and height ($BMI = \text{kg/m}^2$) during their enrollment into KORONA. Patients were asked to specify their household type; options were single (living alone), couple (living with a partner), nuclear family (consisting of only a parent or parents and their children), or extended family (consisting of 3 or more generations). Data on comorbidity was obtained from 2 sources: first, through a questionnaire filled out by a practitioner according to the responses of the patient, and second, through clinical examination. The questionnaire determined comorbidity as any ailment the patient had been diagnosed with or had received treatment for. Comorbidities included cardiovascular disease, hypertension (HTN), gastrointestinal (GI) disease, diabetes mellitus, neoplastic diseases, thyroid disease, pulmonary disease, neurologic diseases, depression, etc. Data regarding drug side effects was obtained through the aforementioned questionnaire, and was based on the patient's response. The questionnaire asked whether or not the patient had experienced drug side effects; patients responded "yes" or "no." Through blood tests, patients' rheumatoid factor and erythrocyte sedimentation rate (ESR) were obtained. Using their ESR, patients' Disease Activity Score in 28 joints (DAS28) was calculated. The DAS28 and Health Assessment Questionnaire (HAQ) were used to evaluate health-related outcomes. Global health (GH) and pain visual analog scale (VAS) scores were also used to evaluate health-related results.

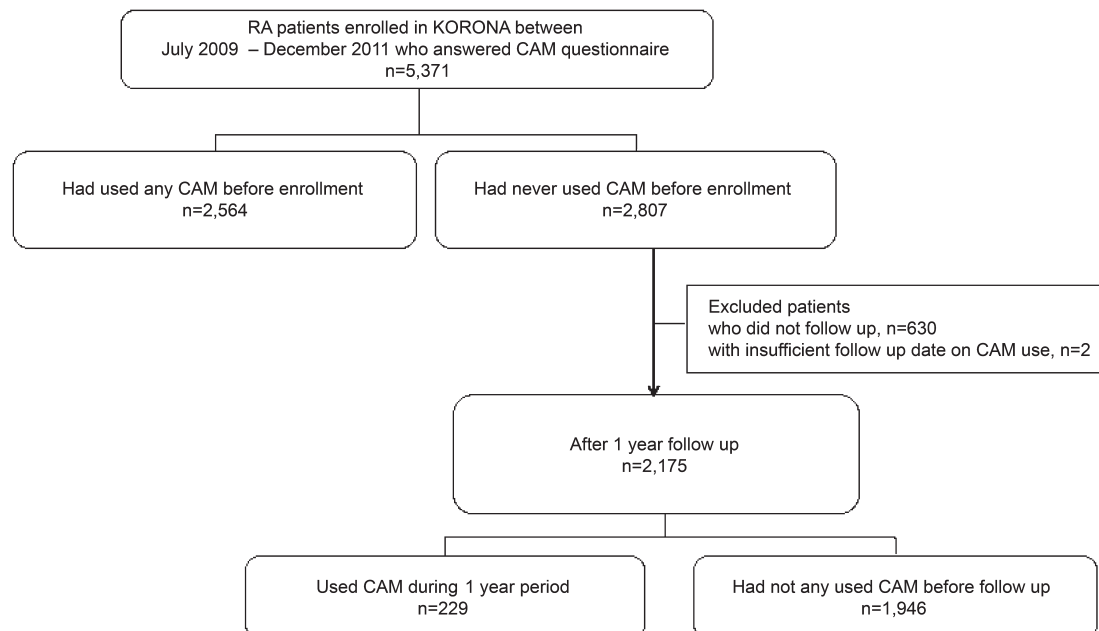


Figure 1. Study participants selected from the KORONA database. KORONA: KOREan Observational study Network for Arthritis; RA: rheumatoid arthritis; CAM: complementary and alternative medicine.

Statistical analysis. Univariate and multivariable logistic regressions were used to investigate factors associated with CAM use in Korean patients with RA with OR and 95% CI. Following the results of univariate logistic regression, variables that were significant at a p value of <0.2 were included in a multivariable logistic regression analysis^{15,16}. After locating all variables statistically significant at a p value of <0.2, we also chose variables that were clinically important, although not statistically significant, to be included in the multivariable logistic regression analysis. These clinically important variables were methotrexate (MTX) use, biologics use, history of drug side effects, HTN, and GI disease. We conducted a Hosmer-Lemeshow goodness-of-fit test for the multivariable model. The Hosmer-Lemeshow goodness-of-fit test for the multivariable model yielded a chi-square of 9.63 ($p = 0.29$), and a C-statistic of 0.63. SAS 9.2 was used for statistical analysis (SAS Institute Inc.). P values less than 0.05 were considered statistically significant.

RESULTS

Types of CAM used by patients with RA. The types of CAM used by Korean patients with RA are shown in Table 1. For those who had received CAM before enrollment, the most common type of CAM used was Chinese acupuncture (1817 patients, 70.9%), followed by herbal medicine (1494 patients, 58.3%) and moxibustion/cupping (757 patients, 29.5%). Until the time of enrollment, patients had most commonly been treated with a combination of herbal medicines and acupuncture treatments (982 patients, 38.3%).

For incident CAM use (i.e., patients who first used CAM between the time of enrollment and the 1-year followup), the most common type of CAM was Chinese acupuncture (117 patients, 51.1%), followed by herbal medicine (56 patients, 24.5%) and “Other,” which primarily included physical therapy and placental extract injections (49 patients, 21.4%). Incident CAM use, however, mostly consisted of only acupuncture treatments (125 patients, 54.6%), followed by only herbal medicines (39 patients, 17.0%; Table 1).

Demographic and clinical features. Of the 2175 patients, 229 (10.5%) reported that they first started treatment with CAM between the time of enrollment and the 1-year followup. Of these 229 patients with RA, 90% were women. The mean age at enrollment of patients who began treatment with CAM during this 1-year period was higher than that of those who did not (54.3 vs 54.2 yrs, respectively). Additionally, the mean disease duration of those who received CAM during this period was longer than that of patients who did not (7.9 vs 7.6 yrs, respectively). However, both of these differences were not significant. Of those patients who received CAM, 24 patients (10.5%) were single, 79 patients (34.5%) lived as part of a couple, 99 patients (43.2%) were from households with nuclear families, and 27 patients (11.8%) lived with extended families. The mean HAQ scores of the 229 patients who received CAM were significantly higher than the mean scores of patients who did not receive CAM ($p < 0.01$), although the differences were not very large. The DAS28 scores of patients who received CAM were also significantly higher than those who did not ($p = 0.01$). Additionally, patients who had depression received more CAM ($p < 0.01$). The mean patient pain and the patient GH VAS scores of those who received CAM were higher than the scores of patients who did not, but this difference was not statistically significant. There was no difference between the 2 groups in terms of conventional medication. Of those who received CAM, 83.0% received MTX and 4.4% received biologics (Table 2).

Predictive factors of new CAM use. Of the 2175 patients, 308 patients (32 had received CAM, 276 had not received CAM) were not included in the multivariable logistic regression

Table 1. Types of CAM used by Korean patients with RA. Multiple responses allowed. Values are n (%).

Category of CAM	CAM	CAM Used Prior to Enrollment, n = 2564	CAM Use Began after Enrollment, n = 229
	Type of CAM		
Herbal medicine	Herbal medicine	1494 (58.3)	56 (24.5)
Acupuncture treatment	Chinese acupuncture	1817 (70.9)	117 (51.1)
	Moxibustion/cupping	757 (29.5)	46 (20.1)
	Bee venom therapy	474 (18.5)	16 (7.0)
Other	Other	367 (14.3)	49 (21.4)
Categories of CAM			
	Only herbal medicine	326 (12.7)	39 (17.0)
	Only acupuncture treatment	889 (34.7)	125 (54.6)
	Only other types of CAM	107 (4.2)	37 (16.2)
	Herbal medicine & acupuncture treatment	982 (38.3)	16 (7.0)
	Acupuncture treatment & other types of CAM	74 (2.9)	11 (4.8)
	Herbal medicine & other types of CAM	22 (0.9)	1 (0.4)
	Herbal medicine & acupuncture treatment & other types of CAM	164 (6.4)	0 (0.0)

CAM: complementary and alternative medicine; RA: rheumatoid arthritis.

analysis on account of missing data. The remaining 1867 were included in the analysis. The 32 excluded patients who had received CAM accounted for 14.0% of the overall number of patients who had received CAM, while 276 who had not received CAM accounted for 14.2% of those who did not. There was no significant difference in any variable important to our study between those patients excluded and those patients included in the multivariable model. The multivariable logistic regression revealed that women (OR 1.89, 95% CI 1.13–3.14) were significantly more likely to start treatment with CAM than men. Patients living with an extended family (OR 1.78, 95% CI 1.08–2.95) and patients living as part of a couple (OR 1.55, 95% CI 1.07–2.24) were also significantly more likely to start treatment with CAM than patients living as part of a nuclear family. Further, patients with depression (OR 3.52, 95% CI 1.65–7.50) were significantly more likely to start treatment with CAM than patients without depression. Patients with higher HAQ scores (OR 1.38, 95% CI 0.99–1.83), less education (OR 1.11, 95% CI 0.79–1.58), and more experience with RA drug side effects (OR 1.15, 95% CI 0.83–1.59) also tended to start treatment with CAM more, but these differences were not statistically significant (Table 3).

DISCUSSION

In our study of South Korean patients with RA we investigated the frequency rate of new CAM use (i.e., incident CAM use) among patients with no experience with CAM, the patterns of this use, and the predictive factors of new CAM use. Our study found that 47.7% of Korean patients with RA, with a mean disease duration of 8.9 years, had received some kind of CAM at the time of enrollment. Additionally, at 1-year followup, 10.5% of patients with no previous CAM experience began receiving CAM for the first time. Finally, we found that patients with depression, female patients, and patients living in extended family households and couple

households were more likely to begin treatment with CAM.

According to 1 study in Japan, 34.6% of patients with RA were treated with CAM¹⁷. Additionally, in Mexico and Israel, the percentages of patients with rheumatic disease who were treated with CAM were 42% and 71%, respectively^{4,18}. However, while these studies included dietary supplements in their definition of CAM, our study did not. Yet, these statistics suggest that patients with RA in Korea receive a comparatively large amount of CAM, despite the narrower definition of CAM used in our study. Unfortunately, these inconsistent definitions of CAM prevent a direct comparison between rates of overall CAM use. However, the use of specific CAM treatments can be directly compared between countries. For example, 33.8% of patients with RA in Korea are treated with Chinese acupuncture (1817 patients of 5371 patients), while 18.6% of patients with rheumatic diseases in Israel (65 of 350 patients) and 12.9% of patients with rheumatic diseases in Mexico (103 of 800 patients) are treated with Chinese acupuncture. In addition, 9.3% of patients with RA in Japan (355 patients of 3815 patients) are treated with Chinese acupuncture and/or moxibustion^{4,17,18}. This comparison of specific treatments reflects the relatively high use of CAM among Korean patients with RA. Previous research has shown that certain forms of CAM, such as Chinese acupuncture, are easily accessible in Korea¹⁹. This may be because of the Korean insurance system, which covers many forms of acupuncture treatment. This accessibility may therefore account for the comparatively high use of CAM among Korean patients with RA.

We also found that household type and sex were related to CAM use. Women received CAM significantly more than males, which supports existing findings that sex is associated with CAM use^{19,20,21}. Patients living as part of a couple or living with their extended family (consisting of 3 or more generations) were treated with CAM more than patients of nuclear families (consisting only of parents and their

Table 2. Demographic and clinical characteristics of new CAM use. Values are n (%) or mean ± SD unless otherwise specified.

Variable	Total, n = 2175	New CAM Use Use, n = 229	No Use, n = 1946	Crude OR (95% CI)	p
Female	1791 (82.3)	206 (90.0)	1585 (81.5)	2.04 (1.31–3.19)	< 0.01
Age at enrollment, yrs	54.2 ± 12.3	54.3 ± 12.4	54.2 ± 12.3	1.001 (0.99–1.01)	0.91
Median (Q1–Q3)	55 (46–63)	56 (47–65)	55 (46–63)		
≥ 65	475 (21.8)	58 (25.3)	417 (21.4)	1.00 (ref)	
≥ 40 to < 65	1431 (65.8)	141 (61.6)	1290 (66.3)	0.79 (0.57–1.09)	0.67
< 40	269 (12.4)	30 (13.1)	239 (12.3)	0.90 (0.57–1.44)	0.15
Age at disease onset, yrs	44.8 ± 12.6	44.4 ± 12.1	44.8 ± 12.7	0.997 (0.99–1.01)	0.62
Median (Q1–Q3)	45 (36–54)	45 (36–54)	45 (36–54)		
≥ 65	104 (5.0)	7 (3.2)	97 (5.2)	1.00 (ref)	
≥ 40 to < 65	1272 (60.7)	137 (62.0)	1135 (60.6)	1.67 (0.76–3.68)	0.20
< 40	719 (34.3)	77 (34.8)	642 (34.3)	1.66 (0.75–3.71)	0.21
Disease duration, yrs	7.6 ± 7.1	7.9 ± 8.2	7.6 ± 6.9	1.01 (0.99–1.03)	0.53
Median (Q1–Q3)	5.6 (2.2–11.2)	5.1 (1.6–11.3)	5.6 (2.3–11.2)		
> 10	640 (30.1)	62 (28.2)	578 (30.3)	1.00 (ref)	
> 5 to ≤ 10	500 (23.5)	52 (23.6)	448 (23.5)	1.08 (0.73–1.60)	0.69
> 1 to ≤ 5	673 (31.7)	63 (28.6)	610 (32.0)	0.96 (0.67–1.39)	0.84
≤ 1	313 (14.7)	43 (19.6)	270 (14.2)	1.49 (0.98–2.25)	0.06
Education					
≥ High school	1237 (57.2)	119 (52.4)	1118 (57.8)	1.00 (ref)	
≤ Middle school	924 (42.8)	108 (47.6)	816 (42.2)	1.24 (0.94–1.64)	0.12
Family income, 10,000 won/mo					
≥ 500	224 (10.4)	22 (9.7)	202 (10.4)	1.00 (ref)	
≥ 200 to < 500	927 (42.9)	99 (43.6)	828 (42.8)	1.10 (0.68–1.79)	0.71
< 200	1011 (46.8)	106 (46.7)	905 (46.8)	1.08 (0.66–1.75)	0.77
Household type					
Nuclear family	1131 (52.2)	99 (43.2)	1032 (53.2)	1.00 (ref)	
Extended family	196 (9.0)	27 (11.8)	169 (8.7)	1.67 (1.06–2.63)	0.03
Couple	624 (28.8)	79 (34.5)	545 (28.1)	1.51 (1.11–2.07)	0.01
Single	217 (10.0)	24 (10.5)	193 (10.0)	1.30 (0.81–2.08)	0.28
BMI, kg/m ²	22.8 ± 3.2	22.7 ± 3.1	22.8 ± 3.2	0.99 (0.95–1.04)	0.75
Median (Q1–Q3)	22.5 (20.5–24.7)	22.7 (20.6–24.3)	22.5 (20.5–24.7)		
≥ 23.0	957 (44.4)	100 (44.1)	857 (44.4)	1.00 (ref)	
≥ 18.5 to < 23.0	1045 (48.5)	111 (48.9)	934 (48.4)	1.02 (0.77–1.36)	0.90
< 18.5	155 (7.2)	16 (7.1)	139 (7.2)	0.99 (0.57–1.72)	0.96
RF positivity	1968 (90.5)	205 (89.5)	1763 (90.6)	0.89 (0.57–1.39)	0.60
HAQ	0.6 ± 0.6	0.7 ± 0.6	0.6 ± 0.6	1.44 (1.17–1.77)	< 0.01
Median (Q1–Q3)	0.5 (0.0–1.0)	0.6 (0.1–1.1)	0.4 (0.0–1.0)		
Patient pain VAS, cm	3.5 ± 2.7	3.8 ± 2.8	3.4 ± 2.7	1.04 (0.99–1.10)	0.09
Median (Q1–Q3)	3 (1–5)	3 (1–6)	3 (1–5)		
Patient's GH VAS, cm	3.7 ± 2.6	4.0 ± 2.7	3.7 ± 2.6	1.05 (0.997–1.11)	0.07
Median (Q1–Q3)	3 (2–5)	4 (2–6)	3 (2–5)		
DAS28-ESR	3.6 ± 1.3	3.8 ± 1.3	3.5 ± 1.3	1.14 (1.03–1.27)	0.01
Median (Q1–Q3)	3.5 (2.6–4.4)	3.8 (2.8–4.7)	3.5 (2.5–4.4)		
< 2.6	509 (25.8)	46 (21.7)	463 (26.3)	1.00 (ref)	
≥ 2.6 to < 3.2	309 (15.7)	31 (14.6)	278 (15.8)	1.12 (0.70–1.81)	0.64
≥ 3.2 to ≤ 5.1	892 (45.2)	104 (49.1)	788 (44.8)	1.33 (0.92–1.91)	0.13
> 5.1	263 (13.3)	31 (14.6)	232 (13.2)	1.35 (0.83–2.18)	0.23
Medication					
MTX	1802 (82.9)	190 (83.0)	1612 (82.8)	1.01 (0.70–1.45)	0.96
Any DMARD	1646 (75.7)	173 (75.6)	1473 (75.7)	0.99 (0.72–1.36)	0.96
Steroids	1510 (69.4)	158 (69.0)	1352 (69.5)	0.98 (0.73–1.32)	0.88
NSAID	1683 (77.4)	171 (74.7)	1512 (77.7)	0.85 (0.62–1.16)	0.30
Biologics	133 (6.1)	10 (4.4)	123 (6.3)	0.68 (0.35–1.31)	0.25
Past history of drug side effects	643 (30.2)	75 (33.3)	568 (29.9)	1.17 (0.88–1.58)	0.28
Comorbidity					
CVD	82 (3.8)	3 (1.3)	79 (4.1)	0.31 (0.10–1.002)	0.05
HTN	543 (25.0)	59 (25.8)	484 (24.9)	1.05 (0.77–1.43)	0.77
Gastrointestinal disease	462 (21.2)	55 (24.0)	407 (20.9)	1.20 (0.87–1.65)	0.28
Diabetes mellitus	179 (8.2)	19 (8.3)	160 (8.2)	1.01 (0.62–1.66)	0.97
Thyroid disease	141 (6.5)	15 (6.6)	126 (6.5)	1.01 (0.58–1.76)	0.96
Depression	41 (1.9)	11 (4.8)	30 (1.5)	3.22 (1.59–6.52)	< 0.01
Pulmonary disease	198 (9.1)	20 (8.7)	178 (9.2)	0.95 (0.59–1.54)	0.84

Numbers of missing data: age at disease onset = 80 (Use = 8, No Use = 72), disease duration = 49 (Use = 9, No Use = 40), education = 14 (Use = 2, No Use = 12), family income = 13 (Use = 2, No Use = 11), household type = 7 (Use = 0, No Use = 7), BMI = 18 (Use = 2, No Use = 16), HAQ = 6 (Use = 2, No Use = 4), patient pain VAS = 2 (Use = 1, No Use = 1), patient's GH VAS = 2 (Use = 1, No Use = 1), DAS28-ESR = 202 (Use = 17, No Use = 185), and past history of drug side effects = 48 (Use = 4, No Use = 44). CAM: complementary and alternative medicine; BMI: body mass index; RF: rheumatoid factor; HAQ: Health Assessment Questionnaire; VAS: visual analog scale; GH: global health; DAS28: Disease Activity Score in 28 joints; ESR: erythrocyte sedimentation rate; MTX: methotrexate; DMARD: disease-modifying antirheumatic drug; NSAID: nonsteroidal antiinflammatory drug; CVD: cardiovascular disease; HTN: hypertension; ref: reference.

Table 3. Predictive factors of new CAM use for Korean patients with RA (n = 1867).

Factor	Adjusted OR	95% CI	p
Sex			
Male	1.00 (ref)		
Female	1.89	1.13–3.14	0.01
Age at enrollment, yrs			
≥ 65	1.00 (ref)		
≥ 40 to < 65	1.01	0.67–1.51	0.98
< 40	1.27	0.68–2.36	0.45
Disease duration, yrs			
> 10	1.00 (ref)		
> 5 to ≤ 10	1.26	0.83–1.92	0.28
> 1 to ≤ 5	1.04	0.69–1.59	0.84
≤ 1	1.56	0.97–2.49	0.06
Education			
≥ High school	1.00 (ref)		
≤ Middle school	1.11	0.79–1.58	0.55
Household type			
Nuclear family	1.00 (ref)		
Extended family	1.78	1.08–2.95	0.02
Couple	1.55	1.07–2.24	0.02
Single	1.22	0.71–2.09	0.48
HAQ	1.38	0.99–1.83	0.05
Patient pain VAS, cm	1.01	0.93–1.10	0.83
Patient's GH VAS, cm	0.97	0.89–1.06	0.49
DAS28-ESR			
< 2.6	1.00 (ref)		
≥ 2.6 to < 3.2	1.08	0.65–1.77	0.78
≥ 3.2 to ≤ 5.1	1.05	0.69–1.60	0.83
> 5.1	0.87	0.45–1.66	0.67
Medication			
MTX	0.95	0.63–1.42	0.80
Biologics	0.59	0.29–1.21	0.15
History of drug side effects			
Yes	1.15	0.83–1.59	0.39
Comorbidity			
CVD	0.31	0.09–1.03	0.06
HTN	0.99	0.70–1.44	1.00
Gastrointestinal disease	1.17	0.82–1.68	0.39
Depression	3.52	1.65–7.50	< 0.01

Chi-square goodness-of-fit = 9.63 (p = 0.29) and C-statistic = 0.63. In the case of continuous variables such as HAQ, Patient pain VAS, and Patient's GH VAS, the presented OR indicated the odds per unit. CAM: complementary and alternative medicine; RA: rheumatoid arthritis; HAQ: Health Assessment Questionnaire; VAS: visual analog scale; GH: global health; DAS28: Disease Activity Score in 28 joints; ESR: erythrocyte sedimentation rate; MTX: methotrexate; CVD: cardiovascular disease; HTN: hypertension; ref: reference.

children). Even though we adjusted for income and age, household type remained a factor significantly related to CAM use. Therefore, it is not enough to simply say that couple households and extended family households receive more CAM than nuclear family households; there must be a deeper reason for this difference in CAM use. This suggests that household type may offer other factors influencing a patient's decision to begin treatment with CAM. For example, in extended families, patients may be recommended CAM by other family members with previous experience

with CAM. Additionally, both extended family and couple households may have more economic freedom to begin treatment with CAM than nuclear families that devote a large portion of their income to children. The fact that household type is a predictive factor of new CAM use may indicate that cultural and personal backgrounds are important influential factors in CAM use. However, additional research is needed on this matter.

Depression was also found to be a factor highly associated with the use of CAM. Patients with RA are more frequently diagnosed with depression than the general population^{22,23}. This association of CAM use and depression supports other existing research that shows pain and depression to be among the chief reasons why patients receive CAM^{7,24,25}. While sex and household type generally do not change for a given patient, depression can be variable. This is an important factor for CAM use because both quality of life and CAM use itself can be directly modified because of changes in level of depression.

Previous research shows that disease duration is positively associated with CAM use⁴; additionally, lower education levels correspond to increasingly higher CAM use²⁰. Our study observed similar trends, although our findings were not statistically significant. While both disease duration and education level are longterm factors that cannot be changed immediately, the patients in our study had just begun treatment with CAM. These factors are not significant in our research because it excluded patients who already had experience receiving CAM; our study instead focused on the new CAM use of patients with long disease duration (mean of over 7 yrs) within a 1-year period. It would be beneficial to study the CAM use of patients with previous experience of CAM; however, our primary purpose was to determine why patients who had experienced RA for a long period of time and who had become accustomed to RA medications began treatment with CAM as an additional treatment. Because of the different purpose of our study, the meaning ascribed to the results of our research may be different from that of other studies.

KORONA is the first nationwide, RA-specific cohort in Korea; it is composed of 23 institutions across South Korea, accounting for about 38% of the tertiary academic hospital rheumatology departments across Korea¹². Because of this, the data provided may help facilitate comparative studies regarding the CAM use of patients with RA in Korea and those of other countries; however, such a comparison may still be inhibited by other factors, such as the fact that Korean insurance covers common types of CAM.

One limitation of our study is the accessibility of CAM in Korea. While theoretically considered as forms of CAM in Korea, herbal medicine and acupuncture treatments such as Chinese acupuncture are largely recognized as integrated medicine; it can therefore be difficult to locate factors strongly associated with their use. Because herbal medicine

and certain acupuncture treatments are not standard in many other countries, it is still possible to locate factors strongly associated with CAM use in general, but because of Korean patients' proximity to these forms of CAM, many patients may receive them without recognizing them as CAM. This is why in our research, as in previously published research, the only factors found to be associated with CAM use in Korea are the aforementioned sex, household type, and depression, while in other countries additional factors may also be found. This creates a difficulty in comparative analyses between the CAM use of Korean patients with RA and patients with RA of other countries. However, it also demonstrates the unique situation of patients with RA who are treated with CAM in Korea.

Another limitation was the lack of questions in the original KORONA surveys concerning the subjective factors of patients' CAM use, such as dissatisfaction with conventional medicine or treatment, unalleviated pain, or experience with undesirable side effects. This means that, while we have been able to locate other risk factors associated with new CAM use, there may be other subjective risk factors to consider that are invisible to our study. We used VAS and HAQ scores in an attempt to gain some insight into subjective risk factors for new CAM use. However, more research is needed on subjective dissatisfaction with RA treatment in patients with RA and on its association with CAM. More research and questioning are also needed on why those who persistently do not receive any CAM continue not to do so.

Overall, although our study does not explain why CAM is used in general, it may offer meaningful insight into specific reasons why patients with RA begin treatment with CAM. Our study found, within 1 year of followup, a frequency rate for new CAM use among patients with no previous experience with CAM of 10.5%. Sex, depression, and household type were significantly associated with new CAM use. Future interviews focusing exclusively on the subjective factors of CAM use are necessary to gain a deeper understanding of the relationship between these factors and its use.

ACKNOWLEDGMENT

The authors wish to acknowledge the assistance from the following investigators who enrolled patients in KORONA: Drs. Joong Kyong Ahn, Sung Jae Choi, Minyoung Her, Chung-Il Joung, Young Mo Kang, Dong-Yook Kim, Hae-Rim Kim, Hyoun Ah Kim, Jinseok Kim, Tae-Jong Kim, Choong Ki Lee, Jaejoon Lee, Sang-Heon Lee, Sang-Hoon Lee, Sung Won Lee, Sung-Hoon Park, Dong Hyuk Sheen, Gwan Gyu Song, and Chang-Hee Suh.

REFERENCES

- Gabriel SE. The epidemiology of rheumatoid arthritis. *Rheum Dis Clin North Am* 2001;27:269-81.
- Choy EH, Panayi GS. Cytokine pathways and joint inflammation in rheumatoid arthritis. *N Engl J Med* 2001;344:907-16.
- Whalley D, McKenna SP, de Jong Z, van der Heijde D. Quality of life in rheumatoid arthritis. *Br J Rheumatol* 1997;36:884-8.
- Alvarez-Hernández E, César Casasola-Vargas J, Lino-Pérez L, Burgos-Vargas R, Vázquez-Mellado J. [Complementary and alternative medicine in patients attending a rheumatology department for the first time. Analysis of 800 patients.] [Article in Spanish] *Reumatol Clin* 2006;2:183-9.
- Efthimiou P, Kukar M. Complementary and alternative medicine use in rheumatoid arthritis: proposed mechanism of action and efficacy of commonly used modalities. *Rheumatol Int* 2010;30:571-86.
- Ramos-Remus C, Raut A. Complementary and alternative practices in rheumatology. *Best Pract Res Clin Rheumatol* 2008;22:741-57.
- Barnes PM, Powell-Griner E, McFann K, Nahin RL. Complementary and alternative medicine use among adults: United States, 2002. *Adv Data* 2004;343:1-19.
- Astin JA. Why patients use alternative medicine: results of a national study. *JAMA* 1998;279:1548-53.
- Jensen P. Alternative therapy for atopic dermatitis and psoriasis: patient-reported motivation, information source and effect. *Acta Derm Venereol* 1990;70:425-8.
- Cameron M, Gagnier JJ, Chrusasik S. Herbal therapy for treating rheumatoid arthritis. *Cochrane Database Syst Rev* 2011;CD002948.
- Rao JK, Mihaliak K, Kroenke K, Bradley J, Tierney WM, Weinberger M. Use of complementary therapies for arthritis among patients of rheumatologists. *Ann Intern Med* 1999;131:409-16.
- Sung YK, Cho SK, Choi CB, Park SY, Shim J, Ahn JK, et al. Korean Observational Study Network for Arthritis (KORONA): Establishment of a prospective multicenter cohort for rheumatoid arthritis in South Korea. *Semin Arthritis Rheum* 2012;41:745-51.
- National Center for Complementary and Alternative Medicine. Complementary, alternative, or integrative health: what's in a name? (2008). [Internet. Accessed July 23, 2015] Available from: www.nccam.nih.gov/health/whatiscam
- Kim YS. Medical trends in South Korea. *Am J Chin Med* 1987;15:155-7.
- Hosmer DW, Lemeshow S. Goodness of fit tests for the multiple logistic regression model. *Communications in statistics* 1980;9:1043-69.
- Hosmer DW Jr, Lemeshow S. *Applied logistic regression*. New York: Wiley; 1989.
- Kajiyama H, Akama H, Yamanaka H, Shoji A, Matsuda Y, Tanaka E, et al. One third of Japanese patients with rheumatoid arthritis use complementary and alternative medicine. *Mod Rheumatol* 2006;16:355-9.
- Breuer GS, Orbach H, Elkayam O, Berkun Y, Paran D, Mates M, et al. Use of complementary and alternative medicine among patients attending rheumatology clinics in Israel. *Isr Med Assoc J* 2006;8:184-7.
- Lee MS, Lee MS, Yang CY, Lee SI, Joo MC, Shin BC, et al. Use of complementary and alternative medicine by rheumatoid arthritis patients in Korea. *Clin Rheumatol* 2008;27:29-33.
- Jacobs JWG, Kraaijaat FW, Bijlsma JW. Why do patients with rheumatoid arthritis use alternative treatments? *Clin Rheumatol* 2001;20:192-6.
- Quandt SA, Chen H, Grzywacz JG, Bell RA, Lang W, Arcury TA. Use of complementary and alternative medicine by persons with arthritis: results of the National Health Interview Survey. *Arthritis Rheum* 2005;53:748-55.
- Frank RG, Beck NC, Parker JC, Kashani JH, Elliott TR, Haut AE, et al. Depression in rheumatoid arthritis. *J Rheumatol* 1988;15:920-5.
- Dickens C, McGowan L, Clark-Carter D, Creed F. Depression in rheumatoid arthritis: a systematic review of the literature with meta-analysis. *Psychosom Med* 2002;64:52-60.
- Waraich P, Goldner EM, Somers JM, Hsu L. Prevalence and incidence studies of mood disorders: a systematic review of the literature. *Can J Psychiatry* 2004;49:124-38.
- Kojima M, Kojima T, Suzuki S, Takahashi N, Funahashi K, Kato D, et al. Alexithymia, depression, inflammation, and pain in patients with rheumatoid arthritis. *Arthritis Care Res* 2014;66:679-86.