Utilization Patterns of Disease-Modifying Antirheumatic Drugs in Elderly Rheumatoid Arthritis Patients

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This study was conducted to investigate disease-modifying antirheumatic drug (DMARD) utilization in Korean elderly patients with rheumatoid arthritis (RA). We used data from January 1, 2005 to June 30, 2006 from the Health Insurance Review and Assessment Service claims database. The study subjects were defined as patients aged 65 yr or older with at least two claims with a diagnosis of RA. DMARD use was compared by the patients' age-group, gender, medical service, and geographic divisions. The patterns of DMARD use in mono- and combination therapy were calculated. RA medication use was calculated by the number of defined daily doses (DDD)/1,000 patients/day. A total of 166,388 patients were identified during the study period. DMARD use in RA patients was 12.0%. The proportion of DMARD use was higher in the younger elderly, females, and patients treated in big cities. Hydroxychloroquine was the most commonly used DMARD in monotherapy, and most of the combination therapies prescribed it with methotrexate. DMARD use in elderly RA patients was noticeably low, although drug prescriptions showed an increasing trend during the study period, clinicians may need to pay more attention to elderly RA patients.

Keywords: Utilization; Antirheumatic Agents; Arthritis, Rheumatoid; Database

INTRODUCTION

Rheumatoid arthritis (RA) causes chronic inflammatory synovitis. Inadequately controlled RA is associated with joint damage and consequent disability with higher health costs, as well as mortality (1). RA affects about 1% of the adult population, which means that this low prevalence leads the average physician to have little experience with its diagnosis or management (2, 3). The prevalence increases with age and reaches its peak in the population aged 65 yr or older (4). The elderly (65 yr or older) made up 9 percent of Korea's population in 2005, and 38 percent of the population will be elderly by 2050 (5).

Disease-modifying antirheumatic drugs (DMARDs) have been used to treat inflammatory arthritis and slow down joint destruction. However, previous guidelines have recommended non-steroidal anti-inflammatory drugs (NSAIDs) and corticosteroids without DMARDs for the initial management of RA until evidence of joint damage appeared (6). In the last decade, treatment approaches for RA have changed drastically. The current guidelines suggest that all patients with RA are candidates for DMARDs and that the ideal time to begin the drugs is within three months after receiving an RA diagnosis (7).

However, some studies have reported that older adults with RA are less likely to receive DMARDs than younger adults despite similar disease activity (8, 9). The aim of this study was to investigate DMARD utilization in elderly patients with RA.

MATERIALS AND METHODS

Data source and study population

Patients were identified from the Health Insurance Review and Assessment Service (HIRA) claims database in Korea. The HIRA database contains information on the demographic characteristics, diagnoses, and prescriptions of approximately 50 million Koreans (10). General information includes an anonymized patient number, age, gender, type of hospital visit (inpatient/outpatient), types of medical services, and geographic division. Diagnosis information consists of the visit date and the diagnosis code from the 10th revision of the International Classification of Diseases (ICD-10). Prescription information is composed of the prescription number, drug brand name, drug generic name, prescription date, days of supply, and amount. We used data from the HIRA database from January 1, 2005 to June 30, 2006 covering 4,159,305 elderly patients with 100,838,744 prescriptions. The study subjects were defined as elderly patients aged 65 yr or older with at least two diagnoses of RA (ICD-10:

M05-M06) on different days and excluded patients who were diagnosed with human immunodeficiency virus (ICD-10: B20-B24) or cancer (ICD-10: C00-C97, D00-D09).

Variable measurement

The study variables used in this study included demographic factors (age group, gender), medical care utilization status (type of hospital visit, medical service, and geographic division), rheumatoid factors, medication use, and comorbidities. Inpatients were defined as patients hospitalized at least once during the study period, while outpatients were patients who only visited the clinic or outpatient department of secondary or tertiary hospitals. Medical services were classified as primary, secondary, and tertiary care. Geographic regions depending on the location of healthcare institutions were classified into three areas, metropolitan cities, urban cities, and rural areas, that is, areas with a population over 1,000,000, with a population between 50,000 to 1,000,000, and with a population under 50,000, respectively. RA patients with at least one diagnosis of sero-positive RA (ICD-10 code: M05) were defined as positive for rheumatoid factor. Comorbidities were noted, including hypertension (ICD-10 code: I10, I15), heart failure (ICD-10 code: I50), ischemic heart disease (ICD-10 code: I20-I25), atrial fibrillation (ICD-10 code: I48), hyperlipidemia (ICD-10 code: E78), stroke (ICD-10 code: I60, I61, I63, I64), diabetes mellitus (DM) (ICD-10 code: E10-E14), and chronic obstructive pulmonary disease (COPD) (ICD-10 code: J40-J44).

Evaluation of treatment for rheumatoid arthritis

In this study, for RA treatment, medication use included DMARDs, corticosteroids, and NSAIDs. Sixteen DMARDs were covered by the national insurance during the study period, including non-biological and biological DMARDs. The non-biological DMARDs comprised methotrexate (MTX), hydroxychloroquine (HCQ), sulfasalazine (SSZ), leflunomide (LEF), bucillamine (Bc), D-penicillamine (DP), minocycline (MC), sodium aurothiomalate (SA), auranofin (AF), azathioprine (AZA), cyclophosphamide (CP), cyclosporine (Cy), and mizoribine (MZ). The biological DMARDs included etanercept (ET), infliximab (IFX), and rituximab (RTX). Among the corticosteroid and NSAID use in this study, we included medications administered orally or by injection. For each RA patient, medication use was defined as being prescribed at least one of these drugs during the study period.

For ascertaining the DMARD prescription pattern in the elderly RA patients, we identified the frequently prescribed DMARDs both in mono- and combination therapies. DMARD monotherapy was defined as only one DMARD prescribed in a prescription. More than one DMARD in one prescription was defined as combination therapy. Corticosteroids and NSAIDs that were prescribed in the same prescription with DMARDs were assessed as comedication.

In order to describe the DMARD prescription patterns in the RA patients, we used the value of the defined daily dose (DDD) (11). The DDD for each drug was identified from the WHO website for the 2013 ATC/DDD Index (12). If there was no information on the DDD value on the WHO website, the value was defined based on the recommended daily medication doses for RA treatment in Korea (13).

Statistical analysis

The patients' baseline characteristics were presented by demographic factors, medical care utilization status, rheumatoid factors, medication use, and comorbidities. The proportion of DMARD use was calculated and compared by demographic factors, medical care utilization status, and geographic division. We also compared the rheumatoid factors, medication use, and comorbidities between DMARD users and non-users. The number of prescriptions with mono and combination DMARD therapies was evaluated. Combination therapies were categorized into two groups: MTX+another DMARD and a DMARD combination without the MTX prescribed. We also calculated the number of prescriptions with DMARD only, DMARD+corticosteroid, DMARD+NSAIDs and DMARD+corticosteroid+NSAIDs. We calculated the number of DDD/1,000 patients/day in each month from the claims data. For each drug, the total DDDs were calculated by summing the doses of the drugs for the month. This number was divided by the population in thousands and then divided by the number of days in that month to give the DDD/1,000 patients/day. If drugs were prescribed before 2005, then the duration of the prescription could last up to 2005, and these prescriptions were difficult to reflect in our data. Therefore, in this study, we estimated the drug consumption for 16 months, excluding the first two months of 2005. The chi-square test was performed to compare the difference in the proportion between classified groups, and the Cochran-Armitage trend test was used to see the trends in the proportions by group. P values less than 0.05 were considered statistically significant. All of the analyses were performed using SAS software version 9.3 (SAS Institute Inc., Cary, NC, USA).

Ethics statement

The study protocol was approved by the institutional review board (IRB) of Seoul National University College of Medicine and Seoul National University Hospital (Protocol ID: 2011-1613). Informed consent was waived by the IRB.

RESULTS

Study populations and baseline characteristics

A total of 166,388 elderly RA patients were identified from January 1, 2005 to June 30, 2006 (Fig. 1). The mean age ± SD of the
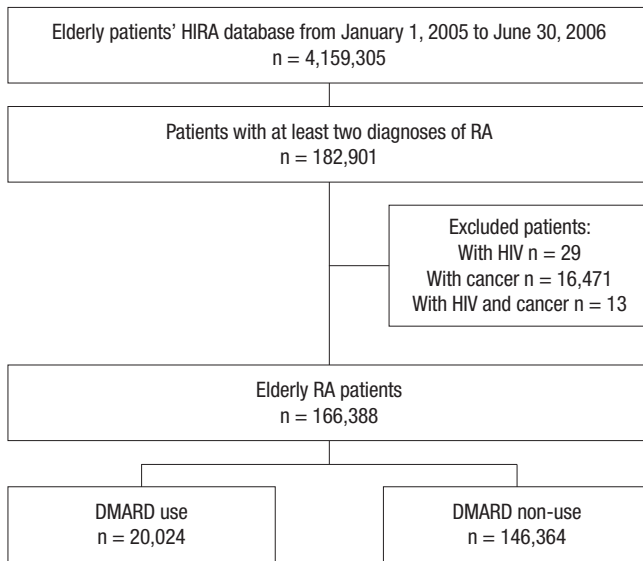
Fig. 1. The flowchart of the study populations. HIRA, Health Insurance Review and Assessment Service; RA, rheumatoid arthritis; HIV, human immunodeficiency virus; DMARD, disease-modifying antirheumatic drug.

Table 1. The characteristics of elderly patients with rheumatoid arthritis

Category	No. of patients (%)
Age, yr (Mean ± SD: 72.5 ± 5.8)	
65-69	63,391 (38.1)
70-74	50,000 (30.1)
75-79	31,363 (18.8)
80+	21,634 (13.0)
Gender	
Male	35,864 (21.6)
Female	130,524 (78.4)
Type of hospital visit	
Inpatient	10,796 (6.5)
Outpatient	155,592 (93.5)
Medical service*	
Primary care	123,980 (74.5)
Secondary care	15,000 (9.0)
Tertiary care	40,192 (24.2)
Geographic division*	
Metropolitan cities	73,814 (44.4)
Urban cities	57,783 (34.7)
Rural areas	42,656 (25.6)
Rheumatoid factor	
Sero-positive	33,658 (20.2)
Medication use*	
DMARD	20,024 (12.0)
Corticosteroids	144,427 (86.8)
NSAIDs	138,109 (85.9)
Comorbidity*	
Hypertension	108,444 (65.2)
Heart failure	13,741 (8.3)
Ischemic heart disease	34,794 (20.9)
Atrial fibrillation	4,841 (2.9)
Hyperlipidemia	54,496 (32.8)
Stroke	21,516 (12.9)
Diabetes mellitus	62,328 (37.5)
COPD	58,848 (35.4)

*Patients can be included in more than one category. DMARD, disease-modifying antirheumatic drug; NSAID, non-steroidal anti-inflammatory drug; COPD chronic obstructive pulmonary disease.

participants was 72.5 ± 5.8 yr, and 130,524 (78.4%) of the patients were women. Almost 93.5% of the patients presented as outpatients, and 74.5%, 9.0%, and 24.2% of the patients received primary, secondary, and tertiary care, respectively. Among the patients 44.4% received medical services in metropolitan cities, 34.7% in urban cities, and 25.6% in rural areas. As for rheumatoid factor, 20.2% of the patients were sero-positive. Among all of the elderly RA patients, only 20,024 (12.0%) patients received at least one DAMRD during the study period, but 86.8% received a corticosteroid prescription, and 85.9% received NSAIDs. With regard to comorbidity, 65.2% of the elderly RA patients had been diagnosed with hypertension, 32.8% with hyperlipidemia, 12.9% with stroke, 37.5% with DM, and 35.4% with COPD (Table 1).

Utilization of DMARDs by patient characteristics

DMARD use by demographic factors and medical care utilization status is shown in Table 2. The proportion of DMARD use in the youngest age group was 15.8%, which was markedly higher than that in the older age groups, with a decreasing trend by groups of increasing age ($P < 0.01$). The proportion was higher in the females than the males (12.4% vs 10.8%, respectively, $P < 0.01$). Among those who presented as inpatients, 28.7% received DMARDs, which was more than twice the proportion of outpatients who received DMARDs (10.9%) ($P < 0.01$). The proportion of DMARD prescription in patients using tertiary care services was 26.0%, which was higher than that of patients visiting secondary care (7.3%) and primary care institutions (8.0%). By geographic division, the proportion of those prescribed DMARDs was higher in patients treated in bigger cities compared to those

Table 2. Disease-modifying antirheumatic drug use in elderly patients with rheumatoid arthritis

Category	Elderly RA patients	DMARD use (No.) (%)	P value
Age (yr)			< 0.01*
65-69	63,391	10,028 (15.8)	
70-74	50,000	6,098 (12.2)	
75-79	31,363	2,813 (9.0)	
80+	21,634	1,085 (5.0)	
Gender			< 0.01†
Male	35,864	3,878 (10.8)	
Female	130,524	16,146 (12.4)	
Type of hospital visit			< 0.01†
Inpatient	10,796	3,099 (28.7)	
Outpatient	155,592	16,925 (10.9)	
Medical service			< 0.01*
Primary care	123,980	9,914 (8.0)	
Secondary care	15,000	1,090 (7.3)	
Tertiary care	40,192	10,452 (26.0)	
Geographic division			< 0.01*
Metropolitan cities	73,814	12,447 (16.9)	
Big cities	57,783	6,885 (11.9)	
Rural areas	42,656	1,512 (3.5)	

*The P value was calculated by the Cochran-Armitage trend test; †The P value was calculated by a chi-square test; RA, rheumatoid arthritis; DMARD, disease-modifying antirheumatic drug.

treated in smaller cities and rural areas: The proportions were 16.9%, 11.9%, and 3.5%, respectively, and showed a decreasing trend ($P < 0.01$).

Comparison between DMARD users and non-users

In the group using DMARDs, there were significantly more sero-positive patients than in the non-use group ($P < 0.01$). Both corticosteroid and NSAID use were significantly higher in patients using DMARDs compared with the rates in non-users ($P < 0.01$). Compared with DMARD non-use patients, DMARD users had a significantly higher prevalence of hyperlipidemia ($P < 0.01$) but had a significantly lower prevalence of other co-

morbidities (atrial fibrillation, $P = 0.02$; others, $P < 0.01$) (Table 3).

Evaluation of DMARDs, NSAIDs, and corticosteroids

Table 4 shows the DMARD prescription patterns in elderly RA patients. The numbers of prescriptions with DMARD monotherapy and combination therapy were 98,273 and 76,977, respectively. In monotherapy, the most frequently prescribed pattern was DMARD+corticosteroids+NSAIDs, and the most frequently prescribed DMARDs were HCQ, MTX, SSZ, Bc, and LEF in that order. In combination therapy, the most prescribed pattern was also DMARD+corticosteroids+NSAIDs. Moreover, prescriptions with MTX comprised almost 80% of the combination therapy cases, and the most frequently prescribed combinations were MTX+HCQ, MTX+HCQ+SSZ, MTX+SSZ, MTX+Bc, MTX+HCQ+Bc, MTX+LEF, and MTX+SSZ+Bc in order of decreasing frequency. In combination therapy without MTX, the most frequently prescribed combinations were SSZ+HCQ, HCQ+Bc, and SSZ+Bc in that order.

Prescriptions of RA medications by DDD

Fig. 2 shows the prescriptions of NSAIDs, DMARDs, and corticosteroids by month from March 2005 to June 2006. The NSAIDs were the most prescribed drugs, and the usage of drugs increased steadily, such that NSAID use increased from 1,234.0 DDD/1,000 patients/day in March 2005 to 1,442.6 DDD/1,000 patients/day in June 2006; DMARD use increased from 282.7 DDD/1,000 patients/day to 369.6 DDD/1,000 patients/day; and corticosteroid use increased from 248.1 DDD/1,000 patients/day to 297.2 DDD/1,000 patients/day.

Table 3. A comparison of disease-modifying antirheumatic drug users and non-users

Category	DMARD use (n = 20,024)	DMARD non-use (n = 146,364)	P value*
Sero-positive RA	6,198 (31.0)	27,460 (18.8)	< 0.01
Medication			
Steroids	19,322 (96.5)	125,105 (85.5)	< 0.01
NSAIDs	17,351 (86.7)	120,758 (82.5)	< 0.01
Comorbidity			< 0.01
Hypertension	12,242 (61.1)	96,202 (65.7)	< 0.01
Heart failure	1,498 (7.5)	12,243 (8.4)	< 0.01
Ischemic heart disease	3,911 (19.5)	30,883 (21.1)	< 0.01
Atrial fibrillation	532 (2.7)	4,309 (2.9)	0.02
Hyperlipidemia	6,771 (33.8)	47,725 (32.6)	< 0.01
Stroke	1,975 (9.9)	19,541 (13.4)	< 0.01
Diabetes mellitus	7,192 (35.9)	55,136 (37.7)	< 0.01
COPD	6,843 (34.2)	52,005 (35.5)	< 0.01

*The P value was calculated by a chi-square test; DMARD, disease-modifying antirheumatic drug; COPD, chronic obstructive pulmonary disease.

Table 4. The patterns of disease modifying antirheumatic drugs in mono- and combination therapy

DMARDs	No. of prescriptions	DMARD only No.* (%)	DMARD+corticosteroid No.* (%)	DMARD+NSAIDs No.* (%)	DMARD+corticosteroid +NSAIDs No.* (%)
Monotherapy	98,273	10,786 (11.0)	17,034 (1.3)	29,169 (29.7)	41,284 (42.0)
HCQ	53,253	5,156 (9.4)	7,617 (13.3)	17,232 (34.1)	23,248 (43.2)
MTX	19,247	2,768 (14.0)	3,811 (17.0)	5,331 (30.2)	7,337 (38.8)
SSZ	10,683	1,357 (12.3)	1,526 (13.4)	3,551 (35.1)	4,249 (39.3)
Bc	7,369	655 (9.1)	1,178 (14.4)	2,291 (33.8)	3,245 (42.7)
LEF	5,872	480 (8.4)	2,233 (34.9)	497 (9.4)	2,662 (47.3)
Others	1,849	370 (20.2)	669 (33.4)	267 (15.8)	543 (30.7)
Combination therapy	76,977	5,824 (7.6)	17,096 (22.2)	12,770 (16.6)	41,287 (53.6)
MTX+other DMARDs	61,352	4,394 (7.2)	13,057 (21.3)	9,794 (16.0)	34,107 (55.6)
MTX+HCQ	27,596	2,092 (7.6)	5,152 (18.7)	5,055 (18.3)	15,297 (55.4)
MTX+HCQ+SSZ	11,018	782 (7.1)	2,623 (23.8)	1,479 (13.4)	6,134 (55.7)
MTX+SSZ	7,476	489 (6.5)	1,336 (17.9)	1,450 (19.4)	4,201 (56.2)
MTX+Bc	5,422	436 (8.0)	1,188 (21.9)	666 (12.3)	3,132 (57.8)
MTX+HCQ+Bc	4,055	280 (6.9)	795 (19.6)	616 (15.2)	2,364 (58.3)
MTX+LEF	1,916	85 (4.4)	758 (39.6)	183 (9.6)	890 (46.5)
MTX+SSZ+Bc	1,626	87 (5.4)	331 (20.4)	183 (11.3)	1,025 (63.0)
MTX+others	2,243	143 (6.4)	874 (39.0)	162 (7.2)	1,064 (47.4)
Other combinations	15,625	1,430 (9.2)	4,039 (25.8)	2,976 (19.0)	7,180 (46.0)
SSZ+HCQ	7,606	656 (8.6)	1,753 (23.0)	1,585 (20.8)	3,612 (47.5)
HCQ+Bc	3,896	457 (11.7)	756 (19.4)	802 (20.6)	1,881 (48.3)
SSZ+Bc	1,115	63 (5.7)	265 (23.8)	228 (20.4)	559 (50.1)
Others	3,008	254 (8.4)	1,265 (42.1)	361 (12.0)	1,128 (37.5)

*No., number of prescriptions; DMARDs, disease-modifying antirheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs; HCQ, hydroxychloroquine; MTX, methotrexate; SSZ, sulfasalazine; Bc, bucillamine; LEF, leflunomide.
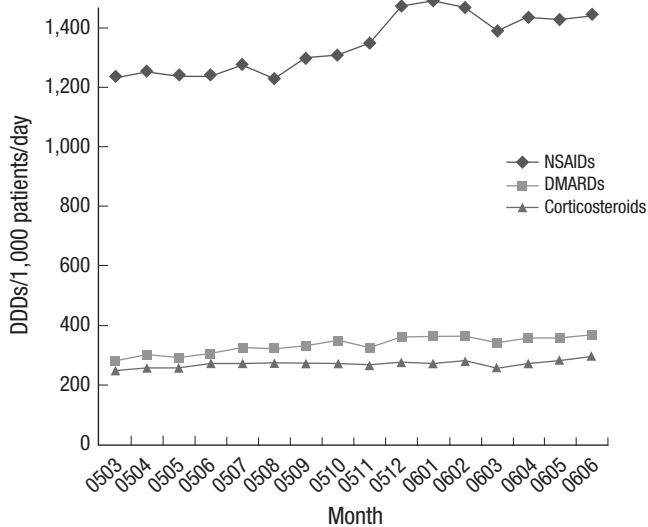
Fig. 2. Prescriptions of rheumatoid arthritis medications by month from March 2005 to June 2006. DDD, defined daily dose; NSAID, non-steroidal anti-inflammatory drug; DMARD, disease-modifying antirheumatic drug.
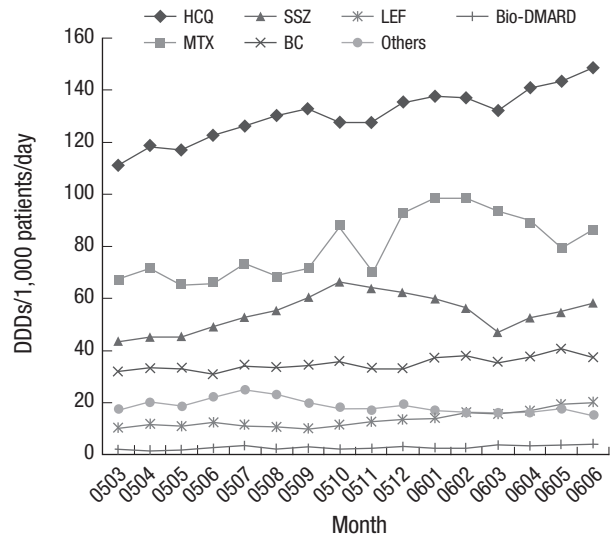

Fig. 3. Prescriptions of disease-modifying antirheumatic drugs by month from March 2005 to June 2006. DDD, defined daily dose; HCQ, hydroxychloroquine; MTX, methotrexate; SSZ, sulfasalazine; BC, bucillamine; LEF, leflunomide.

HCQ was the most commonly used DMARD. The usage of HCQ, MTX, SSZ, LEF, and the biological DMARDs increased from 110.8, 67.2, 43.4, 10.0, and 1.9 DDD/1,000 patients/day in March 2005 to 148.7, 86.5, 58.2, 20.0, and 3.9 DDD/1,000 patients/day in June 2006. On the other hand, Bc showed a fluctuating pattern, and use of the other DMARDs decreased (Fig. 3).

DISCUSSION

In this nationally representative data set on elderly patients' claims with a diagnosis of RA, we found wide variations in DMARD prescriptions based on demographic factors and medical care utilization status. Male sex, advanced age, visiting a primary or secondary care institution, and treated in rural areas were related to a lower number of DMARD prescriptions.

These findings were in line with those of previous studies that found patients aged 85 yr and older had a lower rate of DMARD use than patients 65 to 69 yr of age (14, 15) and lower rates were also found for male patients (15). However, the finding that only 12% of elderly RA patients received DMARDs in our study was noticeably lower than the proportions in other population-based studies (30%-52%) (14-19). In this study, DMARD use was 28.7% in inpatients, but the majority of patients were outpatients (93.5%) and the proportion of DMARD use in these patients was only 10.9%. In addition, about 75% of patients visited primary and secondary care institutions which had low proportion of DMARD prescription. And also due to the low proportion of study subjects identified as RF positive (20.2%), given that DMARD use has been strongly associated with serious conditions such as being RF positive (20). On the other hand, based on the data of the Korean National Health

and Nutrition Examination Surveys (KNHANES) III, conducted in 2005, the self-reported prevalence of RA without treatment was almost 56%, which means that despite patients' knowing they had RA, more than half of the patients had not received any treatment. This may have also contributed to the limited use of DMARDs (21). DMARD prescriptions in patients with coronary and cerebrovascular disease, heart failure, pulmonary disease, and diabetes were not statistically different compared with patients without these diseases (14). In contrast, patients who received DMARDs had significantly lower rates of diagnosis of hypertension, heart failure, ischemic heart disease, stroke, diabetes mellitus, and COPD in our study (all were $P < 0.05$).

The most commonly prescribed DMARD was MTX in several previous studies (22, 23). One study reported SSZ to be the most commonly prescribed DMARD, but the use of MTX showed an increasing trend (16). Despite these findings, patients received HCQ more frequently than other DMARDs both among monotherapy and combination therapy options in our study. In another Korean study on DMARDs using the HIRA database reported that the most commonly prescribed drug was HCQ, followed by MTX, which was similar to our results (24). In combination therapy, nearly 80% of combination therapies were prescribed with MTX, which suggests that the prescriptions appropriately followed guideline recommendations (7). Despite the low proportion of DMARD use in elderly RA patients, increasing patterns of drug use were observed in most of the drugs that treat RA, especially HCQ, MTX, and biological DMARDs.

This study had the following strengths. The study used the national health insurance claims database including the whole population of elderly patients with RA. The HIRA database provides reliable and comprehensive information on drug prescrip-

tions that should reflect the medication use in RA treatment among representative populations in the real world. The database contains various parameters including medical care utilization status and geographic division, and provided significant differences or trends in DMARD use. Furthermore, the prescription date, days of supply, and amount enabled us to obtain and calculate accurate drug prescription information and analyze drug usage patterns.

Nonetheless, our study had some limitations. This study used the national claims database, which is data submitted to HIRA for review, checking, and fee reimbursement purposes, and thus may be limited in identifying the diagnosis accurately (25). However, in a previous validation study, the ICD-10 codes used in the HIRA database were in about 70% agreement overall with clinical information (26). One previous study performed for examining the validity of algorithm for identifying RA (sero-positive) diagnostic codes in the HIRA database reported that the prevalence of NSAIDs and corticosteroids prescription in the true RA patients were 85.90% and 75.59%, the specificity of corticosteroids was 62.25% (27). These results of the study can partly support our study findings. Nevertheless, it is difficult to confirm the accuracy of diagnostic code for sero-negative RA patients due to lack of validity studies on these patients. Sero-positive RA defined in this study, we used the ICD-10 code M05, but HIRA database dose not contain laboratory data, so we could not collect the accurate information on whether sero-positive RA was assessed by quantitative test or qualitative test. And the database was also lack of information about anti-cyclic citrullinated peptide antibodies (anti-CCP). The data we used to observe prescribing trends was from March 1, 2005 to July 30, 2006. This period was only 16 months, which was not long enough to observe DMARD and other drugs prescription trends by year. On the other hand, we were not able to assess all of the biological DMARDs used in this study given that at the time of the study (2005-2006), most biological DMARDs were not covered by insurance. Furthermore, a part of biological DMARDs prescriptions had been omitted from the records of HIRA claims database. Regrettably, the data of this study was relatively old (from January 2005 to June 2006), so it may not reflect current medication pattern exactly. Therefore, further research is needed to investigate current DMARD utilization patterns using recent data, and also needed to perform follow-up studies using long-term data to observe the changing patterns.

In summary, according to the results of this study, DMARD use in Korean elderly RA patients was 12.0%. Prescriptions of DMARDs were greater in number in the younger elderly, females, and those who treated in big cities. The DMARD use patients had a higher proportion of sero-positivity, corticosteroid, and NSAID use, and had a lower rate of comorbidities. HCQ was the most common used DAMRD in monotherapy, and most of the combination therapies were prescribed with MTX.

When prescribing DMARDs, it was most common to add both corticosteroids and NSAIDs in one prescription. Despite the low proportion of DMARD use, the drug prescriptions showed an increase trend during the study period.

DISCLOSURE

The authors have no conflicts of interest to disclose.

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