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RESEARCH ARTICLE

Utilization of oral anticoagulants in Korean nonvalvular atrial fibrillation patients

Hye-Yoon Song[1] · Kyung-Bok Son[1] · Ju-Young Shin[2] · SeungJin Bae[1]

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Abstract

Background Although the majority of clinical guidelines indicate the use of NOAC (nonvitamin K antagonist oral anticoagulant) over vitamin K antagonist in nonvalvular atrial fibrillation patients, there is no information on real-world prescription factors that lead to a specific type of oral anticoagulant selection. *Objective* To evaluate the prescription factors for choosing a specific oral anticoagulant for nonvalvular atrial fibrillation patients in Korea. *Setting* Nationwide sampled database in South Korea. *Methods* In this study, we defined nonvalvular atrial fibrillation patients as having one or more hospitalizations or two or more out-patient visits with a stroke risk score (CHA2DS2-VASc scores) ≥ 2 eligible for oral anticoagulant therapy from Jan 1st, 2016 to Dec 31st, 2016. Baseline characteristics were analyzed, including sex, age, comorbidities, CHA2DS2-VASc, bleeding risk score (mHAS-BLED), prescribing specialty, insurance type, medical institution type and location. Univariate and multivariate logistic regression analyses were conducted for being prescribed NOAC compared with vitamin K antagonist. *Main outcome measure* Adjusted odds ratio of the NOAC group and vitamin K antagonist group. *Results* Of 9,226 patients eligible for oral anticoagulant therapy, 4999 patients (54.2%) received oral anticoagulant therapy, and 4517 patients took NOAC or vitamin K antagonist only during the study period. Prior stroke, transient ischemic attack, thromboembolism, thyroid disease, dyslipidemia, cancer, mHAS-BLED ≥ 5, in-patient care, and specialty in internal medicine and neurology were positive predictors of NOAC use over vitamin K antagonist, whereas young age (≤64), renal dysfunction, and secondary care institution were negative predictors of NOAC use over vitamin K antagonist. *Conclusions* The presence of comorbidities was linked to NOAC use over vitamin K antagonist, which is different from prescription factor studies in other countries and requires further study.

Keywords Anticoagulant · NOAC · Nonvalvular atrial fibrillation · Prescribing · South korea · Vitamin-K antagonist

Impact on practice

- Underutilization of oral anticoagulant therapy in stroke prevention is still a problem in Korea. Only half of the nonvalvular atrial fibrillation patients eligible for oral anticoagulant therapy are treated.
- NOAC prescribing in South Korea is associated with the providers' specialty and the types of medical institutions, as well as comorbidities.
- Clinicians and policy makers should strive to increase NOAC use for nonvalvular atrial fibrillation patients in primary or secondary medical institutions.

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✉ SeungJin Bae
sjbae@ewha.ac.kr

[1] College of Pharmacy, Ewha Womans University, Seoul 03760, Republic of Korea

[2] School of Pharmacy, Sungkyunkwan University, Suwon 16419, Republic of Korea

Introduction

As of 2016, 13.6% of Korea's population was aged 65 or older [1], and cerebral infarction, which occurs when there is irreversible damage to the brain after ischemic stroke, is the second highest in healthcare cost after Alzheimer's in South Korea [2]. The incidence of stroke is approximately 5 times higher in patients diagnosed with atrial fibrillation

compared to that of healthy people [3]. Hence, it is important to address stroke prophylaxis among atrial fibrillation patients, especially in Korea.

Despite the proven safety and efficacy of the vitamin K antagonist (VKA), which is one of the oral anticoagulants, the difficulty in using VKA has resulted in underutilization of oral anticoagulant (OAC) therapy [4–6]. To improve the use of OACs, non-vitamin K antagonist oral anticoagulant (NOACs) has been developed since 2010, including dabigatran, rivaroxaban, apixaban, and edoxaban. The available clinical guidelines do not show a preference among NOACs, although they recommend using NOAC over warfarin in OAC therapy [3, 7, 8]. The Korea Heart Rhythm Society Guidelines for Stroke Prevention Therapy in Korean Patients with Nonvalvular Atrial Fibrillation (NAF) suggested that male patients with CHA2DS2-VASc score ≥ 2 and female patients with CHA2DS2-VASc score ≥ 3 are recommended to receive OAC therapy [9]. Additionally, the guidelines specified that NOAC is recommended in preference to VKA. NOAC use is reimbursed for stroke prevention in patients with AF with a high risk of stroke, namely, patients with a history of stroke/transient ischemic attack (TIA)/thromboembolism (TE) or patients ≥ 75, which pertains to the CHA2DS2-VASc score, or having 2 or more of the six risk factors (chronic heart failure, hypertension, diabetes, vascular disease, age between 65 and 74, and female sex), which pertains to the CHA2DS2-VASc score of 2 as each risk factor equates to 1 point [9]. With the introduction of NOACs to the market, many studies in Korea have noted differences in the prescription patterns of OACs [10, 11]. Yet there has not been a prescription factor analysis in OAC selection for stroke prophylaxis in NAF patients considering various comorbidities that may be present with old age or associated with AF. Although a previous study calculated CHA2DS2-VASc scores, which estimate the risk of stroke [12], few studies considered the risk of bleeding as well using a representative sample in Korea. The risk of bleeding should also be determined preceding the use of OACs as indicated by available guidelines [7, 8, 11], because the use of OAC may reduce the risk of stroke but may increase the risk of bleeding at the same time. Although there are many bleeding risk scores developed, the 2017 Asian Pacific Heart Rhythm Society recommends the use of HAS-BLED for the estimation of bleeding risk in Asian patients [3]. Hence, we have also added a modified HAS-BLED score to estimate bleeding risk in AF patients. These risk evaluation scores allowed our evaluation of claims data to closely resemble the actual physician evaluation process in the clinical setting [11, 13, 14]. The purpose of this study was to estimate which factor(s) positively affects the prescription of NOACs over conventional VKA treatment ('warfarin') using Korean national claims sample data in 2016. Because NOACs are indicated specifically for nonvalvular AF patients in Korea, we focused on NAF patients in our analysis.

Ethics approval

The patient's personal information was anonymized so that the actual individuals could not be identified. Hence, the acquisition of informed consent was waived by the board. This study was waived for review by the Institutional Review Board of Ewha Womans University (IRB no, 160-11).

Methods

Data source

In this study, we used the National Patients Sample data gathered by the Korean Health Insurance Review and Assessment Service (HIRA-NPS), which represents 3% (1.4 million) of the entire Korean population consisting of 10% in-patient data and 90% out-patient data. The study period was from Jan 1st, 2016, to Dec 31st, 2016. The National Patients Sample data passed the validity test and proved to represent the Korean patient population [15].

Patient definition

The validity of the ICD codes in the HIRA claims database has been questioned, and various diagnostic algorithms or definitions have been added to exclude false positive cases [16]. Our definition is based on previous studies that defined NAF as such using the claims database [17, 18]. Specifically, adults who were 20 years old or older and who made 2 or more visits to out-patient medical clinics or who had 1 or more hospitalizations with AF based on the ICD-10 diagnosis code (I480–I484, I489) were defined as NAF patients. To distinguish NAF patients from the AF population, we excluded AF patients who also had the ICD-10 diagnosis code for mitral stenosis (I50, I52, I59) or mechanical heart valve (Z952–Z954), which relate to valvular AF [19]. Considering previous studies that reported a relatively low incidence of adult AF in Korea of 0.77% consisting of 276,246 patients [11], we searched up to the 10th diagnosis to capture as many NAF patients in our study population as possible.

Study drugs

For stroke prophylaxis in NAF patients, two categories of OACs exist: VKA and NOAC. Warfarin is the only available VKA in Korea, and dabigatran, rivaroxaban, apixaban, and edoxaban are the current NOACs reimbursed in Korea.

Definition of the CHA2DS2-VASc score and modified HAS-BLED (mHAS-BLED) score

We calculated the CHA2DS2-VASc scores to evaluate the stroke risk of NAF patients. Many clinical guidelines use CHA2DS2-VASc to determine eligibility for OAC therapy [17, 18]. CHA2DS2-VASc is a 9-point scoring system and consists of various risk factors, including congestive heart failure/LV dysfunction (1 point), hypertension (1 point), age ≥ 75 years old (2 points), diabetes mellitus (1 point), previous stroke /TIA / TE (2 points), vascular disease (1 point), age 65–74 years old (1 point), and female sex (1 point). Previous studies were referred to for the ICD-10 codes of the comorbidities (Supplementary Table 1). For bleeding risk, the HAS-BLED score was used following the Korean and European guidelines [7, 8]. It consists of hypertension (1 point), abnormal renal and liver function (1 point each), previous stroke (1 point), bleeding tendency or predisposition (recent bleed, anemia, etc.) (1 point), labile international normalized ratio (INR) for warfarin user (1 point), age ≥ 65 years old, and drug and alcohol excess (1 point each). The INR is a standardized measure to evaluate whether warfarin therapy is under a controlled range of 2.0–3.0. As the INR is not included in the HIRA-NPS, a modified HAS-BLED (mHAS-BLED) scoring was applied referring to previous studies [20, 21].

Definition of comorbidities

Other than the presence of a disease that counts toward the CHA2DS2-VASc score and mHAS-BLED score, other comorbidities that were independently associated risk factors of AF in the ESC guidelines were considered [7]. Additionally, the presence of pneumonia, rheumatic disease, and cancer was checked as they were diagnoses that easily relate to the elderly population. All comorbidities were confirmed up to the 10^{th} diagnosis code of each patient, and the definition of each comorbidity is presented in Supplementary Table 2.

Types of medical institutions and locations

The types of medical institutions and locations were categorized according to a previous cross-sectional study [22]. Medical institutions were categorized into tertiary care institutions consisting of general hospitals and upper-level general hospitals, secondary care institutions consisting of hospitals and nursing hospitals, and primary care institutions consisting of local clinics and public health clinics consisting of government-sponsored health care facilities. All other medical institutions were grouped in the "Others" category.

Statistical analysis

Because all variables were categorical, χ^2 tests were performed. Then, these variables were evaluated using univariate and multivariate logistic regression analyses. Data analysis was performed using SAS version 9.4 (SAS Institute Inc., Cary, NC, USA). Statistical significance was set at $p < 0.05$.

Results

During the study period from Jan 1st, 2016, to Dec 31st, 2016, adult NAF patients who had visited the hospital more than twice or who had more than one hospitalization record totaled 11,194 patients (Fig. 1). Of 9226 NAF patients eligible for OAC therapy, 4999 patients (54.2%) received OAC therapy, and after we excluded 482 patients who took both NOAC and VKA, 4517 patients were left for the analysis (Fig. 1).

Table 1 shows the characteristics of patients receiving warfarin (VKA) and NOAC. The distribution of the CHA2DS2-VASc score was significantly different in the NOAC group and warfarin group ($p < 0.0001$), with the NOAC group being more likely to be older and with more comorbidities, including hypertension, prior stroke/TIA/TE, vascular disease, renal disease, liver disease, thyroid disease, COPD, dyslipidemia, and cancer. Both the mHAS-BLED and CHA2DS2-VASc scores showed that the NOAC group tended to have higher scores, indicating that patients with higher stroke risk and bleeding risk were more likely to be prescribed NOAC than VKA. NOAC-treated patients were more likely to visit tertiary medical institutions (86.2%) and less likely to visit primary medical institutions, whereas 82.55% of warfarin-treated patients visited tertiary medical institutions. In the secondary and primary medical institutions, patients treated with warfarin were greater than those treated with NOAC. The NOAC group was more likely to be used in the in-patient setting ($p < 0.0001$), and warfarin was more likely to be used by specialists other than neurology or internal medicine.

Table 2 shows the results of univariate and multivariate logistic regression to find the factors associated with any NOAC prescription versus warfarin. Overall, aged 64 or less (adjusted odds ratio (aOR), 0.60; 95% CI, 0.48–0.76), the presence of renal disease (aOR, 0.46; 95% CI, 0.36–0.59), and visit to a secondary care institution (aOR, 0.65; 95% CI, 0.50–0.85) led to a decreased prescription rate of NOAC over warfarin. On the other hand, the presence of prior stroke/TIA/TE (aOR 1.35; 95% CI, 1.09–1.67), thyroid disease (aOR 1.37; 95% CI, 1.14–1.64), dyslipidemia (aOR, 1.28; 95% CI, 1.10–1.49), and cancer (aOR, 1.38; 95% CI, 1.12–1.72) led to an increased prescription rate of NOAC over warfarin. In terms of clinical risk scores, only mHAS-BLED ≥ 5 showed statistical significance

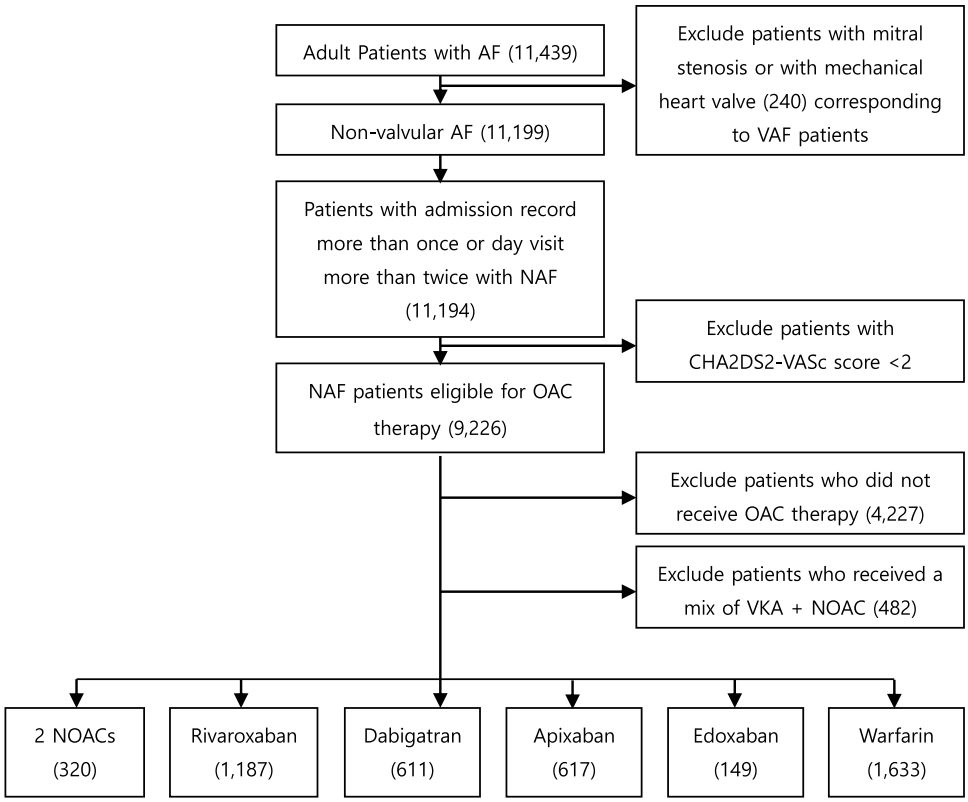

Fig. 1 Case extraction diagram. HIRA, Health Insurance Review and Assessment Service; NPS, National Patients Sample; AF, Atrial fibrillation; VAF, Valvular atrial fibrillation; NAF, Nonvalvular atrial fibrillation; VAF, Valvular atrial fibrillation; OAC, Oral anticoagulants; VKA, Vitamin K antagonist oral anticoagulant

to confirm the prescription rate difference between NOAC and warfarin (aOR, 1.46; 95% CI, 1.06–2.01). In-patient setting and a prescribing specialty in internal medicine and neurology also showed a higher preference of NOAC prescription over warfarin prescription.

Discussion

In this study, we analyzed sample national claims data from Jan 1st, 2016, to Dec 31st, 2016, to examine the prescription factors of OACs in NAF patients. Of the 11,194 identified patients, those who had a stroke risk score ≥ 2 totaled 9226. These patients represented the target population who were eligible for OAC therapy. However, only 4999 of them (or 54.2%) had a record of receiving OACs. Nonetheless, when comparing OAC therapy utilization in NAF patients from a previous study by Lee (2009), the use of OAC therapy had increased. The study reported that the proportion of patients who received OAC therapy had increased from 32.0% in 2008 to 46.0% in 2015. This study attributed the increase in NOAC prescriptions as the main cause for the increase in the utilization of OAC therapy [11]. In the same manner, our study also observed a higher proportion of patients who received NOAC (2884) than warfarin (1633) in 2016, which was also observed in a recent French study [23].

When comparing NOAC to warfarin, the factors that affect OAC selection were age, prior stroke/TIA/TE, renal disease, thyroid disease, dyslipidemia, and cancer. Our result is consistent with a previous Korean study, which suggested that the patients who received warfarin were younger than the patients who received NOAC [11]. The same was also observed in a study that used 2014–2016 HIRA sample data [10]. However, the definition of NAF patients in Ko et al.'s study only confirmed prescription pattern analysis in an outpatient setting [10], so special attention should be paid. In addition to renal disease, the presence of prior stroke/TIA/TE, thyroid disease, dyslipidemia, and cancer led to a higher preference for NOAC prescription over warfarin. This observation is the opposite of the report in Denmark, where the prescription preference for warfarin increased in the presence of renal disease, liver disease, and cancer [24]. On the other hand, the prescription factor analysis study in Taiwanese patients showed that older age, the presence of ischemic heart disease, and concomitant use of anti-hypertensive agents led to increased prescription preference of NOAC over warfarin [25]. This result is consistent with our finding that NOAC preference increased with older age and the presence of prior stroke/TIA/TE. This may be due to small drug interaction as well as the larger benefits in safety and efficacy of using NOAC compared to warfarin in Asian patients [26]. Although global pivotal clinical studies

Table 1 Baseline characteristics of nonvalvular atrial fibrillation patients eligible for oral anticoagulant (OAC) therapy and have received either non-vitamin K antagonist oral anticoagulant (NOA) or vitamin K antagonist (VKA) in Korea from Jan 1, 2016 to Dec 31, 2016

	NOAC total (n = 2,884) n (%)	VKA (n = 1,633) n (%)	*p* value
Gender			0.424
Male	1556 (53.95)	863 (52.85)	
Female	1328 (46.05)	770 (47.15)	
Age			< .0001*
Age ≤ 64	412 (14.29)	349 (21.37)	
Age 65–74	999 (36.64)	541 (33.13)	
Age ≥ 75	1473 (51.07)	743 (45.50)	
Comorbidities			
Heart failure	1363 (47.26)	764 (46.79)	0.7527
Hypertension	2057 (71.32)	1120 (68.59)	0.0448*
Diabetes mellitus	844 (29.26)	482 (29.52)	0.8584
Prior Stroke/TIA/TE	1143 (39.63)	489 (29.94)	< .0001*
Vascular disease	649 (22.50)	326 (19.96)	0.0487*
Renal disease	191 (6.62)	170 (10.41)	< .0001*
Liver disease	1050 (36.41)	509 (31.17)	0.0003*
Bleeding	255 (8.84)	132 (8.08)	0.408
Thyroid disease	483 (16.75)	219 (13.41)	0.0034*
COPD	310 (10.75)	146 (8.94)	0.039*
Dyslipidemia	2281 (79.09)	1186 (72.63)	< .0001*
Pneumonia	450 (15.60)	225 (13.78)	0.0895
Rheumatic disease	157 (5.44)	70 (4.29)	0.0977
Cancer	366 (12.69)	141 (8.63)	< .0001*
CHA2DS2-VASc			< .0001*
2–3	987 (34.22)	694 (42.50)	
4–5	1224 (42.44)	683 (41.82)	
≥ 6	673 (23.34)	256 (15.68)	
mHAS-BLED			< .0001*
0–2	395 (13.70)	349 (21.37)	
3–4	1656 (57.42)	944 (57.81)	
≥ 5	833 (28.88)	340 (20.82)	
Medical institution			0.0045*
Tertiary	2486 (86.2)	1348 (82.55)	
Secondary	154 (5.34)	115 (7.04)	
Primary	236 (8.18)	164 (10.04)	
Public Health Center and Others	8 (0.27)	6 (0.36)	
Insurance			0.1454
NHI	2626 (91.05)	1492 (91.37)	
MedAid	233 (8.08)	135 (8.27)	
PVI	25 (0.87)	6 (0.37)	
Visit type			< .0001*
Out-patient	2245 (77.84)	1419 (86.9)	
In-patient	639 (22.16)	214 (13.1)	
Location			0.1659
Metropolitan	826 (28.64)	450 (27.56)	
City	800 (27.74)	422 (11.88)	
Rural	1258 (43.62)	761 (48.60)	
Prescribing Specialty			< .0001*
Internal medicine	2155 (74.72)	1257 (76.97)	
Neurology	507 (17.58)	194 (11.88)	
Others	222 (7.70)	182 (11.15)	

TIA Transient ischemic attack, *TE* Thromboembolism, *COPD* Chronic obstructive pulmonary disease, *NHI* National health insurance plan, *MedAid* Medical aid program, *PVI* Patriots and veterans insurance plan

All variables were validated with χ^2-test ($p < .05$)

*$p < 0.05$

Table 2 Univariate and multivariate logistic regression of factors associated with any NOAC prescription v. warfarin

Independent variable	Any NOAC v. Warfarin	
	Odds ratio	Adjusted odds ratio
Gender		
Male	1	Not included
Female	0.96 (0.85–1.09)	
Age		
Age ≥ 75	1	1
Age 65–74	0.92 (0.80–1.06)	0.94 (0.80–1.10)
Age ≤ 64	0.59 (0.50–0.70)*	0.60 (0.48–0.76)*
Comorbidities		
Heart failure	1.01 (0.90–1.14)	Not included
Hypertension	1.15 (1.01–1.31)*	1.07 (0.90–1.28)
Diabetes mellitus	0.99 (0.87–1.13)	Not included
Prior stroke/TIA/TE	1.54 (1.35–1.75)*	1.35 (1.09–1.67)*
Vascular disease	1.17 (1.00–1.36)*	1.09 (0.92–1.29)
Renal disease	0.62 (0.50–0.77)*	0.46 (0.36–0.59)*
Liver disease	1.27 (1.11–1.45)*	1.05 (0.89–1.24)
Thyroid disease	1.28 (1.08–1.53)*	1.37 (1.14–1.64)*
COPD	1.26 (1.02–1.55)*	1.10 (0.89–1.37)
Dyslipidemia	1.42 (1.23–1.64)*	1.28 (1.10–1.49)*
Pneumonia	1.16 (0.98–1.38)	Not included
Rheumatic disease	1.26 (0.94–1.68)	Not included
Cancer	1.53 (1.25–1.89)*	1.38 (1.12–1.72)*
CHA2DS2-VASc		
2–3	1	1
4–5	1.27 (1.11–1.45)*	0.89 (0.75–1.07)
≥ 6	1.86 (1.57–2.22)*	0.92 (0.69–1.23)
mHAS-BLED		
0–2	1	1
3–4	1.55 (1.31–1.82)*	1.21 (0.98–1.49)
≥ 5	2.18 (1.79–2.64)*	1.46 (1.06–2.01)*
Medical institution		
Tertiary care	1	1
Secondary care	0.73 (0.57–0.94)*	0.65 (0.50–0.85)*
Primary care	0.79 (0.64–0.98)*	0.88 (0.71–1.10)
Insurance		
NHI	1	Not included
MedAid	0.98 (0.78–1.22)	
Visit type		
Out-patient	1	1
In-patient	1.88 (1.59–2.23)*	2.02 (1.67–2.45)*
Location		
Metropolitan	1	Not included
City	1.03 (0.87–1.22)	
Rural	0.91 (0.79–1.06)	
Prescribing specialty		
Other than internal medicine and neurology	1	1
Internal medicine	1.42 (1.15–1.75)*	1.80 (1.43–2.27)*
Neurology	2.18 (1.68–2.82)*	2.12 (1.58–2.83)*

Independent variables that had $p < .05$ in univariate and multivariate logistic regression analysis between any NOAC(rivaroxaban, dabigatran, apixaban, and edoxaban) v. VKA(warfarin) and significant p values (<.05) were marked with *

NOAC non-vitamin K antagonist oral anticoagulant, *VKA* vitamin K antagonist oral anticoagulant, *TIA* Transient ischemic attack, *TE* Thromboembolism, *COPD* Chronic obstructive pulmonary disease, *NHI* National health insurance plan, *MedAid* Medical aid program

confirmed the safety and efficacy of NOAC in controlled conditions, trials were performed in a controlled environment with fewer comorbidities. The prescription factor difference among NOACs and between Asian and non-Asian patients emphasizes the need for further prescription factor analysis in Asian patients with other diseases that occur frequently among the elderly population.

The prescription of NOACs was significantly higher in tertiary care institutions, which may be due to the "new drug effect" in Korea, implying that when a drug has been recently approved, the use of this drug is more prevalent in tertiary care institutions than in primary care institutions, and the spread was observed to be faster [27]. Because NOACs was introduced in 2011 in Korea, new drug effects may still be present. Additionally, for patients who had controllable INR levels using warfarin in OAC therapy in primary care institutions, they may not have the need to switch to NOACs or to transfer to larger secondary or tertiary care institutions. The prescription preference of NOACs was higher than warfarin when the prescribing specialty was in internal medicine and neurology. In particular, the prescription preference of NOACs was higher in neurology than in internal medicine, which includes cardiology. In tertiary care institutions, stroke prophylaxis in atrial fibrillation is performed by collaboration between cardiology and neurology; thus, NOACs can be similarly preferred by cardiologists, which was observed in a previous study [28]. As our analysis did not specify a subspecialty within internal medicine, the large category of internal medicine may have obscured the magnitude of the preference of NOACs over warfarin among cardiologists, which requires further study.

NOACs cost approximately 20 times more than VKA; thus, we assumed that underprivileged patients, such as patients under the Medical Aid program, are less likely to be prescribed NOACs. However, our analysis showed no significant difference based on insurance status (95% CI 0.78–1.22), which might be attributable to various cost-sharing waiver policies to increase accessibility.

When comparing the prescription factor of NOACs versus warfarin, some observations were a clear indicator of

clinicians' correct understanding of the pharmacology of NOACs, whereas some were new findings that were not supported by information in the clinical guidelines. The presence of renal disease indicated a negative prescription factor for rivaroxaban and dabigatran over warfarin. This observation was clearly linked to the pharmacology of rivaroxaban and dabigatran, as they are known to be 80% and 35% renal-cleared drugs [29, 30].

Table 1 shows that in addition to renal disease and diabetes, the presence of comorbidities was associated with a higher prescription preference for NOACs over warfarin. This result is different from the prescription factor studies in Taiwan, Denmark, and Spain [12, 25]. Although the safety and efficacy of NOACs have been proven in controlled clinical trials, the safety and efficacy of NOACs in the presence of various comorbidities are still unclear. In our study, the prescription preference of NOACs over warfarin was higher among patients with cancer. There have been several systematic reviews and meta-analyses of NOAC use in cancer patients that indicated non-inferior effects of NOACs in venous thromboembolism (VTE) prophylaxis compared to warfarin [31] or superiority in VTE prophylaxis and prevention of major bleeding [32], which may be a clue to the increasd preference of NOACs in cancer patients. However, cancer patients in the clinical trials for NOACs were underrepresented, and the use of NOACs in cancer patients is not endorsed by international guidelines [31, 32], but further study is necessary to support NOAC use for cancer patients. Other comorbidities such as thyroid disease, COPD, and dyslipidemia that showed a higher prescription preference of NOACs over warfarin are not specified in the current international consensus guidelines, such as those of the ESC and the Asia Pacific Heart Rhythm Society. Hence, further analysis of positive prescription factors identified in this study requires reconfirmation.

The strength of our study is that we calculated the stroke risk score (CHA2DS2-VASc) as well as the bleeding risk score (mHAS-BLED) using a nationally representative sample to closely follow the real-world clinician's evaluation process and enhance our understanding of each patient's clinical information.

However, our study should be interpreted with caution. Due to the short time frame, it was not possible to look for comorbidities over one year. Because we regarded a patient as having a certain comorbidity if the patient had a diagnosis history of a disease, we could not confirm the exact timing or activity status (ongoing/recovered) of the comorbidity. Nevertheless, as most comorbidities in our study were chronic illnesses, we assumed that these comorbidities would likely have existed over one year. Last, because the national claims data do not contain laboratory test results, such as the INR of warfarin, the complete HAS-BLED score could not be calculated. Instead, a modified HAS-BLED score has been used, so direct comparison with other studies with absolute HAS-BLED scores is not possible. Additionally, our claims data do not include patients whose CHA2DS2-VASc is lower than 2 because the Korean NHI only reimburses patients whose CHA2DS2-VASc is equal to or higher than 2, and the appropriateness of the prescription is difficult to determine, which is a limitation of our study. Further study using medical chart review should be undertaken.

Conclusion

The NOAC prescriptions in 2016 increased from 46% in 2014 [33] to 51.9% in Korea. However, the utilization of OAC therapy in general is still low compared to the recommended level (54.2%). Clinicians and policy makers should strive to increase NOAC use in primary or secondary medical institutions for those patients who can afford to use them.

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Conflicts of interest The authors declare that they have no conflict of interest.

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