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Clinical investigation

10-year nationwide trends of the incidence, prevalence, and adverse outcomes of non-valvular atrial fibrillation: nationwide health insurance data covering the entire Korean population

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Running title: Increasing burden of atrial fibrillation

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Abstract

Background: Most data on the clinical epidemiology of atrial fibrillation (AF) are reported from Western populations, and data for Asians are limited. We aimed to investigate the 10-year trends of the prevalence and incidence of non-valvular AF and provide prevalence projections till 2060 in Korea. We also investigated the annual risks of adverse outcomes among patients with AF.

Methods: Using the Korean National Health Insurance Service database involving the entire Korean population, a total of 679,416 adults with newly diagnosed AF were identified from 2006 to 2015. The incidence and prevalence of AF and risk of adverse outcomes following AF onset were assessed.

Results: The prevalence of AF progressively increased by 2.10-fold from 0.73% in 2006 to 1.53% in 2015. The trend of its incidence was flat with a 10-year overall incidence of 1.77 per 1,000 person-years. The prevalence of AF is expected to reach 5.81% (2,290,591 patients with AF) in 2060. For a decade, the risk of all-cause mortality following AF declined by 30% (adjusted hazard ratio [HR]: 0.70, 95% confidence interval [CI]: 0.68–0.72), heart failure by 52% (adjusted HR: 0.48, 95% CI: 0.44–0.51), and ischemic stroke by 9% (adjusted HR: 0.91, 95% CI: 0.88–0.93).

Conclusions: The burden of AF among Asian patients is increasing. Although the overall risks of cardiovascular events and death following AF onset have decreased over a decade, the event rates are still high. Optimized management of any associated comorbidities should be part of the holistic management approach for patients with AF.

Keywords: atrial fibrillation; epidemiology; incidence; prevalence; projection; adverse outcomes

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Introduction

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in the general population.[1, 2] The prevalence of AF has been projected to increase to 12 million individuals in the USA by the year 2050 and 17.9 million in Europe by the year 2060, with more than half of these patients aged ≥80 years, leading to a substantial public health and economic burden.[3, 4] The age distribution of AF populations in developed countries is expected to shift in the coming years with older age groups becoming more prominent. With population aging, AF is likely to become a greater public health burden; thus, reliable prevalence and incidence figures are needed for both clinicians and policy-makers.[5]

AF increases the risk of mortality and morbidity resulting from stroke, congestive heart failure, and impaired quality of life, explaining its enormous socioeconomic and healthcare implications.[6] In recent years, important improvements have been made in pharmacological and nonpharmacological treatment of associated diseases, such as hypertension, myocardial infarction, and heart failure.[7, 8] However, the current knowledge on the incidence, prevalence, and associated cardiovascular morbidity and mortality of AF has been predominantly derived from Western countries.[9]

We investigated the temporal trends of the prevalence and incidence of non-valvular AF, projected prevalence of AF to 2060, and risks of cardiovascular events and all-cause mortality using the National Health Insurance Service (NHIS) database of the entire Korean population from 2006 to 2015.

Materials and methods

This nationwide study was based on the national health claims database established by the NHIS of Korea.[10-14] An insured individual should pay a national health insurance, which is proportional to the individual's income. Although the user charge exists, it is mandatory for all Koreans to join the Korean NHIS. The majority (97.1%) of the Korean population is mandatory subscribers. The remaining 3% of the population with low income is covered by the Medical Aid program. Since 2006, the information of Medical Aid beneficiaries has been incorporated into the NHIS database. Therefore, the data extracted from the NHIS database are indeed based on the entire Korean population, not causing selection bias. The following medical information is provided: patients' sociodemographic information, their use of inpatient and outpatient services, pharmacy dispensing claims, and mortality data. Every population in the NHIS database was linked with the Korean social security numbers, and all social security numbers were deleted after constructing the cohort by providing serial numbers to prevent leakage of personal information. These databases are open to researchers whose study protocols are approved by the official review committee. This study was approved by the institutional review board of Yonsei University Health System (4-2016-0179). The need for informed consent was waived.

Incidence, prevalence, and projected number of non-valvular AF

The annual incidence was defined as the rate of acquisition of a new AF diagnosis in the health claims data within a 1-year period. To qualify as an incident case, an AF diagnosis must have occurred between January 1, 2006 and December 31, 2015 (with the index date being the first date of diagnosis within this observation period). AF was diagnosed using the International Classification of Disease 10th Revision (ICD-10) codes I48 (AF and atrial flutter), I48.0 (AF),

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and I48.1 (atrial flutter). We regarded the first date of obtaining the AF-related ICD-10 codes as the newly diagnosed year and excluded the first 4 years (2002 to 2005) to avoid the possibility for misdiagnosis of preexisting AF for incident AF. Moreover, the patients were considered to have AF only when AF was only a discharge diagnosis or confirmed more than twice in the outpatient department to ensure diagnostic accuracy. The diagnosis of AF has previously been validated in the NHIS database with a positive predictive value (PPV) of 94.1%.[11, 14] We excluded patients aged <20 years and patients with valvular heart disease (with a diagnosis of mitral stenosis [ICD-10: I05.0, I05.2, and I34.2] or prosthetic heart valves [ICD-10: Z95.2–Z95.4] and insurance claims for valve replacement or valvuloplasty).

The annual prevalence of AF was calculated by dividing the number of patients with AF alive at the end of each year by the number of the total Korean residents alive at the end of that year. Supplementary Table I shows the number and distribution of the total Korean residents aged ≥20 years. The annual incidence rates of AF in each year were calculated by dividing the number of incident cases of AF by the number of person-years at risk among all Korean residents of that year who had never been diagnosed with AF. The incidence was presented per 1,000 person-years. The incidence and prevalence rates were calculated per sex and age group (20–29, 30–39, 40–49, 50–59, 60–69, 70–79, and ≥80 years).

The projection of the prevalence of AF was also calculated using a prevalence model as previously described.[3, 15] The details of the prevalence model we used are described in the "Projected number of AF" section in the Supplementary Methods.

Definitions of comorbidities and adverse outcomes

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We obtained information on selected comorbidities from the inpatient and outpatient hospital diagnoses (all available primary and secondary diagnoses). Comorbidities were defined using the medical claims according to the ICD-10 codes and prescription medication use at the time of AF diagnosis. To ensure diagnostic accuracy, the patients were considered to have comorbidities (including heart failure, hypertension, diabetes, previous ischemic stroke/transient ischemic attack [TIA], previous intracranial bleeding, previous myocardial infarction, peripheral arterial disease [PAD], chronic kidney disease [CKD], and malignant neoplasm) when the condition was a discharge diagnosis or was confirmed more than twice in an outpatient setting, which is similar to the methods of previous studies that used the NHIS data.[10-14] Economic status was categorized into three groups based on the total amount of national health insurance premiums paid by the insured individual in each year, which is proportional to the individual's income: low, intermediate, and high economic status.

We followed up all patients with incidental AF and investigated the epidemiological trends of five adverse outcomes, including all-cause mortality, ischemic stroke, intracranial bleeding, heart failure admission, and myocardial infarction. The diagnostic accuracies of myocardial infarction (PPV: 86.5%), ischemic stroke (PPV: 88–95%), and intracranial bleeding (PPV: 78–92%) in the Korean NHIS have been validated previously.[13, 16] The definitions of comorbidities and adverse outcomes are presented in Supplementary Table II.

Statistical analysis

Data were presented as means ± standard deviations or medians ± interquartile ranges (IQRs) for continuous variables and proportions for categorical variables. The Cochran-Armitage

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trend test was used for analyzing the temporal trends of categorical variables. The nonparametric

test for trend by Jonckheere-Terpstra was used for continuous variables.

We investigated the risks of adverse outcomes in two different manners: (i) We

calculated the annual risk (%/year) of adverse outcomes among the total patients with prevalent

AF and non-AF population of Korea by dividing the number of the first lifetime event that

occurred in each year by the total number of patients at the start of the year who had never

experienced the event. Since the risks of ischemic stroke, intracranial bleeding, and myocardial

infarction might be associated with the use of antithrombotic therapies, we analyzed these risks

among the patients who did not receive antithrombotic therapies within 90 days after enrollment.

Adverse outcomes among the non-AF Korean population were evaluated using an age- and sex-

matched cohort derived from the Korean NHIS-National Sample Cohort database. The details of

the non-AF cohort are presented in the "Non-AF cohort from the Korean National Health

Insurance Service-National Sample Cohort database" section of the Supplementary Methods. (ii)

We also investigated the association between the calendar years of AF diagnosis and adverse

outcomes on the 2-year follow-up after AF diagnosis using Cox-proportional hazard regression

analysis. We estimated the hazard ratios (HRs) of 7 calendar years of AF diagnosis (2007-2013)

with 2006 as the reference calendar year. The HRs were adjusted for age, sex, economic status,

and comorbidities at the time of diagnosis, including heart failure, hypertension, diabetes,

previous ischemic stroke/TIA, previous intracranial bleeding, previous myocardial infarction,

PAD, CKD, and malignant neoplasm.

All tests were two-tailed, with P values of <0.05 considered significant. Statistical

analyses were conducted using SAS version 9.4 (SAS Institute, Cary, NC, USA), R version 3.4.1,

and SPSS version 23.0 (SPSS Inc., Chicago, IL, USA).

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Results

Patient characteristics

During a total of 384,266,047 person-years of follow-up, we identified 679,416 patients in the general population with first-time AF diagnosed between 2006 and 2015. The characteristics of the patients with newly diagnosed AF in Korea between 2006 and 2015 are presented in Table I. The AF diagnoses were almost equally distributed between the men and women and stable over time. The proportion of the men increased modestly from 51.7% in 2006 to 54.2% in 2015 (P value for trend <0.001). The median age of the patients with AF increased from 65 (IQR: 53–74) years in 2006 to 71 (IQR: 59–79) years in 2015 (P value for trend <0.001). The proportion of the elderlies aged 70–79 and ≥80 years gradually increased from 25.6% and 12.0% in 2006 to 29.0% and 23.2% in 2015 (both P values for trend <0.001), respectively. The proportion of the patients with intermediate and high economic status increased significantly, while the proportion of the patients with low economic status decreased from 49.1% in 2006 to 30.0% in 2015 (all P values for trend <0.001).

The comorbidity burden increased over time. The most prevalent comorbidities during the 10-year period were hypertension (71.1%), heart failure (24.9%), malignant neoplasm (23.0%), diabetes (22.7%), and ischemic stroke (19.6%).

Table I. Characteristics of the patients with newly diagnosed AF in Korea between 2006 and 2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Overall	P value for trend
Newly diagnosed AF, n	66,903	66,986	65,829	66,100	67,071	66,743	68,461	69,642	69,961	71,720	679,416	
Age, median (IQR)	65 (53–74)	65 (53–74)	66 (54–75)	67 (54–75)	67 (55–75)	68 (55–76)	68 (56–76)	70 (58–78)	70 (58–78)	71 (59–79)	68 (56–76)	<0.001
20–29 years, %	2.7	2.8	2.5	2.4	2.2	2.0	1.8	1.4	1.5	1.7	2.1	<0.001
30–39 years, %	5.1	5.2	5.0	4.7	4.5	4.3	3.8	3.3	3.2	3.2	4.2	<0.001
40–49 years, %	11.2	11.2	10.5	10.2	9.7	8.9	8.4	7.1	7.0	7.0	9.1	<0.001
50–59 years, %	16.9	17.1	17.1	16.5	16.6	17.1	17.4	16.1	15.8	14.9	16.5	<0.001
60–69 years, %	26.5	25.6	25.3	24.9	24.1	23.4	22.9	21.0	20.8	21.1	23.5	<0.001
70–79 years, %	25.6	25.9	26.7	27.4	27.7	28.5	29.1	30.6	30.0	29.0	28.1	<0.001
≥80 years, %	12.0	12.2	13.0	13.9	15.1	15.8	16.7	20.4	21.8	23.2	16.5	<0.001
Sex, %												
Male	51.7	52.4	52.3	51.9	52.7	53.3	53.3	54.1	54.1	54.2	53.0	<0.001
Female	48.3	47.6	47.7	48.1	47.3	46.7	46.7	45.9	45.9	45.8	47.0	<0.001
Economic status, %												
Low	49.1	44.3	40.5	38.1	41.8	38.8	36.6	30.5	29.7	30.0	37.8	<0.001

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Intermediate	20.6	38.2	23.9	24.1	23.9	23.9	23.5	24.0	25.0	25.0	25.2	<0.001
High	30.3	17.5	35.6	37.8	34.3	37.3	40.0	45.5	45.3	45.0	37.0	<0.001
Comorbidities, %												
Heart failure	22.2	22.8	23.4	23.7	24.0	24.5	25.5	26.5	27.7	28.2	24.9	<0.001
Hypertension	64.1	66.5	68.4	70.0	71.7	71.8	73.4	75.1	74.9	74.2	71.1	<0.001
Diabetes	18.5	19.6	20.5	21.6	22.3	22.9	23.8	25.3	26.0	26.2	22.7	<0.001
Ischemic stroke	14.2	16.0	17.1	19.0	20.2	20.1	21.2	22.6	23.0	22.2	19.6	<0.001
Intracranial bleeding	1.8	2.0	2.0	2.2	2.6	2.5	2.6	2.7	2.8	2.9	2.4	<0.001
MI	7.3	7.7	8.2	8.5	8.1	8.0	8.3	8.5	8.8	9.1	8.3	<0.001
PAD	5.3	6.4	7.8	10.2	11.4	12.1	13.2	14.5	15.0	15.5	11.2	<0.001
CKD	3.8	4.4	4.8	5.3	5.6	5.9	6.9	7.4	8.1	8.4	6.1	<0.001
Malignant neoplasm	15.9	17.9	19.6	21.6	22.8	24.2	25.5	25.8	27.2	28.3	23.0	<0.001
CHA_2DS_2-VASc score, mean (SD)	2.74 (1.92)	2.84 (2.00)	2.95 (2.04)	3.08 (2.10)	3.16 (2.13)	3.18 (2.16)	3.29 (2.18)	3.54 (2.05)	3.59 (2.07)	3.60 (2.10)	3.20 (2.10)	<0.001
HAS-BLED score, mean (SD)	2.07 (1.38)	2.19 (1.43)	2.30 (1.45)	2.42 (1.47)	2.50 (1.48)	2.54 (1.49)	2.62 (1.50)	2.72 (1.50)	2.75 (1.52)	2.75 (1.54)	2.49 (1.59)	<0.001

AF, atrial fibrillation; CKD, chronic kidney disease; IQR, interquartile range; MI, myocardial infarction; PAD, peripheral artery disease; SD, standard deviation.

Prevalence, incidence, and projected number of AF

Figure 1 shows the temporal trends of the prevalence of AF in Korea. The prevalence progressively increased by 2.10-fold from 0.73% in 2006 to 1.53% in 2015 (P value for trend <0.001). The prevalence was significantly greater in the men than in the women for all years (P <0.001) (Figure 1A). Across all age groups, the prevalence consistently increased over the study period, except for the prevalence among those aged 20–29 years, which decreased significantly (all P values for trend <0.001) (Figure 1B). The prevalence of AF increased with older age, ranging from 0.09% among those aged 20–29 years to 8.15% among those aged ≥80 years in 2015 (P value for trend <0.001). The annual prevalence of AF between 2006 and 2015 stratified by sex and age is presented in Supplementary Table III.
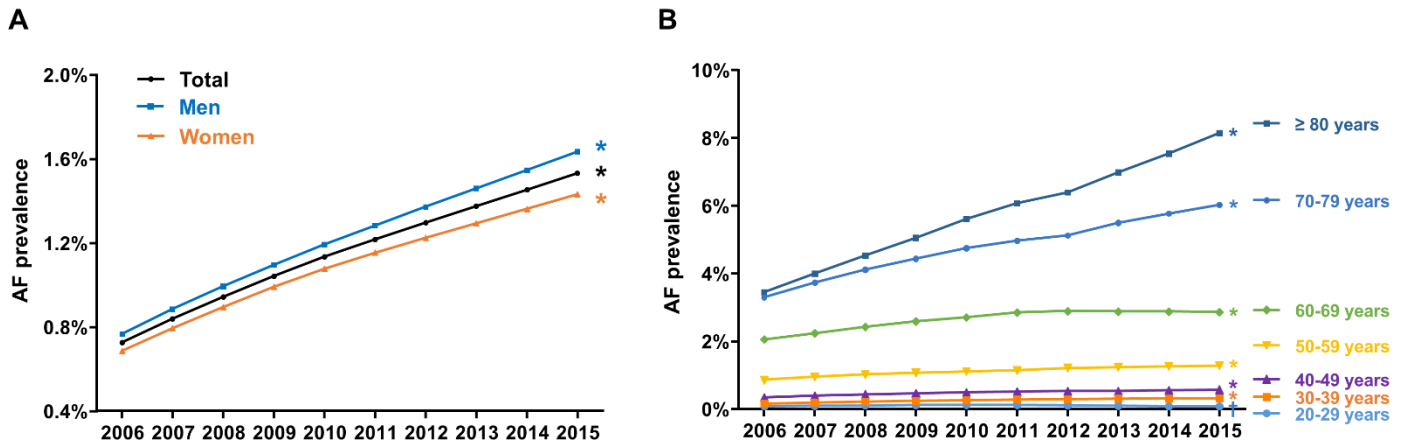

Figure 1. Annual prevalence of AF between 2006 and 2015 stratified according to sex (A) and age (B)

*P value for increasing trends <0.001. †P value for decreasing trends <0.001. AF, atrial fibrillation.

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Figure 2 shows the incidence of AF from 2006 to 2015. The annual trend of AF incidence was almost flat with a 10-year overall incidence of 1.77 per 1,000 person-years. The 10-year overall incidence in the men was 1.89 per 1,000 person-years, which was 1.16 times higher than 1.65 per 1,000 person-years in the women (P <0.001); the tendency was consistent over the study period (Figure 2A). The annual AF incidence in the subjects aged ≥80 years significantly increased from 12.1 in 2006 to 14.3 per 1,000 person-years in 2015 (P value for trend <0.001), while the incidence in all other age groups decreased (all P values for trend <0.001) (Figure 2B and Supplementary Table IV).
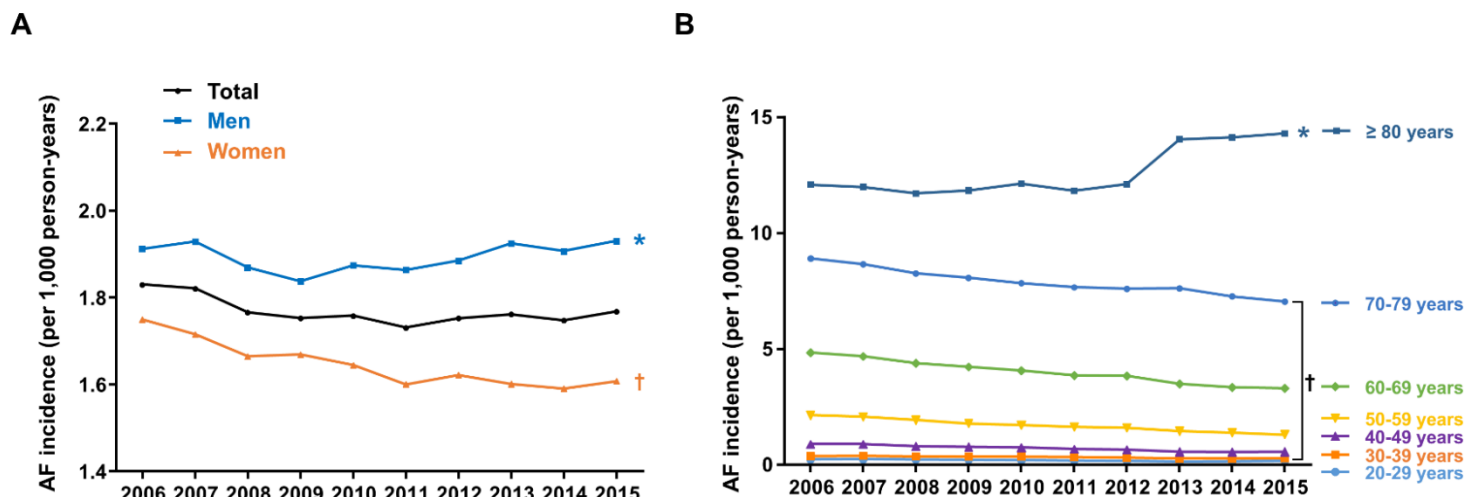

Figure 2. Annual incidence of AF between 2006 and 2015 stratified according to sex (A) and age (B)

[*]P value for increasing trends <0.001. [†]P value for decreasing trends <0.001. AF, atrial fibrillation.

Using the prevalence model previously described and assuming that the incidence of AF and mortality remained constant beyond 2015, the projected number of adults with AF will be

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2,290,538 (prevalence rate: 5.35%) in 2050 and 2,290,591 (prevalence rate: 5.81%) in 2060

(Figure 3).
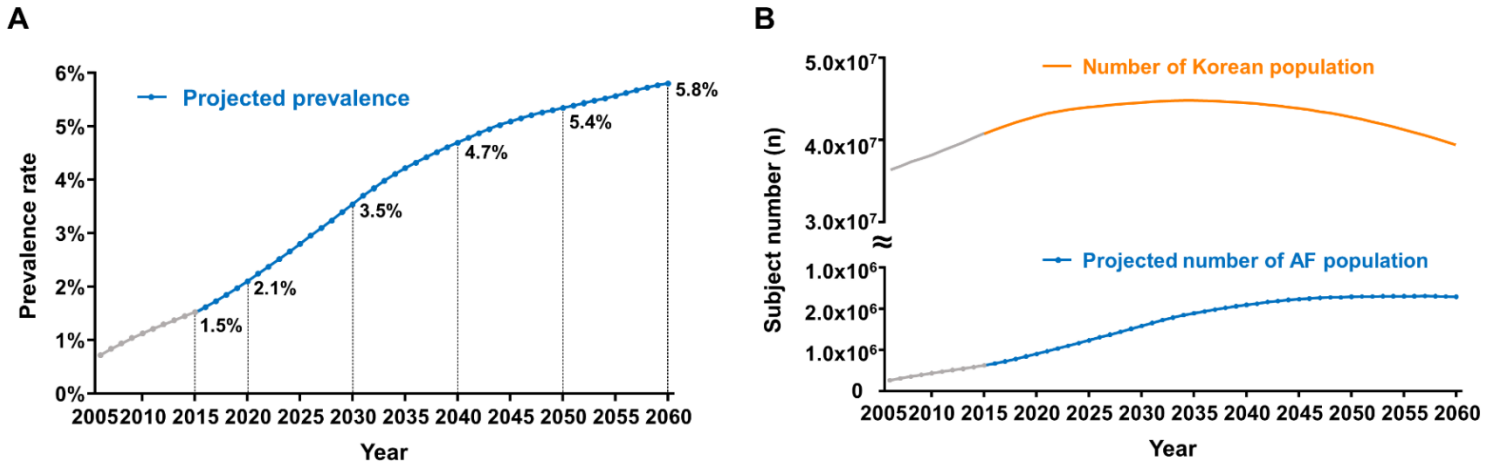
Figure 3. Projected prevalence rate (A) and number (B) of AF

AF, atrial fibrillation.

Trends of the CHA$_2$DS$_2$-VASc and HAS-BLED scores

The distributions according to the CHA$_2$DS$_2$-VASc and HAS-BLED scores among the

patients with incident AF are presented in Figure 4. The proportion of the patients with

CHA$_2$DS$_2$-VASc scores of ≥2 increased from 68.8% to 81.2% from 2006 to 2015 (P value for

trend <0.001). The proportion of the patients with a high bleeding risk according to the HAS-

BLED score of ≥3 increased from 39.3% in 2006 to 59.1% in 2015 (P value for trend <0.001).

A

CHA$_2$DS$_2$-VASc score

B
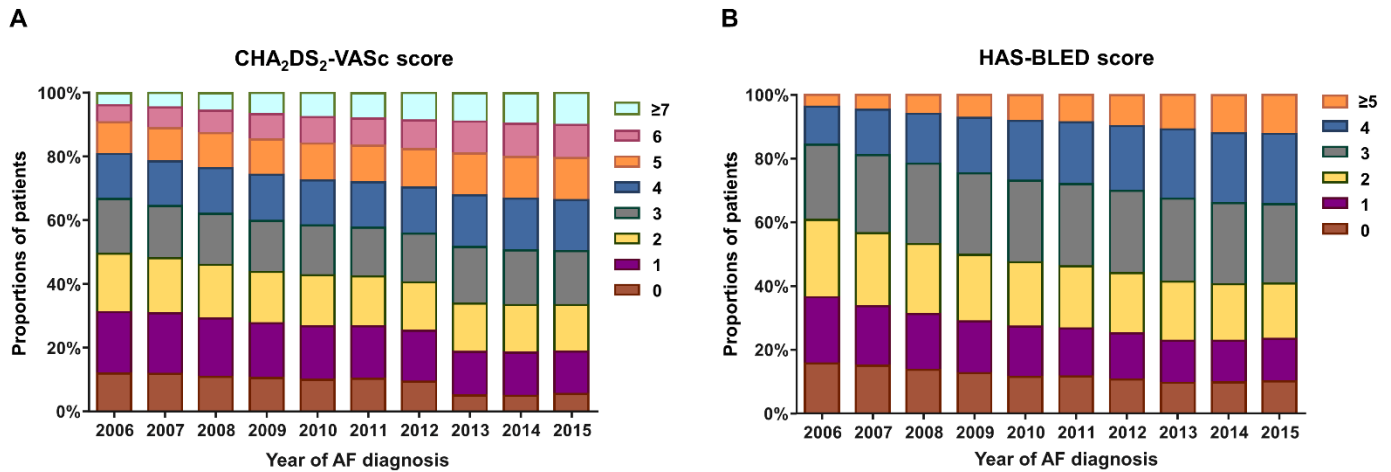
HAS-BLED score

Figure 4. Temporal trends of the distribution of the patients with newly diagnosed AF according to the CHA$_2$DS$_2$-VASc and HAS-BLED scores between 2006 and 2015

AF, atrial fibrillation.

Trends of the adverse outcomes among the patients with AF

The annual trends of the adverse event rates among the patients with prevalent AF and non-AF Korean population are presented in Figure 5. Among the patients with prevalent AF, the annual event rates for all-cause mortality, ischemic stroke, intracranial bleeding, heart failure admission, and myocardial infarction declined for a decade (all P values for trend <0.001). However, these did not change significantly among the non-AF Korean population.

A

B
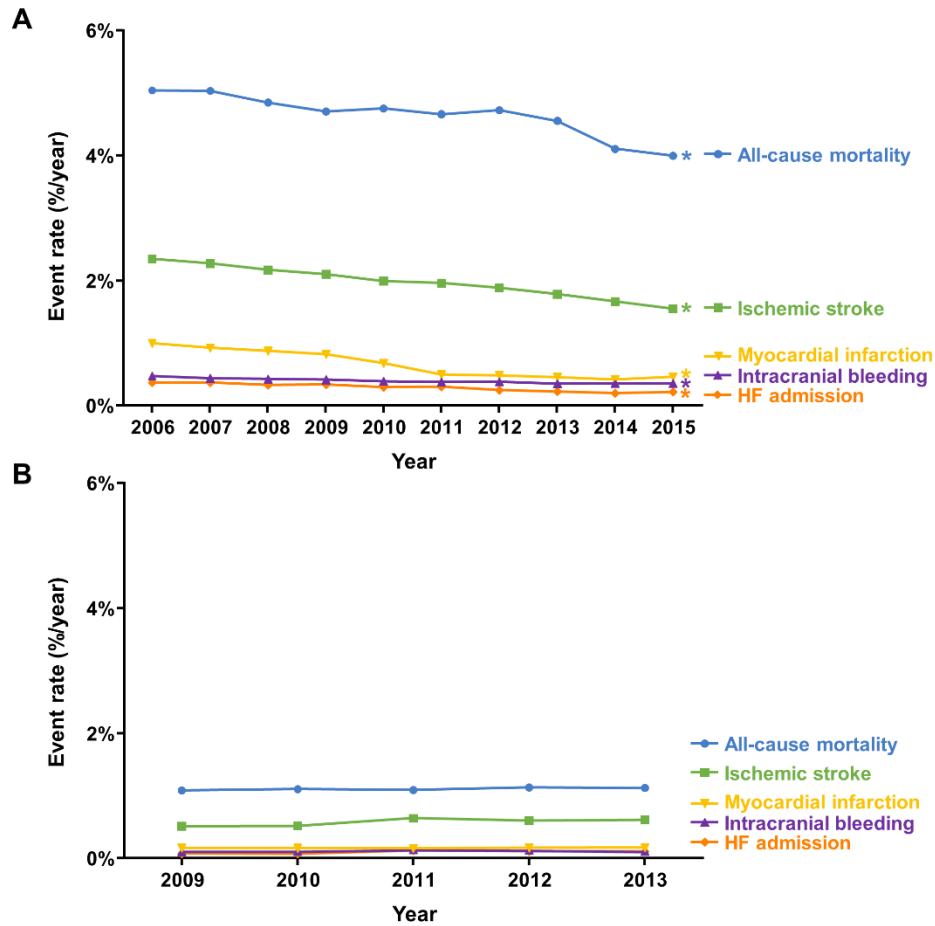
Figure 5. Temporal trends of the 1-year adverse event rates of the (A) patients with prevalent AF and (B) non-AF Korean population in each year

[*]P value for trends <0.001. The 1-year adverse event rates (%/year) were calculated by dividing the number of the first lifetime event that occurred in each year by the total number of patients at the start of the year who had not experienced that event before. AF, atrial fibrillation; HF, heart failure.

The temporal trends of the 2-year risks of adverse outcomes following AF diagnosis are presented in Figure 6. The adjusted risk of the patients diagnosed with AF in 2013 for all-cause mortality declined by 30% (adjusted HR: 0.70, 95% confidence interval [CI]: 0.68–0.72), heart

failure by 52% (adjusted HR: 0.48, 95% CI: 0.44–0.51), myocardial infarction by 59% (adjusted

HR: 0.41, 95% CI: 0.39–0.43), ischemic stroke by 9% (adjusted HR: 0.91, 95% CI: 0.88–0.93),

and intracranial bleeding by 26% (adjusted HR: 0.74, 95% CI: 0.70–0.79), compared with those

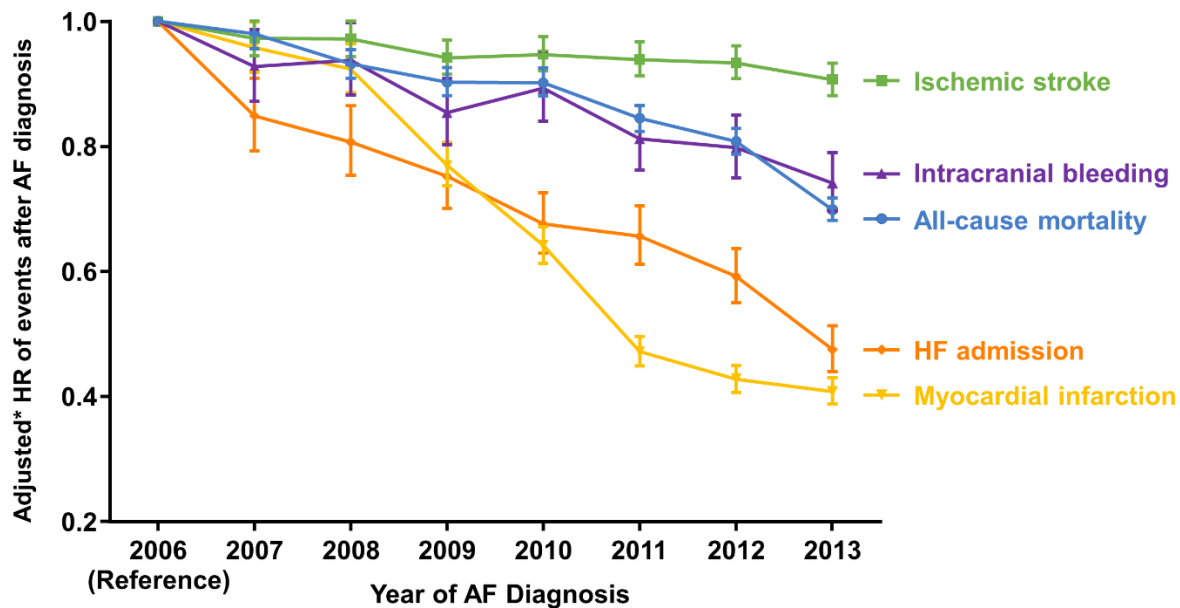of the patients diagnosed in 2006 (Figure 6 and Supplementary Table V).

Figure 6. Temporal trends of the adjusted HRs of the adverse outcomes in the 2-year

follow-up after AF diagnosis

The HR was adjusted for age, sex, economic status, and comorbidities. AF, atrial fibrillation; HF,

heart failure; HR, hazard ratio.

Discussion

To the best of our knowledge, the current study used the largest nationwide cohort consisting of the entire Korean population to estimate the current and future non-valvular AF incidence and prevalence. Our principal findings are as follows: (i) The prevalence of AF progressively increased by 2.10-fold from 0.73% in 2006 to 1.53% in 2015; (ii) the trend of annual AF incidence was flat with a 10-year overall incidence of 1.77 per 1,000 person-years; (iii) the prevalence of AF was estimated to be 5.81% in 2060; and (iv) the risks of all-cause mortality, ischemic stroke, intracranial bleeding, heart failure, and myocardial infarction following onset of AF decreased markedly over a decade.

Prevalence, incidence, and projected number of AF

Over the course of 10 years of observation, we observed an increasing prevalence and a flat incidence of AF. The increase in the prevalence is in line with the findings for most Western populations.[4, 17-19] Across all age groups and both sexes, the prevalence consistently increased over the study period with higher absolute numbers in the older patients and men. The prevalence of AF in Korea was similar to the recently reported AF prevalence rates from 1.1% to 1.6% in other Asian countries (1.07% in Taiwan,[17] 1.5% in Singapore,[20] and 1.6% in Japan[21]). The prevalence of AF is generally lower in Asia than in Western countries (i.e., Caucasians).[22, 23] Although the precise mechanisms behind the differences in AF epidemiology between Asians and Caucasians remain unclear, part of the global variation may be attributable to the better surveillance in developed countries, and the prevalence of AF in some Asian countries is probably underestimated.[22, 24] Furthermore, the longer life expectancy and more prevalent

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cardiovascular risk factors and diseases, including smoking, obesity, hypertension, ischemic heart diseases, and diabetes, in developed Western countries may play important roles.[24]

Most prior data on AF incidence rates were reported from studies performed in Europe and North America. The reported AF incidence rate ranges from 3.3 to 9.9 per 1,000 person-years among studies conducted in Europe[23, 25, 26] and from 3.3 to 19.2 per 1,000 person-years among predominantly USA-based cohort studies.[3, 19, 27] The 10-year overall incidence of AF in the present study was 1.77 per 1,000 person-years, which is lower than that in Europe and the USA. However, our AF incidence rate is comparable to those described in a Taiwanese nationwide cohort study (i.e., 1.51 per 1,000 person-years).[17] Consistent with our findings, the annual trend of AF incidence was stable in Taiwan.

Similar to the growing burden of AF worldwide,[22] the AF prevalence and the absolute number of patients with AF would continuously increase over the coming decades in Korea based on our projected estimations. Indeed, the AF prevalence in Korea was estimated to be 5.35% in 2050, which is higher than the projected AF prevalence of 4.01% in Taiwan.[17]

Risks of adverse outcomes

Over the last 5 decades, the AF-associated mortality decreased by 25% in the Framingham heart study.[19] In Korea, we observed a 20% reduction in the mortality rate over a decade from 5.0% per year in 2006 to 4.0% per year in 2015. The improved survival after AF onset may arise from (1) earlier detection (lead time) owing to heightened awareness, (2) changed diagnostic criteria (as described above), (3) enhanced surveillance of patients with AF, (4) advances in the guideline-recommended treatments for AF, including oral anticoagulation to reduce risks of embolization, and (5) more aggressive treatment of complications and

comorbidities, such as hypertension, ischemic heart disease, heart failure, and

hypercholesterolemia.[18]

Given the high mortality associated with heart failure and stroke,[28, 29] the 52% reduction

in heart failure subsequent to AF observed over the study period and the 9% reduction in the risk

of ischemic stroke were likely to have contributed substantially to the improved survival.

Although our results showing a declining associated risk for heart failure and stroke following

AF are in line with those for other Western populations,[18] the 1-year rates of heart failure and

stroke were 0.2% and 1.8% per year, respectively, which are still higher than 0.1% and 0.6% per

year of the age- and sex-matched non-AF population in 2013.

Limitations

The present study has several limitations given the nature of the nationwide registry

dataset we used. Such studies using administrative databases might be susceptible to errors from

coding inaccuracies. To minimize this problem, we examined the nationwide cohort and applied

the definition already validated in previous studies that used the Korean NHIS sample cohort.[11,
13, 14, 16] Since we defined AF cases only with ICD-10 codes, it is possible that either paroxysmal

or asymptomatic AF cases, which were not ascertained by these codes, were not recorded. Also,

we could not analyse paroxysmal, persistent, and permanent AF subgroups separately. Patients

younger than 20 years were excluded from the study population. This approach can omit some

patients with AF. However, the prevalence among children and adolescents could be

underestimated owing to the lack of symptoms, fewer visits to medical institutions, and lack of

routine ECG check-up. Therefore, most previous studies have included only adult populations.[17-
21, 23] Although it would be relevant to stratify all adverse outcomes according to antithrombotic

therapies, we provided the risks of ischemic stroke, intracranial bleeding, and myocardial

infarction, which could be altered by antithrombotic therapies, only among the patients who did

not receive antithrombotic therapies. By investigating the risk of first lifetime events which were

not affected by antithrombotic therapies, we attempted to understand the disease course after

new-onset AF more clearly. Despite these limitations, this study evaluated longitudinal data from

the entire Korean adult population. Therefore, our findings may reflect the "real-world" AF

burden on a nationwide scale.

Conclusion

The burden of AF among Asian patients is increasing. Although the overall risks of death, ischemic stroke, intracranial bleeding, heart failure, and myocardial infarction following onset of AF have decreased over a decade, the absolute event rates are still high. Optimized management of any associated comorbidities should be part of the holistic management approach for patients with AF.

Disclosures

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