

# Incidence and Risk Factors for Atrial Fibrillation in Korea: the National Health Insurance Service Database (2002–2010)

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**Background and Objectives:** Atrial fibrillation (AF) is a common arrhythmia that is known as an important independent risk factor for stroke. However, limited information is available on AF in Korea. This study evaluated the incidence of AF, its associated co-morbidities and risk factors for AF in Korea.

**Subjects and Methods:** The National Health Insurance Service database between 2002 and 2010 was used in the study. Individuals <30 years old and those diagnosed with AF between 2002 and 2004 were excluded. Hazard ratios (HRs) according to co-morbidities and risk factors for AF were determined using a Cox proportional hazard model. Population attributable fractions (PAFs) of AF risk factors were determined.

**Results:** During a 6-year follow-up period, 3517 (1.7%) developed AF. The incidence rates in men and women aged 30–39 years were 0.82 and 0.55 per 1000 person-years, respectively; the incidence rates further increased with age to 13.09 and 11.54 per 1000 person-years in men and women aged ≥80 years, respectively. The risk factors for incident AF were age, sex, body mass index (BMI), hypertension, ischemic heart disease (IHD) and heart failure. After adjusting for variables related to AF, the risk of AF was significantly associated with hypertension (HR 1.667), IHD (HR 1.639), heart failure (HR 1.521), and the PAFs for age, sex, BMI, hypertension, IHD, heart failure and diabetes mellitus were 30.6%, 10.1%, 3.4%, 16.6%, 8.2%, 5.3% and 0.8%, respectively.

**Conclusion:** Incidence of AF increased with age and was higher in men than in women. A larger proportion of AF events was attributable to hypertension than to other co-morbidities. **(Korean Circ J 2016;46(4):515–521)**

**KEY WORDS:** Atrial fibrillation; Incidence; Comorbidity.

## Introduction

Atrial fibrillation (AF) is a common arrhythmia and an important cause of cardiovascular morbidity and mortality.<sup>1</sup> AF is also

associated with a 4 to 5-fold increased risk of stroke and is responsible for approximately 15% of all strokes.<sup>2,3</sup> The incidence and prevalence of AF increase with older age<sup>4,5</sup> and are higher in men than in women.<sup>6,7</sup> The prevalence of AF in the United States is estimated at 2.3 million and is expected to increase to 5.6 million by 2050.<sup>4</sup> In the Rotterdam Study, the prevalence of AF was 5.5% in subjects aged ≥55 years, and the incidence rate in subjects aged 80–84 years was 21 per 1000 person-years.<sup>8</sup> Assessment of Medicare beneficiaries in the United States showed that the incidence of AF over a 14-year period ranged from 27.3 to 28.3 per 1000 person-years; moreover, AF was associated with various co-morbidities and mortality, and its incidence rates were consistently higher in men than in women and in whites than non-whites.<sup>9</sup> In Asia, the prevalence of AF is approximately 1%, lower than in Caucasians (1–2%).<sup>4,10</sup> Moreover, it is estimated that by 2050, 72 million individuals in Asia will be diagnosed with AF, which is more than double the combined numbers of patients in Europe and the United States, due to proportionally larger number of aged individuals in Asian

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countries.<sup>11-13)</sup>

To date, few epidemiologic studies have assessed the prevalence of AF in Korea, and none have examined its incidence.<sup>14)15)</sup> The Korean Genome and Epidemiology Study reported that the prevalence of AF was 0.4% in adults aged 40-69 years, increasing to 1.0% in individuals aged 60-69 years.<sup>14)</sup> Another study found that the prevalence of AF was 0.7% in subjects aged  $\geq 40$  years and 2.1% in those aged  $\geq 65$  years.<sup>15)</sup> These studies may have underestimated the prevalence of AF because they enrolled study population aged 40-69 years<sup>14)</sup> or healthy individuals.<sup>15)</sup>

Many studies have reported that risk factors for AF include increased age, male sex, hypertension, diabetes mellitus, obesity, heart failure, valve disease, myocardial infarction and alcohol consumption.<sup>7)16-18)</sup> The Copenhagen City Heart Study reported that AF was a much more pronounced risk factor for stroke and cardiovascular death in women than in men.<sup>19)</sup>

The prevalence of AF is expected to increase in proportion to the aging of the Korean population and thus likely to become a greater public health problem. Effective prevention of AF and care of patients with this condition require reliable determination of its prevalence and incidence.<sup>20)</sup> Therefore, the purpose of this study was to determine the incidence of AF, its associated co-morbidities and risk factors and the contribution of co-morbidities to AF incidence using data from the Korean National Health Insurance Service (NHIS).

## Subjects and Methods

### Data source

The NHIS is a mandatory universal health insurance system that covers about 97% of the Korea population; it includes a centralized healthcare claims database that provides a nationwide source of information on healthcare resource utilization. The remaining 3% of the population is covered by the Medical Aid program, a public assistance program providing healthcare for the poor. Data in the NHIS database included demographic information, anthropometric measurements, biochemical test results, medical treatment, and disease diagnoses according to the Korean Classification of Diseases-6 (KCD-6), which is a similar system to the International Classification of Diseases-10 (ICD-10). Data made publicly available from the NHIS database from 2002 through 2010 were reviewed. The study protocol was approved by the Institutional Review Board of the Health Insurance Review and Assessment Service.

### Study population and materials

Patients were defined as having AF if they had the KCD-10 disease

codes I48 (atrial fibrillation and atrial flutter), I48.0 (atrial fibrillation), and I48.1 (atrial flutter). To avoid classifying those with pre-existing AF as incident cases, subjects with AF between 2002 and 2004 were excluded. The NHIS database included 207896 subjects aged  $\geq 30$  years who underwent at least one health-screening between 2002 and 2004. After excluding the 1883 subjects who had been diagnosed with AF between 2002-2004, 206013 subjects (121226 men and 84787 women) remained eligible for analysis.

Covariates included demographic characteristics (age and sex), anthropometric measurements (body mass index [BMI], systolic blood pressure [SBP] and diastolic blood pressure [DBP]), biochemical test results (glucose, total-cholesterol and hemoglobin concentrations) and co-morbidities (hypertension, ischemic heart disease [IHD], heart failure and diabetes mellitus). Subjects were divided into 10-year age groups; i.e., 30-40, 40-50, 50-60, 60-70, 70-80, and  $\geq 80$  years. BMI was calculated as weight in kilograms divided by height in meters squared. Co-morbidities present during the period between 2002-2004 were retrospectively assessed in subjects subsequently diagnosed with incident AF by searching for the KCD-10 disease codes for 4 co-morbidities, hypertension (KCD-10 I10-I15), ischemic heart disease (KCD-10 I20-I25), heart failure (KCD-10 I11.0, I13.0, I13.2, I50) and diabetes mellitus (KCD-10 E10-E14) (Supplementary Table in the online-only Data Supplement).

### Statistical analysis

Characteristics of the study population during the window period were determined. Continuous variables were expressed as mean  $\pm$  standard deviation and compared using t-tests, and categorical variables were expressed as frequency (percentage) and compared using chi-square tests. Incidence of AF was determined overall and by sex and age group, with incidence calculated as the number of patients with incident AF during each year of the 6-year follow-up period divided by the total person-years at risk among all subjects that year who did not have AF at the beginning of the year.

To assess risk factors for AF incidence, hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox's proportional hazard regression analyses. We evaluated unadjusted and multivariable-adjusted HRs of incident AF according to the co-morbidities. Unadjusted and multivariable-adjusted population attributable fractions (PAFs) of AF co-morbidities were ascertained, with multivariable-adjusted PAFs adjusted for age, sex, BMI and the other co-morbidities. All statistical tests were two-tailed, and  $p < 0.05$  were considered statistically significant. All statistical analyses were performed using SAS software (version 9.4; SAS Institute, Cary, NC, USA).

## Results

During the 6-year follow-up period, 3517(1.7%) individuals aged ≥30 years in South Korea were newly diagnosed with AF, including 2043(58.1%) males and 1474(41.9%) females. Table 1 showed the characteristics of the study population according to the incidence of AF during the window period. The incidence of AF differed significantly among groups assorted by age; BMI; SBP; DBP; concentrations of glucose, total-cholesterol, and hemoglobin; and by the presence of hypertension, IHD, heart failure and diabetes mellitus. Among subjects with incident AF during 2005–2010, 50.0% had hypertension, 20.9% had IHD, 14.8% had heart failure and 26.0% had diabetes mellitus.

The incidences of AF during the follow-up period according to sex and age groups were shown in Table 2. The overall incidence rate was 2.87/1000 person-years. The incidence was consistently higher among men than women and increased substantially with age. The incidence rates in men and women aged 30–39 years were

0.82 and 0.55 per 1000 person-years, respectively, increasing with age to 13.09 and 11.54 per 1000 person-years in men and women aged ≥80 years, respectively.

Table 3 showed the risk factors for incident AF after adjusting for variables related to incident AF. The risk factors for incident AF were age, sex, BMI, hypertension, IHD and heart failure ( $p < 0.05$  each). The association between total-cholesterol concentration and incident AF showed borderline significance, but the HR was approximately 1 (HR=0.999, 95% CI=0.998–1.000). Hypertension was the strongest risk factor for incident AF.

The HRs of co-morbidities for incident AF were presented in Table 4. Unadjusted and age- and sex-adjusted risks for AF were significantly increased by hypertension, IHD, heart failure and diabetes mellitus. After adjustments for age, sex, BMI and co-morbidities, all except diabetes mellitus remained significant. Consistent with the risk factors for incident AF, the HR of hypertension was the strongest (HR=1.667, 95% CI=1.537–1.807).

Table 5 presented unadjusted and multivariable-adjusted PAFs

**Table 1.** Demographic and clinical characteristics of subjects with and without AF during the window period (2002–2004)

Characteristic	Overall (n=206013)	Incident AF		p
		Yes (n=3517)	No (n=202496)	
Age (years)				<0.001
30–39	53278 (25.9)	242 (6.9)	53036 (26.2)	
40–49	66143 (32.1)	629 (17.9)	65514 (32.4)	
50–59	42890 (20.8)	799 (22.8)	42091 (20.8)	
60–69	30501 (14.8)	1090 (31.0)	29411 (14.5)	
70–79	11363 (5.5)	628 (17.9)	10735 (5.3)	
≥80	1838 (0.9)	129 (3.7)	1709 (0.8)	
Sex				0.167
Male	121226 (58.8)	2043 (58.1)	119183 (58.9)	
Female	84787 (41.2)	1474 (41.9)	83313 (41.1)	
BMI (kg/m <sup>2</sup> )	23.8±3.1	24.3±3.4	23.8±3.1	<0.001
SBP (mmHg)	125.4±17.4	131.6±19.6	125.3±17.4	<0.001
DBP (mmHg)	78.7±11.4	81.1±12.2	78.6±11.4	<0.001
Glucose (mg/dL)	96.6±30.8	101.4±32.4	96.5±30.7	<0.001
Total-cholesterol (mg/dL)	196.6±37.7	199.2±39.2	196.5±37.7	<0.001
Hemoglobin (g/dL)	14.0±1.5	13.9±1.5	14.0±1.5	<0.001
Co-morbid condition				
Hypertension	43743 (21.2)	1757 (50.0)	41986 (20.7)	<0.001
Ischemic heart disease	14378 (7.0)	735 (20.9)	13643 (6.7)	<0.001
Heart failure	8304 (4.0)	519 (14.8)	7785 (3.8)	<0.001
Diabetes mellitus	27873 (13.5)	914 (26.0)	26959 (13.3)	<0.001

Data presented as mean±standard deviation or n (%). AF: atrial fibrillation, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure

and 95% CIs for AF. The sex-adjusted PAF for age was 40.2%. After adjusting for all covariates, the PAF for age ( $\geq 60$  years), sex (male) and BMI ( $\geq 25$  kg/m<sup>2</sup>) were 30.6%, 10.1% and 3.4%, respectively. The unadjusted PAFs for hypertension, IHD, heart failure and diabetes mellitus were 36.9%, 15.2%, 11.3% and 14.6%, respectively. After adjustments for age, sex, BMI and co-morbidities, the PAFs for hypertension, IHD, heart failure and diabetes mellitus were 16.6%, 8.2%, 5.3% and 0.8%, respectively. The PAF for age of established AF was highest. The PAF for hypertension was greater than other co-morbidities, and the PAF for diabetes mellitus was not significant in the full model.

## Discussion

To our knowledge, this is the first study to investigate the incidence of AF in Korea using the nationwide NHIS database. The study population consisted of subjects aged  $\geq 30$  years without AF during the window period. In our study, the incidence of AF

increased with older age and was higher in men than in women, consistent with previous reports.<sup>5)9)21)</sup> The risk factors for incident AF were age, sex, BMI, hypertension, IHD and heart failure. A larger proportion of AF events was attributable to hypertension than to other co-morbidities.

Several reports<sup>14)15)</sup> described the prevalence of AF in Korea. The Korean Genome and Epidemiology Study showed that the overall prevalence of AF was 0.4% and was 1.0% in subjects aged 60–69 years.<sup>14)</sup> To compare these findings and the results of our study, we conducted additional analysis for the incidence of AF using 9986 Korean adults (4726 men and 5260 women) who enrolled in the Korean Genome and Epidemiology Study. During an 8-year follow-up period, the incidence rates in men and women aged 60–69 years were 3.01 and 1.80 per 1000 person-years, respectively. However, the high follow-up loss rate (approximately 35%) suggested that these results may have been underestimated. Our assessment of the NHIS database showed that the incidence rates of AF in men and women aged 30–39 years were 0.83 and 0.55 per 1000 person-years, respectively; the incidence rate further increased to 13.09

**Table 2.** Incidence of AF during the 6-year follow-up period according to age and sex

	N	Cases (%)	Person-year	Incidence rate (per 1000 person-year)
Overall (years)	206013	3517 (1.71)	1223496	2.87
30-39	53278	242 (0.45)	318761	0.76
40-49	66143	629 (0.95)	394606	1.59
50-59	42890	799 (1.86)	254495	3.14
60-69	30501	1090 (3.57)	179161	6.08
70-79	11363	628 (5.53)	65922	9.53
$\geq 80$	1838	129 (7.02)	10551	12.23
Male (years)	121226	2043 (1.69)	719957	2.84
30-39	40539	200 (0.49)	242501	0.82
40-49	37332	384 (1.03)	222610	1.72
50-59	22608	484 (2.14)	133905	3.61
60-69	14834	589 (3.97)	86863	6.78
70-79	5095	325 (6.38)	29418	11.05
$\geq 80$	818	61 (7.46)	4660	13.09
Female (years)	84787	1474 (1.74)	503539	2.93
30-39	12739	42 (0.33)	76260	0.55
40-49	28811	245 (0.85)	171996	1.42
50-59	20282	315 (1.55)	120590	2.61
60-69	15667	501 (3.20)	92298	5.43
70-79	6268	303 (4.83)	36504	8.30
$\geq 80$	1020	68 (6.67)	5891	11.54

AF: atrial fibrillation

**Table 3.** Multivariate analysis of risk factors for incident AF

Variables	HR(95% CI)	p*
Age (years)		
30-39 vs. ≥80	0.090 (0.072-0.112)	<0.001
40-49 vs. ≥80	0.183 (0.150-0.223)	<0.001
50-59 vs. ≥80	0.310 (0.256-0.375)	<0.001
60-69 vs. ≥80	0.520 (0.432-0.626)	<0.001
70-79 vs. ≥80	0.755 (0.624-0.914)	0.004
Sex		
Male vs. female	1.302 (1.195-1.418)	<0.001
BMI	1.024 (1.015-1.034)	<0.001
SBP	1.001 (0.998-1.003)	0.682
DBP	1.001 (0.996-1.005)	0.812
Glucose	1.000 (0.999-1.001)	0.572
Total-cholesterol	0.999 (0.998-1.000)	0.044
Hemoglobin	1.013 (0.984-1.042)	0.390
Co-morbidity		
Hypertension	1.651 (1.517-1.796)	<0.001
Ischemic heart disease	1.638 (1.497-1.792)	<0.001
Heart failure	1.521 (1.371-1.687)	<0.001
Diabetes mellitus	1.059 (0.973-1.153)	0.183

\*by Cox proportional hazard regression analysis. AF: atrial fibrillation, HR: hazard ratio, CI: confidence interval, BMI: body mass index, SBP: systolic blood pressure, DBP: diastolic blood pressure

**Table 4.** HR of incident AF according to co-morbidity

Co-morbidity	HR (95% CI)		
	Unadjusted	Model 1	Model 2
Hypertension	3.762 (3.521-4.019)	2.102 (1.955-2.260)	1.667 (1.537-1.807)
IHD	3.595 (3.314-3.899)	2.187 (2.012-2.378)	1.639 (1.498-1.792)
Heart failure	4.234 (3.857-4.647)	2.300 (2.089-2.534)	1.521 (1.372-1.687)
Diabetes mellitus	2.267 (2.102-2.444)	1.364 (1.262-1.474)	1.048 (0.966-1.136)

Model 1: adjusted for age and sex. Model 2: adjusted for age sex, body mass index and other co-morbidities. HR: hazard ratio, AF: atrial fibrillation, CI: confidence interval, IHD: ischemic heart disease

**Table 5.** PAFs(%) and 95% CIs of established AF

	PAF (95% CI)	
	Unadjusted	Multivariate adjusted <sup>†</sup>
Age (≥60 years)	40.1 (38.0-42.0)	30.6 (28.4-32.7)
Sex (Male)	-1.9 (-)*	10.1 (7.6-12.5)
BMI (≥25 kg/m <sup>2</sup> )	8.5 (6.5-10.5)	3.4 (1.3-5.4)
Hypertension	36.9 (34.8-38.8)	16.6 (14.3-18.9)
IHD	15.2 (13.8-16.6)	8.2 (6.8-9.7)
Heart failure	11.3 (10.1-12.6)	5.3 (4.0-6.5)
Diabetes mellitus	14.6 (13.0-16.2)	0.8 (-0.9-2.4)

\*The CI for the PAF estimate is not shown because the SMR estimate was less than 1. <sup>†</sup>Adjusted for age sex BMI and co-morbidities. PAF: population attributable fraction, CI: confidence interval, AF: atrial fibrillation, BMI: body mass index, IHD: ischemic heart disease

and 11.54 per 1000 person-years, in men and women aged  $\geq 80$  years, respectively. These rates were lower than in previous studies. For example, in the Rotterdam Study, the incidence rates of AF were 21 per 1000 person-years in subjects aged 80–84 years and 33–39 per 1000 person-years in the Medicare cohort.<sup>8)9)</sup> Similar to other studies, we found that incidence rates were higher among men than women in all age groups.<sup>5)9)21)</sup>

After multivariable adjustment, older age, male sex, BMI, hypertension, IHD and heart failure were significantly associated with the incidence of AF in this study. Moreover, after adjusting for age, sex, BMI and co-morbidities, the risk of AF was significantly associated with hypertension, IHD and heart failure. The Framingham Heart Study showed that the risks of AF in men and women were increased by hypertension 1.5- and 1.4-fold, respectively, and by heart failure 4.5- and 5.9-fold, respectively.<sup>7)</sup> The lifetime risk for development of AF in adults aged  $\geq 40$  years was increased 7–10% by antecedent congestive heart failure or myocardial infarction.<sup>21)</sup> In addition, obesity, sleep apnea, and metabolic syndrome have been linked to the development of AF.<sup>22)23)</sup>

Hypertension, IHD, heart failure and diabetes showed adjusted HRs for incident AF of 1.667, 1.639, 1.521 and 1.048, respectively. The HR was greater for hypertension than for these other co-morbidities, and the HR for diabetes was no longer significant after adjustment for variables related to AF. Moreover, after adjusting for age, sex, BMI and other co-morbidities, hypertension (36.9%) had a higher PAF for established AF than other co-morbidities, whereas the PAF for diabetes mellitus was not significant. The Multi-Ethnic Study of Atherosclerosis calculated age- and sex-adjusted PAFs to determine the relative contribution of major risk factors for AF (diabetes mellitus, hypertension, BMI and current smoking) among different race-ethnic groups,<sup>24)</sup> showing that hypertension was the most important contributor to AF events, affecting 22.2% of non-Hispanic whites, 33.1% of non-Hispanic blacks, 46.3% of Chinese, and 43.9% of Hispanics. In addition, similar to our results, that study showed that the PAFs for diabetes were quite small.

Our study had several limitations. First, patients with atrial flutter were included among those with AF, and participants with paroxysmal AF were not distinguished from those with persistent AF. Therefore, some participants may only have had a single episode of paroxysmal AF. However, individuals with an index AF event have high rates of recurrence and conversion to persistent AF.<sup>25)</sup> In addition, paroxysmal and persistent AF are similarly associated with risk for stroke.<sup>26)</sup> Second, patients with AF were identified according to KCD-10 codes and not confirmed by electrocardiography. Thus, the AF group may have included some patients without the disease. Conversely, the frequency of AF and co-morbidities may have been underestimated if the event did not result in a claim. However, a

recent validation study of KCD-10 diagnostic codes in the Korean NHIS database has shown that about 70% of primary, secondary, and tertiary diagnosis codes in NHIS records coincide with those from medical records. Moreover, the accuracy of diagnosis codes tended to be higher for claims from hospital admissions than from office visits, and for claims for severe than for mild conditions.<sup>27)</sup>

Nevertheless, our study had several strengths, including the sample size, which was larger than in previous studies. Furthermore, our study investigated the incidence of and risk factors for AF and its HR and PAF for co-morbidities in Korea.

In conclusion, this nationwide survey on the incidence of AF using medical claim data from the NHIS showed that the incidence of AF increased with age and was higher in men than in women. The risk of AF was significantly associated with hypertension, IHD and heart failure. A higher proportion of AF events was attributable to hypertension than to other co-morbidities. These findings suggest the importance of managing hypertension to prevent AF and the establishment of appropriate prevention strategies to reduce AF morbidity and mortality.

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This study used NHIS data (No. NHIS-2014-2-010) and made clear that all results were not related to NHIS.

## Supplementary Materials

The online-only Data Supplement is available with this article at <http://dx.doi.org/10.4070/kcj.2016.46.4.515>.

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**Supplementary Table.** Definitions of co-morbidities of AF

Co-morbidity	KCD-6	Name of disease
Hypertension	I10	Essential (primary) hypertension
	I11	Hypertensive heart disease
	I12	Hypertensive renal disease
	I13	Hypertensive heart and renal disease
	I15	Secondary hypertension
Ischemia	I20	Angina pectoris
	I21	Acute myocardial infarction
	I22	Subsequent myocardial infarction
	I23	Certain current complications following acute myocardial infarction
	I24	Other acute ischemic heart diseases
	I25	Chronic ischemic heart disease
Heart failure	I11.0	Hypertensive heart disease with (congestive) heart failure
	I13.0	Hypertensive heart and renal disease with (congestive) heart failure
	I13.2	Hypertensive heart and renal disease with both (congestive) heart failure and renal failure
	I50	Heart failure
Diabetes mellitus	E10	Insulin-dependent diabetes mellitus
	E11	Non-insulin-dependent diabetes mellitus
	E12	Malnutrition-related diabetes mellitus
	E13	Other specified diabetes mellitus
	E14	Unspecified diabetes mellitus

AF: atrial fibrillation, KCD-6: Korean classification diseases-6