

## ORIGINAL RESEARCH ARTICLE

## Increasing trends in hospital care burden of atrial fibrillation in Korea, 2006 through 2015

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**ABSTRACT**

**Objective** Temporal changes in the healthcare burden of atrial fibrillation (AF) are less well known in rapidly ageing Asian countries. We examined trends in hospitalisations, costs, treatment patterns and outcomes related to AF in Korea.

**Methods** Using the National Health Insurance Service (NHIS) database involving the entire adult Korean population (n=41 701 269 in 2015), we analysed a nationwide AF cohort representing 931 138 patients with AF. We studied all hospitalisations due to AF from 2006 to 2015.

**Results** Overall, hospitalisations for AF increased by 420% from 767 to 3986 per 1 million Korean population from 2006 to 2015. Most admissions occurred in patients aged  $\geq 70$  years, and the most frequent coexisting conditions were hypertension, heart failure and chronic obstructive pulmonary disease. Hospitalisations mainly due to major bleeding and AF control increased, whereas hospitalisations mainly due to ischaemic stroke and myocardial infarction decreased. The total cost of care increased even after adjustment for inflation from €68.4 million in 2006 to €388.4 million in 2015, equivalent to 0.78% of the Korean NHIS total expenditure. Overall in-hospital mortality decreased from 7.5% in 2006 to 4.3% in 2015. The in-hospital mortality was highest in patients  $\geq 80$  years of age (7.7%) and in patients with chronic kidney disease (7.4%).

**Conclusions** AF hospitalisations have increased exponentially over the past 10 years in Korea, in association with an increase in comorbid chronic diseases. Mortality associated with AF hospitalisations decreased during the last decade, but hospitalisation costs have markedly increased.

**INTRODUCTION**

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in the general population, and is associated with increased mortality and morbidity.<sup>1</sup> The number of persons with AF has been projected to increase to 12.1–15.9 million in the USA by 2050 and 17.9 million in Europe by 2060, with more than half of these patients  $\geq 80$  years of age.<sup>2–4</sup> Consequently, the healthcare burden of AF is growing considerably, and is mainly related to hospitalisations.<sup>5–7</sup> The total cost related to AF care was estimated as US\$6–US\$26 billion in the USA and it accounts for 1% of the national healthcare burden in the UK.<sup>5–7</sup>

While the global burden of AF has increased over recent decades, most studies about the epidemiology and care burden of AF are based on the predominantly white populations of North America or Europe.<sup>8</sup> The actual disease burden of AF in Asia is rapidly increasing given the larger proportional increase in the elderly population.<sup>9 10</sup> However, the impact of AF on hospitalisations and mortality, and the economic burden of AF is less understood in Asian populations. A nation-level study of the temporal trends in healthcare burden of AF is essential for establishing the burden of AF and appropriate healthcare planning. Therefore, we used a national insurance database to evaluate a contemporary AF-related hospital care burden. We examined temporal trends in hospitalisations, the effects of comorbid diagnoses, costs, treatment patterns and outcomes related to AF in Korea.

**METHODS****Data sources**

This study is based on the national health claims database established by the National Health Insurance Service (NHIS) of Korea.<sup>11</sup> The NHIS is the single insurer managed by the Korean government, and the majority (97.1%) of the Korean population are mandatory subscribers, while the remaining 3% of the population are medical aid subjects. The NHIS database contains information on medical aid subjects as well; therefore, it is based on the entire Korean population. The following medical information is provided: sociodemographic information, patient use of inpatient and outpatient services, pharmacy dispensing claims and mortality data. Every population in the NHIS database was linked by Korean social security numbers, and all social security numbers were deleted after constructing the cohort by using serial numbers to prevent leakage of personal information. These databases are open to researchers, whose study protocols are approved by the official review committee. Informed consent was waived.

**Study population**

Between 1 January 2006 and 31 December 2015, 931 138 patients with AF were identified from the entire Korean population. AF was diagnosed using the International Classification of Disease 10th Revision (ICD-10) codes I48 (AF and atrial flutter), I48.0 (AF) and I48.1 (atrial flutter). To ensure diagnostic accuracy, patients were defined as having

AF only when it was a discharge diagnosis or confirmed more than twice in the outpatient department.<sup>12–17</sup> Diagnosis of AF has previously been validated in the NHIS database with a positive predictive value of 94.1%.<sup>15–17</sup> Patients aged <20 years or with valvular AF (with a diagnosis of either mitral stenosis (ICD-10: I05.0, I05.2 and I34.2) or prosthetic heart valves (ICD-10: Z95.2–Z95.4) or insurance claims for valve replacement or valvuloplasty) were excluded.

All hospitalisations due to AF from 2006 to 2015 and the cost of each inpatient stay were studied. AF hospitalisations and inpatient costs were obtained in two different ways: 1) overall AF hospitalisation (AF as any diagnosis of up to five discharge diagnoses) and 2) AF hospitalisation due to each main cause including major bleeding, ischaemic stroke, AF control (AF as principal discharge diagnosis), myocardial infarction (MI), heart failure, sick sinus syndrome (SSS) or pacemaker (PM) related, and radiofrequency catheter ablation (RFCA) for AF. All costs were calculated in Korean won (KRW) and converted into Euros

(1 EUR=1282.7 KRW). Cost was adjusted for inflation by calculating in terms of the 2015 cost using the Korean Consumer Price Index data.<sup>18</sup>

### Comorbidities, economic status and medications

Comorbidities were defined using medical claims according to ICD-10 codes and prescription medication use. To ensure diagnostic accuracy, patients were considered to have comorbidities when it was a discharge diagnosis or was confirmed more than twice in an outpatient setting, similar to previous studies with the NHIS.<sup>12–13 15–17</sup> The definitions of comorbidities and main hospitalisation causes are presented in online supplementary table 1. Economic status variables were categorised into three groups based on the total amount of national health insurance premiums paid by an insured person in each year, which is proportional to the person's income: low, intermediate and high economic status. Prescription medication use was ascertained

**Table 1** Characteristics of patients with AF hospitalisations

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	P value for trend
Total Korean AF population, n	269448	315854	359695	402024	442657	481682	520070	558651	598614	639349	
Patients with hospitalisations, n (%)	16639 (6.2)	20539 (6.5)	24948 (6.9)	28345 (8.2)	33214 (7.1)	36025 (7.5)	41421 (8.0)	46012 (8.2)	51223 (8.6)	58160 (9.1)	<0.001
Sex, %											
Male	55.4	54.8	53.9	54.6	54.3	54.3	54.1	54.0	53.9	53.6	<0.001
Female	44.6	45.2	46.1	45.4	45.7	45.7	45.9	46.0	46.1	46.4	<0.001
Age, mean (SE)	69.5 (0.9)	70.0 (0.8)	70.6 (0.7)	70.9 (0.7)	71.1 (0.6)	71.4 (0.6)	71.9 (0.5)	72.3 (0.3)	72.9 (0.5)	73.3 (0.5)	<0.001
20–49 years, %	6.0	5.8	5.2	5.1	4.8	4.4	4.2	3.6	3.6	3.4	<0.001
50–59 years, %	10.9	10.5	9.8	9.9	10.0	10.1	10.2	10.0	9.4	8.9	<0.001
60–69 years, %	27.7	26.2	24.7	23.9	22.9	22.2	20.9	19.5	18.5	18.3	<0.001
70–79 years, %	37.5	38.4	39.2	39.0	39.3	38.9	38.8	39.5	38.9	37.6	<0.001
≥80 years, %	18.0	19.1	21.0	22.2	23.0	24.4	25.9	27.4	29.7	31.9	<0.001
Economic status, %											
Low	45.1	46.3	45.3	44.1	42.9	42.5	41.2	39.9	38.1	36.5	<0.001
Intermediate	20.9	20.6	25.0	24.3	24.1	24.0	24.1	24.2	24.2	24.4	<0.001
High	34.0	33.2	29.7	31.6	32.9	33.5	34.7	35.9	37.7	39.1	<0.001
Practice level of initial AF diagnosis											
Primary care hospital	3.7	4.5	5.4	6.0	6.6	7.5	8.3	8.7	9.0	9.2	<0.001
Secondary care hospital	9.7	9.9	10.7	12.3	12.6	11.2	9.8	9.4	9.7	9.5	<0.001
Tertiary referral hospital	85.3	83.4	82.4	80.0	79.2	79.5	79.9	79.7	79.0	78.8	<0.001
Others (nursing/public health centre)	1.3	2.2	1.6	1.6	1.6	1.7	2.0	2.2	2.3	2.4	<0.001
Comorbidities, %											
Heart failure	69.6	70.2	69.5	69.8	69.6	70.4	70.8	71.4	72.8	73.8	<0.001
Hypertension	95.3	95.8	96.0	96.4	96.3	96.1	96.3	96.6	96.6	96.6	<0.001
Diabetes mellitus	36.2	37.4	38.9	39.8	40.8	41.7	42.5	42.9	43.5	44.2	<0.001
Previous ischaemic stroke	37.3	39.4	41.6	42.9	44.3	45.4	46.3	47.4	47.6	48.1	<0.001
Previous MI	25.7	25.7	25.4	25.1	24.3	22.8	22.0	21.6	21.0	20.9	<0.001
PAD	12.9	14.4	16.6	19.3	21.2	22.5	23.6	24.6	25.7	26.1	<0.001
Previous major bleeding*	13.9	15.6	16.8	17.9	18.2	18.2	18.7	19.0	19.3	19.2	<0.001
COPD	43.7	46.3	48.1	49.2	50.0	50.4	51.3	52.0	52.6	52.6	<0.001
CKD	10.8	11.7	12.2	13.5	13.7	14.0	15.4	16.5	16.8	18.1	<0.001
CHA <sub>2</sub> DS <sub>2</sub> -VASc score, mean (SE)	4.75 (0.02)	4.88 (0.01)	5.02 (0.01)	5.09 (0.01)	5.15 (0.01)	5.19 (0.01)	5.26 (0.01)	5.33 (0.01)	5.40 (0.01)	5.45 (0.01)	<0.001
HAS-BLED score, mean (SE)	3.08 (0.01)	3.20 (0.01)	3.28 (0.01)	3.35 (0.01)	3.38 (0.01)	3.41 (0.01)	3.43 (0.01)	3.46 (0.01)	3.48 (0.01)	3.48 (0.01)	<0.001

\*Major bleeding includes intracranial bleeding and gastrointestinal bleeding.

AF, atrial fibrillation; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PAD, peripheral artery disease.

**Table 2** Trends of AF hospitalisation per 1 million Korean population between 2006 and 2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Relative increase*, %	P value for trend
Overall	767	997	1275	1529	1854	2048	2497	2914	3397	3986	420	<0.001
Age (years)												
20–49	58	71	85	92	111	117	124	121	131	145	150	<0.001
50–59	497	572	656	748	855	886	1013	1108	1162	1303	162	<0.001
60–69	2013	2370	2689	3058	3483	3666	4136	4342	4449	4856	141	<0.001
70–79	5249	6777	8504	9488	11 120	11 631	13 227	15 148	17 246	19 242	267	<0.001
≥80	8185	10 805	14 459	17 890	21 402	24 034	29 887	35 174	41 429	48 388	491	<0.001
Sex												
Male	827	1039	1302	1561	1853	2037	2457	2817	3204	3727	350	<0.001
Female	707	956	1249	1497	1856	2059	2535	3009	3588	4242	500	<0.001
Main cause of hospitalisation												
Major bleeding†	241	348	440	516	592	638	735	793	869	966	301	<0.001
Ischaemic stroke‡	179	211	247	270	302	326	348	357	369	387	116	<0.001
AF control‡	89	114	134	158	184	214	260	282	318	350	294	<0.001
MI	142	170	192	207	215	189	204	216	239	274	94	<0.001
Heart failure	297	388	450	502	555	589	619	651	690	732	146	<0.001
SSS or PM related	20	24	23	25	27	33	36	44	49	52	20	<0.001
RFCA for AF	8	9	8	15	20	25	30	31	34	40	413	<0.001

\*2015 value minus 2006 value divided by 2006 value multiplied by 100.

†Major bleeding includes intracranial bleeding and gastrointestinal bleeding.

‡Admission for anticoagulation, rate and rhythm control for AF (AF as principal discharge diagnosis).

AF, atrial fibrillation; MI, myocardial infarction; PM, pacemaker; RFCA, radiofrequency catheter ablation; SSS, sick sinus syndrome.

by identifying NHIS database claims. Medication use among patients with AF in a given year was defined when the medication was prescribed for >180 days in the particular year.

**Statistical analysis**

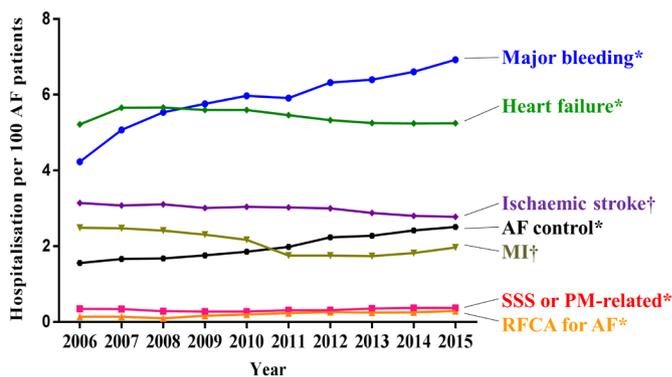
AF hospitalisations are presented as numbers per 1 million Korean population and as numbers per 100 patients with AF in a given year. Hospitalisations per 1 million Koreans were the number of hospitalisations in a given year divided by the total number of Korean residents who were alive in that year. Online supplementary table 2 shows the number and distribution of total Korean residents aged ≥20 years. Hospitalisations per 100 patients with AF were the number of hospitalisations in a given year divided by the total number of Korean patients with AF in that year and multiplied by 100. The Cochran-Armitage trend test was used to analyse temporal trends of categorical variables. For continuous variables such as hospitalisation costs, the non-parametric test for trends by Jonckheere-Terpstra was used. All tests were two-tailed, with P<0.05 considered to be statistically significant. Statistical analyses were conducted with SAS V.9.4 (SAS Institute, Cary, North Carolina, USA) and SPSS V.23.0 statistical package (SPSS, Chicago, Illinois, USA).

**RESULTS**

**AF hospitalisations, demographics and comorbidities**

The characteristics of patients with AF who were hospitalised are presented in table 1. The proportion of patients with AF who were hospitalised in a given year compared with the total Korean patient population with AF in that year increased from 6.2% in 2006 to 9.1% in 2015. The proportion of females showed a modest increase, changing from 44.6% in 2006 to 46.4% in 2015 (P<0.001). The mean age increased from 69.5 (SE: 0.9) years in 2006 to 73.3 (SE: 0.5) years in 2015 (P<0.001). The proportion of elderly patients aged ≥70 years increased from 55.5% in 2006 to 69.5% in 2015 (P<0.001).

The most frequent coexisting conditions in hospitalised patients with AF were hypertension, heart failure and chronic obstructive pulmonary disease. Over the study period, the prevalence of several comorbid diseases increased significantly, with the largest increase of peripheral artery disease (2.0-fold; 12.9%–26.1%). Chronic kidney disease (CKD) also increased by 1.7-fold, from 10.8% in 2006 to 18.1% in 2015. CHA<sub>2</sub>DS<sub>2</sub>-VASc score and HAS-BLED score also significantly increased over the decade. The proportion of patients with intermediate and high economic status also increased significantly, while the proportion of low economic status decreased. The proportion of patients with AF initially diagnosed in primary care hospitals increased significantly, whereas the proportion of those diagnosed in secondary or tertiary referral hospitals decreased.



**Figure 1** Temporal trends of AF hospitalisation per 100 patients with AF according to main hospitalisation causes between 2006 and 2015. \*P value for increase trends <0.001. †P value for decrease trends <0.001. AF, atrial fibrillation; MI, myocardial infarction; PM, pacemaker; RFCA, radiofrequency catheter ablation; SSS, sick sinus syndrome.

**Table 3** Trends of AF hospitalisation cost between 2006 and 2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Relative increase*, %	P value for trend
Overall	68.4	90.1	111.3	135.8	172.1	187.7	223.9	262.4	314.7	388.4	468	<0.001
Age (years)												
20–49	3.9	4.9	5.3	5.4	7.0	7.6	7.5	8.1	9.1	11.3	187	<0.001
50–59	6.9	8.6	9.4	12.8	15.0	16.6	19.9	23.3	25.7	31.0	349	<0.001
60–69	19.3	23.8	27.2	31.7	38.7	40.2	45.4	48.5	54.8	67.9	251	<0.001
70–79	26.1	36.2	46.1	54.8	69.1	75.2	88.6	104.2	124.3	145.9	460	<0.001
≥80	12.1	16.7	23.4	31.0	42.3	48.2	62.4	78.4	100.8	132.3	991	<0.001
Sex												
Male	39.0	50.0	60.3	73.7	90.3	97.9	116.1	133.9	158.0	194.5	399	<0.001
Female	29.4	40.1	50.9	62.0	81.8	89.9	107.8	128.5	156.7	194.0	559	<0.001
Economic status												
Low	29.0	39.4	48.5	59.8	75.5	82.8	96.1	111.3	127.5	149.4	415	<0.001
Intermediate	14.0	18.3	27.8	30.7	38.6	42.2	49.8	59.0	69.5	87.9	531	<0.001
High	25.4	32.4	34.9	45.3	58.0	62.7	77.9	92.1	117.7	151.1	494	<0.001
CHA <sub>2</sub> DS <sub>2</sub> -VASc												
0–1	2.5	3.1	3.2	3.9	4.9	5.7	6.3	6.7	6.8	8.2	223	<0.001
≥2	65.8	87.1	108.0	131.7	167.2	182.0	217.5	255.8	307.9	380.2	478	<0.001
Main cause of hospitalisation												
Major bleeding†	37.1	48.8	57.8	68.7	80.5	81.3	92.1	96.9	110.4	123.6	233	<0.001
Ischaemic stroke	22.8	27.6	32.9	37.1	41.9	45.5	46.9	48.4	51.4	61.1	168	<0.001
AF control‡	5.9	7.6	8.0	10.5	13.3	15.9	19.5	21.1	26.9	33.2	468	<0.001
MI	16.7	19.3	19.7	20.9	21.7	18.7	19.7	20.5	23.7	28.5	71	<0.001
Heart failure	16.1	21.9	24.9	28.4	33.1	35.4	37.8	41.5	46.1	52.1	223	<0.001
SSS or PM related	4.3	5.2	4.2	4.7	5.2	6.1	7.2	9.2	10.6	11.7	172	<0.001
RFCA for AF	2.2	2.7	2.1	4.0	5.4	7.2	8.9	9.0	12.0	16.4	660	<0.001

All costs are adjusted for inflation by calculating in terms of 2015 cost according to Korean Consumer Price Index data and presented as million €.

\*2015 value minus 2006 value divided by 2006 value multiplied by 100.

†Major bleeding includes intracranial bleeding and gastrointestinal bleeding.

‡Admission for anticoagulation, rate and rhythm control for AF (AF as principal discharge diagnosis).

AF, atrial fibrillation; MI, myocardial infarction; PM, pacemaker; RFCA, radiofrequency catheter ablation; SSS, sick sinus syndrome.

### Trends of AF hospitalisations

From 2006 to 2015, the overall hospitalisation rate per 1 million Korean population increased significantly from 767 to 3986 per 1 million Koreans (relative increase, 420%;  $P<0.001$ ; table 2). The significant increase of hospitalisation rate was observed across all age groups. The largest increase in hospitalisation rate was observed in the group aged  $\geq 80$  years (491%), followed by the group aged 70–79 years (267%). The relative rates of increase were higher in females than males (500% vs 350%;  $P<0.001$ ). Therefore, the hospitalisation rate was higher in men from 2006 to 2009, but was higher in women since 2010. Hospitalisation due to major bleeding increased by 301%, from 241 to 966 per 1 million Koreans from 2006 to 2015 ( $P<0.001$ ). Hospitalisation due to ischaemic stroke, AF control, MI and heart failure also increased by 116%, 294%, 94% and 146%, respectively (all  $P<0.001$ ).

The overall hospitalisation rate per 100 patients with AF also increased significantly from 13.4 in 2006 to 28.6 in 2015 (relative increase 113%;  $P<0.001$ ). The increasing trend was consistent across all subgroups according to economic status and CHA<sub>2</sub>DS<sub>2</sub>-VASc score (all  $P<0.001$ , online supplementary table 3). Mean hospitalisations per 100 patients with AF with high CHA<sub>2</sub>DS<sub>2</sub>-VASc score ( $\geq 2$ ) were consistently higher than those with CHA<sub>2</sub>DS<sub>2</sub>-VASc score from 0 to 1. Figure 1 shows the temporal trends of AF hospitalisations per 100 patients with AF according to main hospitalisation cause. The hospitalisations per 100 patients with AF mainly due to major bleeding,

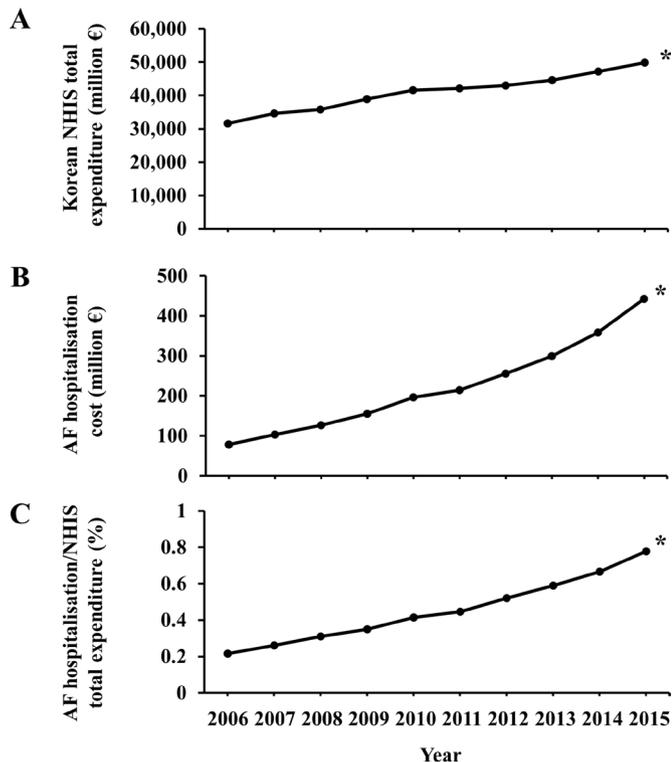
AF control, heart failure and SSS or PM related increased by 64%, 61%, 1% and 8%, respectively (all  $P<0.001$ ). The magnitude of the increase in hospitalisation rates per 100 patients with AF was highest with RFCA for AF (110%;  $P<0.001$ ). However, hospitalisations mainly due to ischaemic stroke ( $-12\%$ ;  $P<0.001$ ) and MI ( $-21\%$ ;  $P<0.001$ ) per 100 patients with AF decreased.

### Trends of AF hospitalisation costs

Table 3 shows temporal trends of AF hospitalisation costs. After adjusting for inflation, the overall cost of AF hospitalisations increased exponentially from €68.4 million in 2006 to €388.4 million in 2015 (relative increase, 468%;  $P<0.001$ ). Across all subgroups according to age, sex, economic status and CHA<sub>2</sub>DS<sub>2</sub>-VASc score, the inpatient costs increased significantly (all  $P<0.001$ ).

The total inpatient costs mainly due to major bleeding increased from €37.1 million in 2006 to €123.6 million in 2015 (relative increase, 233%;  $P<0.001$ ). Total inpatient costs mainly due to ischaemic stroke, AF control and MI also increased by 168%, 468% and 71%, respectively (all  $P<0.001$ ).

Over the same period, the annual Korean NHIS total expenditure increased by 58% from €31 589 million to €49 898 million.<sup>19</sup> The proportion of AF hospitalisation cost to Korean NHIS total expenditure increased from 0.22% in 2006 to 0.78% in 2015 (figure 2, online supplementary table 4).



**Figure 2** Temporal trends of medical cost between 2006 and 2015. (A) Korean NHIS total expenditure (million €), (B) total AF hospitalisation cost (million €) and (C) the proportion of total AF hospitalisation cost to Korean NHIS total expenditure (%). \*P value for trends <0.001. AF, atrial fibrillation; NHIS, National Health Insurance Service.

Mean cost per hospitalisation for overall AF hospitalisation decreased by 3% from €2407 to €2337 (P<0.001). Mean cost per hospitalisation mainly due to ischaemic stroke, AF control, heart failure and RFCA for AF increased over the decade; however, mean cost per hospitalisation due to major bleeding and MI decreased over this period (table 4).

**Trends of AF treatment patterns**

Table 5 shows the trends in AF treatment patterns. The use of oral anticoagulants significantly increased by 36% (from 26.8% to 36.4%; P<0.001), with increasing trends in both

warfarin and non-vitamin K-dependent oral anticoagulant use. The use of P2Y<sub>12</sub> inhibitors and statins increased by 165% and 160%, respectively, whereas aspirin use decreased by 19% (all P<0.001). Usage of digoxin decreased by 49%, while that of class Ic anti-arrhythmic drugs increased by 80% (both P<0.001).

**In-hospital mortality and length of stay**

Table 6 shows the trends of in-hospital mortality following AF hospitalisation. Overall in-hospital mortality significantly decreased from 7.5% in 2006 to 4.3% in 2015 (relative decrease 42%, P<0.001). The in-hospital mortality was highest in patients aged ≥80 years (7.7%) and in those with CKD (7.4%) and major bleeding (7.3%).

While mean lengths of hospital stay mainly due to major bleeding, ischaemic stroke, AF control, SSS or PM related and RFCA for AF decreased, those due to heart failure and MI increased over the time period from 2006 to 2015 (see online supplementary table 5).

**DISCUSSION**

The main findings of our analysis of AF hospitalisation over a 10-year period in Korea are as follows: (1) AF hospitalisations have increased significantly for the last decade; (2) the majority of admissions occurred in elderly patients aged ≥70 years, and those aged ≥80 years demonstrated the largest increase of admissions and the greatest in-hospital mortality among all age groups; (3) the total costs of AF care were increased even after adjusting for inflation, with the proportion of AF hospitalisation costs to Korean NHIS total expenditure increasing to 0.78% in 2015 and (4) mortality associated with AF hospitalisations decreased significantly.

**Increased AF hospitalisation**

Our finding of increased AF hospitalisation rates is consistent with other nationwide studies.<sup>20 21</sup> The increase of AF hospitalisation might be attributable to ageing of the general population and the increasing prevalence of risk factors including hypertension, diabetes mellitus and obesity.<sup>12 17</sup> Almost 80% of hospitalised patients were ≥70 years of age, consistent with previous studies.<sup>3 21</sup> Patients aged ≥80 years had the largest hospitalisation rate for any age group throughout the 10-year period, and had an exponential increase from 8185 in 2006 to 48 388 per 1 million people per year in 2015. Moreover, the in-hospital

**Table 4** Mean cost per hospitalisation

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Relative increase*, %	P value for trend
Overall AF hospitalisation, €	2407	2404	2290	2304	2380	2318	2238	2218	2250	2337	-3	<0.001
Main cause of hospitalisation, €												
Major bleeding†	4155	3725	3448	3456	3481	3224	3133	3009	3085	3067	-26	<0.001
Ischaemic stroke	3431	3486	3501	3566	3556	3525	3364	3342	3389	3780	10	<0.001
AF control‡	1776	1783	1562	1728	1840	1878	1875	1848	2047	2271	28	<0.001
MI	3175	3020	2685	2617	2581	2504	2416	2343	2403	2492	-22	<0.001
Heart failure	1465	1505	1451	1469	1527	1515	1524	1569	1623	1707	16	<0.001
SSS or PM related	5887	5887	4872	4854	4816	4570	4992	5119	5255	5391	-8	<0.001
RFCA for AF	7407	7554	6895	7111	7023	7204	7249	7176	8601	9742	32	<0.001

All costs are adjusted for inflation by calculating in terms of 2015 cost according to Korean Consumer Price Index data and presented as €.

\*2015 value minus 2006 value divided by 2006 value multiplied by 100.

†Major bleeding includes intracranial bleeding and gastrointestinal bleeding.

‡Admission for anticoagulation, rate and rhythm control for AF (AF as principal discharge diagnosis).

AF, atrial fibrillation; MI, myocardial infarction; PM, pacemaker; RFCA, radiofrequency catheter ablation; SSS, sick sinus syndrome.

**Table 5** Trends of AF treatment patterns between 2006 and 2015

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Relative increase*, %	P value for trend
OAC	26.8	27.5	27.2	27.8	28.0	29.5	30.3	32.0	33.5	36.4	36	<0.001
Warfarin	26.8	27.5	27.2	27.8	28.0	29.5	30.3	30.0	31.0	28.4	6	<0.001
NOAC	0.0	0.0	0.0	0.0	0.0	0.0	0.0	1.9	2.5	9.8		<0.001
Aspirin	46.2	47.0	47.1	47.6	47.1	45.9	45.5	44.2	41.7	37.4	-19	<0.001
P2Y <sub>12</sub> inhibitor	5.9	7.6	9.4	11.2	11.1	11.0	11.9	13.4	15.2	15.7	165	<0.001
Statin	16.0	19.3	21.4	24.9	28.2	30.3	33.2	36.0	38.9	41.5	160	<0.001
β-Blocker	44.7	46.0	46.6	47.9	47.7	47.8	45.8	44.2	42.1	40.1	-10	<0.001
Calcium channel blocker	20.8	21.3	21.8	22.5	22.5	22.4	21.9	21.5	21.1	20.6	-1	<0.001
Digoxin	32.7	30.5	28.3	26.7	24.8	23.6	21.8	20.2	18.5	16.7	-49	<0.001
AAD class Ic	6.0	6.4	6.7	7.2	7.7	8.9	9.6	10.0	10.4	10.8	80	<0.001
AAD class III	5.9	5.9	5.8	5.5	5.4	5.4	5.4	5.5	5.8	6.0	1	0.287

Values are percentages of each drug user type among patients with AF hospitalisations.

\*2015 value minus 2006 value divided by 2006 value multiplied by 100.

AAD, anti-arrhythmic drug; AF, atrial fibrillation; NOAC, non-vitamin K-dependent oral anticoagulant; OAC, oral anticoagulant.

mortality in this age group was highest among all age groups. It is expected that the number of elderly Koreans aged  $\geq 75$  years will increase from 2.05 million in 2010 to 5.08 million in 2030, and to 11.0 million in 2060.<sup>22</sup> Increasing AF hospitalisations with

high mortality in this elderly group will give rise to an increased public healthcare burden and associated healthcare costs.

Since 2010, women had higher AF hospitalisation rates than men, with a higher rate of increase during 10 years. This sex

**Table 6** In-hospital mortality for AF hospitalisation

	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	Overall	Relative increase*, %	P value for trend
Overall, %	7.5	7.4	7.3	6.6	6.6	6.1	6.0	5.5	4.8	4.3	5.7	-42	<0.001
Age (years), %													
20–49	3.1	3.3	3.1	2.3	2.2	1.8	1.8	1.9	1.5	1.7	2.1	-45	<0.001
50–59	4.6	4.4	4.1	3.5	2.9	2.8	2.9	2.2	2.0	1.9	2.8	-59	<0.001
60–69	5.7	5.6	5.5	5.1	4.8	4.2	3.9	3.7	3.2	2.7	4.1	-53	<0.001
70–79	8.0	7.9	7.3	6.6	6.6	6.1	5.9	5.5	4.6	4.1	5.7	-49	<0.001
$\geq 80$	11.3	10.7	11.0	9.6	9.5	8.8	8.5	7.4	6.4	5.7	7.7	-50	<0.001
Sex, %													
Male	7.7	7.7	7.6	6.8	6.9	6.4	6.3	5.9	5.4	4.8	6.1	-38	<0.001
Female	7.3	7.1	7.1	6.4	6.3	5.9	5.8	5.2	4.3	3.9	5.3	-46	<0.001
Economic status, %													
Low	6.5	6.6	6.7	6.2	6.3	6.0	6.0	5.4	4.6	4.2	5.5	-35	<0.001
Intermediate	7.2	7.9	7.8	7.1	6.9	6.0	5.7	5.7	5.0	4.2	5.8	-41	<0.001
High	8.9	8.2	8.1	7.0	6.9	6.5	6.3	5.7	4.9	4.5	5.9	-50	<0.001
CHA <sub>2</sub> DS <sub>2</sub> -VASc, %													
0–1	4.3	4.2	3.6	3.2	3.2	2.6	2.4	2.2	1.8	1.8	2.7	-58	<0.001
$\geq 2$	7.6	7.5	7.5	6.7	6.7	6.2	6.1	5.6	4.9	4.4	5.8	-43	<0.001
Comorbidities, %													
Heart failure	7.5	7.7	7.7	7.0	7.0	6.6	6.4	5.9	5.1	4.6	6.0	-40	<0.001
Hypertension	7.3	7.3	7.2	6.6	6.5	6.1	6.0	5.5	4.8	4.3	5.7	-41	<0.001
Diabetes mellitus	10.0	9.2	9.5	8.3	8.2	7.7	7.4	6.8	5.7	5.2	7.0	-49	<0.001
Previous ischaemic stroke	8.3	8.0	7.6	7.0	6.6	6.1	6.0	5.5	4.6	4.1	5.6	-50	<0.001
Previous MI	9.6	8.8	8.7	8.0	7.7	7.6	7.0	6.6	5.6	5.1	6.9	-47	<0.001
PAD	8.1	7.6	7.3	6.5	6.9	6.4	6.5	6.0	5.2	4.7	5.9	-41	<0.001
Previous major bleeding†	11.4	10.1	9.8	9.0	8.4	7.9	7.9	7.1	5.9	5.1	7.3	-55	<0.001
COPD	7.6	7.9	8.1	7.3	7.3	6.9	6.8	6.3	5.4	5.0	6.3	-35	<0.001
CKD	10.8	10.1	9.8	9.4	9.1	8.3	8.0	7.1	6.5	5.5	7.4	-49	<0.001

\*2015 value minus 2006 value divided by 2006 value multiplied by 100.

†Major bleeding includes intracranial bleeding and gastrointestinal bleeding.

AF, atrial fibrillation; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; MI, myocardial infarction; PAD, peripheral artery disease.

difference is similar to that reported in previous studies in the USA and Scotland,<sup>21 23</sup> and might be explained by a higher symptom burden and stroke risk in women with AF.<sup>24</sup>

### Hospitalisation costs

In this study, total hospital costs per year increased exponentially by 468% over a 10-year follow-up. The annual Korean NHIS total expenditure increased by only 58%, while the proportion of AF hospitalisation cost to Korean NHIS total expenditure increased to 0.78% in 2015. Consistent with our findings, many previous studies have shown that the number of AF-related hospital costs have increased with ageing of the population and more prevalent risk factors such as hypertension and diabetes.<sup>20 21</sup> Moreover, the number of RFCA shows a consistent increase over the past decade, which could contribute to the rise of hospital costs.

The mean length of hospital stays due to various causes, except heart failure and MI, decreased from 2006 to 2015 and mean cost per hospitalisation showed a slight decrease of -3% for the same period (perhaps related to the strong regulation of medication price and medical practice by the strict reimbursement system of Korea); however, the total cost increased significantly over the 10-year period. Increasing number of hospitalisations, ageing and increasing patients' comorbidities and complexities are some drivers of these increasing costs, causing a major economic problem on the healthcare system.

Compared with some other countries,<sup>21</sup> the mean length of hospital stay in Korea was significantly longer. This might be related to cheaper hospitalisation costs and generous reimbursement policies in Korea. Therefore, we should focus on limiting hospitalisations and on shortening the lengths of hospital stay. There are some potential means to reduce the cost of AF care, such as emergency department observation unit for acute onset AF, rhythm versus rate control and low molecular weight heparin use in patients hospitalised for AF.<sup>25-27</sup>

### Treatment pattern and in-hospital mortality

Previous studies have reported that global burden of AF has increased exponentially.<sup>21 28</sup> However, patients with AF showed a modest decrease in in-hospital mortality over the 10-year study period in our study. The rising prevalence and longer survival after onset of AF might be attributable, in part, to early disease detection due to improvements in surveillance methods and general medical care.

Along with decreased in-hospital mortality, we showed declines over time in stroke and MI admissions occurring in patients with AF. Our findings are in line with data that show a decline in stroke rates, including thromboembolic strokes, during the past few decades.<sup>29</sup> In contrast, the number of hospitalisations mainly due to major bleeding among patients with AF increased over a 10-year period. These dual findings of decreasing stroke and MI and increasing bleeding admissions seemed to coincide with increased use of oral anticoagulants and P2Y<sub>12</sub> inhibitors along with decreased use of aspirin. The switching of antithrombotic therapy from aspirin to oral anticoagulant as well as the increased use of P2Y<sub>12</sub> inhibitors might help explain the decreased stroke and MI admissions and increased bleeding admissions.

### Limitations

The present study has several limitations. Such studies using administrative databases might be susceptible to errors from coding inaccuracies. To minimise this problem, we examined the nationwide cohort and applied the definition that we already

validated in previous studies that used a Korean NHIS sample cohort.<sup>13 15-17</sup> 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. We could not distinguish index admissions from re-admissions in the NHIS database, potentially leading to an overestimation of the number of hospitalisations. This study examines only in-hospital mortality without follow-up outcomes. However, this study analysed longitudinal data from the entire adult Korean population, using the largest nationwide Asian database available in the literature. Therefore, our findings should reflect the 'real-world' AF burden on a nationwide scale.

### CONCLUSIONS

Hospitalisation rates for AF among Korean adults increased exponentially from 2006 to 2015, in association with an increase in comorbid chronic diseases. Mortality associated with AF hospitalisations decreased during the last decade, but hospitalisation costs have markedly increased. Prevention of AF hospitalisations and streamlined integrated AF management should be pursued in a holistic manner to lessen the healthcare burden of AF.<sup>30</sup>

### Key questions

#### What is already known on this subject?

- ▶ The healthcare burden of atrial fibrillation (AF) is growing considerably, and is mainly related to hospitalisations. However, the impact of AF on hospitalisations and mortality, and the economic burden of AF is less understood in Asian populations.

#### What might this study add?

- ▶ AF hospitalisations have increased exponentially among Korean adults from 2006 to 2015, in association with an increase in comorbid chronic diseases. Mortality associated with AF hospitalisations decreased during the last decade, but hospitalisation costs have markedly increased.

#### How might this impact on clinical practice?

- ▶ Prevention of AF hospitalisations and streamlined integrated AF management should be pursued in a holistic manner to lessen the healthcare burden of AF.

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**Patient consent** Not required.

**Ethics approval** This study was approved by the Institutional Review Board of Yonsei University Health System (4-2016-0179).

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