

## Review Article



# Risk Factor Management for Atrial Fibrillation

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### Conflict of Interest

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## ABSTRACT

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in the general population. Many cardiovascular diseases and concomitant conditions increase the risk of the development of AF, recurrent AF, and AF-associated complications. Knowledge of these factors and their management is hence important for the optimal management of patients with AF. Recent studies have suggested that lowering the blood pressure threshold can improve the patients' outcome. Moreover, adverse events associated with a longer duration of hypertension can be prevented through strict blood pressure control. Pre-hypertension, impaired fasting glucose, abdominal obesity, weight fluctuation, and exposure to air pollution are related to the development of AF. Finally, female sex is not a risk factor of stroke, and the age threshold for stroke prevention should be lowered in Asian populations. The management of diseases related to AF should be provided continuously, whereas lifestyle factors should be monitored in an integrated manner.

**Keywords:** Atrial fibrillation; Risk factors; Hypertension; Obesity

## INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia in the general population.<sup>1-3)</sup> AF increases the risk of mortality and morbidity resulting from stroke, congestive heart failure, dementia, and impaired quality of life, which explains its enormous socioeconomic and healthcare implications.<sup>3,4)</sup> The prevalence of AF progressively increased by 2.10-fold from 0.73% in 2006 to 1.53% in 2015 in Korea. The prevalence of AF in the Korean population is expected to reach 5.81% (2,290,591 patients with AF) by 2060.<sup>3)</sup>

The incidence of AF has been shown to be positively correlated with age, male sex, diabetes, hypertension, congestive heart failure, valve disease, and myocardial infarction (MI).<sup>3,5,6)</sup> The management of risk factors or comorbidities, including lifestyle factors, is an important component of an integrated AF management.<sup>3,7)</sup> An integrated approach to AF management is the basis of consistent guideline-based treatment of AF, and such guideline adherence helps improve patient outcomes.

## HYPERTENSION

Hypertension is highly prevalent in the adult population with AF, especially among persons older than 60 years, and affects approximately 1 billion adults worldwide.<sup>1)2)8)</sup> According to the Seventh Report of the Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure guidelines, 62.2% of Korean patients with AF had hypertension.<sup>9)</sup> After applying the 2017 American College of Cardiology/American Heart Association guidelines for hypertension, 79.4% had hypertension, adding 17.2% cases as newly re-defined hypertension (130–139/80–89 mmHg). The Korean population with hypertension (hazard ratio [HR], 1.80; 95% confidence interval [CI], 1.62–1.99;  $p < 0.001$ ) had an increased risk of new-onset AF (**Table 1**).<sup>5)</sup> Hypertension and pre-hypertension are independently associated with AF.<sup>10)11)</sup> Indeed, AF can be considered a manifestation of target organ damage due to hypertension.

**Table 1.** Baseline characteristics and risk of atrial fibrillation

Characteristics	Number (n=171,324)	HR* (95% CI)	p value
<b>Sex</b>			
Female	67,142	1	
Male	104,182	1.65 (1.49–1.82)	<0.001
<b>Age (years)</b>			
40–49	100,269	1	
50–59	47,917	1.67 (1.49–1.87)	<0.001
60–69	19,215	3.60 (3.19–4.07)	<0.001
70–79	3,923	5.04 (4.18–6.06)	<0.001
<b>BMI (kg/m<sup>2</sup>)</b>			
<18.5	3,141	1.10 (0.87–1.39)	0.97
18.5–19.9	9,322	1.06 (0.84–1.35)	0.93
20.0–22.4	41,575	1	
22.5–24.9	59,984	1.03 (0.91–1.17)	0.60
≥25.0	57,302	1.24 (1.10–1.41)	<0.001
<b>Hypertension</b>			
No	113,929	1	
Yes	57,395	1.80 (1.62–1.99)	<0.001
<b>DM</b>			
No	156,609	1	
Yes	14,715	0.95 (0.83–1.10)	0.53
<b>Dyslipidemia</b>			
No	123,995	1	
Yes	47,329	1.12 (1.02–1.24)	0.01
<b>MI</b>			
No	169,470	1	
Yes	1,584	1.60 (1.17–2.18)	<0.003
<b>Excessive alcohol intake (≥5 times/week)</b>			
No	165,296	1	
Yes	6,028	0.99 (0.80–1.22)	0.99
<b>Excessive exercise (≥5 times/week)</b>			
No	160,315	1	
Yes	11,009	0.95 (0.80–1.12)	0.55
<b>Heavy smoking (≥30 pack-years)</b>			
No	153,404	1	
Yes	19,374	1.10 (0.96–1.26)	0.13

BMI = body mass index; CI = confidence interval; DM = diabetes mellitus; HR = hazard ratio; MI = myocardial infarction. \*HRs were adjusted for clinical variables including age, sex, initial BMI, hypertension, diabetes mellitus, dyslipidemia, excessive alcohol intake (drinking ≥5 times/week), excessive exercise (exercise ≥5 times/week), and heavy smoking (smoking ≥30 pack-years).

### What is the ideal blood pressure treatment threshold for atrial fibrillation?

The presence of hypertension in patients with AF has been identified to be an independent risk factor for stroke, increasing the risk by 1.8- to 2-fold compared with that in the absence of hypertension. Uncontrolled high blood pressure enhances the risk of stroke and bleeding events and may lead to recurrent AF.<sup>12)</sup> Therefore, good blood pressure control should form an integral part of the management of patients with AF, as a component of the holistic approach to AF management.<sup>7)</sup> However, the optimal blood pressure treatment threshold for patients with AF with hypertension has not been well identified.

Two recent studies suggested that blood pressure should be more strictly controlled in patients with AF.<sup>9,11)</sup> Patients with newly re-defined hypertension had a greater risk of major cardiovascular events (HR, 1.07; 95% CI, 1.05–1.10), ischemic stroke (HR, 1.12; 95% CI, 1.08–1.16), intracranial hemorrhage (HR, 1.12; 95% CI, 1.01–1.23), and admission for heart failure (HR, 1.06; 95% CI, 1.01–1.11) than non-hypertensive patients (<130/80 mmHg).<sup>9)</sup> In patients with AF under hypertension treatment, a U-shaped relationship for major cardiovascular events was evident, with 120–129/<80 mmHg as the optimal blood pressure treatment target (Figure 1). The benefit-to-harm ratio of optimal blood pressure control (120–129/<80 mmHg) relative to suboptimal blood pressure control (130–139/80–89 mmHg) was >1.00 for all subgroups stratified by the 10-year cardiovascular disease risk (<10%, 10–20%, and >20%), suggesting that patients with AF with treated hypertension would have greater benefit than harm from optimal blood pressure control regardless of the estimated cardiovascular disease risk (Figure 2).<sup>9)</sup>

### Effect of hypertension duration on ischemic stroke risk in atrial fibrillation

The increase of hypertension duration was associated with an increased risk of ischemic stroke. A 1-year increase of hypertension duration continuously increased the adjusted risk of ischemic stroke until 7 years and reached a plateau with an adjusted HR of 1.6. The risk of ischemic stroke linearly increased with the increase of hypertension duration in patients aged

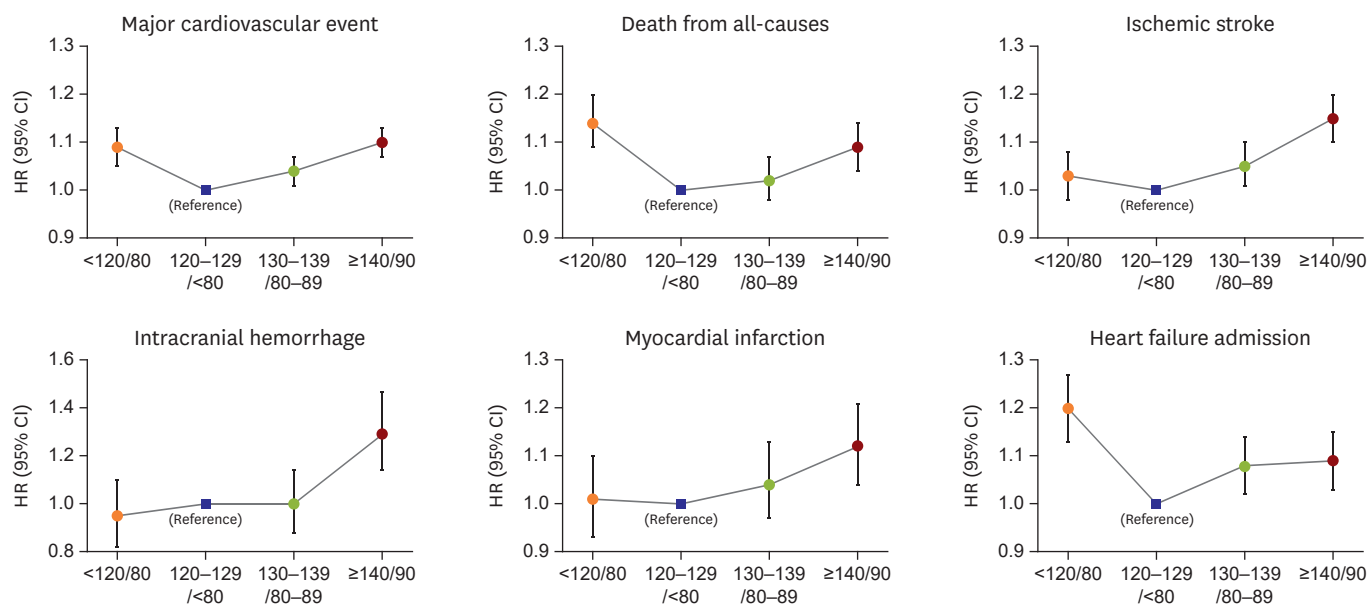
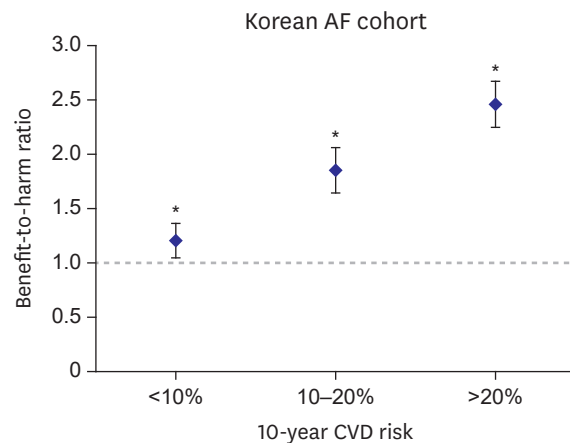


Figure 1. Risk of adverse outcomes according to blood pressure. CI = confidence interval; HR = hazard ratio.



**Figure 2.** Benefit-to-harm ratios of optimal (120–129/<80 mmHg) versus suboptimal blood pressure control (130–139/80–89 mmHg) according to 10-year predicted cardiovascular risk subgroups.

AF = atrial fibrillation; CVD = cardiovascular disease.

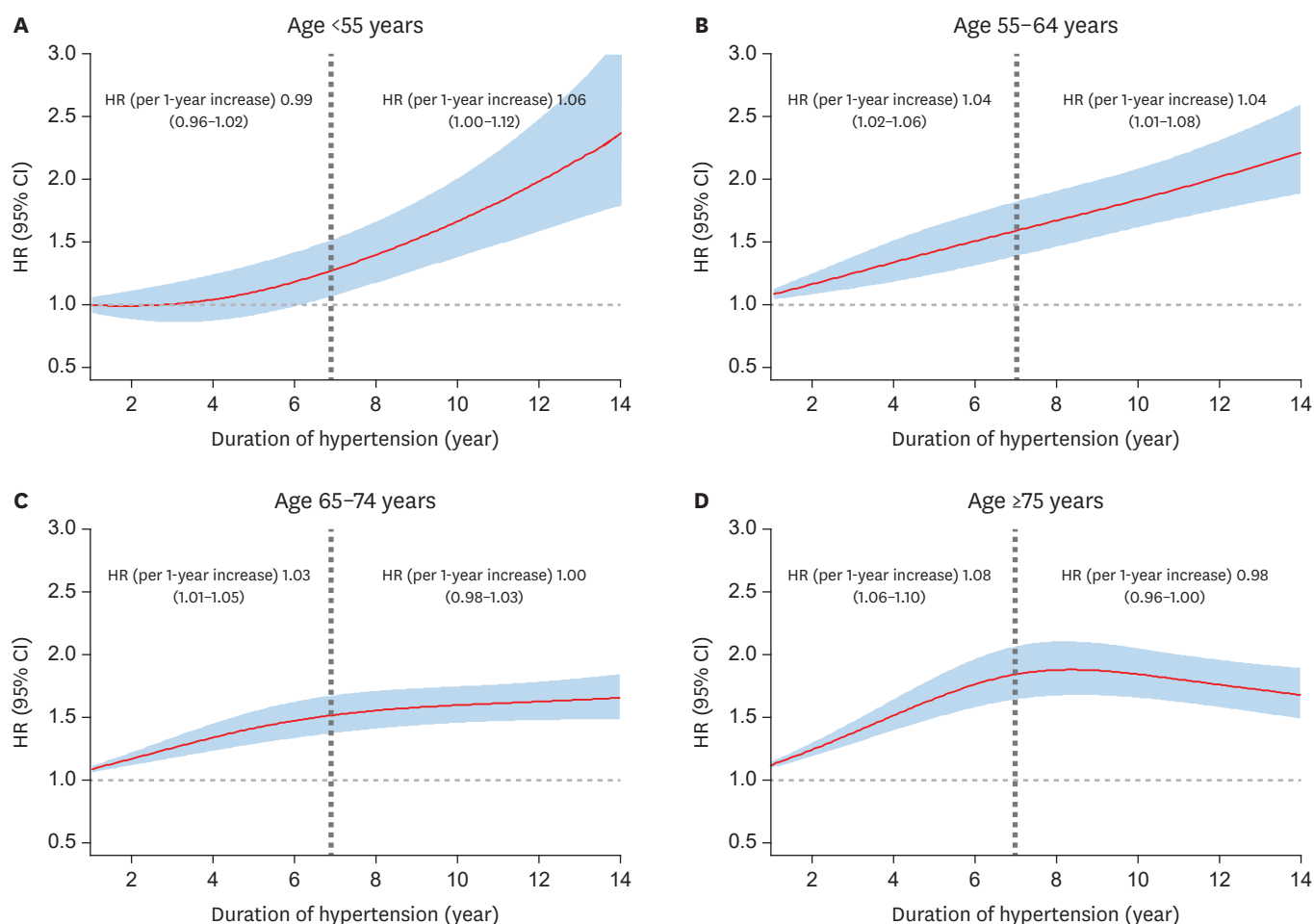
\*If a p value is less than 0.05, it is flagged with one star.

<65 years, whereas the risk reached a plateau in those aged  $\geq 65$  years (**Figure 3**). In all baseline and pre-AF average systolic blood pressure subgroups, a longer duration of hypertension before AF was associated with a higher ischemic stroke risk than a shorter duration of hypertension.<sup>13</sup> However, this long-term effect of hypertension duration can be attenuated by long-term strict systolic blood pressure control throughout the entire duration of hypertension. The effect of long-term hypertension was not observed in patients with strictly well-controlled pre-AF average systolic blood pressure of <120 mmHg (**Figure 4**).<sup>13</sup>

## DIABETES

Diabetes and AF frequently coexist because of their associations with other risk factors. Diabetes is a risk factor for stroke and other complications in AF.<sup>214</sup> In patients with AF, a longer duration of diabetes seems to confer a higher risk of thrombo-embolism, albeit without a greater risk of oral anticoagulant (OAC)-related bleeding.<sup>15</sup>

An impaired fasting glucose (IFG) is a prior stage to diabetes, which is a well-known risk factor for AF. Because IFG is common worldwide and is considered clinically normal, treatments for this condition are rare. Lee et al.<sup>11</sup> reported that in healthy Asian populations without comorbidities, IFG and pre-hypertension were important risk factors for AF. Subjects with IFG (HR, 1.16) had a higher risk of AF, and diastolic blood pressure (HR, 1.11) was a stronger indicator for the occurrence of AF than systolic blood pressure. As the risks IFG, pre-hypertension, and body mass index (BMI)  $\geq 25$  kg/m<sup>2</sup> increased, the risk of AF also increased. Even in a healthy population, subjects with all 3 risks had a much higher AF risk (HR, 1.50) than those without. IFG related to AF was more prominent in subjects with BMI <25 kg/m<sup>2</sup> (HR, 1.18) than in those with BMI  $\geq 25$  kg/m<sup>2</sup>, and subjects with both IFG and pre-hypertension had a greater AF risk (HR, 1.27) than those without (**Figure 5**).<sup>11</sup> The BMI-dependent effects of pre-hypertension and IFG also showed a similar pattern for AF-related stroke, HF, and mortality in a healthy population.<sup>11</sup>



**Figure 3.** Duration of hypertension and risk of ischemic stroke in patients with AF according to different age categories. (A) Age <55 years. (B) Age 55-64 years. (C) Age 65-74 years. (D) Age ≥75 years. Patients with hypertension duration under 1 year are used as reference. AF = atrial fibrillation; CI = confidence interval; HR = hazard ratio.

**A Pre-AF average SBP <120 mmHg**

HTN duration	No. of patients	No. of events	Rate (95% CI)	Adjusted HR (95% CI)
Non-hypertensive	13,067	368	3.17 (2.85-3.51)	Ref
HTN with duration <3 years	12,706	603	5.70 (5.26-6.18)	1.11 (0.97-1.28)
HTN with duration 3 to 5 years	3,516	221	7.76 (6.77-8.85)	1.03 (0.84-1.26)
HTN with duration ≥5 years	10,001	766	10.29 (9.58-11.05)	1.18 (1.00-1.39)

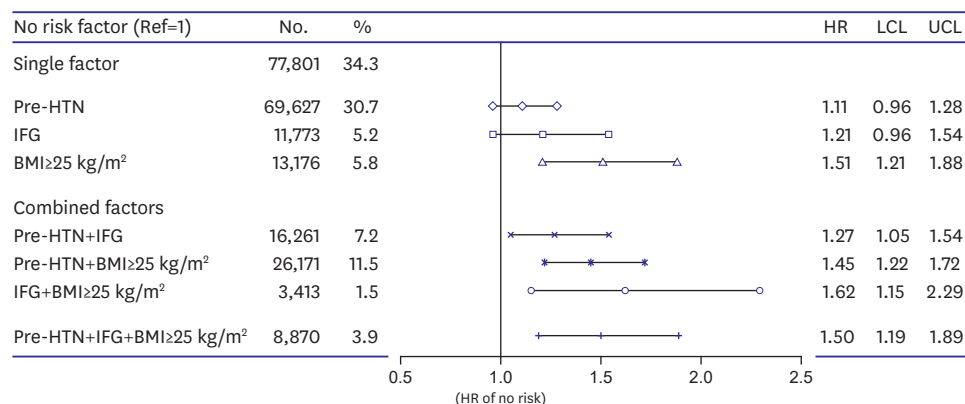
HR (95% CI) plot: 0.8, 1.0, 1.3, 2.0. p value for trends <0.01.

**B Pre-AF average SBP 120-139 mmHg**

HTN duration	No. of patients	No. of events	Rate (95% CI)	Adjusted HR (95% CI)
Non-hypertensive	13,067	368	3.17 (2.85-3.51)	Ref
HTN with duration <3 years	30,596	1,811	7.17 (6.84-7.50)	1.38 (1.22-1.55)
HTN with duration 3 to 5 years	12,940	989	9.66 (9.06-10.28)	1.53 (1.33-1.76)
HTN with duration ≥5 years	48,233	4,469	12.78 (12.40-13.16)	1.64 (1.46-1.86)

HR (95% CI) plot: 0.8, 1.0, 1.3, 2.0. p value for trends <0.01.

**Figure 4.** Risk of ischemic stroke according to the duration of hypertension in patients with AF. (A) Baseline SBP <120 mmHg. (B) Baseline SBP 120-139 mmHg. AF = atrial fibrillation; CI = confidence interval; HR = hazard ratio; HTN = hypertension; SBP = systolic blood pressure.



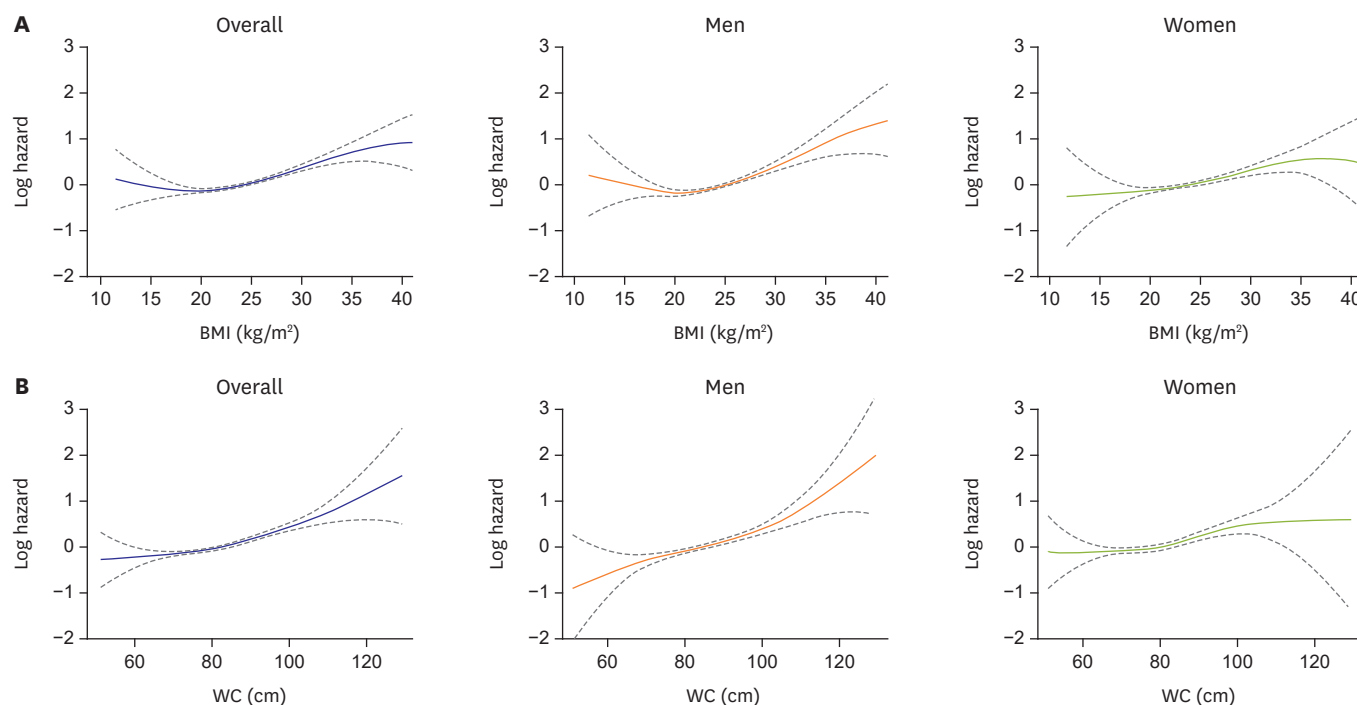
**Figure 5.** Incidence and risk of AF based on the combination of risk factors. AF = atrial fibrillation; BMI = body mass index; HR = hazard ratio; HTN = hypertension; LCL = lower confidence limit; IFG = impaired fasting glucose; UCL = upper confidence limit.

## OBESITY

Obesity is linked to AF and is considered a conventional risk factor for adverse cardiovascular events.<sup>16-19)</sup> Large epidemiological studies have observed strong associations between obesity and the incidence of AF and AF-related complications.<sup>16-19)</sup> Obesity is associated with an increased left atrial size and a decreased left ventricular diastolic function, which, in turn, leads to an increased left atrial pressure.<sup>18)</sup> In addition, dynamic changes in left atrial size and pressure likely affect both the atrial substrate and the triggers for AF.<sup>17)</sup> In the Korean population, a high BMI ( $\geq 25$  kg/m<sup>2</sup>; HR, 1.24; 95% CI, 1.10–1.41) was associated with a greater AF risk compared with a BMI of 20–22.5 kg/m<sup>2</sup> (Table 1).<sup>5)</sup>

Waist circumference and waist-to-hip circumference ratio are also associated with a higher risk of AF.<sup>20)</sup> Visceral adiposity is associated with incident cardiovascular disease after adjustment for clinical risk factors and generalized adiposity.<sup>21)</sup> The prevalence of overweight and obesity is much lower in Asian populations than in Western populations.<sup>1)19)</sup>

Baek et al.<sup>19)</sup> showed that abdominal obesity is an important, potentially modifiable risk factor for AF in non-obese Asians. After multivariable adjustment, each 1 standard deviation (3.7 kg/m<sup>2</sup> and 9.4 cm) increase in BMI or waist circumference was associated with an increase of 8% ( $p < 0.001$ ) and 12% ( $p < 0.001$ ), respectively. Spline curves between BMI and waist circumference, and the HR of new-onset AF are presented in Figure 6. A non-linear J-shaped association was found between continuous BMI variables and AF risk. AF risk positively increased with the increase of waist circumference. Interestingly, the overall J-shaped and linear patterns in the association seem to be mainly driven by the patterns for men. Abdominal obesity was associated with new-onset AF in the underweight ( $p < 0.001$ ), normal ( $p < 0.001$ ), and overweight ( $p < 0.001$ ) groups, but not in the obese group ( $p = 0.894$ ). These data suggest that interventions to decrease abdominal obesity may reduce the population burden of AF.<sup>19)</sup>

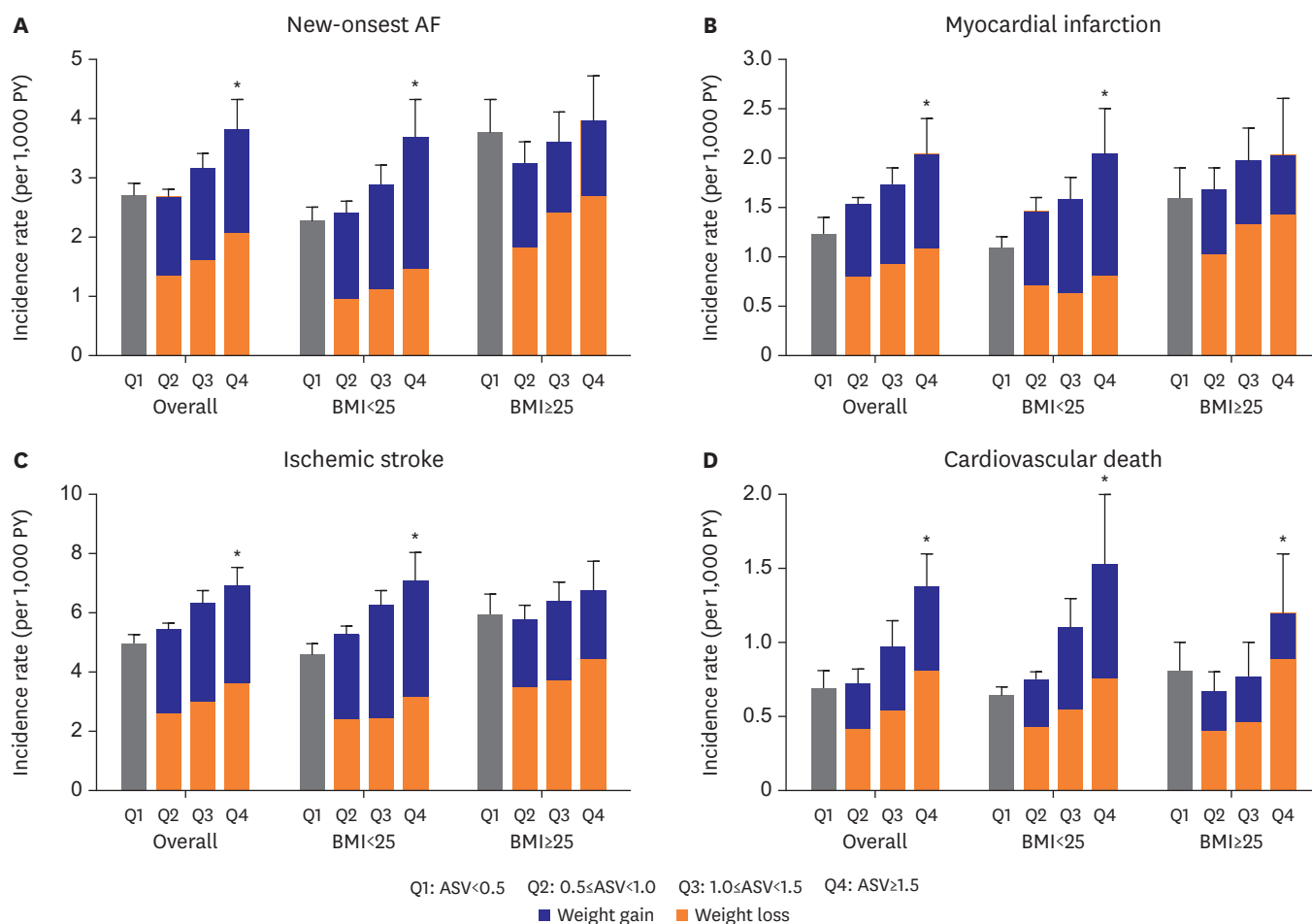


**Figure 6.** Spline curves between BMI and WC, and the HR of new-onset AF. Although there was a non-linear J-shaped association between continuous BMI variables and AF risk (A), the AF risk increased positively as WC increased (B). AF = atrial fibrillation; BMI = body mass index; HR = hazard ratio; WC = waist circumference.

## WEIGHT FLUCTUATION

The use of baseline weight or BMI measurements alone cannot capture the dynamic BMI changes that may influence the incidence of AF.<sup>17)</sup> Patients in the normal or underweight BMI category may experience undesired weight loss due to other medical problems, which may affect the incidence of AF in the general population.<sup>22)</sup> The Atherosclerosis Risk in Communities study found that a weight loss or gain of >5% of the initial body weight was positively associated with AF.<sup>22)</sup> In addition, the LEGACY study reported incremental increases in AF burden with weight fluctuations.<sup>23)</sup>

In the underweight and normal Asian population, BMI variability, especially weight gain, increased the risk of incident AF and MI but not the risk of stroke.<sup>5)</sup> **Figure 7** shows the incidence of new-onset AF, MI, ischemic stroke, and cardiovascular death per 1,000 person-years according to BMI variability. In initially underweight and normal individuals (initial BMI <25 kg/m<sup>2</sup>), the highest BMI variability (Q4) was associated with a significantly higher incidence of AF than a stable BMI variability (Q1). Furthermore, the highest BMI variability, especially weight gain, was related to higher systolic and diastolic blood pressure, fasting blood glucose level, and total cholesterol level than those with a more stable BMI variability. The Korean population with dyslipidemia (HR, 1.12; 95% CI, 1.02–1.24; p=0.01) had an increased risk of new-onset AF (**Table 1**).<sup>5)</sup> This finding suggests that avoiding weight fluctuation, especially weight gain, is important to prevent AF and to decrease the risk of MI in the underweight and normal Asian populations.<sup>5)</sup>



**Figure 7.** Incidence rate according to BMI variability. New-onset AF (A), MI (B), ischemic stroke (C), and cardiovascular death (D). Q1: ASV<0.5; Q2: 0.5≤ASV<1.0; Q3: 1.0≤ASV<1.5; Q4: ASV≥1.5.

AF = atrial fibrillation; ASV = average successive variability; BMI = body mass index; MI = myocardial infarction.

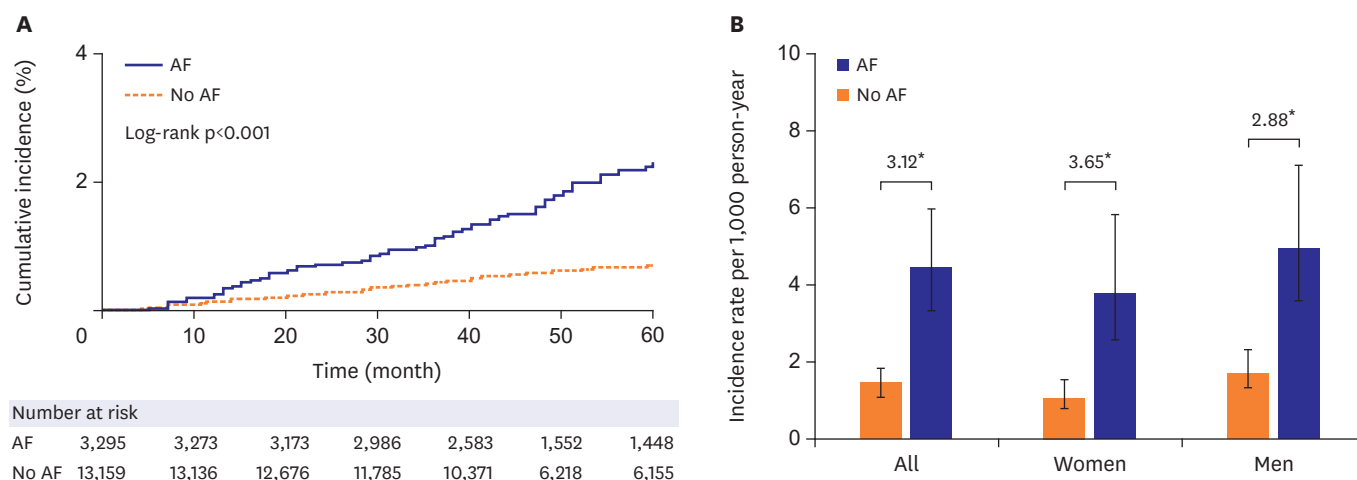
\*Asterisks indicate that there is a significant difference between overall Q1 and Q4 ( $p<0.05$ ).

## MYOCARDIAL INFARCTION

AF is a common arrhythmia of acute MI (AMI) that has been shown to be related to increased in-hospital and long-term mortality rates.<sup>24)</sup> Various pathologic mechanisms including elevated left ventricular end-diastolic pressure, increased atrial pressures, acute deterioration of left ventricular function, left atrial enlargement, atrial ischemia, or infarction can contribute to the development of AF in the AMI setting.<sup>24)</sup> Inflammatory markers, mainly C-reactive protein, have been reported to be related to future AF development.<sup>25)26)</sup> Accordingly, Hwang et al.<sup>27)</sup> reported that C-reactive protein could be strongly related to early AF in patients with AMI, especially in those with a less dilated left atrium.

In addition to being an established complicating factor for MI, recent studies have revealed that AF increased the risk of MI.<sup>28)</sup> Lee et al.<sup>29)</sup> reported that AF was associated with a 3-fold increased risk of MI (HR, 3.1; 95% CI, 2.22–4.37) in both men (HR, 2.91; 95% CI, 1.91–4.45) and women (HR, 3.52; 95% CI, 2.01–6.17) (**Figure 8**). The risk of AF-associated MI was higher in patients free of hypertension, diabetes, ischemic stroke, and dyslipidemia at baseline. The cumulative incidence of AF-associated MI was lower in patients under anticoagulant and





**Figure 8.** AF and MI. (A) Cumulative incidence of MI related to AF in the propensity scored-matched cohort. (B) Age-adjusted incidence rate and incidence rate ratios of MI.

AF = atrial fibrillation; MI = myocardial infarction.

\*If a p value is less than 0.05, it is flagged with one star.

statin treatments. This finding suggests that that AF complications beyond stroke should extend to total mortality to include MI.<sup>29)</sup>

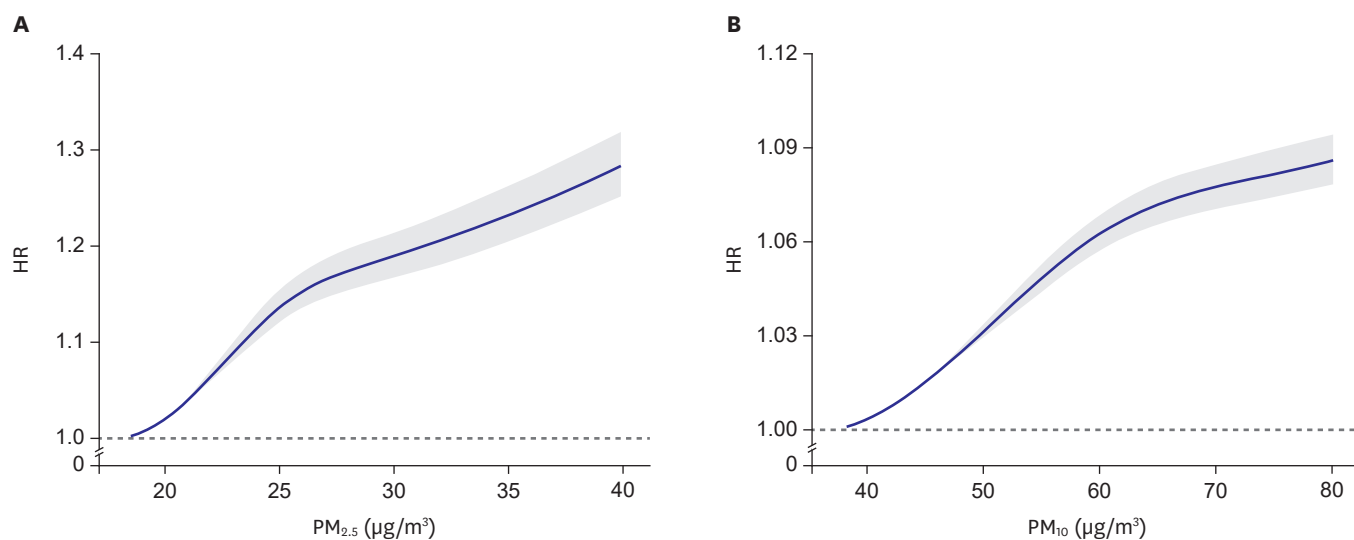
## AIR POLLUTION

Epidemiological studies have suggested that exposure to elevated levels of ambient particulate matter (PM)  $< 2.5 \mu\text{m}$  ( $\text{PM}_{2.5}$ ) or  $< 10 \mu\text{m}$  ( $\text{PM}_{10}$ ) in aerodynamic diameter is consistently associated with adverse cardiac events.<sup>30-33)</sup> Although many studies for these adverse cardiovascular outcomes have been performed, the correlations between short-term exposures to  $\text{PM}_{2.5}$  and incident AF were uncertain.<sup>34)</sup> However, these studies were performed in the European countries and United States, where the air pollution levels are much lower than in Asian countries. Therefore, the effect sizes could be low in those studies.

Kim et al.<sup>35)</sup> reported that long-term exposure to  $\text{PM}_{2.5}$  (HR 1.18 for  $10 \mu\text{g}/\text{m}^3$  increments,  $p < 0.001$ ) and  $\text{PM}_{10}$  (HR 1.03 for  $10 \mu\text{g}/\text{m}^3$  increments,  $p < 0.001$ ) is associated with an increased incidence of new-onset AF in the Asian general population (**Figure 9**). It is more profound in obese male subjects older than 60 years and in those with a history of hypertension or previous MI.<sup>35)</sup>

## PREDICTION OF STROKE RISK

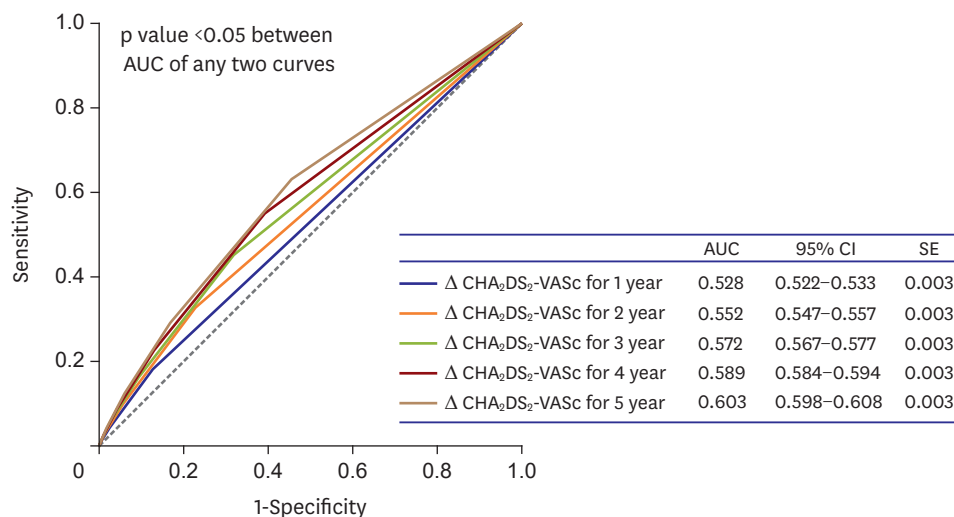
Stroke prevention is the principal management priority in patients with AF, given its association with a 5-fold increase in stroke risk.<sup>315)36)</sup> The  $\text{CHA}_2\text{DS}_2\text{-VASc}$  score is now used in most guidelines for stroke prevention in patients with AF.<sup>315)</sup> The adjusted incidence rates (per 100 person-years) of ischemic stroke were 3.79 in Korea, being 0.26 in low-risk patients ( $\text{CHA}_2\text{DS}_2\text{-VASc}$  score 0 [men] or 1 [female]), 1.18 in intermediate-risk patients ( $\text{CHA}_2\text{DS}_2\text{-VASc}$  score 1 [men]), and 5.30 in high-risk patients ( $\text{CHA}_2\text{DS}_2\text{-VASc} \geq 2$ ).<sup>2)</sup> The more recent focus of stroke prevention in patients with non-valvular AF has shifted away from predicting “high-risk” patients toward initially identifying patients at a “truly low-risk” of ischemic



**Figure 9.** Concentration-response relationships between incident AF and long-term exposures to air pollution. (A) PM<sub>2.5</sub>. (B) PM<sub>10</sub>. AF = atrial fibrillation; HR = hazard ratio; PM<sub>2.5</sub> = particulate matter <2.5 µm; PM<sub>10</sub> = particulate matter <10 µm.

stroke in whom OAC has no net clinical benefit.<sup>8)</sup> Korean patients who were categorized as “low-risk” by the CHA<sub>2</sub>DS<sub>2</sub>-VASC score (i.e., score of 0 point in men or 1 point in female) consistently had an event rate of <1%/year.<sup>2)</sup>

Stroke risk as assessed by the CHA<sub>2</sub>DS<sub>2</sub>-VASC score is dynamic and changes over time. The rates of ischemic stroke increased when patients accumulated risk factors and were reclassified into higher CHA<sub>2</sub>DS<sub>2</sub>-VASC score categories. Assessment of stroke risk is needed at every patient contact, as accumulation of risk factors with increasing CHA<sub>2</sub>DS<sub>2</sub>-VASC score translates to greater stroke risks over time (Figure 10).<sup>14)</sup>



**Figure 10.** ROC curves of delta CHA<sub>2</sub>DS<sub>2</sub>-VASC scores in predicting ischemic stroke. AUC = area under the curve; CI = confidence interval; ROC = receiver operating characteristic; SE = standard error.

### Female sex

In Koreans, the risk of incident AF was higher in men than in women (HR, 1.65; 95% CI, 1.49–1.82) (Table 1).<sup>5)</sup> On multivariable analysis, significant associations between CHA<sub>2</sub>DS<sub>2</sub>-VASc risk factors and ischemic stroke were observed; however, the significance of vascular disease or diabetes mellitus was attenuated after multivariable adjustment, and female sex (HR, 0.73; 95% CI, 0.64–0.84) had a lower risk of ischemic stroke than male sex (Table 2).<sup>2)37)</sup> Several cohort studies have shown that female sex is a risk factor for stroke, albeit dependent on age.<sup>38)39)</sup> Recently, female sex was suggested as a risk modifier for stroke in patients with AF.<sup>40)</sup> However, Asian cohort studies have indicated that female sex was not an independent risk factor for ischemic stroke, again suggesting some potential ethnic differences in the risk of stroke between Asian and non-Asian populations.<sup>3)</sup> Consistent with previous Asian studies, female sex was not a risk factor for stroke in a Korean cohort; instead, it was associated with a lower stroke risk of ischemic stroke than that of male sex.<sup>2)37)</sup>

### Age threshold

The risk of incident AF was increased with advancing age (Table 1).<sup>5)</sup> Older age is also the most important risk factor for ischemic stroke in AF among the 7 individual risk factors included in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score, particularly for low- to intermediate-risk patients.<sup>41-43)</sup> However, the appropriate age threshold (e.g., CHA<sub>2</sub>DS<sub>2</sub>-VASc score, 1 point for age 65–74 years, 2 points for age ≥75 years) is still controversial, as actual age thresholds may differ between different countries and ethnic groups. Moreover, the ability of a risk scoring scheme to identify patients with AF who are at a “truly low-risk” of stroke is even more important in Asians because the stroke risk among Asian populations may be much higher than that among Western populations.<sup>44-47)</sup>

Older age is the most important predictor of ischemic stroke in Korean and Taiwan patients with AF.<sup>43)48)</sup> Patients aged 65–74 years without other risk factors showed a significantly higher risk of stroke than those with 1 risk factor other than age. Lowering the current age threshold (age ≥65 years) in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score to age ≥55 years might be appropriate in Asian patients with AF.<sup>43)</sup>

**Table 2.** Associations between baseline factors and ischemic stroke in patients without anticoagulant treatment<sup>4)</sup>

Characteristics	Number with event	Ischemic stroke			
		Univariable		Multivariable	
		HR	95% CI	HR	95% CI
Age (years)					
<65	161/2,594	Ref.		Ref.	
65–74	320/1,700	3.44	2.84–4.16	2.11	1.73–2.58
>75	338/1,561	4.70	3.90–5.68	3.11	2.51–3.85
Female sex	385/2,835	0.94	0.82–1.07	0.75	0.63–0.86
Ischemic stroke/TIA	411/1,433	3.81	3.32–4.37	2.58	2.23–2.97
Atherosclerotic disease					
MI	139/764	1.49	1.24–1.79	0.97	0.81–1.17
Peripheral arterial disease	113/611	1.45	1.19–1.76	0.95	0.78–1.17
Vascular disease*	221/1,206	1.54	1.32–1.80	0.98	0.84–1.15
HF	380/1,869	2.16	1.88–2.48	1.23	1.06–1.42
Hypertension	750/4,422	4.04	3.16–5.17	1.85	1.43–2.40
Diabetes	216/1,168	1.53	1.31–1.79	1.13	0.96–1.32
ESRD	23/89	2.36	1.56–3.57	2.03	1.33–3.09
COPD	134/673	1.72	1.43–2.07	1.13	0.94–1.37
Aspirin use	505/2,636	1.93	1.68–2.23	1.30	1.12–1.50

CI = confidence interval; COPD = chronic obstructive pulmonary disease; ESRD = end-stage renal disease; HF = heart failure; HR = hazard ratio; MI = myocardial infarction; TIA = transient ischemic attack.

\*Vascular disease includes previous MI, peripheral arterial disease, or aortic plaque.

## CONCLUSION

The management of diseases (obesity, hypertension, heart failure, diabetes mellitus, sleep apnea) related to AF should be provided continuously, whereas lifestyle factors such as smoking and drinking should be monitored in an integrated manner.<sup>3)</sup> However, in lean Asian populations, strict blood pressure control and management of IFG should be emphasized. Avoiding abdominal obesity and weight fluctuation, as well as controlling the exposure to air pollution might reduce the development of AF. Finally, female sex is not a risk factor for stroke in Asian populations. Lowering the current age threshold (age  $\geq 65$  years) in the CHA<sub>2</sub>DS<sub>2</sub>-VASc score to age  $\geq 55$  years might be appropriate in Asian patients with AF. Knowledge of these factors and their management will enable optimal management and can improve the outcome of patients with AF.

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