Table 2. Multivariable-adjusted hazard ratios (95% confidence intervals) of incident atrial fibrillation according to the various blood pressure categories

SBP	Normal SBP	Systolic prehypertension	Systolic hypertension	Trend *P*
Person years	37,548	28,607	22,503	
Cases	53	83	117	
Incidence/1,000 person-year	1.41	2.90	5.20	
Age- and sex-adjusted	1	1.34 (0.94–1.91)	1.90 (1.34–2.69)	<0.001
Model 1 adjusted	1	1.31 (0.92–1.87)	1.80 (1.26–2.57)	<0.001
Model 2 adjusted	1	1.29 (0.91–1.85)	1.74 (1.22–2.49)	0.002
Model 2 and DBP adjusted	1	1.29 (0.88–1.90)	1.74 (1.12–2.69)	0.010
DBP	**Normal DBP**	**Diastolic prehypertension**	**Diastolic hypertension**	**Trend *P***
Person years	48,459	20,950	19,249	
Cases	98	63	92	
Incidence/1,000 person-year	2.02	3.01	4.78	
Age- and sex-adjusted	1	1.22 (0.88–1.68)	1.64 (1.23–2.20)	<0.001
Model 1 adjusted	1	1.18 (0.85–1.64)	1.51 (1.11–2.05)	0.008
Model 2 adjusted	1	1.16 (0.84–1.61)	1.47 (1.08–1.99)	0.014
Model 2 and SBP adjusted	1	1.03 (0.73–1.46)	1:14 (0.77–1.69)	0.513
Blood pressure category	**Normal BP**	**Prehypertension**	**Hypertension**	**Trend *P***
Person years	33,751	29,093	25,814	
Cases	50	81	122	
Incidence/1,000 person-year	1.48	2.78	4.73	
Age- and sex-adjusted	1	1.25 (0.87–1.80)	1.70 (1.20–2.40)	0.002
Model 1 adjusted	1	1.22 (0.84–1.75)	1.58 (1.11–2.26)	0.008
Model 2 adjusted	1	1.20 (0.83–1.73)	1.53 (1.07–2.19)	0.016
Pulse pressure	**<40 mm Hg**	**40–59 mm Hg**	**≥60 mm Hg**	**Trend *P***
Person years	27,639	44,938	16,053	
Cases	41	121	90	
Incidence/1,000 person-year	1.48	2.69	5.61	
Age- and sex-adjusted	1	1.25 (0.87–1.81)	1.78 (1.19–2.67)	0.003
Model 1 adjusted	1	1.29 (0.89–1.86)	1.78 (1.18–2.67)	0.004
Model 2 adjusted	1	1.29 (0.90–1.87)	1.75 (1.17–2.64)	0.005
Model 2 and SBP adjusted	1	1.14 (0.76–1.70)	1.28 (0.73–2.25)	0.399

Abbreviations: BP, blood pressure; DBP, diastolic blood pressure; SBP, systolic blood pressure.
Model 1: Adjusted by age, sex, body mass index, hypercholesterolemia and diabetes, current smoking and drinking status.
Model 2: Adjusted by Model 1 factors, cohort groups, chronic kidney disease, and histories of stroke, coronary heart disease, chronic heart failure, and premature contractions.

respectively (*P* for interaction between SBP and BMI = 0.04, Figure 1).

DISCUSSION

Our findings indicated that systolic and/or diastolic hypertension, higher pulse pressure, and overweight are risk factors for incident AF. Among these various components of BPs, only systolic hypertension was an independent predictor of incident AF after further adjustment. Overweight also remained a significant factor after further adjustment by both SBP and DBP. Interaction of SBP and BMI with risk of incident AF was observed. Hence, to our knowledge, this is the first positive association on the interaction of SBP and BMI with risk of incident AF in a general population.

In the Women's Health Study, high-normal SBP and DBP were associated with incident AF,[5] and after further

Table 3. Multivariable-adjusted hazard ratios (95% confidence intervals) of incident atrial fibrillation according to body mass index categories

Body mass index category	Underweight	Normal weight	Overweight	Trend *P*
Person years	6,631	64,641	17,385	
Cases	16	166	71	
Incidence/1,000 person-year	2.41	2.57	4.08	
Age- and sex-adjusted	0.98 (0.58–1.65)	1	1.43 (1.08–1.90)	0.023
Model 1 adjusted	1.02 (0.61–1.73)	1	1.35 (1.02–1.80)	0.075
Model 2 adjusted	1.02 (0.60–1.72)	1	1.35 (1.01–1.80)	0.081
Model 2 and systolic and diastolic BPs adjusted	1.05 (0.62–1.78)	1	1.34 (1.01–1.79)	0.096

Abbreviation: BP, blood pressure.
Model 1: Adjusted by age, sex, normal BP, prehypertension, hypertension, hypercholesterolemia and diabetes, current smoking and drinking status.
Model 2: See Table 2 footnote.

Table 4. Cox proportional hazards models for various types of blood pressure and body mass index as predictors of development of atrial fibrillation

Blood pressure component	Units	Age-adjusted HRs (95% CI)	Model 1-adjusted HRs (95% CI)	Model 2-adjusted HRs (95% CI)	Model 3-adjusted HRs (95% CI)
Systolic BP	per 20 mm Hg	1.25 (1.11–1.39)	1.22 (1.08–1.37)	1.22 (1.08–1.37)	1.24 (1.06–1.47)[a]
Diastolic BP	per 10 mm Hg	1.15 (1.04–1.28)	1.11 (1.00–1.24)	1.10 (0.99–1.24)	0.97 (0.84–1.12)[b]
Pulse pressure	per 10 mm Hg	1.13 (1.04–1.22)	1.13 (1.04–1.22)	1.12 (1.04–1.22)	1.03 (0.89–1.19)[b]
BMI	per 1 kg/m^2	1.27 (1.02–1.11)	1.06 (1.01–1.10)	1.05 (1.01–1.10)	1.05 (1.01–1.10)

Abbreviations: BMI, body mass index; BP, blood pressure; CIs, confidence intervals; HR, hazard ratio.
Model 1: age, sex, (body mass index or BP categories (normal BP, prehypertension, and hypertension)), smoking, drinking, hyperlipidemia, diabetes mellitus, and impaired fasting glucose.
Model 2: See Table 2 footnote.
Model 3: [a]Model 2 and diastolic BP adjustment; [b]Model 2 and systolic BP adjustment.

adjustment of both SBP and DBP, systolic hypertension was still associated with incident AF, but DBP was attenuated, which was similar to the current study. In a healthy Norwegian cohort study in men, the upper-normal SBP (128–138 mm Hg) and DBP (≥80 mm Hg) had 2- and 1.7-folds increased risk of incident AF, however, did not reveal an association between pulse pressure and incident AF.[6]

The Framingham Heart Study showed that a 20-mm Hg increase in pulse pressure was associated with a 1.26-increased risk of AF.[7] SBP was positively associated with AF, but when DBP was added in this model, only pulse pressure still consistent with AF. In our study, high pulse pressure (≥60 mm Hg) and diastolic hypertension were associated with incident AF. However, after further adjustment for SBP, the associations were attenuated. The difference in these results might be due in part to the body composition (mean BMI = 22.5 and 25.7 kg/m^2 in Japanese and U.S. populations, respectively). Increasing BMI is a strong risk factors for ventricular diastolic dysfunction[19] and increasing pulse pressure.[20] Previous Japanese prospective studies show that SBP is the highest important predictor of incident cardiovascular disease, among the various BP variables, but pulse pressure is less important.[21] Compared with normal BP group, controlled hypertension group does not increased risk of incident AF. However, uncontrolled hypertension is a risk factor for incident AF (HR = 1.53, 95% CI = 1.06~2.21, Supplemental Table III). Controlled hypertension is important to prevent AF. Arterial stiffness, left ventricular hypertrophy, and increased left atrial size are important mediators of the relationship between BP and incident AF.[22]

We found that overweight was linked to a 1.35-fold increased risk of incident AF in this population, and still associated with incident AF after adjustment for both SBP and DBP. In previous cohort studies, the increased risks of incident AF were observed in obese,[11,12,14] and in overweight.[14] The previous cohort studies showed around 4–5% increased risk of each 1-kg/m^2 increase in BMI,[11,12,14] which is compatible with the results of our study. Recently, a Japanese cohort study has shown that obesity was a 2.2-fold increased risk of incident AF,[23] but nonassociations with overweight and hypertension were observed. Due to the low frequency of our obese subjects (1.6%), we could not calculate the risk of AF associated with obesity.

Increasing body weight has an important association with left atrial enlargement,[24] because it causes left ventricular hypertrophy[25] and elevated blood flow volume,[26] and increases the vulnerability of the atrium that triggers

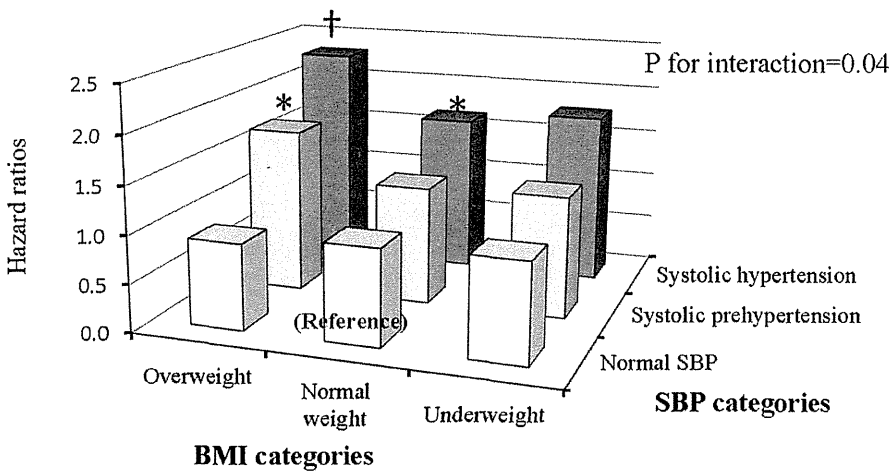

Figure 1. Multivariable-adjusted hazard ratios of incident atrial fibrillation according to combinations of systolic blood pressure (normal SBP and systolic prehypertension and hypertension) and body mass index (underweight, normal weight, and overweight) categories. Data are expressed as multivariable-adjusted hazard ratios adjusted for Model 2. *$P < 0.05$, compared with normal weight and normal SBP as references. †$P < 0.001$, compared with normal weight and normal SBP as a reference. Abbreviations: BMI, body mass index; SBP, systolic blood pressure.

AF.[27] The pathogenesis of increasing body weight is related to increasing BP,[28] and involves metabolic dysregulation,[29] the sympathetic nervous system,[30] renin-angiotensin-aldosterone system activity,[31] and renal sodium reabsorption.[32] In the present study, we observed an interaction between BMI and BP for incident AF. Weight gain has previously been associated with left ventricular hypertrophy[25] and an increased risk of hypertension.[28] Participants with both higher SBP and overweight may experience the mutual exacerbation of left ventricular hypertrophy and hypertension, and consequently, a synergistically increased risk of AF.

Our study has several limitations. The primary limitation is a dilution bias; this study was based on a baseline survey of BP and BMI, which may have led to a misclassification of these risk factors for AF. A previous study has suggested, however, that BP measurements taken on a single day are accurate.[33] Second, we did not perform Holter electrocardiography cyclopedically, even if we perform Holter electrocardiography, we may have missed participants with paroxysmal AF. Third, even with the moderate sample size and 12.8-year follow-up, the numbers of incident AF were limited. A study with a larger sample size is required to validate to the associations. Fourth, 1,408 participants without follow-up were excluded from our baseline data. Compared with the followed-up subjects, the subjects without follow-up had higher percentage of men and smoking and higher prevalence of hypertension, DM, and hyperlipidemia. However, the prevalence of AF at the baseline was not significant in the 2 groups (Supplemental Table IV). Fifth, we did not use follow-up data of BMI and BP, but baseline data. We can predict the future AF by healthy examinations as a baseline in this study. Near future, we will conduct the different study using updated measures to account for changes in BMI over time frame and to characterize the short-term impact that BMI could have on AF risk, and even how weight-loss and -gain influence on BP level. Finally, we did not have types of antihypertensive agents at the baseline.

In conclusion, hypertension and overweight are important risk factors for incident AF. Interaction of these 2 risk factors with risk of incident AF was observed. For AF prevention, it is important to not have these 2 risks. For early detection of AF, it is also important for a person with those 2 risk factors to take an electrocardiogram regularly.

SUPPLEMENTARY MATERIAL

Supplementary materials are available at *American Journal of Hypertension* (http://ajh.oxfordjournals.org).

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DISCLOSURE

The authors declared no conflict of interest.

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