Prevalence and Incidence of Atrial Fibrillation in the General Population Based on National Health Insurance Special Health Checkups — TAMA MED Project-AF —

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Background: Although National Health Insurance special health checkups have been useful for the diagnosis of metabolic syndrome, they are insufficient to identify atrial fibrillation (AF). In Tama City in Tokyo, 12-lead electrocardiogram has been included as an essential examination in special health checkups to diagnose AF since 2008.

Methods and Results: In subjects aged 40–74 years at entry, prevalence of AF was 0.8% (men, 1.7%; women, 0.2%) in 2008 and 1.4% (men, 2.9%; women, 0.4%) in 2015. Of 10,430 subjects without AF in 2008 (mean age, 64.9±7.1 years; men, 40.4%), AF developed in 133 between 2008 and 2015. The incidence rate of new-onset AF was 2.5/1,000 person-years during an observation period of 52,707 person-years. On multivariate Cox regression analysis in subjects without a history of cardiac disease, hypertension (HR, 1.58; 95% CI: 1.01–2.47, P=0.045) and body mass index (BMI; /1-kg/m² increase; HR, 1.07; 95% CI: 1.00–1.12, P=0.049) were significant risk factors for new-onset AF in addition to age and male sex.

Conclusions: Prevalence of AF increased between 2008 and 2015. Age, male sex, hypertension, and BMI were significant predictors for future incidence of AF in the general population without overt cardiac disease. Controlling hypertension and BMI may prevent new-onset AF in the general population.

Key Words: Atrial fibrillation; General population; Health checkup; Incidence; Prevalence

Atrial fibrillation (AF) is a common arrhythmia and a strong risk factor for cardiogenic thromboembolism.^{1,2} In order to reduce the incidence of cardiogenic stroke, both prevention of new-onset AF and early detection of undiagnosed AF prior to the initiation of appropriate anticoagulation therapy are important³ in the general healthy population. In Japan, special health checkups, so-called “Tokutei kenshin”, were introduced in 2008 to identify lifestyle-related diseases intended for individuals who have national health insurance. Although the special health checkups are useful for the diagnosis of metabolic syndrome,⁴ they are insufficient to diagnose AF because the recording of electrocardiograms (ECG) is not mandatory. Therefore, in Tama City in the suburbs of Tokyo, 12-lead ECG has been included as an essential examination in special health checkups to diagnose AF since 2008. Using the ECG findings of the special health

checkups, the aim of this study was to clarify the prevalence and incidence of AF in apparently healthy individuals in the general population and identify the risk factors for new-onset AF in subjects who did not have AF in 2008.

Methods

TAMA MED Project-AF

The TAMA MED Project-AF was conducted as a retrospective cohort study to clarify the prevalence and incidence of AF in the general population. The study protocol conformed to the Declaration of Helsinki and was approved by the institution ethics committee. A consecutive series of subjects who had national health insurance and underwent annual special health checkups at a clinic or hospital belonging to the TAMA CITY Medical Association were recruited. All participants were aged 40–74 years at the

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	2008	2015	P-value*
No. subjects	12,137	12,303	
Age (years)	65.2±7.6	67.0±7.3	<0.001
Sex, men	5,050 (41.6)	5,034 (40.9)	0.272
BMI (kg/m ²)	22.6±3.2	22.6±3.3	0.121
SBP (mmHg)	128.7±16.5	127.2±16.5	<0.001
DBP (mmHg)	76.2±10.4	74.5±10.4	<0.001
Current smoker	2,772 (22.8)	2,697 (22.2)	0.082
Past history	8,011 (66.0)	8,747 (72.1)	<0.001
Present illness	2,679 (22.1)	2,525 (20.8)	0.003
Comorbidities			
Cardiac disease†	578 (4.8)	749 (6.1)	<0.001
Hypertension	4,928 (40.6)	5,235 (42.6)	0.002
DM	1,441 (11.9)	1,603 (13.0)	0.006
Stroke/TIA	412 (3.4)	488 (4.0)	0.096
Metabolic syndrome	1,659 (13.7)	1,837 (14.9)	0.007
Blood examinations			
HDL-C (mg/dL)	63.7±16.7	64.5±16.6	<0.001
LDL-C (mg/dL)	126.7±30.1	124.6±30.4	<0.001
Triglycerides (mg/dL)	115.8±78.8	114.4±80.1	0.176
HbA1c (NGSP) (%)	5.6±0.7 [‡]	5.7±0.6	<0.001
AST (IU/L)	24.8±11.1	24.5±11.7	0.052
ALT (IU/L)	21.9±14.0	21.2±14.2	0.001
γ-GTP (IU/L)	37.4±48.6	35.2±50.2	<0.001
Urinalysis			
Urine sugar	279 (2.3)	280 (2.3)	0.876
Urine protein	646 (5.3)	517 (4.2)	<0.001
Medication			
For hypertension	3,602 (29.7)	4,206 (34.2)	<0.001
For diabetes mellitus	743 (6.1)	1,011 (8.2)	<0.001
For dyslipidemia	1,924 (15.9)	2,693 (21.9)	<0.001

Data given as n (%) or mean±SD. †Self-reported. ‡HbA1c (JDS)+0.4%. *Comparison between 2008 and 2015. γ-GTP, γ-glutamyl transpeptidase; ALT, alanine transaminase; AST, aspartate transaminase; BMI, body mass index; DBP, diastolic blood pressure; DM, diabetes mellitus; HbA1c, glycated hemoglobin; HDL-C, high-density lipoprotein cholesterol; JDS, Japan Diabetes Society; LDL-C, low-density lipoprotein cholesterol; NGSP, National Glycohemoglobin Standardization Program; SBP, systolic blood pressure; TIA, transient ischemic attack.

time of entry because the special health checkups are open for subjects aged ≥40 years, and individuals aged ≥75 years are not eligible for this insurance. Age at the end of the fiscal year was recorded in the Tama City database and was used for subsequent analyses. All participants completed the questionnaire, which included items to evaluate self-reported past history, such as cardiac disease, stroke, gastrointestinal disease, renal disease, malignancy, and so on; present illness (the presence of any subjective symptom at the time of special health checkups, including non-cardiac symptoms); habitual status, including current smoking; and medication use. The following measurements were obtained for all participants: body height and weight, body mass index (BMI), waist circumference, and systolic and diastolic blood pressure (SBP and DBP). According to an ordinance of the Ministry of Health, Labour and Welfare referred to as Article 157 in 2007, the following essentials were examined: fasting plasma glucose (FPG) or glycated hemoglobin (HbA1c), serum high-density lipoprotein cholesterol (HDL-C), serum low-density lipoprotein cholesterol (LDL-C), triglycerides, aspartate transaminase, alanine transaminase, γ-glutamyl transpep-

tidase (γ-GTP), and urine sugar and protein. Hypertension was defined as SBP ≥140 mmHg, DBP ≥90 mmHg, and/or receiving antihypertensive medication. Diabetes mellitus was defined as FPG ≥126 mg/dL, HbA1c ≥6.1% (Japan Diabetes Society) or ≥6.5% (National Glycohemoglobin Standardization Program), and/or receiving medical treatment containing oral hypoglycemic agents and/or insulin. In addition, a standard 12-lead ECG was recorded for all participants as a Tama City-specific mandatory optional examination. AF was diagnosed directly by physicians or based on automatic analysis of 12-lead ECG in each clinic or hospital, regardless of the electrocardiograph model and vendor. All annual health checkups in 2015 were used to clarify the most recent prevalence of AF. To calculate the incidence rate of new-onset AF, individuals who did not have AF in 2008 were enrolled for this analysis.

Statistical Analysis

Data are presented as mean±SD. The significance of differences in means was analyzed using Student's t-test. Frequencies of parameters were compared using the chi-squared test. Kaplan-Meier curves were generated to show

Table 2. No. Cases and Prevalence of AF in Tama City

Age (years) (at the end of the year)	Men			Women			Overall		
	No. subjects	No. with AF	Prevalence of AF (%)	No. subjects	No. with AF	Prevalence of AF (%)	No. subjects	No. with AF	Prevalence of AF (%)
2008									
40–44	173	0	0	195	0	0	368	0	0.0
45–49	173	0	0	190	0	0	363	0	0.0
50–54	167	1	0.6	272	0	0	439	1	0.2
55–59	305	1	0.3	623	1	0.2	928	2	0.2
60–64	745	13	1.7	1,492	1	0.1	2,237	14	0.6
65–69	1,653	33	2.0	2,217	4	0.2	3,870	37	1.0
70–74	1,661	30	1.8	1,927	10	0.5	3,588	40	1.1
75	173	7	4.0	171	0	0.0	344	7	2.0
Total	5,050	85	1.7	7,087	16	0.2	12,137	101	0.8
2015									
40–44	104	0	0	132	0	0	236	0	0
45–49	206	0	0	204	0	0	410	0	0
50–54	188	0	0	220	0	0	408	0	0
55–59	207	1	0.5	325	0	0	532	1	0.2
60–64	391	4	1.0	919	1	0.1	1,310	5	0.4
65–69	1,628	44	2.7	2,443	9	0.4	4,071	53	1.3
70–74	2,009	78	3.9	2,668	17	0.6	4,677	95	2.0
75	301	17	5.6	358	4	1.1	659	21	3.2
Total	5,034	144	2.9	7,269	31	0.4	12,303	175	1.4

AF, atrial fibrillation.

the cumulative incidence of AF from 2008 to 2015, and the time to events was compared between sex, age, BP, and BMI classes on log-rank test. A Cox proportional hazard model was used to investigate the influence of clinical factors on new-onset AF. Hazard ratios (HR) and 95% confidence intervals (CI) for the presence of categorical variables and for each 1-unit increase of continuous variables were calculated. Explanatory variables for multivariate analysis were adopted for significant variables in univariate analysis except for SBP, DBP, and medication for hypertension, to avoid multicollinearity with hypertension. HbA1c and medication for diabetes mellitus were also not included to avoid multicollinearity with diabetes mellitus. In addition, to detect significant risk factors except cardiac disease, multivariate analysis was conducted after exclusion of subjects with a history of cardiac disease. The prediction ability of risk factors was determined using area under the receiver operating characteristic (ROC) curve (AUC), and the optimal cut-offs for new-onset AF were determined as the values at maximum Youden index (=sensitivity+specificity–1) on the ROC curves. Two-tailed $P<0.05$ was considered statistically significant. All statistical analysis was performed using SPSS version 23.0 (IBM, Armonk, NY, USA).

Results

Prevalence of AF

Of 12,149 participants in 2008, 12 were excluded due to a deficit of system data. Characteristics for all subjects in 2008 and 2015 are shown in **Table 1**. The prevalence of hypertension, diabetes, metabolic syndrome, and medication for comorbidities was higher in 2015 than in 2008. The number of cases of AF and prevalence of AF in 12,137 participants at the time of initiation of the special health

checkups in 2008 and those most recently in 12,303 participants in 2015 are shown in **Table 2**, **Figure 1**. The overall prevalence rate of AF was 0.8% (men, 1.7%; women, 0.2%) in 2008 (**Table 2**) and 1.4% (men, 2.9%; women, 0.4%) in 2015 (**Table 2**). The prevalence of AF was higher in men than in women, and increased from 2008 to 2015, especially in men. In 2015, an increasing trend in the prevalence of AF with age class was clearly observed in both men and women (**Figure 1**). When age was divided into 10-year classes, the prevalence of AF in age classes 50–59, 60–69, and 70–79 years was 0.3%, 2.4%, and 4.1% in men and 0%, 0.3%, and 0.7% in women, respectively, in 2015 (**Supplementary Figure 1**).

Subjects Without AF in 2008: Baseline Characteristics

Of 12,137 participants, 101 who had AF at the time of entry and 1,606 who underwent special health checkups only once in 2008 were excluded. Consequently, a total of 10,430 subjects who did not have AF in 2008 and underwent annual checkups at least once between 2009 and 2015 were enrolled to calculate the incidence rate of new-onset AF. Baseline characteristics of subjects without AF in 2008 ($n=10,430$) are listed in **Supplementary Table 1**. Characteristics are also shown separately for participants who subsequently developed AF (onset-AF, $n=133$) and who did not (no-AF, $n=10,297$) until 2015. Age, BMI, SBP and DBP, γ -GTP; and the frequency of current smokers, any past history, cardiac disease, hypertension, diabetes mellitus, and metabolic syndrome in the onset-AF group were significantly higher than in the no-AF group, whereas LDL-C in the onset-AF group was significantly lower than in the no-AF group (**Supplementary Table 1**). Consequently, the frequency of receiving medical treatment for hypertension and diabetes mellitus in the onset-AF group were significantly higher than in the no-AF group (**Supplementary**

Figure 1. No. cases and prevalence of atrial fibrillation (AF) in Tama City in 2015. The subjects consisted of 12,303 individuals (5,034 men and 7,269 women) who underwent annual special health checkups in the TAMA CITY Medical Association in 2015. Age is given at year end.

Table 1). After exclusion of subjects with a history of cardiac disease, baseline characteristics of subjects without AF in 2008 (n=9,992) are shown in **Supplementary Table 2**.

Incidence of New-Onset AF

Of 10,430 subjects without AF in 2008 (mean age, 64.9 ± 7.1 years; men, 40.4%), AF developed in 133 (1.3%) between 2008 and 2015. The overall incidence rate of new-onset AF was 2.5/1,000 person-years during an observation period of 6.9 years (52,707 person-years; **Figure 2**). It was 4.5/1,000 person-years (20,468 person-years) in men and 1.3/1,000 person-years (32,239 person-years) in women, respectively. The cumulative rate of new-onset AF in men was significantly higher than that in women ($P < 0.001$, log-rank test; **Figure 3A**). There was a significant difference in the rate of new-onset AF by age class ($P < 0.001$, log-rank test; **Figure 3B**). After exclusion of 438 subjects with a history of cardiac disease (n=9,992), AF developed in 105 (1.1%) until 2015 and the incidence rate of new-onset AF was 2.1/1,000 person-years during an observation period of 7.0 years (50,810 person-years). The number of subjects who underwent the special health checkups completely every year was 4,723 (45.3% of all). Of these subjects, AF developed in 67 (1.4%) until 2015 and the incidence rate of new-onset AF was 2.0/1,000 person-years during an observation period of 7.0 years (32,869 person-years). It was not different from that in 10,430 subjects ($P = 0.146$, log-rank test).

Predictors for New-Onset AF

On univariate analysis, age, male sex, BMI, a history of cardiac disease, hypertension, diabetes mellitus, SBP, DBP, HbA1c, triglycerides, and γ -GTP were positively correlated with new-onset AF; meanwhile, LDL-C, current smoking, and receiving medication for hypertension and diabetes mellitus were negatively correlated with new-onset AF (**Table 3**). On multivariate analysis, only age (/1-year increase; HR, 1.07; 95% CI: 1.03–1.12, $P = 0.001$), male sex (HR, 2.76; 95% CI: 1.67–4.57, $P < 0.001$), and a history of cardiac disease (HR, 4.47; 95% CI: 2.73–7.32, $P < 0.001$) were

Figure 2. Kaplan-Meier curves for new-onset atrial fibrillation (AF) in Tama City between 2008 and 2015. In 10,430 subjects without AF in 2008 (mean age, 64.9 ± 7.1 years, men 40.4%), AF developed in 133 (1.3%) until 2015.

significant risk factors for new-onset AF (**Table 3**). Given that a history of cardiac disease, as obtained from the self-reported questionnaire in the special health checkups, contains various unknown cardiac diseases, further analysis was performed to clarify the predictors for new-onset AF in subjects without an obvious history of cardiac disease. In 9,992 subjects without a history of cardiac disease, hypertension (HR, 1.58; 95% CI: 1.01–2.47, $P = 0.045$) and BMI (/1-kg/m² increase, HR, 1.07; 95% CI: 1.00–1.12, $P = 0.049$) were significant risk factors for new-onset AF in addition to age and male sex (**Table 4**).

Table 3. Significant Indicators of New-Onset AF (Cox Proportional Hazard Model, n=10,430)				
Variables	Univariate†		Multivariate‡	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Cardiac disease	7.146 (4.707–10.849)	<0.001	4.467 (2.727–7.319)	<0.001
Hypertension	2.144 (1.520–3.023)	<0.001	1.435 (0.960–2.145)	0.078
DM	1.845 (1.156–2.871)	0.007	1.143 (0.686–1.905)	0.608
Age (/1-year increase)	1.100 (1.058–1.144)	<0.001	1.071 (1.027–1.117)	0.001
Sex (men)	3.546 (2.451–5.128)	<0.001	2.755 (1.667–4.566)	<0.001
BMI (/1-kg/m ² increase)	1.072 (1.037–1.109)	<0.001	1.046 (0.983–1.114)	0.154
SBP (/1-mmHg increase)	1.024 (1.015–1.033)	<0.001	–	–
DBP (/1-mmHg increase)	1.035 (1.019–1.051)	<0.001	–	–
HbA1c (/1% increase)	1.254 (1.030–1.528)	0.024	–	–
LDL-C (/1-mg/dL increase)	0.988 (0.982–0.993)	<0.001	0.995 (0.988–1.002)	0.131
Triglycerides (/1-mg/dL increase)	1.002 (1.000–1.003)	0.006	1.001 (0.999–1.002)	0.292
γ-GTP (/1-IU/L increase)	1.004 (1.002–1.005)	<0.001	1.002 (1.000–1.005)	0.092
Current smoking	0.680 (0.468–0.988)	0.043	1.051 (0.669–1.651)	0.829
Medication for hypertension	0.450 (0.320–0.634)	<0.001	–	–
Medication for DM	0.453 (0.265–0.775)	0.004	–	–

†Non-significant variables in univariate analysis are not shown. ‡SBP and DBP, HbA1c, and medications for hypertension and DM were not included in multivariate analysis to avoid multicollinearity. Abbreviations as in Table 1.

Influence of Hypertension, BP, and BMI on New-Onset AF
Given that hypertension and BMI were associated with an increase in the risk of new-onset AF in the multivariate Cox hazard model, additional Kaplan-Meier curves were generated to show the cumulative incidence of AF based on the presence of hypertension (Figure 4A), BMI class (Figure 4B), and the quartiles of SBP and DBP (Supplementary Figure 2). There were significant differences in the incidence of AF between the presence of hypertension, BMI classes, and BP quartiles based on log-rank test (Figure 4, Supplementary Figure 2). The prediction ability (AUC) of SBP and BMI for new-onset AF was 0.610 (95% CI: 0.562–0.658, $P < 0.001$) and 0.583 (95% CI: 0.533–0.633, $P = 0.001$), respectively. The cut-offs of SBP

and BMI, for which interventions are possible, were 129.5 mmHg (sensitivity, 66.9%; specificity, 51.6%) and 22.5 kg/m² (sensitivity, 63.2%; specificity, 51.7%), respectively.

Discussion

The major findings of the present study were as follows. First, the prevalence of AF increased between 2008 and 2015; and was 1.4% (men, 2.9%; women, 0.4%) in subjects aged 40–74 years at entry in the general population in 2015. Second, the incidence rate of new-onset AF was 2.5/1,000 person-years (4.5/1,000 person-years in men and 1.3/1,000 person-years in women). Third, age, male sex,

Table 4. Significant Indicators of New-Onset AF After Exclusion of Subjects With a History of Cardiac Disease (Cox Proportional Hazard Model, n=9,992)

Variables	Univariate [†]		Multivariate [‡]	
	HR (95% CI)	P-value	HR (95% CI)	P-value
Cardiac disease (excluded)	—		—	
Hypertension	2.288 (1.552–3.372)	<0.001	1.582 (1.011–2.474)	0.045
DM	1.900 (1.156–3.123)	0.011	1.263 (0.721–2.213)	0.414
Age (/1-year increase)	1.108 (1.059–1.159)	<0.001	1.093 (1.041–1.148)	<0.001
Sex (men)	3.534 (2.342–5.348)	<0.001	2.632 (1.513–4.587)	<0.001
BMI (/1-kg/m ² increase)	1.078 (1.041–1.116)	<0.001	1.072 (1.000–1.120)	0.049
SBP (/1-mmHg increase)	1.026 (1.016–1.036)	<0.001	—	
DBP (/1-mmHg increase)	1.037 (1.019–1.055)	<0.001	—	
HbA1c (/1% increase)	1.269 (1.023–1.575)	0.030	—	
LDL-C (/1-mg/dL increase)	0.990 (0.983–0.996)	0.003	0.887 (0.594–1.322)	0.555
Triglycerides (/1-mg/dL increase)	1.002 (1.001–1.003)	0.004	1.001 (0.999–1.002)	0.203
γ-GTP (/1-IU/L increase)	1.003 (1.001–1.005)	0.002	1.001 (0.998–1.005)	0.348
Medication for hypertension	0.489 (0.331–0.720)	<0.001	—	
Medication for DM	0.396 (0.221–0.707)	0.002	—	

[†]Non-significant variables in univariate analysis are not shown. [‡]SBP and DBP, HbA1c, and medication for hypertension and DM were not included in multivariate analysis to avoid multicollinearity. Abbreviations as in Table 1.

Figure 4. Kaplan-Meier curves for new-onset atrial fibrillation (AF) in Tama City between 2008 and 2015 according to (A) presence of hypertension (HT) and (B) body mass index class (kg/m²).

hypertension, and BMI were significant predictors for the future incidence of AF in the general population without overt cardiac disease.

Prevalence of AF

The prevalence of AF has been investigated in several previous studies in Western countries^{2,5–7} and in Japan.^{8–10} In the USA in 1991, the overall prevalence of AF was 0.89%; was 2.3% in adults aged >40 years; and was 5.9% in those aged >65 years, indicating that AF prevalence increased with age.² In England and Wales, the prevalence of AF in 1998 was 1.21% in men and 1.27% in women.⁵ In a recent systematic review of 184 population-based studies of AF from 1980 to 2010,⁷ the prevalence of AF in 2010 was

0.60% in men and 0.37% in women. It increased from 1990 and was consistently higher in men than in women and in elder individuals than in young individuals.⁷

In Japan, based on national surveys of cardiovascular diseases in 1980, 1990, and 2000, the estimated number of persons with AF rapidly increased.⁸ After 2000, a population-based study supported by the Japanese Circulation Society (JCS), of 630,138 participants aged ≥40 years,⁹ found that the overall prevalence of AF in Japan was 0.86% (men, 1.35%; women, 0.43%) in 2003. The prevalence of AF in men was consistently higher than that in women in all age groups.⁹ The age-specific prevalence of AF increased with age, especially at age ≥80 years.⁹ In another community-based study in Japan of 41,436 adult

residents aged ≥ 40 years in Kurashiki City in 2006, the overall prevalence of AF was 1.6%.¹⁰ In the present study, the increasing trend of the age-specific prevalence of AF was similar to that found in preceding studies.^{9,10} The latest overall prevalence of AF was 1.4% in the present study, which was higher than that in the JCS study,⁹ and slightly lower than that in the Kurashiki City study.¹⁰ Given that the subject background and generations were different between the present study and the previous studies, it would be difficult to compare the prevalence directly between the studies. In the present study, the prevalence of AF increased from 0.8% to 1.4%, especially in men from 1.7% to 2.9%, between 2008 and 2015. The reason for the increasing prevalence of AF from 2008 to 2015 may be explained by the increase in the frequency of comorbidities such as hypertension, diabetes, and metabolic syndrome (Table 1).

Incidence of New-Onset AF

The incidence of AF has been investigated in several epidemiological studies. In the Framingham study, the overall incidence of AF was 0.2% per year in men.¹¹ AF was identified in 26 men and in 16 women aged 70–79 years per 1,000 people during a follow-up period of 2 years; thus, the highest rate was in the 70s age range.¹¹ In the Cardiovascular Health Study, the incidence of AF increased with age, and the overall rate was 19.2/1,000 person-years.¹² In the report of a community-based study from Olmsted County, Minnesota, the age- and sex-adjusted incidence rates of AF per 1,000 person-years were 3.04 in 1980 and 3.68 in 2000.¹³ The incidence of AF increased with age and generation, and was higher in older adults than that in younger adults, similar to that in the Framingham study¹⁴ and the Cardiovascular Health Study.¹²

In Japan, similar to the reports from Western countries,^{11–14} the incidence of AF increased with age in both men and women.^{15–17} In an observational cohort study with 28,449 participants aged ≥ 20 years (mean, 59.2 years) based on annual health checkups in Niigata, the incidence of AF per 1,000 person-years was 4.1 in men and 1.3 in women.¹⁵ In another community-based study with 30,010 participants aged ≥ 40 years (median, 73 years) in Kurashiki, the incidence of AF per 1,000 person-years was 13.0 in men and 7.4 in women.¹⁶ The difference in the incidence of AF between these studies may be due to the difference in age of the populations. In a recent study in the Japanese general population aged 30–79 years, the Suita study, AF developed in 311 participants during the 95,180 person-years; thus, the incidence rate of AF was 3.3/1,000 person-years.¹⁷ In the present study, the incidence rate of AF was lower than that in the preceding cohort studies,^{15,17} even in subjects with a history of cardiac disease.

Risk Factors for New-Onset AF in the General Population

In the Framingham Heart Study, age, hypertension, diabetes mellitus, congestive heart failure, valvular disease, and myocardial infarction (only in men) were found to be significant risk factors for new-onset AF.¹⁴ In the Suita study in Japan, the risk factors for new-onset AF included age, systolic hypertension, overweight, excessive drinking, coronary artery disease, current smoking, arrhythmia other than AF, cardiac murmur, and non-HDL-C.¹⁷ These factors were scored from –5 to 9 points; consequently, the 10-year probability of new-onset AF with scores ≤ 2 , 10–11, or ≥ 16 was $\leq 1\%$, 9%, and 27%, respectively.¹⁷ Age and

hypertension were common risk factors in both studies.^{14,17} In the present study, although many variables were associated with new-onset AF on univariate analysis, only age, male sex, and a history of cardiac disease were independent risk factors for new-onset AF on multivariate analysis. These results did not conflict with those in previous reports.^{14,17} Additional analysis was performed in the participants without a history of cardiac disease to determine the pure predictors for new-onset AF in the healthy general population without overt cardiac disease. Hypertension and BMI were identified as independent risk factors for new-onset AF in addition to age and male sex in the general population without overt cardiac disease. This also did not conflict with previous reports.^{14,17}

Interventions are available for hypertension and BMI even in the general population via health-care promotion.¹⁸ Given that the cut-offs of SBP and BMI for new-onset AF were 129.5 mmHg and 22.5 kg/m² in the present study, SBP < 130 mmHg and standard body weight could be targets for the management of these risk factors to prevent new-onset AF in the healthy general population. In the Cardio-Sis study, in which non-diabetic patients with SBP ≥ 150 mmHg were randomly assigned to either target SBP groups < 140 mmHg (usual control) or < 130 mmHg (tight control), the incidence rate of new-onset AF in the tight control group was significantly lower than that in the usual control group (HR, 0.46; 95% CI: 0.22–0.98).¹⁹ In contrast, in a population-based case-control study, the incidence rate of new-onset AF in participants with SBP < 120 mmHg was significantly higher than that in those with SBP 120–129 mmHg (OR, 1.99; 95% CI: 1.10–3.62), indicating a J-curve.²⁰ In participants with SBP ≥ 120 mmHg, however, SBP elevation of 14 mmHg was associated with an increase in the risk of new-onset AF by 33%.²⁰ Therefore, BP control must be important to prevent new-onset AF, but it remains controversial whether lower target BP is better. Obesity is also recognized as a risk factor for new-onset AF.^{21,22} In a cohort of the Framingham study, a 4% increase in AF risk per 1-unit increase in BMI was observed in both men and women even after adjusting for several clinical confounding factors.²¹ In a recent report of the REVERSE-AF study to evaluate the impact of body weight and risk factor management on the progression of AF, $\geq 10\%$ weight loss resulted in 88% who reversed from persistent AF to paroxysmal or no AF.²³ Body weight control would also be an important strategy to prevent new-onset AF.

Study Limitations

The present study had several limitations. First, participants of special health checkups were limited by age and insurance. People who have social insurance and/or are aged < 40 or ≥ 75 years at entry were not eligible for these special health checkups. Therefore, the overall prevalence and incidence of AF must be underestimated. Second, the diagnostic accuracy of the automatic ECG analysis was not validated. Given that electrocardiographs varied in model and vendor, diagnostic algorithms were not standardized. In addition, because the ECG recording was acquired only once per year at the time of annual health checkups, paroxysmal AF was not always detected. These issues could also be causes for underestimation of the prevalence and incidence of AF. Third, the cardiac disease histories obtained via the self-reported questionnaires during the special health checkups were not validated. These limitations may be similar to those in other cohort studies

based on health checkups in the general population. In addition, the number of new-onset AF cases (n=133) was small even for a 7-year follow-up period, and information of alcohol intake was lacking in the present study.

Conclusions

Prevalence of AF increased between 2008 and 2015. Age, male sex, hypertension, and BMI were significant predictors for future incidence of AF in the general population without overt cardiac disease. Given that interventions are available for hypertension and BMI, appropriate control of these factors may be important to prevent new-onset AF in the general population.

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Disclosures

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Supplementary Files

Please find supplementary file(s);
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