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Original article

Influence of abdominal obesity and habitual behaviors on incident atrial fibrillation in Japanese

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ABSTRACT

Background: As atrial fibrillation (AF) increases with the aging of the population, it is urgently required to clarify modifiable factors to prevent AF. However, evidence regarding the independent influence of abdominal-obesity and habitual behaviors on incident AF is limited among Japanese.
Methods and Results: Those aged 40–79 years undergoing periodic health checkups during 2008–2014 were followed-up in 2015 ($n = 96,841$) and the independent risk of incident AF was estimated using multivariate Cox proportional hazards regression models after adjustment for potential covariates. Participants were classified into four groups according to the baseline body mass index (BMI: kg/m^2) (normal-BMI or overweight: $<$ or $\geq$25) and waist circumference (WC: cm) (normal-WC or abdominal-obesity: $<$ or $\geq$85 for male, $\geq$90 for female). Baseline habitual behaviors, smoking status, alcohol intake, and physical activity, were also included as modifiable factors. Among 65,984 eligible participants, 349 developed AF over mean follow-up of 5.5 ± 1.6 years. Increase of both BMI and WC significantly elevated the risk of AF. Compared to the normal-BMI and normal-WC group, the normal-BMI but abdominal-obesity and the overweight and abdominal-obesity groups in males and the overweight and abdominal-obesity group in females had significantly elevated risk of AF. Among modifiable behavioral factors including abdominal-obesity, alcohol intake ($\geq$40 g/day) and abdominal-obesity significantly elevated the risk of AF in males, and abdominal-obesity was the strongest risk factor in both sexes, but smoking and physical activity were not significant. However, an aggregation of these four behavioral factors increased the risk of AF more than 2.5 times in both sexes.
Conclusions: Abdominal-obesity could be a crucial risk factor in prediction of AF in Japanese, and an aggregation of four behavioral factors increased the risk of AF almost three times. To prevent incident AF, practicing healthy habitual behaviors is recommended.

Introduction

Atrial fibrillation (AF) is a quivering or an irregular arrhythmia and is one of the major causes of stroke and heart failure [1,2]. Estimated prevalence of AF has doubled in the last decade due to the global aging of the population [3]. The global burden of AF has greatly affected healthcare costs [4] and patients' quality of life [5], thus early detection of modifiable risk factors for AF prevention would be beneficial [6]. Although multiple risk factors (e.g. obesity [7,8], hypertension [9], diabetes [10], chronic kidney disease (CKD) [11]) have been suggested to be evident as increasing the risk of incident AF, obesity has become a major risk factor [12] because of the increased prevalence [13].

Although body mass index (BMI: kg/m^2) has been used as a measurement of obesity to estimate the risk of AF, a large number of studies has suggested that abdominal-obesity measured by waist circumference (WC) is more closely associated with the risk of obesity-related disorders such as hypertension, diabetes, and coronary heart disease [14,15], which are the risk factors of AF. However, it is unclear whether WC is more independently predictive than BMI of the risk of incident AF from already known risk factors of AF. On the other hand, habitual behaviors including

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smoking, excess alcohol intake, and vigorous physical activity have been suggested to increase the risk of incident AF [16]. All these behaviors are strongly correlated with WC; however, evidence regarding independent influence of WC on incident AF from habitual behaviors is unclear. Further, independent associations of smoking cessation [17], modest amounts of alcohol intake [18], and moderate intensity of physical activity [19] with incident AF remain unclear. To our knowledge, however, there is no study that examined the independent influence of WC and habitual behaviors on the risk of incident AF longitudinally in Japan.

The aims of this study were to clarify the independent influence of abdominal-obesity and habitual behaviors on incident AF in a large Japanese population longitudinally.

Methods

Study participants

This retrospective cohort study was based on the periodic complete medical checkups ("Ningen Dock") at Seirei Center for Health Promotion and Preventive Medicine in Hamamatsu City, Japan. A total of 96,841 participants aged 40–79 years, who underwent checkups from April 2008 to March 2014, were included, and the data of the first checkup was used as a baseline. For this study, those who had AF or atrial flutter at the baseline and past electrocardiograms (ECGs), clinical history of AF, and no subsequent checkup were excluded. Consequently, 69,593 participants who had received at least one checkup after the next year of the baseline from April 2009 to December 2015 remained. Further, those people who had any missing data regarding measures of body weight, height and/or WC ($n = 493$), critical values from specimens ($n = 130$) [20], or possible influential conditions on body weight, WC, and incident AF [e.g. chronic renal failure dialysis period (serum creatinine > 8 mg/dl or estimated glomerular filtration rate (eGFR) < 15 mL/min/1.73 m^2) ($n = 33$), artificial dialysis ($n = 25$), medical history of collagen-related diseases ($n = 539$), cancer ($n = 2562$), heart surgery ($n = 213$), and pacemaker implantation ($n = 54$)] at baseline were excluded.

Ethical considerations

Informed consent was obtained from all participants according to the guidelines of the Council for International Organizations of Medical Sciences at each checkup. They were informed that the health checkup results anonymizing personal information would be used as population data for epidemiological studies. The study was approved by the Ethics Review Committee of the University of Tokyo (Approval ID: 11105) and the Seirei Center (Approval ID: 27-10).

Biochemical measurements and potential confounding factors

The medical checkups were conducted following the standardized protocol of the Ministry of Health, Labour and Welfare [21] and Japan Society of Ningen Dock [22]. Body weight was measured with an electronic scale (TBF-210® Tanita, Tokyo, Japan) to the nearest 0.1 kg. Height was measured without shoes to the nearest 0.1 cm. BMI was calculated as weight (kg) divided by height (m) squared and categorized into normal-BMI or overweight ($<$ or $\geq$25 kg/m^2). WC (cm) was measured in a standing position at the umbilical level to the nearest 0.1 cm and classified into normal-WC or abdominal-obesity ($<$ or $\geq$85 cm for male and $<$ or $\geq$90 cm for female) [23]. After at least 1 min of seated rest, blood pressure (BP) was recorded as the lower of two consecutive measurements, which were recorded more than 2 min apart.

As potential confounding factors, the following at the baseline were categorized: age: 40–49, 50–59, 60–69 and 70–79 years; BP: systolic blood pressure ($<$ or $\geq$130 mmHg) and/or diastolic blood pressure ($<$ or $\geq$85 mmHg) and/or use of antihypertensive medication; blood lipids: triglyceride ($<$ or $\geq$150 mg/dl) and/or high-density lipoprotein cholesterol ($<$ or $\geq$40 mg/dl) and/or low-density lipoprotein cholesterol ($<$ or $\geq$140 mg/dl) and/or use of antidyslipidemia medication; fasting glucose: fasting plasma glucose ($<$ or $\geq$110 mg/dl) and/or use of hypoglycemic medication; and renal function: eGFR ($<$ or $\geq$60 mL/min/1.73 m^2) calculated using the abbreviated Modification of Diet in Renal Disease equation [24]. Information on the history of heart disease (including coronary heart disease, chronic heart failure, myocardial disease, and valvar disease), stroke (including cerebral infarction, intracerebral hemorrhage, and subarachnoid hemorrhage), current medications (for hypertension, diabetes, and dyslipidemia), and habitual behaviors was collected using standardized self-reported questionnaires and confirmed by physicians and/or nurses one by one.

Definition of incident AF and the endpoint of follow-up

Diagnoses of AF until December 31, 2015 were identified both from 12-lead ECGs performed and self-report when the participants received checkups. All ECGs performed were analyzed and confirmed by experienced cardiologists after being analyzed by the software (FCP-7431® Fukuda Denshi, Tokyo, Japan), which is characterized by a high sensitivity (95.1%) and specificity (100%) in coding AF [25]. In case of disagreement between the automated analysis by the ECG and an experienced cardiologist, we selected the diagnosis by the cardiologist. AF was defined as the absence of P waves before each QRS complex, irregular atrial electrical activity with fibrillatory waves varying in size, shape, and timing, and completely irregular RR intervals. The date of incident AF was defined as whichever came earlier of the first presentation of AF/atrial flutter on an ECG or the self-reported information on physician-diagnosed AF during the follow-up period.

The endpoint of the follow-up period for each participant was defined based on one of the following options that occurred first: (i) the year of the first AF event confirmed by ECG or interview at the checkups, (ii) year of the last health checkup, or (iii) December 2015 (censored).

Definition of abdominal-obesity and habitual behaviors

Four modifiable habitual behaviors were defined as follows: abdominal-obesity: normal-WC or abdominal-obesity. Smoking status: never or smoking (former and current). Alcohol intake: modest or excess alcohol intake ($<$ or $\geq$40 g of pure alcohol/day for male and $<$ or $\geq$20 g/day for female) [26]. Physical activity: inactive or active ($<$ or $\geq$1 hour of walking or equivalent intensity of physical activity/day).

Statistical analysis

The baseline characteristics between those who developed AF or not were compared using the unpaired *t*-test for continuous variables and the chi-square test for categorical variables. Cox proportional hazards regression models were used to estimate the relative risk of AF, and hazard ratios (HR) and 95% confidence intervals (CI) were calculated after adjustment for potential confounding factors of age, BP, blood lipids, fasting glucose, smoking status, alcohol intake, physical activity, renal function, and history of cardiac disease and stroke. First, the HRs of incident AF by 1 SD increase of WC and BMI were estimated, respectively. Secondly, to examine the interplay of WC and BMI, the participants

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