Body Size and Atrial Fibrillation in Japanese Outpatients

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Background: Although recent studies have suggested that height and body mass index (BMI) independently affect the prevalence of atrial fibrillation (AF), their combined effects have not been fully examined in Japanese patients.

Methods and Results: Patients without organic cardiac diseases, hypertension and diabetes mellitus were screened from a prospective, single hospital-based cohort of the Shinken Database 2004–2007 (n=4,719). Both height and BMI significantly increased the crude rate of AF prevalence and the effects were significant even after adjustment by age, sex and left atrial dimension. The relative risks (RRs) for AF in the height and BMI categories were 2.07 (95% confidence interval [CI] 1.70–2.52) and 1.78 (95%CI 1.46–2.17), respectively, in the highest tertile compared with the lowest tertile. The RRs in the highest combined tertile was high to 2.98 (95%CI 2.07–4.28) compared with the lowest combined tertile, an unignorable figure for AF prevalence in the future.

Conclusions: Height and BMI synergistically affected the prevalence of AF in Japanese patients. With respect to the recent increase in body size of the Japanese population, the present study predicts that there will be more occurrences of AF than previously predicted. (Circ J 2010; 74: 66–70)

Key Words: Atrial fibrillation; Epidemiology; Risk factors

Atrial fibrillation (AF) is the most common arrhythmia in developing countries, which has almost doubled each decade. Together with appropriate management of arrhythmias that is closely associated with an increase in total and cardiovascular mortality, as well as cardiovascular morbidity, including stroke and heart failure, primary AF prevention is of great interest and requires appropriate identification of people at high risk for AF.

Recently, obesity, as represented by an increase in body mass index (BMI), has been implicated as a risk factor for AF. Moreover, in a large-scale cross-sectional study of impaired left ventricular function, stature measured by height was also identified as a strong risk factor for AF, and it was very recently expanded to a healthy population.

In Japan, with the change in dietary habits, there has been a rapid increase in the prevalence of metabolic disorders. Moreover, a temporal increase in height has also been observed in the Japanese population. Although these changes might lead to an increase in the prevalence of AF, based on reports from Western countries, the effect of body size on the occurrence of AF is still unknown in the Japanese population.

In the present study, we analyzed the relationships between height, BMI, and the prevalence of AF, using data from the Shinken Database 2004–2007, a single hospital-based cohort in an urban city in Japan.

Methods

Study Patients

The Shinken Database comprises all the new patients visiting the Cardiovascular Institute Hospital ("Shin-ken", in Japanese), excluding patients with active cancer and foreign travelers. The principal aim of the hospital-based database is to monitor the prevalence and prognosis of cardiovascular diseases in Japan. The registry of the data began in April 2004 and the data are accumulated annually.

The data used in the present study were derived from the database between April 2004 and March 2008, which was specifically named as the Shinken Database 2004–2007 (n=8,917). To eliminate the effects of other comorbidities, we excluded patients with coexisting organic cardiac diseases, hypertension and diabetes mellitus, which left 5,795 patients. Of these, measurements of body size (including height and...
Body Size and Prevalence of AF

Weight and echocardiography data were available for 4,719 patients, who became the study patients of the present study.

Data Collection
For each patient, after obtaining an ECG and chest X-ray, cardiovascular status was evaluated using echocardiography, an exercise test, 24-h Holter recording and blood laboratory data, whenever appropriate, according to the attending physician’s decision within 3 months after the initial visit. In the database, the following information at the initial visit was collected: patient’s data (sex, age, height and weight), coexisting cardiac diseases (congestive heart failure, valvular diseases, myocardial infarction, angina pectoris, hypertrophic cardiomyopathy and dilated cardiomyopathy) and other coexisting diseases (hypertension, diabetes mellitus and history of disabling cerebral infarction, transient ischemic attack and intracranial bleeding).

Definition of AF
In the present study, AF was diagnosed by ECG recordings, including 12-lead surface ECGs and 24-h Holter recordings within 3 months after the initial visit. It was also diagnosed by a medical history of AF, which was reported by physicians previously consulted.

Because the definition of the clinical type of AF is rather complex and could be altered during the follow-up, AF was simply categorized into 2 clinical types (paroxysmal or persistent) according to its duration, which was reported by the attending physicians from the available clinical data and history.

Statistical Analysis
All analyses were performed using SPSS (SPSS Inc, Chicago, IL, USA) for Windows (Microsoft Corp, Redmond, WA, USA), version 14.0 software. Statistical significance was set at P<0.05.

For the patient characteristics, data (except percentages) are presented as mean±SD. The prevalence of AF was determined in each stratified category of height and BMI tertile. The effects of each parameter on the prevalence of AF were evaluated by the relative risks (RRs), with categorical data adjusted using the multivariate model with Poison regression analysis. The multivariate model included height, BMI (calculated as weight in kilograms divided by height in meters squared), age, sex and left atrial dimension (LAD). Tests for trend were performed for the height and BMI categories in both the whole population and each body index category.

Borderlines of Tertile
In the population of the present study, the tertiles for height (cm), BMI (kg/m²) and LAD (mm) were determined as follows: (1) height; <158.7 (n=1,577), 158.7–167.9 (n=1,579), 167.9< (n=1,563), (2) BMI; <21.34 (n=1,572), 21.34–24.17 (n=1,574), 24.17< (n=1,573) and (3) LAD; <31 (n=1,540), 31–35 (n=1,582), 35< (n=1,597).

Ethical Issues
The Ethical Committee in the Cardiovascular Institute granted permission for this study and all patients gave written informed consent.

Results
Characteristics of the Study Patients
The characteristics of the study patients are shown in Table 1. The population (n=4,719; age 53.8±15.3 years, males 2,576 (54.6%)) included 577 patients with AF (12.2%, paroxysmal 369, persistent 208). The average height, BMI and LAD were 163.2±9.4 cm, 23.0±3.5 kg/m² and 34.0±5.9 mm, respectively.

Effect of Height and BMI on the Prevalence of AF
Figure shows the prevalence of AF in the categories of height and BMI, thus demonstrating clear effects of these body indices. In the same BMI tertile group, a taller height increased the prevalence of AF. Likewise, in the same height tertile, a larger BMI increased the prevalence of AF.

The synergistic effects of height and BMI on AF remained after adjustment for age, sex and LAD (Table 2). For height, the middle and high tertiles significantly increased the overall
Table 2. Adjusted* RR of Height and BMI for AF, Shinken Database 2004–2007

<table>
<thead>
<tr>
<th>BMI</th>
<th>Height</th>
<th>P-trend</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Low (95%CI)</td>
<td>Middle (95%CI)</td>
<td>High (95%CI)</td>
</tr>
<tr>
<td>Low</td>
<td>1.00 (reference)</td>
<td>1.13 (0.73–1.76)</td>
<td>1.72 (1.16–2.57)</td>
</tr>
<tr>
<td>Middle</td>
<td>1.38 (0.91–2.10)</td>
<td>1.51 (1.00–2.28)</td>
<td>2.70 (1.87–3.91)</td>
</tr>
<tr>
<td>High</td>
<td>1.58 (1.05–2.37)</td>
<td>2.34 (1.60–3.41)</td>
<td>2.98 (2.07–4.28)</td>
</tr>
<tr>
<td>P-trend</td>
<td>0.14</td>
<td>0.044</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>1.00 (reference)</td>
<td>1.37 (1.11–1.71)</td>
<td>2.07 (1.70–2.52)</td>
</tr>
</tbody>
</table>

CI, confidence interval; RR, relative risk. Other abbreviations see in Table 1.

*Adjusted by age, sex and left atrial dimension.

prevalence of AF compared with the low tertile (RR [95% confidence interval (CI)], 1.37 [1.11–1.71] and 2.07 [1.70–2.52], respectively; P<0.001) and this height-related increase also remained significant in every BMI category (P<0.001 in the middle and high BMI tertile and P=0.004 in the low BMI tertile). For BMI, the middle and high tertiles significantly increased the overall prevalence of AF (RR [95%CI], 1.45 [1.18–1.79] and 1.78 [1.46–2.17], respectively; P<0.001) and this BMI-related increase also remained significant in every height category (P<0.001 in the middle and high height tertiles and P=0.044 in the low height tertile). These RR for the prevalence of AF synergistically increased with the increment in the height and BMI tertiles, which reached 2.98 [95%CI 2.07–4.28] in the highest combined tertile group compared with that in the lowest combined tertile group.

Discussion

Major Findings
The present study clearly showed strong effects of a large body size on the prevalence of AF in Japanese outpatients without coexisting morbidity, including organic cardiac diseases, hypertension and diabetes mellitus. In addition, their synergistic effects remained significant after adjustment by age, sex and LAD. These simple observations have not been reported previously in Japan.

Effect of Body Size on the Prevalence of AF
Among the various risk factors for AF, body stature is likely to be unnoticed in daily routine clinical practice. Recently, with the increased threat of metabolic syndrome as a dangerous risk factor for cardiovascular disease,31 the significant effect of obesity on the incidence and prevalence of AF has been indicated in several population-based studies32–34 and meta-analyses.35 Furthermore, the effects of obesity-associated comorbidities, including diabetes mellitus, hypertension and ischemic heart disease, have been indicated as possible underlying mechanisms. However, the effect of a large body size itself (BMI and/or height) on AF was ignored until recently.

Several recent reports from Western countries have demonstrated that a large body size has an epidemiologically strong impact on AF, predicting an increase in AF.36–38 Although body size is very different between those countries and Japan, the present study of Japanese outpatients also clearly showed a strong effect of body size on the prevalence of AF. Actually, patients in the tallest height or largest BMI tertile groups had ~2-fold greater risk for the prevalence of AF compared with those in the shortest height or smallest BMI groups. Moreover, patients in both the tallest height and largest BMI group had ~3-fold greater risk compared with those in both the shortest height and smallest BMI groups. This is the first study to quantitatively demonstrate the combined effects of height and BMI in Japanese patients.

Relationship Between Body Size and LAD
The strong relationship between body size and AF can be easily explained by the basic relationship between LAD and AF development,24 which could be supported by the multiple wavelet theory explaining that AF requires a critical LA surface area,25 because a large body size may predict an increase in the LA volume. Actually, previous studies have reported significant relationships between body size and LAD.26–30 As for obesity, left ventricular hypertrophy,31,32 increased total blood volume,33 clusters of metabolic syndrome34 and obstructive sleep apnea5,35 have been proposed as plausible mechanisms for an increase in LA volume. In contrast, for height the mechanism of its strong relationship to LAD28–30 could be explained by the association with the thoracic size,36 which would physically affect the primary size of the LA.

Despite the close relationship between body size and LAD, some reports suggest that body size and LAD independently affect AF,12 which is similar to the results of the present study. Although the mechanism is still unclear, it might be explained by the hypothesis that body size affects a different axis of the LA other than the anteroposterior one. In fact, using computed tomography, Guthaner et al37 reported that the maximum transverse diameter of the LA was sometimes in the normal range, even in patients with severe mitral valve diseases, different from the maximum anteroposterior LAD. In this regard, the transverse and anteroposterior diameters of the LA could be regulated differently. The echocardiographic LAD represents only the anteroposterior diameter and thereby misses the transverse and longitudinal information. Therefore, if the hypothesis is true, body size and the echocardiographic anteroposterior LAD would regulate the real size of the LA differently, which consequently leads to the synergistic effects on the development of AF. Of course, it is unclear whether height and BMI are closely associated with the transverse or longitudinal axis of the LA, which requires further study.

Effect of Increasing Body Size on AF in Clinical Practice
AF incidence has increased over time,38–40 and it is expected to increase explosively in the future.1 Although the aging of society is a reasonable cause, AF is known to increase in similar age demographics according to time,38–40 and the reasons have been unknown for a long time. In a report from the Framingham study,38 the prevalence of AF in male/female
patients aged 65–74 years increased from 2.9/2.9% (1968–1970) to 7.8/4.4% (1987–1989); moreover, in those aged 75–84 years it increased from 3.9/2.5% (1968–1970) to 11.7/5.2% (1987–1989). Similarly, in Japan, AF has increased over time, and is also expected to increase explosively in the future. Osawa et al. and Inoue et al. separately estimated that the number of people with AF was approximately 700,000, and it is expected that will increase to more than 1,000,000 in 2020–2030, because of the increase in the aged population. In addition, it has been reported that the prevalence of AF increases over time within similar age demographics, just as in Western countries; a longitudinal community-based study with biannual examination including ECGs reported that the prevalence of AF at the age of 70 years increased from ~0.5% to 2% over a decade. Although the reason for the time trends has not been clearly explained, our results suggest that the increase might be, at least in part, attributable to the increasing body size of the Japanese population.

In the annual report by the Ministry of Health, Labor and Welfare in Japan, the average height and weight of Japanese males/females aged 20 years in 1955 was 162.2/151.7 cm and 55.6/50.3 kg, respectively, which substantially increased to 169.8/158.3 cm and 65.8/54.2 kg in 2005. Furthermore, in males/females aged 20 years in 1955 was 162.2/151.7 cm and 55.6/50.3 kg, respectively, which substantially increased to 169.8/158.3 cm and 65.8/54.2 kg in 2005. Furthermore, in the report from the Hisayama study, the prevalence of obesity (defined as BMI ≥25kg/m²) in males/females increased from 7.0/12.9% in 1961 to 29.3/24.0% in 2002. Given the recent trends in Japan towards an increase in body size, our data also imply that there will be more occurrence of AF in Japan than previously predicted as a result of aging, so continued close monitoring of the population of people with AF in Japan is required.

Study Limitations
First, the present study had a selection bias because the population was limited to patients visiting a single cardiovascular hospital in an urban city in Japan. Furthermore, the study patients were limited to those without cardiovascular diseases, hypertension or diabetes mellitus. Therefore, the results of the present study can not be expanded to the general population, and it should be re-examined in large-scale population-based studies. Second, AF was diagnosed by medical history and clinical examinations, including ECG and Holter recordings, a method that is well-known for underestimating the prevalence of AF because it neglects asymptomatic AF. Third, the effects of lipid profiles on AF was not evaluated in the present study, so it could not be completely denied that the effect of BMI in the present study might be, at least in part, derived from that of a lipid disorder.

Although limited, the present study has clearly shown a strong effect of body size on the prevalence of AF, which addresses the need for more intensive efforts to prevent the arrhythmia in our society.

References
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