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Original article

Coronary artery diseases in Japanese patients with nonvalvular atrial fibrillation $\!\!\!\!^{\star}$

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ABSTRACT

Background: Both the prevalence of atrial fibrillation and coronary artery disease (CAD) is increasing in aged societies. However, limited data are available regarding the prevalence of CAD and the incidence of coronary events in Japanese patients with nonvalvular atrial fibrillation (NVAF).

Methods and results: The data in this study were derived from Shinken Database 2004–2010, which includes 15,227 new patient visitors to the Cardiovascular Institute between June 2004 and March 2011. In the database, 1835 patients were diagnosed with NVAF (mean age 63 years, mean CHADS2 score 1.1 ± 1.1 , and 75% were men). The prevalence of CAD at the initial visit was 118 patients (6.4%). They were older age and had a greater prevalence of men, more history of congestive heart failure and more history of cardiovascular risk factors rather than those without. During the follow-up period of 532 ± 599 days, coronary events (myocardial infarction, unstable angina, and stable angina) occurred in 51 patients (1.9%/year). Multivariate analysis showed that a history of CAD (p < 0.001) and older age (p = 0.024) were independent predictors of the incidence of future coronary events.

Conclusions: In Japanese patients with NVAF, both the presence of CAD and the occurrence of coronary events are not uncommon. History of CAD and older age are strongly associated with the incidence of coronary events.

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Introduction

Atrial fibrillation (AF) is the most common cardiac arrhythmia in clinical practice. AF is associated with multiple symptoms, with significant morbidity and mortality and with decreased quality of life. The prevalence of AF in the US population is expected to increase from 2.3 million in 2001 to 5.6 million in 2050 [1]. Since the current prevalence of AF is somewhat lower or comparable to that observed

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in Western countries, the AF population is expected to increase also in Japan. The mortality rate of AF patients is almost twice that of patients with normal sinus rhythm. Notably, this observation has been attributed to an increased cardiac death due to underlying heart disease [2–5] rather than to thromboembolism [6].

In Western countries, coronary artery disease (CAD) is highly prevalent among patients with AF and may be one of its underlying causes [7]. Furthermore, AF may be the sole manifestation of CAD [8]. Interestingly, epidemiological data have indicated that ischemic heart disease is one of the most common underlying causes of death among patients with AF [9]. These observations have therefore led to an increased interest in the evaluation of underlying CAD in patients with nonvalvular atrial fibrillation (NVAF).

The present study aimed to investigate the prevalence of CAD and the incidence of coronary events in Japanese patients with NVAF in a single-hospital-based cohort study.

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Methods

Study patients

The Shinken database comprises all new patients visiting the Cardiovascular Institute in Tokyo, Japan ("Shinken" is an abbreviated name in Japanese for the name of the hospital), and excludes patients with active cancer and any foreign travellers. The principal aim of this hospital-based database is surveillance of the prevalence and prognosis of cardiovascular diseases in the urban areas of Japan [10-12]. The registry started in June 2004, and patients have been continually registered to the database annually thereafter. Information about patients' health status and the incidence of cardiovascular events and mortality are maintained in the database by its link to the hospital's medical records and by a mail enquiry sent to patients approximately once or twice per year. The data in the present study were derived from this database between June 2004 and March 2010 (Shinken Database 2004-2010), which included 15,227 new visiting patients. The database contained 1835 patients with the diagnosis of NVAF.

Data collection

For each patient, an electrocardiogram and a chest radiograph were obtained, and the cardiovascular status was then evaluated using echocardiography, exercise test, and 24-h Holter monitor records from the initial visit according to the attending physicians. The following information was collected from the database: (1) patient data (age, sex, and type of AF), (2) cardiovascular diseases, (3) cardiovascular risk factors, and (4) use of medications. The body mass index was calculated as weight in kilograms divided by height in meters squared. The CHADS₂ score is calculated by adding 1 point each for congestive heart failure, hypertension, age \geq 75 years, and diabetes mellitus, and by adding 2 points for a previous stroke or transient ischemic attack [13]. In the present study, patients were divided into 3 CHADS₂ score categories (0, 1, and \geq 2).

Definitions of AF, CAD, and coronary events

In the present study, AF was diagnosed based on electrocardiography at the initial visit, which included 12-lead surface electrocardiograms or 24-h Holter monitor records. AF was also diagnosed based on any medical history of AF from referring physicians.

The definition of CAD included: (1) history of percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) and (2) \geq 50% coronary stenosis as documented by coronary angiography (CAG) results and the detection of ischemia on stress testing including the treadmill stress test, radioisotope single-photon emission computed tomography, and/or fractional flow reserve (FFR) during CAG. FFR, an index of coronary stenosis severity, can be calculated from the ratio of hyperemic distal to proximal coronary pressure.

Coronary events were defined as hospitalization for myocardial infarction, unstable angina, or stable angina. The incidence of coronary events was presented using the person-year method.

Statistical analysis

In baseline characteristics, continuous variables and categorical variables are expressed as mean \pm SD and absolute numbers (percentage), respectively. A chi-square test and an unpaired Student's *t*-test were used for the comparison of categories and continuous variables between 2 groups, respectively. The cumulative incidence of coronary events was estimated by the Kaplan–Meier method. The incidence of coronary events according to the significant univariate

variables was calculated by the person-year methods. Univariate and multivariate Cox regression analyses were performed to identify the predictors for the incidence of coronary events. In multivariate model, co-factors significantly associated with incidence of coronary events in the univariate models were considered in the stepwise method. All statistical analyses were performed using SPSS (SPSS Inc., Chicago, IL, USA) for Windows (Microsoft Corp., Redmond, WA, USA), version 19.0 software. Statistical significance was set at p < 0.05.

Ethical issues

The ethical committee at the Cardiovascular Institute granted ethical permission for this study, and all the patients provided written informed consent.

Results

Characteristics of the total study patients

Table 1 shows the baseline characteristics of the study patients. In this study, 1835 patients (age, 63.2 ± 12.6 years; 1388 men) were enrolled. Among them, 45.4% had tobacco use (current and past), 44.9% hypertension, 25.2% dyslipidemia, and 16.3% diabetes mellitus. The mean CHADS₂ score of the study patients was 1.1 ± 1.1 (CHADS₂ = 0, n = 685; CHADS₂ = 1, n = 589; CHADS₂ ≥ 2, n = 561). Forty-seven percent of patients were treated with warfarin, and 39% with aspirin.

Prevalence of CAD

In the total study patients, patients with a history of CAD were 118 (6.4%) at the initial visit. They were older age and had a higher prevalence of men, more history of congestive heart failure and more history of cardiovascular risk factors than those without. Additionally, they had higher CHADS₂ score than those without $(2.3 \pm 1.2 \text{ vs. } 1.0 \pm 1.1, p < 0.001)$.

Incidence of coronary events

During the follow-up of 532 ± 599 days, 51 patients (1.9%/year) experienced coronary events. The Kaplan-Meier curves for the incidence rate of coronary events are shown in Fig. 1. Oral anticoagulants prescription was not associated with the incidence of coronary events in this study. Univariate Cox regression analysis showed that older age (p = 0.002), men (p = 0.048), hypertension (p=0.004), diabetes mellitus (p=0.004), history of heart failure (p = 0.004), history of CAD (p < 0.001), and CHADS₂ score ≥ 2 (p < 0.001) were associated with the incidence of coronary events (Table 2). Multivariate Cox regression analysis including univariate factors showed that older age (p=0.024) and history of CAD (p < 0.001) were the independent determinants of incidence of coronary events (Table 3). We demonstrated the incidence of coronary events according to the significant univariate values (Fig. 2). Among them, coronary events occurred more frequently in patients with conventional coronary risk factors (i.e. older age, men, hypertension, diabetes mellitus, history of congestive heart failure) and a history of CAD. In addition, coronary events occurred in 11 patients (1.1%/year) in the CHADS₂ = 0, 12 (1.4%/year) in CHADS₂ = 1, and 28 (3.6%/year) in CHADS₂ ≥ 2, respectively. Hence, there was a significant linear trend between CHADS₂ scores and annual coronary events rate.

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