# Trends in the proportions of stroke subtypes and coronary heart disease in the Japanese men and women from 1995 to 2009 

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#### Abstract

Background: The limited evidence on trends in the proportions of stroke subtypes and coronary heart disease in Japan. Methods and results: Stroke and coronary heart disease registrations from three periods including 1995 to 1999,2000 to 2004, and 2005 to 2009 were examined for residents aged 55-74 years for each period who were admitted with acute cardiovascular disease. Subjects who experienced an onset of stroke, or coronary heart disease, or moved at the beginning of each period were excluded. There were 3181 cases of strokes and 768 cases of coronary heart disease in 1995-2009. The age-adjusted proportion of intraparenchymal hemorrhage was $34 \%, 25 \%$, and $24 \%(p=0.02)$ for men, and $27 \%, 29 \%$, and $30 \%$ ( $p=0.41$ ) for women; ischemic stroke was $57 \%, 68 \%$, and $73 \%(p=0.002)$ for men, and $46 \%, 52 \%$, and $58 \%$ ( $p=0.02$ ) for women; and embolic infarction was $23 \%, 31 \%$, and $32 \%(p<0.001)$ for men, and $21 \%, 23 \%$, and $30 \%(p=0.009)$ for women, respectively. The proportions of sudden cardiac death and myocardial infarction among total coronary heart disease did not change during the three periods for either sex. Conclusions: Between 1995-1999 and 2005-2009, the proportion of intraparenchymal hemorrhage among all types of stroke decreased for men, while the proportions of ischemic stroke among all types of stroke and embolic infarction among ischemic stroke increased for both men and women.


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## 1. Introduction

Past epidemiologic studies have indicated that the proportion of hemorrhagic stroke among all types of stroke was higher in Asians than in Americans and Europeans [1-4]. For ischemic stroke subtypes, the proportion of large-artery occlusive infarction in Americans [5] was much greater than that in Japanese ( $61 \%$ versus $25 \%$ $26 \%$ ) [4]. The higher proportions of hemorrhagic stroke and lower proportions of large-artery occlusive infarction in Japanese may be explained in part by the higher prevalence of hypertension [6], and lower serum total cholesterol levels [7] from 1980 to 2000 in Japan. In addition, the proportions of hemorrhagic and ischemic strokes
did not change substantially from 1992 to 2002 among Japanese people age $\geq 40$ years [4]. On the other hand, from 1964 to 2003, the incidence of stroke declined substantially for Japanese men and women, while the incidence of coronary heart disease increased for urban men, but not for rural men and women aged 40-69 years [8]. Similarly, the Hisayama study reported that from 1961 to 2000, the incidence of stroke declined, while the incidence of coronary heart disease was unchanged for both sexes aged $\geq 40$ years [1].

We investigated the proportion of stroke subtypes among all types of stroke, sudden cardiac death (SCD), and myocardial infarction among coronary heart disease in a large Japanese cohort from the Japan Public Health Center-basedprospective (JPHC) study.

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## 2. Methods

### 2.1. Surveyed populations

The JPHC study was conducted in 1990-1994 with a population aged 40 to 69 at 11 public health center areas throughout Japan. There were a total of 140,420 registered residents in the JPHC study from the baseline survey [9].

In this study, all types of stroke and coronary heart disease registrations were examined from 1995 to 2009 with residents aged $55-74$ years for each year ( $40-69$ years at baseline survey). We excluded subjects who experienced an onset of stroke, or coronary heart disease at the beseline survey. The study protocol was approved by the human ethics review committees of the National Cancer Center, Osaka University Graduate School of Medicine and each registered hospital.

### 2.2. Confirmation of stroke and coronary heart disease incidence

The objective of the present study was to determine the incidence of stroke and coronary heart disease. A total of 78 hospitals were registered in the sampling areas of the JPHC cohort. They were all major hospitals where acute stroke and coronary heart disease cases would be admitted. At each hospital, all medical records of stroke and coronary heart disease events were reviewed by hospital physicians, public health center physicians, or research physicians who were blind to the baseline data, using the standard format of registration. Stroke and coronary heart disease events were registered if they occurred after the return of the baseline questionnaire or after January 1, 2010. To complete the review of fatal stroke and coronary heart disease cases, we also conducted a systematic search of death certificates and medical records at the registered hospitals. These records were reviewed by a panel of physician epidemiologists.

Stroke was confirmed based on medical records and meeting the criteria of the National Survey of Stroke [10], which requires a constellation of neurological deficits of sudden or rapid onset lasting at least 24 h or until death. Strokes were classified as ischemic stroke (lacunar, large-artery occlusive, embolic, and unclassified infarctions), and hemorrhagic stroke (intracerebral or subarachnoid hemorrhage), primarily based on computed tomography (CT), magnetic resonance imaging (MRI) or autopsy findings [11]. Infarcts $\leq 1.5 \mathrm{~cm}$ in diameter at the based ganglion and/or pons on brain imaging were classified as lacunar infarction, while infarcts $>1.5 \mathrm{~cm}$ involving cortical areas were classified as largeartery occlusive infarction [11,12]. The definition of embolic infarction required the same criteria as ischemic infarction, plus either a source of possible cerebral emboli in a vessel or the presence of an embolus in the brain, or medical record evidence of a possible source of embolus. A stroke case diagnosed clinically but showing no lesions on CT, MRI, or autopsy was classified as a stroke of undetermined type.

Coronary heart disease was defined as myocardial infarction and SCD. Incidence of myocardial infarction and SCD were confirmed in the medical records according to the criteria of the MONICA (Multinational MONItoring of trends and determinants in CArdiovascular disease) project [13], which required evidence from electrocardiograms, cardiac enzymes, and/or autopsy. Based on a combination of all findings available for review, we classified diagnoses as "definite myocardial infarction" and "possible myocardial infarction". The definite and possible myocardial infarction were combined and presented as myocardial infarction. In the absence of a diagnosis for myocardial infarction, deaths that occurred within 1 h from onset or within 1 h of having been observed alive and symptom-free were regarded as SCD. We
excluded candidate cases if they survived for over 1 h after symptom onset, or if there was another apparent cause of death, such as stroke, cancer, or accident.

### 2.3. Statistical analyses

For the analysis, all types of stroke and coronary heart disease registrations were examined from three periods including 1995 to 1999, 2000 to 2004, and 2005 to 2009 with residents aged 55-74 years for each period. We excluded subjects who experienced an onset of stroke, or coronary heart disease, or moved at the beginning of each period. The sex-specific age-adjusted incidence of stroke and its subtypes, and coronary heart disease were tested by the Poisson regression analysis in each period. We also tested the age-adjusted linear trends in all types of stroke and coronary heart disease incidence, the proportions of stroke subtypes among all types of stroke or ischemic stroke, and SCD among total coronary heart disease across the three study periods using the Poisson regression analysis. All $p$ values for statistical tests were two-tailed and a $p$ value $<0.05$ was considered statistically significant. We used SAS (version 9.3) for all statistical analyses.

## 3. Results

A total census population consisted of 23,902 men and 27,826 women in 1995-1999, 26,898 men and 31,247 women in 2000-2004, and 30,408 men and 35,054 women in 2005-2009. Participants were aged 55-74 years. All participants were divided into 5 -year age groups between 40 and 69 years at baseline survey (Fig. 1)

Table 1 shows the crude number at risk, and incidence of all types of stroke and coronary heart disease in the survey periods. There were 3181 cases ( 1902 men and 1279 women) of all stroke incidences, including 892 cases in 1995-1999, 1092 cases in 2000-2004, and 1197 cases in 2005-2009. For coronary heart disease, there were 238 cases from 1995 to 1999, 252 cases from 2000 to 2004, and 278 cases from 2005 to 2009. The number of stroke and coronary heart disease incidents was the lowest among women aged 55-59 years in each study period.

Table 2 shows the incidence of stroke and coronary heart disease, proportion of stroke subtypes among all types of stroke, and proportions of SCD and myocardial infarction among total coronary heart disease. The age-adjusted incidence of coronary heart disease during the three periods, and the incidence of stroke between 2000-2004 and 2005-2009 trend to decreased for both sexes. The age-adjusted incidence of stroke was 470,497 , and 460 per 100,000 individuals per year ( $p=0.61$ ) for men, and 282, 279, and 241 per 100,000 individuals per years ( $p=0.02$ ) for women, respectively. The corresponding age-adjusted incidence of coronary heart disease was 156,136 , and 121 per 100,000 individuals per years ( $p=0.05$ ) for men, and 43, 39, and 30 per 100,000 individuals per years ( $p=0.01$ ) for women, respectively.

The proportion of intraparenchymal hemorrhage for men and subarachnoid hemorrhage for both sexes among all types of stroke declined, while the proportion of ischemic stroke among all types of stroke increased for both sexes throughout the three periods. However, this trend did not reach statistical significance for subarachnoid hemorrhage. The age-adjusted proportion of intraparenchymal hemorrhage was $34 \%, 25 \%$, and $24 \%$ ( $p=0.02$ ) for men, and $27 \%$, $29 \%$, and $30 \%(p=0.41$ ) for women, respectively; subarachnoid hemorrhage was $8 \%, 6 \%$, and $3 \%(p=0.08)$ for men, and $25 \%, 18 \%$, and $12 \%(p=0.06)$ for women, respectively; and ischemic stroke was $57 \%, 68 \%$, and $73 \%(p=0.002)$ for men, and $46 \%, 52 \%$, and $58 \%$ ( $p=0.02$ ) for women, respectively. The proportions of SCD and myocardial infarction among coronary heart

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