Original Contribution

Cardiovascular disease prevalence and insulin resistance in the Kyushu-Okinawa Population Study and the Framingham Offspring Study

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KEYWORDS:

Cardiovascular disease risk factor; Insulin resistance; Small dense LDL cholesterol; Ethnicity; Community-based cohort study **BACKGROUND:** Age-adjusted cardiovascular disease (CVD) prevalence rates are significantly lower in Japan than in the United States.

OBJECTIVE: Our aim was to compare CVD risk in participants in Fukuoka and Framingham.

METHODS: We measured glucose, insulin, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol (LDL-C), small dense LDL-C, and triglycerides in men and women from Fukuoka (n = 1108) and age (median, 53 years), gender, and age-matched subjects from the Framingham (n = 1101). Blood pressure, body mass index, use of medications, and history of CVD were also assessed.

RESULTS: CVD prevalence rates were more than 6-fold higher in Framingham men and women than their Fukuoka counterparts (P < .001). Median body mass index, LDL-C, insulin levels, and insulin resistance assessment in Fukuoka men and women were significantly (P < .01) lower than in Framingham; however, diabetes prevalence in Fukuoka men was significantly (P < .01) higher than in Framingham men, whereas female rates were similar, as were levels of systolic blood pressure. High-density lipoprotein cholesterol and surprisingly small dense LDL-C levels were significantly (P < .001) higher in Fukuoka than in Framingham. Standard risk factors do not account for the large differences in CVD prevalence rates between the 2 populations, and population differences in insulin resistance may explain

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some of these differences.

CONCLUSIONS: Our data are consistent with the concept that the CVD prevalence rate in a Japanese population is much lower than those observed in the United States, and that these differences cannot be explained by standard CVD risk factors, but may relate to marked population differences in insulin resistance.

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Introduction

Cardiovascular disease (CVD) is a leading cause of death and disability in both Japan and the United States. 1,2 It has been well documented that the Japanese population has a substantially greater longevity and less age-adjusted death from CVD than subjects of Caucasian origin living in the United States.² Based on World Health Organization statistics for 2013, life expectancies in Japan and the United States at birth for men were 80 and 76 years and for women were 87 and 81 years, respectively. At age 60 years in Japan and the United States, the expected additional years of life in men were 23 and 22 years and in women were 29 and 24 years, respectively. Much of these differences are due to a higher prevalence of CVD and a higher ageadjusted mortality from coronary heart disease (CHD) in the United States vs Japan. Age-standardized death rates per 100,000 male and female subjects in the population for CHD and stroke based on World Health Organizations statistics in 2008 were 31.2 and 36.7 in Japan and 80.5 and 25.4 in the United States. Therefore, overall CVD and CHD death rates were higher in the United States by 1.56-fold and 2.58-fold, respectively, but stroke death rate in the United States was 69% of those noted in Japan.²

Major risk factors for atherosclerotic CVD (ASCVD) based on the recently developed American College of Cardiology/American Heart Association (ACC/AHA) risk factor calculator for the United States population includes gender, age, race, total cholesterol, high-density lipoprotein cholesterol (HDL-C), systolic blood pressure, treatment for hypertension, diabetes, and current smoking.³ Individuals with an ASCVD 10-year risk of ≥7.5% have been recommended for statin therapy in addition to lifestyle modification.^{3,4} It is well documented that the low-density lipoprotein cholesterol (LDL-C) lowering induced by statin therapy results in significant reductions in CVD morbidity and mortality.⁵ It has been recently reported that small dense LDL-C (sdLDL-C) may be a better marker and predictor of CVD than total LDL-C as reported from the Framingham Offspring Study, the Atherosclerosis Risk in Communities Study, and the Multi-Ethnic Study of Atherosclerosis.^{6–8} However, whether ethnic differences in those CVD risk markers are account for differences in CVD and CHD death rates has not been clarified.

Our goal was to compare CVD prevalence rates and CVD risk factors in men and women participating in a population study in Fukuoka, Japan, with age- and

gender-matched participants from the Framingham Offspring Study.

Methods

Study population and design

The Japanese population consisted of a subset of the Kyushu-Okinawa Population Study (KOPS), a communitybased prospective observational study of CVD and its risk factors. KOPS has been underway since 2004 in 4 areas in Japan's Kyushu Province including Okinawa and consists of 18,762 community-dwelling native Japanese women and men.^{9,10} The participants of this analysis were notified, by local newspaper and public announcements, of a free annual health examination in Kasuya town given by the Department of General Internal Medicine of Kyushu University Hospital. Kasuya town is a suburb of the Fukuoka metropolitan area in the southwestern area of Japan with a population of approximately 38,000.

A total of 1836 Fukuoka residents (544 men, 1292 women, age range 22-96 years) underwent a health examination. Of these 1836 residents, 62 did not agree to study participation, 33 were aged ≥80 years, and 37 had incomplete data and were excluded. After exclusions, 1704 residents agreed to participate in the study and signed a consent form (participation rate 92.8%). Data collected on each Japanese subject included a complete medical history including information on medication use, as well as dietary and lifestyle interview. In addition, all subjects had a complete physical examination including blood pressure measurements and had blood drawn after an overnight 12hour fast. In all individuals, height, weight, and waist circumference were measured with light clothes on and without shoes. Body mass index (BMI; kilogram per square meter) was calculated as a measure of weight relative to height. To ensure the validity of the data, all physicians who participated in the study were staff members of the Department of General Internal Medicine of Kyushu University Hospital who had been trained with regard to the study protocol and the medical procedures. KOPS was carried out in accordance with the principles of the Declaration of Helsinki and approved by the Kyushu University Hospital Ethics Committee.

United States subjects were selected from participants in cycle 6 of the Framingham Offspring Study, a long-term

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