Changes in Coronary Heart Disease Risk Among Japanese

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Heart disease is the second most prominent cause of mortality in Japan, and coronary heart disease (CHD) accounts for approximately half of heart disease–related deaths. The CHD mortality rate in Japan has been one-third to one-fifth that in the United States, even when validated fatal CHD and sudden cardiac deaths were compared. However, there is growing concern about a possible increase in the incidence of and mortality from CHD because of the westernization of lifestyles such as high-fat diets and sedentary work patterns associated with socioeconomic development since the 1960s.

The present report reviews original articles on population-based surveys of the mortality, incidence, and risk factors of CHD. It focuses on their trends since the 1960s because Japan has experienced rapid changes in lifestyles and environment accompanying socioeconomic development and maturation.

Methods

To identify the relevant literature, PubMed was searched for articles published from 1963 through June 2007. The following search keywords were used: coronary heart disease or coronary artery disease or ischemic heart disease or myocardial infarction; mortality or incidence or risk factor; Japan or Japanese; and epidemiology. Bibliographies of key articles were reviewed and experts in the field were consulted to identify all of the major population-based studies.

Trends in Mortality From CHD

Age-adjusted mortality rates from CHD declined 50% for men and 65% for women between 1969 and 1992 and has continued to decline. According to the World Health Organization database, the age-adjusted annual CHD mortality rate in 2000 was 37 per 100,000 for men and 18 per 100,000 for women, which was the lowest among developed countries.

There are, however, sex, age, and regional variations in CHD mortality trends. The age-adjusted CHD mortality rates declined from 57 per 100,000 in 1969 to 2010 to 0.4 per 1000 person-years in 1979 to 1986 and then plateaued until 1987 to 1994.

More recently, Osaka male residents 40 to 69 years of age have shown a trend for CHD incidence to increase from 0.6 per 1000 person-years in 1980 to 1987 to 1.3 per 1000 person-years in 1996 to 2003. Male residents in Takashima City had an increasing incidence of CHD for all ages from 0.7 per 1000 person-years in 1990 to 1992 to 1.0 per 1000 person-years in 1999 to 2001; the CHD increase was observed primarily for those 65 years of age, and information on risk factor trends was not available.

However, the CHD incidence remained low and did not change materially among female residents in Osaka (~0.4 per 1000 person-years) and Takashima (~0.3 per 1000 person-years), nor did the incidence change over time among men and women 40 to 69 years of age in a rural community of Akita Prefecture (~0.7 per 1000 person-years for men and 0.1 per 1000 person-years for women). No significant trends in CHD incidence were observed among the Hiroshima/Nagasaki cohort between 1958 and 1984 (~2 per 1000 person-years for men and 0.8 per 1000 person-years for women of all ages), for the Hisayama cohort between 1961 and 2000 (~2 per 1000 person-years in men and 1 per 1000 person-years in women ≥40 years of age), or for residents of Okinawa between 1998 and 1999 (myocardial infarction, ~1 per 1000 persons-years for men and 0.04 per 1000 person-years for women ≥40 years of age).

Coronary Risk Factors and Their Trends

Major risk factors for CHD from cohort studies and their trends from national studies and population-based studies were reviewed. Trends for the coronary risk factors were examined by use of the same standardized methods and criteria for blood pressure, smoking, overweight, alcohol intake, and diet and by the Centers for Disease Control—National Heart, Lung, and Blood Institute Lipid Standardization Program and the US Cholesterol Reference Laboratory Network for blood lipids.

Smoking and Its Trend

There was a consistent association between smoking and risk of incidence or mortality from CHD. The multivariable hazard ratio of CHD incidence or mortality for current smoking compared with never or previous smoking was ~2 to 3 for either sex, with a dose-response relationship between the number of cigarettes smoked and the risk of CHD.

As for an effect of environmental tobacco smoke, age-adjusted CHD mortality was 30% higher for nonsmoking wives with nonsmoking husbands than among those in the rest of Japan. The risk of CHD was generally lower for ex-smokers than current smokers, which suggests that smoking cessation lowers risk. A recent large cohort study showed that a decline in risk of CHD after smoking cessation occurred within 2 years and reached the level for diagnosis to ensure the validity of CHD surveillance. The age-adjusted incidence of CHD among male employees 40 to 59 years of age in Osaka increased from 0.4 per 1000 person-years in 1963 to 1970 to 1.5 per 1000 person-years in 1979 to 1986 and then plateaued until 1987 to 1994.

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never smokers 10 to 14 years after cessation.23 In that study, the benefit of smoking cessation was observed similarly among the 40- to 64- and 65- to 79-year age subgroups. The benefit of smoking cessation also was confirmed for patients with a history of myocardial infarction for the prevention of subsequent cardiac events.24 In Japan, the prevalence of current smoking has declined from 82% in 1965 to 46% in 2005 for men ≥20 years of age, whereas that for women declined slightly from 16% in 1965 to 12% in 2005.1-23 However, for women 20 to 29 years old, the prevalence of smoking increased from 7% in 1965 to 21% in 2005.1-23 Population-based studies have identified similar downward trends in smoking for middle-aged men.10,11

High Blood Pressure and Its Trend
High blood pressure has been identified as a risk factor for CHD, and both systolic and diastolic blood pressure levels were positively associated with CHD risk.13,26 The multivariable hazard ratio of CHD incidence for high blood pressure (systolic blood pressure ≥135 mm Hg, diastolic blood pressure ≥85 mm Hg, and/or use of antihypertensive medication) was ~2 for men and 1.5 for women.28 According to a national survey, mean systolic blood pressure for persons ≥30 years of age declined from 142 mm Hg in 1961 to 137 mm Hg in 2000 for men and from 141 to 132 mm Hg for women,29 whereas changes in mean diastolic blood pressure levels were not substantial: from 82 to 83 mm Hg for men and from 81 to 78 mm Hg for women.29 The prevalence of high blood pressure (systolic blood pressure ≥140 mm Hg and/or diastolic blood pressure ≥90 mm Hg) in 2000 was 52% for men and 40% for women ≥30 years of age.29

Similar blood pressure declines were observed between the 1960s and the 1990s in population-based studies of rural men and women and urban women.11 For urban men, either residents or company employees, systolic blood pressure declined modestly between the 1960s and the 1990s, but diastolic blood pressure started to increase in the 1980s.10,11 The prevalence of hypertension decreased, along with downward trends in mean systolic blood pressure levels.10,11 The prevalence of antihypertensive medication use rose substantially between the 1960s and the 1970s, but it did not change substantially thereafter.7,10,11

Blood Lipids and Their Trends
High serum total cholesterol has been a risk factor for CHD.3,13,19,20,26-34 Serum total cholesterol levels were positively associated with risk of CHD, although mean levels of total cholesterol are lower in Japan than in Western countries.13,19,20,26-34 The multivariable hazard ratio of CHD mortality for high (≥220 mg/dL) compared with lower (<180 mg/dL) total cholesterol was 1.6 to 1.8 for both men and women, whereas that for very high (≥260 mg/dL) compared with very low (<160 mg/dL) total cholesterol was ~3.5 for both men and women.33,34

Serum high-density lipoprotein (HDL) cholesterol was inversely associated with risk of CHD.13 Nonfasting serum triglycerides also were associated with the risk of CHD even after adjustment for HDL cholesterol and other coronary risk factors.35 According to a national survey, mean total serum cholesterol levels increased from 186 mg/dL in 1980 to 200 mg/dL in 2000 among men ≥30 years of age and from 191 to 208 mg/dL among women of the same age.29 The prevalence of high total cholesterol (≥220 mg/dL) increased from 15% to 27% for men and 19% to 35% for women, and that of total cholesterol ≥260 mg/dL increased from 2% to 5% for men and from 3% to 8% for women.29 The increase in total cholesterol levels and prevalence of high total cholesterol was observed primarily between the 1980s and the 1990s and plateaued thereafter. Mean serum HDL cholesterol levels have been higher for Japanese than for whites36 and increased from 50 mg/dL in 1990 to 53 mg/dL in 2000 for men and from 53 to 61 mg/dL for women.29 In addition, mean serum triglyceride levels increased between 1990 and 200 for both men and women.29

Similar trends in blood lipids were observed in population-based studies of men and women in rural and urban communities and of male employees in metropolitan areas between the 1960s and the 2000s.7,10,11 and in a large hospital/clinic-based study.37 The prevalence of the use of lipid-lowering medication increased over time by up to 3% for men and 9% for women, although it was much lower than that of antihypertensive medication.10,11

Diabetes Mellitus and Its Trend
Non–insulin-dependent diabetes mellitus may be a risk factor for CHD, although the evidence from community-based cohort studies has been limited. The CHD incidence was twice as high for diabetics as nondiabetics.38 The multivariable hazard ratio of CHD mortality for diabetics (casual blood glucose ≥200 mg/dL and/or history of diabetes) was ~1.5 for men and 2.5 for women,39 and that for diabetics (fasting glucose ≥140 mg/dL, nonfasting glucose ≤200 mg/dL, and/or on treatment) compared with nondiabetics (fasting glucose <100 mg/dL or nonfasting glucose <140 mg/dL) was ~1.5 for men and 3.5 for women.40

No national survey has examined a long-term trend for the prevalence of diabetes mellitus, but the data between 1997 and 2002 showed no change for men and women ≥20 years of age.40 According to community-based studies, the prevalence of diabetes increased from 2% to 8% in the 1980s to 6% to 13% in the 1990s among middle-aged men and from 1% to 5% in the 1980s to 3% to 9% in the 1990s among middle-aged women.11

Overweight and Its Trend
Overweight could be a risk factor for CHD, but its independent contribution to CHD risk may be minor.41,44 Compared with persons with a body mass index (BMI) of 23.0 to 24.9 kg/m², the multivariable hazard ratio of CHD mortality for overweight (BMI ≥27.0 kg/m²) was ~2 for men and 1.5 for women.40 As for CHD incidence, high BMI (BMI ≥30 versus 23.0 to 24.9 kg/m²) was associated with doubling of the risk of CHD for men but not for women.40 In that study, men who were not overweight at 20 years of age but gained ≥10 kg afterward showed double the risk of CHD compared with those with stable weight.44

Mean BMI and the prevalence of overweight have increased consistently among men since the 1980s but did not change among women, according to a national survey.29,45 Mean BMI increased from 22.5 kg/m² in 1980 to 23.4 kg/m² in 2000 and the prevalence of overweight (BMI ≥25.0 kg/m²) increased from 19% to 28% for men ≥30 years of age; the corresponding mean values and prevalence for women were from 22.8 to 22.8 kg/m² and 23% to 23%, respectively.45 Population-based studies showed similar increasing trends among rural and urban men but not women between the 1960s and the 2000s.9-11

Alcohol Intake and Its Trend
Light to moderate alcohol intake has been associated with a 30% to 60% reduced risk of CHD compared with no intake.46-48 Furthermore, the protection by light to moderate alcohol intake against acute myocardial infarction was found for both the presence and absence of alcohol-induced flushing.48

No national survey has yielded long-term trends in alcohol intake. However, a population-based study showed that the prevalence of heavy drinkers (46 g ethanol/d) declined while the prevalence of light to moderate drinkers (1 to 45 g ethanol/d) increased between the 1980s and the 1990s among both rural and urban men.49 The prevalence of any type of drinkers was low and did not change for either rural or urban women.49

Fish and Soy Intakes and Their Trends
Dietary intakes of fish and soy were associated with a reduced risk of CHD incidence.50,51 Compared with men and women with the lowest fish intake (once a week or median intake of 23 g/d), the multivariate hazard ratio of CHD mortality for the highest versus the lowest quintiles of fish intake was 0.4 for women, but men did not

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show such associations. The inverse association between isoflavone intake and risk of myocardial infarction was observed primarily among postmenopausal women.51

According to the national nutrition survey, mean fish intake for adult men and women was ≈80 g/d in the 1960s and 90 g/d between the 1970s and the 2000s.52 Mean intake of beans was ≈70 g/d and did not change over time.52

**Physical Activity and Its Trend**

Physical activity was associated with a reduced risk of CHD mortality.53 The multivariable hazard ratios of CHD mortality for the highest versus the second-lowest category of walking (≥1.0 versus 0.5 h/d) or sports participation (≥5 versus 1 to 2 h/week) were ≈0.8 and 0.5, respectively.53

No robust data are available for long-term trends in physical activity. However, a decline in physical activity is suggested, particularly for men, because of the stable or declined energy intake,54 the increased BMI,59,60 the mechanization of the work environment, and motorization.7

**Discussion**

Japan is unique among developed countries in that, since the 1960s, it has had the lowest mortality from CHD, according to vital statistics1,2 and population-based studies.3–5 which has been further declining for both men and women.8,9 Mean systolic blood pressure levels7–11,13,29 and the prevalence of smoking1,10,11,25 declined, but mean serum total cholesterol and triglycerides7–11,29,37 levels increased for both men and women. The decline in CHD mortality is attributable to large declines in blood pressure levels and the prevalence of smoking, which may have offset the potentially adverse effects of increased total cholesterol levels during the past decades. High total cholesterol would need a longer incubation period to maximize the effect on CHD risk.54,55

Trends in CHD mortality and coronary risk factors have not been uniform and may vary by sex, age, and region. In the 2 largest metropolitan areas, Tokyo and Osaka, where 17% of the total Japanese population resides, the CHD mortality decline was small for men 30 to 49 years of age compared with those residing in the rest of Japan.9

The higher sustained cholesterol levels, together with a recent rise in diastolic blood pressure and declines in systolic blood pressure levels and the prevalence of smoking, may explain in part the slowed decline in CHD mortality in middle-aged urban men compared with rural men. Urban men have a higher fat intake than rural men (22% to 26% versus 19% of total energy for men 40 to 59 years of age)10,11 and lower physical activity (1600 versus 1800 calories consumed per day).56 According to an autopsy study,57 the pathology of myocardial infarction among urban men was larger infarction associated with hypercholesterolemia-derived atherosclerosis of coronary arteries as also observed in Western populations, whereas for rural men, the pathology of myocardial infarction was smaller, disseminated infarction associated with hypertension-derived atherosclerosis of coronary arteries.

The annual CHD incidence rate for middle-aged Japanese was ≈2 per 1000 for men and ≤1 per 1000 for women; that for Americans was 5 to 6 per 1000 for men and 2 to 3 per 1000 for women.58,59 The low CHD incidence for Japanese men and women is explained by more favorable lipid profiles and glucose metabolism, along with lower BMI levels. Lifestyle factors, including low total and saturated fat intake7,8,10,55,60 and high fish50,52 and soy intake51,52 for men and women, as well as light to moderate alcohol intake49,61 for men, may be major contributing factors.

There were sex, age, and area variations in trends in CHD incidence. The CHD incidence tripled among urban male employees 40 to 59 years of age between the 1960s and the 1990s, subsequently doubled for urban male residents 40 to 69 years of age between the 1980 and the 2000s, and increased by ≈50% for rural or semirural male residents of all ages.12 The number of CHD incident cases was too small to draw definite inferences from previous trend studies.10–12 However, the CHD increase was consistent with findings of a Japanese migrant study that the incidence of CHD was higher among Japanese men living in Hawaii and California than among Japanese men living in Japan.62 The gradient of CHD incidence corresponded to the difference in saturated fat intake and serum total cholesterol levels, supporting environmental effects on CHD risk.62 For female residents and rural male residents, there was no material change in CHD incidence.7,11–14

The decline in CHD mortality, in conjunction with an increase or no change in CHD incidence in Japan, may be accounted for by improvements in medical treatment for CHD and/or decreased severity of CHD during the past decades. In fact, the number of emergency medical centers equipped with an intensive care unit or a cardiac care unit in Japan stood at 17 in 1978, 103 in 1989, and 201 in 2007.1 In addition, the in-hospital case fatality rates at hospitals with cardiac care units declined by >50% between the early 1980s and the late 1990s, probably because of improvements in treatment, including thrombolytic therapy and percutaneous transluminal coronary angioplasty.63

There is no robust evidence on long-term changes in the severity of CHD. A series of autopsy studies showed a decline in the coronary atherosclerosis score for Japanese men and women between the 1960s and the 1980s,64 suggesting that the severity of CHD may have declined in association with major declines in blood pressure levels and the prevalence of smoking.

The risk of CHD mortality and its incidence for Japanese women are half or lower than for Japanese men. The probable reason for the lower CHD risk among women is the lower coronary risk factors such as blood pressure levels, serum triglycerides, and the prevalence of smoking and diabetes mellitus and the higher levels of serum HDL cholesterol. Serum total cholesterol levels are lower in premenopausal women but higher in postmenopausal women compared with men of the same age group. However, the premenopausal lower total cholesterol levels may have a major impact on the sex difference in CHD because increased cholesterol levels after menopause probably would not be around long enough to lead to the development of CHD in many Japanese women.

The percentages of preventable CHD were 45% in men and 18% in women for control of smoking, 34% in men and 17% in women for control of hypertension, 5% in men and 8% in women for control of hypercholesterolemia (≥260 mg/dL), and 5% in men and 9% in women for control of diabetes mellitus. These percentages were estimated from the population-attributable risk percent65 using data on hazard ratios (for current
smoking, 2.5 in both men and women; for high blood pressure, 2 in men and 1.5 in women; for hypercholesterolemia, 3.5 in both men and women; and for diabetes, 1.5 in men and 3 in women) and prevalence of risk factors (for current smoking, 54% in men and 15% in women; for high blood pressure, 52% in men and 40% in women; for hypercholesterolemia, 2.0% in men and 3.4% in women; and for diabetes, 10% in men and 5% in women). Therefore, most of the male CHD cases (461 000 patients and 41 970 deaths in 2005)1,66 in Japan would be preventable if these major coronary risk factors were controlled.

Conclusions
This review presented distinctive trends for the mortality from, incidence of, and risk factors for CHD in Japan. Although it is hard to predict future CHD trends in Japan, middle-aged men, especially in urban areas, may be the victims of an impending epidemic of CHD, as is the case in some developing countries.67 The potential epidemic, although it should be confirmed by continued surveillance, is an important issue for both public health and clinical practice.

Disclosures
None.

References
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