Cardiovascular Disease Epidemiology in Asia

– An Overview –

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Cardiovascular disease (CVD) is the leading cause of death in the world and half of the cases of CVD are estimated to occur in Asia. Compared with Western countries, most Asian countries, except for Japan, South Korea, Singapore and Thailand, have higher age-adjusted mortality from CVD. In Japan, the mortality from CVD, especially stroke, has declined continuously from the 1960s to the 2000s, which has contributed to making Japan into the top-ranking country for longevity in the world. Hypertension and smoking are the most notable risk factors for stroke and coronary artery disease, whereas dyslipidemia and diabetes mellitus are risk factors for ischemic heart disease and ischemic stroke. The nationwide approach to hypertension prevention and control has contributed to a substantial decline in stroke mortality in Japan. Recent antismoking campaigns have contributed to a decline in the smoking rate among men. Conversely, the prevalence of dyslipidemia and diabetes mellitus increased from the 1980s to the 2000s and, therefore, the population-attributable risks of CVD for dyslipidemia and diabetes mellitus have increased moderately. To prevent future CVD in Asia, the intensive prevention programs for hypertension and smoking should be continued and that for emerging metabolic risk factors should be intensified in Japan. The successful intervention programs in Japan can be applied to other Asian countries. (*Circ J* 2013; **77**: 1646–1652)

Key Words: Cardiovascular disease; Epidemiology; Ischemic heart disease; Risk factors; Stroke

Cardiovascular disease (CVD) is the leading cause of death in the world; the estimated number of deaths from CVD in 2008 was 17.3 million, comprising almost 30% of all deaths.¹ Further, global CVD deaths are projected to increase to 23.4 million, comprising 35% of all deaths in 2030.² Because half of the world's cardiovascular burden is estimated to occur in Asia, to prevent CVD in Asia is a critical issue for world health. We therefore reviewed epidemiological studies for the mortality, incidence and risk factors of CVD in Asia.

Mortality From CVD in Asia

Figure 1 shows the age-adjusted mortality from CVD for men and women according to country in 2004, for which data are available from the World Health Organization database.¹ Central Asian countries had the highest age-adjusted mortality from CVD, followed by West Asian, South Asian, and South-East Asian countries. Compared with Western countries, most Asian countries, except for Japan, South Korea, Singapore and Thailand, had higher age-adjusted mortality from CVD.

As shown in Figure 2, most Asian countries, except for Japan, Kuwait and Singapore, had 2- to 5-fold higher age-adjusted mortality from cerebrovascular disease (stroke) com-

pared with Western countries; the annual age-adjusted mortality from stroke was 82–215 per 100,000 for Asian countries and 26–46 per 100,000 for Western countries.¹ Concerning ischemic heart disease (IHD), Japan, South Korea and Thailand tended to have lower age-adjusted mortality than Western countries, except for France, although West and Central Asians had higher age-adjusted mortality from IHD compared with Western countries (Figure 3).¹ The age-adjusted IHD mortality in other East and South-East Asian countries was similar to that in Western countries. The age-adjusted mortality from stroke was higher than that of IHD in East Asian countries and Thailand, while that of IHD was higher than that of stroke in other West, Central, South and South-East Asian and Western countries. Therefore, there may be differences in the distribution of cardiovascular risk factors between East and other Asian countries because many previous epidemiological studies have found different risk factor profiles.^{3,4}

Trends in Mortality From CVD in Asia

In Japan, the mortality from CVD, especially stroke, has declined continuously from the 1960s to the 2000s. Between 1951 and 1980, stroke was the leading cause of death in Japan, but it is now the fourth leading cause of death after cancer,

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heart disease, and pneumonia.⁵ The crude mortality rate for stroke in 2011 was 97.0 per 100,000 for men and 99.3 per 100,000 for women, and that for myocardial infarction was 39.0 per 100,000 for men and 19.8 per 100,000.⁵ Japanese deaths from CVD accounted for 25% (10% for stroke and 15%

for heart disease) of all-cause deaths in 2011, whereas it accounted for 40% (22% for stroke and 18% for heart disease) of all deaths in 1980. The nationwide approach to hypertension prevention and control has contributed to a substantial decline in stroke mortality in Japan.^{6,7}

Strategies for hypertension prevention and control include annual systematic cardiovascular screening, referral of high-risk individuals to local clinics for antihypertensive medication, health education for hypertensive patients at blood pressure (BP) screening sites and during home visits by public health nurses, and community-wide media-disseminated education to encourage participation in BP screening and reducing salt intake.⁶

South Korea has a similar trend for stroke mortality to Japan. The age-adjusted mortality from CVD decreased from

172 per 100,000 in 1984 to 73 per 100,000 in 1999 for men, and from 136 per 100,000 to 70 per 100,000 for women, which accounted for the 57% decrease in CVD for men and 48% decrease in CVD for women during the 15-year period.⁸ Looking into the components of CVD, the age-adjusted mortality from stroke and hypertensive heart disease decreased markedly while that of heart disease increased during the 15-year period.⁵ In 1999, the age-adjusted mortality from stroke for men and women was 41.6 and 42.8 per 100,000, respectively, accounting for approximately 40% decrease in stroke for men

Figure 5. Trends in the age-adjusted incidence rate of ischemic heart disease in men aged 40–69 years.¹¹

and approximately 25% decrease in stroke for women during the 15-year period. On the other hand, the age-adjusted mortality from IHD for men and women was 11.9 and 7.5 per 100,000, respectively, which was 3.8- and 3.6-fold higher than for men and women in 1984.

In China, the leading cause of death is CVD, and the age-adjusted mortality from stroke was higher than that of IHD (157 per 100,000 vs. 63 per 100,000) in 2005.¹ Approximately 3 million Chinese died from CVD annually, which accounted for 41% of deaths from any causes in 2009.⁹ The mortality from CVD in rural residents was higher than that in urban areas; the crude mortality from stroke was 126 per 100,000 in urban residents and 152 per 100,000 in rural residents, and the corresponding mortality from IHD was 95 per 100,000 and 71 per 100,000. The mortality from CVD increased, especially in rural residents, from 1990 to 2009 in China.⁹ In Singapore, the age-standardized mortality from CVD decreased substantially from 99 per 100,000 in 1976 to 59 per 100,000 in 1994, and there was a 3–5% decline in the mortality from stroke annually from 1976 to 1994.¹⁰ For West, Central and South Asian countries, the data on CVD mortality trends have been limited.

Trends in the Incidence of CVD in Japan

When we conduct epidemiological studies for accurate estimation of cardiovascular risk factors and evaluation of population-based prevention programs for CVD, it is very important to investigate incidence. Several population-based cohort studies, such as the Circulatory Risk in Community Study (CIRCS), the Hisayama Study, and a study of Hiroshima and Nagasaki atomic bomb survivors, have reported changes in the incidence of CVD from the 1960s to the present in Japan. In the 1960s, the incidence of stroke was higher in the northeast than in the southwest areas of Japan, and the incidence of stroke has dramatically decreased in the northeast.¹¹ The CIRCS reported that the age-adjusted incidence of stroke decreased from 974 per 100,000 in 1964–1971 to 231 per 100,000 in 1996–2003 for men (76% decline), and the corresponding incidence for

women was from 424 per 100,000 to 106 per 100,000 (75% decline) in a rural community in Akita (Figure 4). Further, the incidence of stroke in a suburban community in Osaka also declined moderately; the age-adjusted incidence of stroke decreased from 268 per 100,000 in 1964–1971 to 118 per 100,000 in 1996–2003 for men (56% decline) and the corresponding incidence for women was from 125 per 100,000 to 80 per 100,000 (36% decline) (Figure 4). The Hisayama study also reported that the age-adjusted incidence of stroke declined by 56% for men and 35% for women from the first cohort in 1961 to the third cohort in 1988.¹²

As for trends in IHD incidence, no change was observed in Akita, Hiroshima and Nagasaki prefectures from the 1960s to the 1990s.^{11,13} However, the incidence of IHD increased twice from 1964–1971 to 1996–2003 among men in Osaka; the age-adjusted incidence was 54 per 100,000 in 1964–1971 and 127 per 100,000 in 1996–2003 (Figure 5).¹¹ Further, the age-adjusted incidence of IHD increased from 67 per 100,000 in 1990–1992 to 101 per 100,000 in 1999–2001 among men in Takashima City, Shiga Prefecture.¹⁴ Therefore, several population-based epidemiological studies have indicated an increase in the incidence of IHD among men in urban and/or suburban areas of Japan in the past decades.

Trends in Cardiovascular Risk Factors in Japan

In Japan, many population-based prospective studies, such as CIRCS,¹⁵ the Hisayama¹⁶ and Tanushimaru¹⁷ studies, NIPPON DATA,¹⁸ the Japan Collaborative Cohort (JACC) study,¹⁹ Japan Public Health Center-based prospective (JPHC) study,²⁰ and the Ibaraki Prefectural Health Study (IPHS),²¹ have been conducted to explore risk factors for CVD. High BP was identified as a strong risk factor for CVD, especially for stroke, and both systolic and diastolic BP levels were associated with cardiovascular risk in a dose-response fashion.¹⁵ In CIRCS, the population-attributable risk fraction (PAF) of hypertension for stroke was 56% in the first cohort (baseline; 1963–1971), 64% in the second cohort (baseline; 1975–1984) and 43% in the third co-

hort (baseline; 1985–1994).¹⁵ According to the national survey for cardiovascular risk factors, the mean systolic BP for persons aged ≥ 30 years declined from 142 mmHg in the year 1961 to 137 mmHg in the year 2000 for men, and from 141 mmHg to 132 mmHg for women.⁵ Because higher BP levels, even in normotensive individuals, were associated with a higher risk of stroke incidence, the early management of hypertension and primary prevention of high BP are important to reduce further the incidence of stroke in Japan.

Smoking and diabetes mellitus also have been identified as risk factors for both stroke and IHD in Japan.^{22–24} On the other hand, most of the studies in Japan have reported null findings on the association between elevated total or low-density lipoprotein (LDL) cholesterol levels and the risk of total or ischemic stroke,²⁵ but a consistent positive association of total or LDL cholesterol levels with the risk of IHD.^{26–28} In contrast, many epidemiological studies in the United States have reported a positive association between serum total and LDL cholesterol levels and the risk of ischemic stroke.^{29–31} This discrepancy may be explained in part by different proportions of stroke subtypes between Japan and the United States. The proportions of stroke subtypes for Japanese were approximately 20% for large artery occlusive infarction, 20–30% for intracerebral hemorrhage and 40% for lacunar infarction,³² whereas in the US populations they were 40%, 5–10%, and 15–20%, respectively.³³ The association between dyslipidemia and risk of ischemic stroke might vary by stroke subtype. The Atherosclerosis Risk in Communities (ARIC) study reported that total cholesterol levels were positively associated with the risk of non-lacunar stroke, but not lacunar stroke.³⁴ Recently, population-based Japanese studies also have shown that elevated total or LDL cholesterol levels were a significant risk factor for developing non-lacunar infarction, but not lacunar infarction.^{35,36} On the other hand, lower total or LDL cholesterol levels were

found to be associated with increased risk of intracerebral hemorrhage among Japanese^{21,37} and US blacks and whites.^{38,39}

Serum total, LDL or non-high-density lipoprotein (HDL) cholesterol levels or the LDL/HDL cholesterol ratio have been positively associated with risk of IHD, whereas HDL cholesterol levels were inversely associated with the risk.^{26–28,40,41} To predict 5-year probabilities of developing acute myocardial infarction, the non-HDL cholesterol model was found to have better predictive ability (area under the receiver-operating curve [AUC]=0.825) than the total cholesterol model (AUC=0.815).²⁷ According to a national survey of cardiovascular risk factors among persons aged ≥ 30 years, mean total serum cholesterol levels increased from 186 mg/dL in the year 1980 to 200 mg/dl in the year 2000 among men, and from 191 mg/dl to 208 mg/dl among women.⁴² The prevalence of high total cholesterol (≥ 220 mg/dl) increased from 15% to 27% for men and from 19% to 35% for women. Therefore, the PAF of dyslipidemia for IHD might appear to have increased from the 1980s to the 2000s in Japan. In CIRCUS, the PAF of hypercholesterolemia for IHD among men aged 40–69 years was 7% in the second cohort (baseline; 1975–1984) and 12% in the third cohort (baseline; 1985–1994).⁴³

Type 2 diabetes mellitus is an established risk factor for IHD among Japanese,^{24,44,45} and a risk factor for ischemic stroke, probably both for large artery occlusive infarction and lacunar infarction.²³ The prevalence of diabetes mellitus (HbA_{1c} $\geq 6.1\%$ and/or medication use) increased slightly for men aged ≥ 20 years (10% in 1997, 13% in 2002, 15% in 2007, and 16% in 2011), but did not change for women (7% in the prior 3 periods and 8% in 2011).⁴⁶ In the JPHC study, the PAFs of borderline diabetes and diabetes for IHD were 6.9% and 6.3%, respectively, among men and women aged 40–69 years.²⁴

Smoking is another of the most important risk factors for IHD among Japanese and also a risk factor for ischemic

stroke.^{47,48} Compared with individuals who never smoked or who are not currently smoking, the multivariable-adjusted hazard ratio of IHD incidence or mortality for current smokers is approximately 2 to 3 for either sex, with a dose-response relationship between the number of cigarettes smoked per day and the risk.^{49,50} Although the prevalence of current smoking has declined from 82% in 1965 to 32% in 2010 for men aged ≥ 20 years and from 16% to 8% for women,⁴⁶ the prevalence among men is still higher in Japan than in Western countries. Therefore, the population-attributable risk for current smoking is notably high among Japanese, especially men; the PAF of smoking for IHD was 46% for men and 9% for women.⁵⁰ Because smoking-cessation benefits include risk reduction of CVD within several years,⁴⁹ a nationwide approach to addressing smoking cessation should be continued to reduce the risk of CVD in Japan.

Vascular Pathology in Relation to Different Profiles of CVD in Japanese and Western Populations

There are 2 major types of vascular pathology leading to stroke, stroke subtypes and IHD.^{37,51} One is atherosclerosis, a large vascular pathology typically observed in the aorta, coronary arteries, carotid arteries and basal cerebral arteries, and characterized by lipid accumulation with proliferative changes leading to plaque formation (Figure 6). Major risk factors for atherosclerosis are dyslipidemia, glucose abnormality and metabolic syndrome, as well as hypertension and smoking.^{37,51}

The other pathology is arteriolosclerosis, a small vascular pathology typically occurring in small penetrating arterioles in the basal ganglia of the brain, characterized by necrosis or apoptosis of smooth muscle cells within the media, leading to the formation of micro-aneurysms (intraparenchymal hemorrhage) and fibrous proliferative changes (lacunar stroke) (Figure 6). Risk factors for arteriolosclerosis are primarily hypertension, and secondarily glucose abnormality and metabolic syndrome.^{37,51}

Atherosclerosis is very common in Western populations and is reflected in high IHD mortality, whereas the same is true for arteriolosclerosis in Japanese, reflecting high stroke mortality. The recent rise in IHD incidence among urban or suburban men suggests a potential increase in atherosclerosis among Japanese subpopulations.

These ethnic differences in the prevalence of vascular pathology and CVD may be primarily due to differences in diet between Japanese and Western populations. Higher sodium, lower calcium and lower animal protein intakes, and for men higher alcohol consumption, may contribute to the higher prevalence of hypertension and higher risk of stroke for Japanese.^{52–56} On the other hand, lower saturated fat (meat) and higher n3 polyunsaturated fat (fish) intakes may contribute to the lower prevalence of hypercholesterolemia and lower risk of IHD for Japanese.^{57,58}

Conclusions

Compared with Western countries, most Asian countries have higher mortality from stroke, and East Asian countries have lower mortality from IHD, but Central Asian countries have higher mortality from both stroke and IHD. Nationwide approaches to hypertension and smoking prevention and control should be continued and that for emerging metabolic risk factors should be intensified in Japan. Because mortality from

stroke among other Asian countries is still high, intensive prevention, especially for hypertension, may be of value to prevent CVD in Asia.

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