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Cardiovascular Disease and Risk Factors in Asia
A Selected Review

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Cardiovascular disease (CVD) prevention in Asia is an important issue for world health, because half of the world’s population lives in Asia. Asian countries and regions such as Japan, the Republic of Korea, the People’s Republic of China, Hong Kong, Taiwan, and the Kingdom of Thailand have greater mortality and morbidity from stroke than from coronary heart disease (CHD), whereas the opposite is true in Western countries. The reasons why this specific situation is observed in countries with rapid and early-phase westernization, such as Japan and South Korea, are very interesting.

The Seven Countries Study conducted by Keys et al in 1957 found that Japanese populations had lower fat intake, lower serum total cholesterol, and lower CHD than populations in the United States and Scandinavia, in spite of higher smoking rates. The serum total cholesterol level in Japan has increased rapidly since World War II in accordance with an increase in dietary fat intake from 10% of total energy intake per capita per day to 25%. Despite this increase, the specific characteristic of lower CHD incidence and mortality than that in Western countries has persisted. Whether Japanese people and certain other Asian populations have different risk factors for CHD than Western populations has been a subject of discussion for quite some time.

In this article, we discuss the existence of higher stroke rates and lower CHD rates in Asian countries than in Western countries and the respective risk factors for this on the basis of extensive reviews of cohort studies. We also discuss whether these risk factors differ from those of Western countries. Along with this, we examine the relationship between serum total cholesterol and total stroke and its subtypes. We also address the emerging problems and important issues for CVD prevention in Asia.

An extensive article search for this review was performed with a primary focus on cohort studies and researchers’ names by country in Asia. For mortality data, statistics were obtained from the World Health Organization.

Mortality and Morbidity of Stroke and CHD

Mortality
The available data from the World Health Organization on age-adjusted mortality for men and women combined from cerebrovascular disease (stroke) and CHD are shown in Figure 1. The left panel of Figure 1 shows age-adjusted stroke mortality for some selected Asian countries and some Western countries, Australia, and New Zealand in 2002 for comparison. In general, stroke mortality in Asian countries except Japan and Singapore is higher than in Western countries; however, it is worth mentioning that Japan had the highest stroke mortality in the world in 1965. It rapidly decreased by approximately 80% during the period from 1965 to 1990. The present stroke mortality rate in Japan is similar to that in Western countries. Interestingly, stroke mortality trends in China and South Korea now show similar characteristics to the Japanese trend observed in the past. The recent age-adjusted stroke mortality rate in China is reported to be decreasing in urban areas, whereas in rural areas, mortality is still increasing or is stable. In South Korea, age-adjusted stroke mortality is also decreasing but remains at a higher level. Other Asian countries, including Middle Eastern countries, Central Asian countries, and South Asian countries except Singapore, have higher stroke mortality than Western countries. Therefore, it can be concluded that Asian countries in general have higher stroke mortality than Western countries.

For age-adjusted CHD mortality, it is of interest that East Asian countries have lower mortality than other Asian countries, except Thailand. As observed in the Seven Countries Study, East Asian countries still have lower CHD mortality than what is seen in Mediterranean countries. A large cohort study in China also confirmed that age-adjusted stroke mortality was 3 times higher than CHD mortality. Therefore, it is a specific characteristic that East Asian countries have
higher stroke mortality but lower CHD mortality than Western countries. Other Asian countries have higher CHD and stroke mortality than East Asian countries or Western countries. Central Asian countries that belonged to the past Soviet Union have both the highest age-adjusted stroke mortality rates and the highest age-adjusted CHD mortality rates of all Asian countries, followed by other Middle East Asian and South Asian countries (Figure 1).

Incidence of Stroke and Myocardial Infarction

Data on age-adjusted incidence of stroke and myocardial infarction for men and women 35 to 64 years of age in 1985 to 1987 are available from the World Health Organization Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA) Project. Results from a Japanese registration database with the same diagnostic criteria are compared with the MONICA results in Figures 2 and 3. The Japanese data were surveyed during the period 1989 to 1993. Stroke incidence rates of 6 Japanese populations and 1 Chinese population are scattered in the middle levels (Figure 2), whereas the incidence of acute myocardial infarction in China and in 6 Japanese populations was far lower than that of the Western populations (Figure 3). In South Korea, it was also observed that stroke incidence was higher than myocardial infarction. Thus, East Asian countries, including Japan, have a lower incidence of and mortality from CHD than stroke.

When trends in mortality and incidence of CHD compared with stroke are addressed, the diagnostic method used and improved case findings may have an influence on the statistics obtained in less developed countries. However, even if this is the case, the specific characteristics in East Asian countries hold true.

Subtype of Stroke

Stroke mortality and incidence are higher in East Asian countries than in Western countries. In addition, the incidence of hemorrhagic stroke in East Asian countries is relatively higher than in Western countries. The ratio of cerebral infarction to cerebral hemorrhage is approximately 2:1 to 3:1 in East Asian countries, whereas it is 5:1 to 10:1 in Western countries (Data Supplement Table I); however, this feature has become less prominent in recent years because of the decline in hemorrhagic stroke incidence and mortality. In addition, lacunar stroke is the dominant type of ischemic stroke in Japan, whereas in Western countries, large thromboembolic stroke prevails. Lacunar stroke decreased by 50% in Japan from 1961 to 2000 in the Hisayama study as a result of blood pressure reductions and a decreased smoking rate.

Risk Factors for Stroke and CHD

Similar to the well-established traditional risk factors for stroke and CHD in Western countries, hypertension, smoking, and diabetes mellitus (DM) are the main risk factors for stroke in Asia. A large-scale meta-analysis project, the Asia Pacific Cohort Studies Collaboration (APCSC), which includes 44 separate cohorts (from mainland China, Hong Kong, Taiwan, Japan, South Korea, Singapore, Thailand,
New Zealand, and Australia) and data from >650,000 individuals, showed that hypertension, smoking, and DM were major risk factors for fatal and nonfatal stroke. However, the APCSC found that the slope of the relationship between blood pressure and fatal and nonfatal stroke was steeper in Asian countries than in Australia and New Zealand. In addition, the slope of the relationship between systolic blood pressure and hemorrhagic stroke was steeper than that of the relationship between systolic blood pressure and ischemic stroke.

Serum total cholesterol is a risk factor for CHD in Asian countries. It has been clearly shown in Asian cohort studies that serum total cholesterol level is positively related to CHD morbidity and mortality. Serum total cholesterol was not a risk factor for total stroke, although it was a weak risk factor for cerebral infarction, and low cholesterol was a weak risk factor for cerebral hemorrhage, especially in hypertensive individuals, on the basis of observational cohort studies. On the other hand, a large, individual-based meta-analysis showed that cholesterol-lowering therapy with statins could prevent total stroke or ischemic stroke without increasing the rate of hemorrhagic stroke. This discrepancy should be studied further to clarify the reasons for it.

In Japan, lacunar stroke is more prevalent than large-artery atherothrombotic ischemic stroke. The main risk factors for lacunar stroke are hypertension, smoking, and DM, although the Hisayama study showed that serum total cholesterol was also a risk factor for lacunar stroke. Large-artery atherothrombotic ischemic stroke may be related to serum total cholesterol; however, this remains to be investigated. There are no reports clearly showing a positive relationship between serum total cholesterol and atherothrombotic stroke in China and Korea. On the basis of observational cohort studies, it is understood that serum total cholesterol is not a risk factor for total stroke and is even less important for ischemic stroke in East Asian countries.

Smoking is a major risk factor for stroke (total, ischemic, and subarachnoid strokes) and CHD even in Asian countries, where CHD is generally lower than in Western countries, except Singapore. Smoking is not as clearly a risk factor for cerebral hemorrhage as for subarachnoid hemorrhage and ischemic stroke.
Blood Pressure and the Prevalence of Hypertension

Blood pressure is higher and hypertension is more prevalent in East Asia than in South Asia. High-quality standardization for blood pressure measurement is needed for the comparison of blood pressure levels and for comparison of the prevalence of hypertension across countries and populations. The International Study of Macro- and Micro-Nutrients and Blood Pressure (INTERMAP) and several other studies found that blood pressure levels and hypertension prevalence in the northern part of China were higher than in the southern part of China. The difference in blood pressure between the northern and southern populations is explained in part by the difference in salt consumption.

Trends in blood pressure levels reported by the Japanese National Nutrition and Health Survey showed that blood pressure was highest in 1965 and declined substantially during the years 1965 to 1990 for men and women in all age groups; for instance, an approximately 16-mm Hg decline in systolic blood pressure was recorded in men 60 to 69 years old. Concomitantly, stroke mortality declined greatly by \( \approx 80\% \) in Japan from 1965 to 1990. Notably, salt consumption in the northern part of Japan was 26 to 27 g/d, estimated by 24-hour urine collection, in the 1950s and is now \( \approx 13\) g/d.

Current, well-standardized epidemiological studies have shown that Japanese populations have similar levels of blood pressure as Americans. The International Cooperative Study of Electrolyte Excretion and Blood Pressure (INTERSALT) and the INTERMAP study show that salt consumption in northern Chinese populations is greater than in Japanese populations. The Korean population also has a higher salt consumption than the Japanese population. Therefore, high salt consumption and high blood pressure continue in East Asian countries, although substantial reductions in both have been observed in Japan.

The APCSC reported that the population-attributable fraction of hypertension for CVD is as high as 60% in Asian countries. In addition, the total number of individuals with hypertension in China and India is expected to increase to \( \approx 500\) million by 2025. However, awareness of hypertension in Asia is \( <50\% \) in China and India (although not so in Japan), and these rates of awareness are far lower than in Western countries. In addition, the treatment rate is lower in Asia, especially in low-income countries. Therefore, we must increase awareness of hypertension and implement all possible policies to reduce and prevent it. However, there are several barriers to this goal, including drug cost, the need for a primary healthcare system to identify high-risk individuals, and policy barriers that prevent implementation of programs to lower blood pressure.
High Smoking Rate

The smoking rate for men in Asian countries (except Singapore, Hong Kong, and India) in 2000 remains high at 40% to 60%.\(^1\) Although it has declined substantially over the last 2 decades (Figure 4).\(^8\)\(^{50–54}\) The smoking rate for women in all Asian countries is far lower, at 3% to 15%, than in Western countries.\(^1\)\(^{46–49}\) It is a specific characteristic in Asia that women smoke and drink much less than men.\(^1\)\(^{46–49}\)

Because smoking is a potent risk factor not only for CHD but also for stroke, the population-attributable fraction of smoking for CVD is high, at 30%, second only to high blood pressure.\(^{45,49}\) The impact of smoking on the population-attributable fraction in men is much stronger than in women (13% to 27% versus 2% to 7%, respectively, with regard to heart disease),\(^{49}\) although smoking is strongly related to the excess of cardiovascular morbidity and mortality in both men and women.\(^{49,55}\) The full impact of smoking on CVD may appear in the future, because the epidemic of smoking is a more recent phenomenon in China than in other Asian countries, eg, Japan (Figure 4). In any case, quitting smoking, especially among men, could greatly reduce the prevalence of CVD in Asia.

Increases in Serum Total Cholesterol

Serum total cholesterol levels in Asian countries are generally lower than in the United States and other Western countries\(^2\) (Figure 5). Among Asian countries, the serum total cholesterol level from 1982 to 1985 was highest in Singapore. Age-adjusted CHD mortality in Singapore was also higher than in East Asian countries.\(^2,4\) The serum total cholesterol level and age-adjusted mortality due to CHD in Singapore have decreased in recent years.\(^4\) Among most other Asian countries, serum total cholesterol increased from \(\approx 4.1\) mmol/L (160 mg/dL) to \(4.9\) mmol/L (190 mg/dL) for middle-aged men, and these increases are similar to those of the Japanese population from 1970 to 1980.\(^{56–57}\) These increases in serum total cholesterol level in Asian countries are compatible with the increase in intake of total and saturated fat.\(^1,\)\(^{56–58}\) Total fat intake in the National Nutrition Survey of Singapore in 1998 was 31% of total energy intake, whereas that in Japan in 1998 was \(\approx 26%\).\(^{1,4}\) Accordingly, the INTERMAP study in 1996 to 1999 showed that the fat energy intake of Chinese populations for men 40 to 59 years of age was 20%, whereas it was...
24% for the Japanese population, 34% for the US population, and 33% for the United Kingdom population. The National Nutrition Survey in South Korea showed that average fat intake per capita per day was 19% of total energy intake, which was lower than that in China and Japan.

Prevalence of Glucose Intolerance and DM
Glucose intolerance and DM are risk factors for CHD and stroke in Asia, as in Western countries. However, Asian populations are presently less obese than Western populations; the body mass index is approximately 20 to 24 kg/m² in Asian but is 26 to 29 kg/m² in the West. Because body mass index is increasing in most Asian countries, the prevalence of glucose intolerance and DM may increase further. APCSC results show that the hazard ratios of DM for ischemic stroke and CHD are similar (≈2) for both Asian and Western countries.

The prevalence of DM has been increasing throughout Asia, and the speed of increase is much faster than in Western countries. The World Health Organization estimated that of 171 million individuals with DM worldwide, >80 million lived in Asia in 2000. The World Health Organization projects these numbers will double by the year 2030, with the greatest increase in Asia. Therefore, we should carefully monitor obesity trends in Asia that cause DM, metabolic syndrome, or risk factor clustering for CVD.

Migrant Studies on CVD, DM, and Atherosclerosis in Asian Populations
Migrant studies of Asian populations to Western countries generally show increases in CHD, type 2 DM, and atherosclerosis. Migrant studies of Japanese in the United States, eg, the Honolulu Heart Program, show that Japanese Americans have higher CHD rates than Japanese people living in Japan, whereas stroke rates in Japanese Americans are lower than in the Japanese in Japan and in whites. Likewise, migrant studies of Asian Indians show an increase in CHD among those living in Western countries. Migrant Asian populations, including Chinese, Indians, and Japanese, have a higher prevalence of type 2 DM not only when compared with their counterparts in their home countries but also compared with whites living in countries where Asians have migrated.

A recent multiethnic study of 6700 men and women in the United States showed that the presence of coronary artery calcification predicts future CHD similarly in whites and Chinese Americans, although the latter have lower prevalence and slower progression of coronary artery calcification. Among men in a post–World War II birth cohort, Japanese Americans and whites had a similarly high prevalence of coronary artery calcification that was significantly higher than that in Japanese people living in Japan.

Conclusions
In Asian countries, stroke is more prominent than CHD. This is most likely due to a higher prevalence of hypertension and a lower level of serum total cholesterol in Asian countries. The population-attributable fraction of hypertension for CVD is as high as 60% in Asian countries. High blood pressure accompanies high salt intake in East Asia, whereas low serum total cholesterol accompanies lower fat intake. Reduction in salt consumption in East Asian countries, including Japan, is important for the reduction of CVD, especially stroke. Prevention of smoking is also an important strategy for reducing CVD in most Asian countries, especially for men. The population-attributable fraction of smoking for CVD is ≈30%. Recent westernization in Asian countries has increased fat consumption, which has been followed by an increase in serum total cholesterol. This may have caused the increase in CHD in Asian countries. The prevalence of obesity is also increasing, and this may also increase the prevalence of DM, glucose intolerance, and the metabolic syndrome. Management of these traditional risk factors for CVD is important for the prevention of CVD in Asian and Western countries.

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Disclosures
None.

References


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