Do Diets Good for Longevity Really Exist?

—Lessons from the eating habits of countries with long-lived populations—

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Abstract

In Georgia, a Eurasian country from which "Caspian Sea yogurt (Matsoni)" was introduced to Japan, people eat a variety of fruits and vegetables of various colors as well as yogurt, all of which are effective for inhibiting the harmful effects of excess intakes of salt, and reactive oxygen species, causes of hypertension and aging. In addition, people there commonly eat boiled meat, which is lower in cholesterol than meat cooked in other ways and good for preventing atherosclerosis.

Okinawa, Japan's southern prefecture, has a reputation for being home to the world's longest lived inhabitants, while Guiyang, a city in Guizhou Province of China, is also noted for its long-lived inhabitants. These areas are known for their high consumption of soybeans as in tofu (bean curd) and other soy products. It has become apparent that isoflavones, functional estrogen-like components of soybeans, are effective not only for lowering blood pressure and cholesterol levels, but also for preventing osteoporosis.

It has been found that docosahexaenoic acid (DHA), amino acids, and taurine, which are contained in fish, have a preventive effect against lifestyle-related diseases. Obesity and hypercholesterolemia are less frequent, and thus the incidence of myocardial infarction is lower among Japanese and Chinese people who consume soy and fish in their daily diets.

If salt intake is reduced to 6–7 g per day, the mortality from stroke decreases sharply. The Japanese traditional diet, which is rich in soybeans and fish, is ideal for the prevention of lifestyle-related diseases, only if the salt content is reduced appropriately.

Key words Stroke, Myocardial infarction, Soy isoflavones, Taurine

Vascular Health Is the Key to Longevity

Average life expectancy and longevity

Japan's population has a long average life expectancy, with the average life expectancy for Japanese women at 86 years, the longest in the world, and that for Japanese men, 79 years, the second longest in the world. However, the actual situation is such that, as the population ages, stroke, which was formerly more common, remains the leading cause of being bedridden or demented in Japan's elderly. This means that Japan's long average life expectancy is one of long life rather than a healthy long life, a long-cherished dream of most humans. The major factors that interfere with healthy longevity include vascular diseases. It has become apparent from the results of the WHO-CARDIAC Study (Cardiovascular Diseases and Alimentary Comparison Study) covering 61 regions in 25 nations of the world that cardiovascular diseases, which become more common with aging, can be prevented by modifying daily eating habits.[1–4]

Stroke and quality of life (QOL)

The WHO-CARDIAC Study revealed a clear

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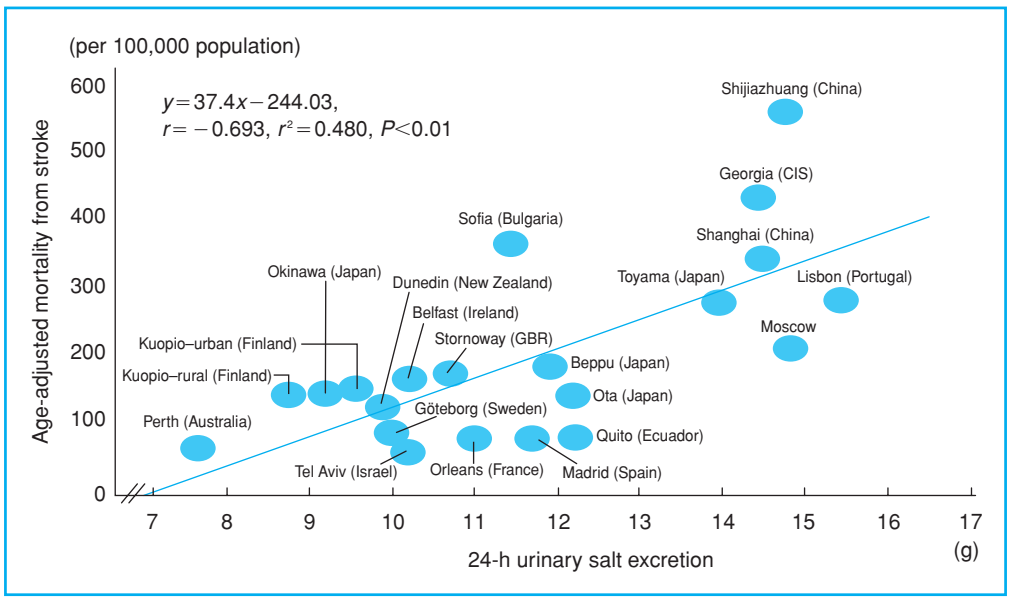

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Fig. 1 Salt and mortality from stroke (in men)
Relationship between mean 24-h urinary salt excretion and age-adjusted mortality from stroke in the WHO-CARDIAC Study.

inverse correlation between age-adjusted mortality from stroke and average life expectancy. The incidence of stroke, a disease that used to be more prevalent in Japan, has decreased over the past four decades as a result of improvements in nutrition, life environment, and health care. However, in Japan, stroke remains the third leading cause of death, and about half of all those who are bedridden or demented are victims of cerebrovascular disorders. Delays in vascular aging by preventing hypertension can lower the risk of stroke, resulting in improved QOL of the elderly. This is a useful way to increase longevity.

Myocardial infarction and average life expectancy

The WHO-CARDIAC Study has shown that there is a strong, significant inverse correlation between age-adjusted mortality from myocardial infarction (x) and average life expectancy (y), which is expressed as $y = 0.043x + 52.41$ ($r^2 = 0.66$, $P<0.01$). This indicates that the prevention of myocardial infarction, among others, contributes to the prolongation of life span.[4] Atherosclerosis leads to myocardial infarction. Low-density lipoprotein (LDL) (also called bad cholesterol), which delivers cholesterol to the blood vessel wall, is recognized as a foreign substance and taken up by macrophages when oxidized. Macrophages that have taken up a large amount of oxidized LDL become vacuolated (foam cells) and accumulate in and around the vascular intima, resulting in atherosclerosis. If this condition occurs in the coronary artery of the heart, the artery is often occluded by thrombus formation, resulting in myocardial infarction. Cholesterol levels, however, can be controlled by diets. Since rice is the main staple of Japan, cholesterol levels are generally lower in the Japanese population than others. It can be said that the long life expectancy of the Japanese people is supported by their consumption of rice. In France, where life expectancy is the second to that of Japan, the incidence of myocardial infarction is low despite high cholesterol levels, as discussed later, probably because people tend to consume antioxidant nutrients.

Mechanism of Longevity Based on Nutrition

Nutrients for stroke prevention: Na, K, Na/K

The major underlying cause of hypertension, which

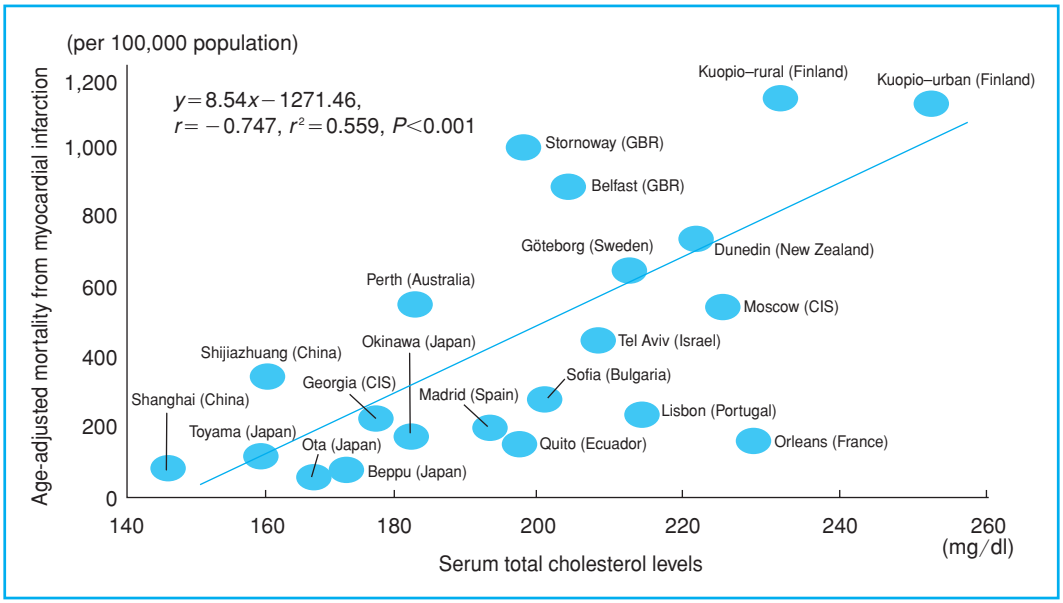

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Fig. 2 Serum cholesterol levels and mortality from myocardial infarction (in men)
Relationship between mean serum total cholesterol levels and age-adjusted mortality from myocardial infarction in the WHO-CARDIAC Study.

can trigger stroke, and atherosclerosis, in which cholesterol is also involved, is an excessive intake of salt. If a large amount of sodium chloride is ingested on a regular basis, sodium (Na) accumulates in cells as they age. In some individuals who have a genetic predisposition, Na accumulation occurs more readily. Na accumulation in the cells leads to water uptake, causing swelling of the cells and hypertrophy of the vascular wall. When this occurs, the intracellular content of ionized calcium (Ca) increases through Na-Ca exchange, causing blood vessel constriction and proliferation of vascular wall cells. Consequently, blood vessels have a thick wall and a narrow lumen, leading to increased peripheral vascular resistance that results in hypertension. On the other hand, fat and cholesterol absorbed from the intestinal tract enter the blood via lymph fluid. If there is excessive intake of sodium chloride, the volume of lymph fluid increases, thereby facilitating the absorption of cholesterol and fat to induce atherosclerosis and obesity.

Thus, there is a distinct relationship between salt intake and stroke, as proven by a positive correlation found between 24-h urinary salt excretion and age-adjusted mortality from stroke (Fig. 1).[2–4] The average daily salt intake of Japanese people is 11–13 g. The results of the WHO-CARDIAC Study suggest that salt intake decreased to 6–7 g/day may reduce mortality from stroke to nearly zero. An analysis carried out in Japan also has indicated that a decrease of 2 g in daily salt intake may prolong average life expectancy by one year.

In addition, the higher the intake of potassium (K), the better the renal excretion of Na; this helps to prevent hypertension and stroke.[2–3] A significant positive correlation has been shown between the 24-h urinary Na/K ratio and age-adjusted mortality from stroke in various regions in the world.[2–4] Increased intake of K causes a decrease in the incidence of stroke. Frequent ingestion of vegetables and fruits that are rich in K and dietary fiber is also important in maintaining vascular health because dietary fiber suppresses Na absorption from the intestinal tract. Magnesium (Mg) and Ca, which are abundant in dairy products, also prevent the adverse effects of Na. It is also thought that soy and fish proteins prevent the harm caused by the excessive intake of salt because the urea produced as their

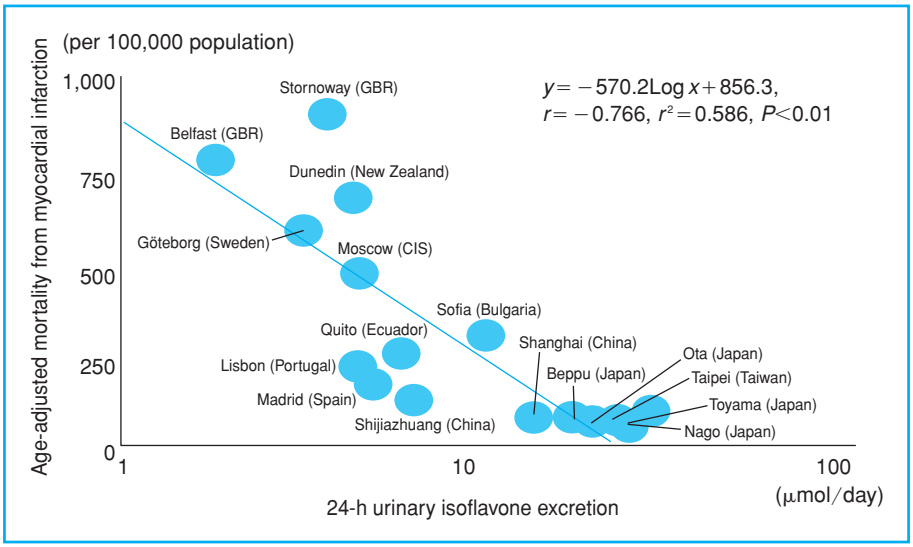

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Fig. 3 Isoflavone and mortality from myocardial infarction (in men)
Relationship between mean 24-h urinary isoflavone excretion and age-adjusted mortality from myocardial infarction in the WHO-CARDIAC Study.

metabolite helps in the urinary excretion of Na from the kidneys.

Elucidation of the relationship between these minerals and stroke has progressed in the experimental setting following the development of stroke-prone spontaneously hypertensive rats (SHRSP).[5–7] In actuality, in the Caucasus region, home to many centenarians, people consume a lot of vegetables and fruits even though salt intake is high. Consumption of meat is about 1.5-fold higher than that in Japan, but boiling meat, which decreases the ingestion of fat, is commonly eaten. This dietary habit is considered to reduce the harm caused by Na and to prevent stroke, thereby contributing to longevity.

Nutrient sources of longevity and the prevention of myocardial infarction

"Moderate levels" of cholesterol

Figure 2 shows the relationship between serum total cholesterol levels and age-adjusted mortality from myocardial infarction. When the serum cholesterol level is high, the mortality of myocardial infarction increases. However, when the serum cholesterol level is low, stroke is more likely to occur.[2–4] Therefore, it can be said that maintaining cholesterol at "moderate" levels (180–200 mg/dl) makes an individual less susceptible to the two major cardiovascular diseases, stroke and myocardial infarction. Cholesterol levels as measured in Okinawa, where people are known to be the longest-lived in the world, are in this "moderate" range. The Okinawan diet is ideal from this point of view. This provides a clue to the longevity of people throughout the world that can be achieved through vascular health.

Suppression of oxidative stress

Since atherosclerosis is influenced by reactive oxygen species oxidizing LDL cholesterol, antioxidant nutrients suppress the aging of blood vessels. Nitric oxide (NO) produced in the vascular endothelium causes blood vessels to dilate and therefore less prone to thrombosis. Nitric oxide loses this activity when oxidized, and LDL cholesterol also serves as a cause of atherosclerosis when oxidized. Therefore, aggressive ingestion of antioxidant nutrients may eliminate reactive oxygen species. Antioxidant nutrients including vitamins A, C, and E are contained in a wide variety of foodstuffs, such as green and yellow vegetables, fruit pigments, herbs and spices, cereal, and pulses. These phytochemicals include pigments of the anthocyanin family present in grapes and prunes, catechin in tea, isoflavones in soybeans, and sesaminol in sesame; many phytochemicals are polyphenols.

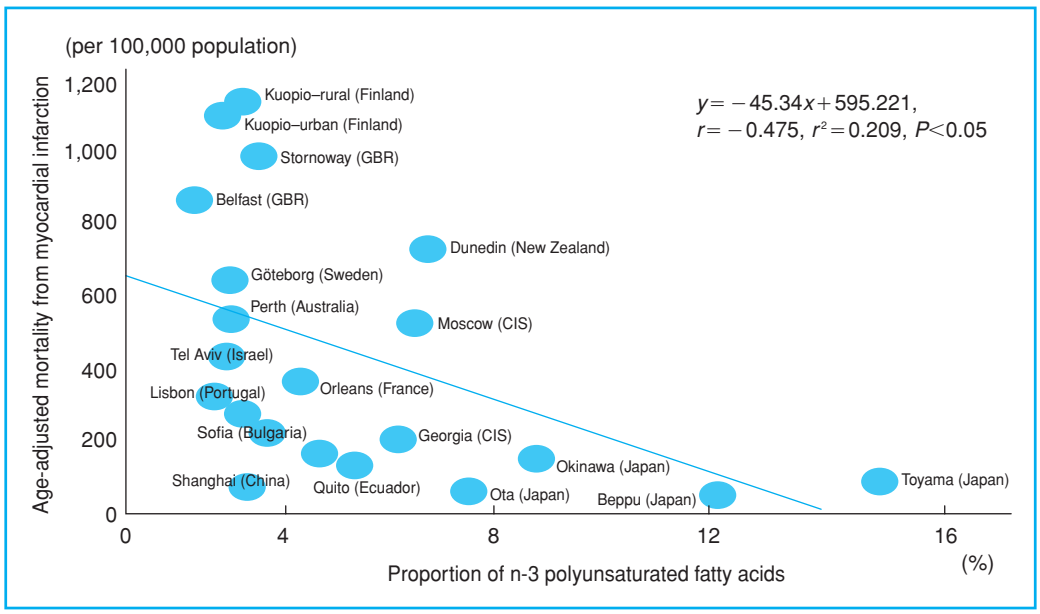

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Fig. 4 N-3 polyunsaturated fatty acid and mortality from myocardial infarction (in men)
Relationship between the mean ratio of n-3 polyunsaturated fatty acids to total fatty acids in plasma phospholipids and the age-adjusted mortality from myocardial infarction in the WHO-CARDIAC Study.

The mortality from myocardial infarction is relatively low in France despite generally high serum cholesterol levels, as observed in Orleans City. In contrast, in Stornoway, Scotland, people's cholesterol levels are lower than in Orleans, but myocardial infarction is more common. Factors common to areas characterized by low mortality from myocardial infarction include low cholesterol levels as well as high levels of vegetable and fruit consumption that enable the adequate ingestion of antioxidant nutrients.

Soy protein and isoflavones

In SHRSP rats, which are genetically prone to develop stroke, the ingestion of soy protein achieved better survival rates and prolongation of average life span.[5–7] This is because soy protein strengthens the vascular wall, and urea produced by metabolism of the protein promotes the urinary excretion of sodium and thus attenuates the development of hypertension. Soybeans also contain other useful components, such as soy oligosaccharides, which help intestinal bacteria work effectively, soy saponins, which suppress the generation of lipid peroxides, tocopherols, and soy isoflavones, which currently are a focus of attention.

Figure 3 shows the inverse correlation between the age-adjusted mortality from myocardial infarction and the amount of isoflavones contained in 24-h urine samples collected in various parts of the world, as demonstrated first in our study.[4,8] The higher the amount of isoflavones in 24-h urine, the lower the mortality from myocardial infarction. Since the urinary isoflavone level is positively correlated with soy intake, sufficient ingestion of soybeans reduces the risk of myocardial infarction. Soy protein adsorbs bile acids made from cholesterol in the intestinal tract and aids in its excretion as feces, leading to decreased cholesterol levels. At the same time, soy isoflavones increase LDL receptors in the liver to facilitate the hepatic processing of LDL cholesterol into bile acids, thereby facilitating a further decrease in serum LDL cholesterol levels. As a result, the risk of myocardial infarction decreases.

When the relation with the mortality from cancer was examined, the amount of soy isoflavones in 24-h urine was found to be inversely correlated with the age-adjusted mortality from breast cancer and prostate cancer. It is presumed

that the weak estrogen-like activity of isoflavones is effective, and isoflavones decrease the risk of breast cancer by occupying estrogen receptors. In elderly Japanese-Americans living in Hawaii, the bone density and the amount of isoflavones in 24-h urine were positively correlated. In an intervention study using soy isoflavones in Japanese-Brazilians, deoxypyridinoline, a marker of bone resorption, was decreased. Based on these findings, soy isoflavones are expected to prevent osteoporosis. Thus, soybean seems to be a promising foodstuff that can prevent lifestyle-related diseases and exert an anti-aging effect.[4,8] In actuality, as shown by the WHO-CARDIAC Study, cardiovascular disease and cancer are less frequent in Guizhou Province of China, the place that seems to be the origin of soy food culture and is still associated with a high consumption of soy products. Similar to Okinawa, long-lived people are also common in Guizhou.

Fish as a source of longevity

In Japan, there is concern that the westernization of eating habits may increase mortality from myocardial infarction. In the WHO-CARDIAC Study, fatty acids in the phospholipids in the blood were analyzed, and it was found that there was a significant inverse correlation between mortality from myocardial infarction and the ratio of n-3 (ω-3) polyunsaturated fatty acids to total fatty acids (Fig. 4).[2–4] It can be said that the high consumption of fish and seafood rich in n-3 polyunsaturated fatty acids, such as DHA and EPA, and the high consumption of α-linolenic acid contained in soybeans lead to a decreased incidence of myocardial infarction. When Japanese-Brazilians who had low daily ingestion of fish were given DHA 2 g/day, blood pressure and the atherosclerosis index (LDL/HDL ratio) were shown to decrease. DHA is considered to be effective for the prevention of myocardial infarction and stroke.

When a large amount of fish is ingested, taurine is excreted in quantity into urine. Through its sympatho-inhibitory effect, taurine attenuate excessive blood pressure responses to stress in both rats and humans. Another beneficial effect is that taurine acts on cholesterol metabolism at the gene level to increase bile production. Therefore, high excretion of taurine is associated clearly with lower mortality from myocardial infarction. DHA is contained abundantly in fish that has blue-silver skin such as mackerel, and taurine is contained profusely in octopus, squid, and shellfish. Decreases in the intake of fish and seafood lead to increased risk of hypertension and hyperlipidemia and exert an adverse effect on the aging of blood vessels. Therefore, the ingestion of seafood as well as soybeans is extremely important for longevity. It can be concluded that the traditionally high ingestion of both seafood and soybeans is sustaining the long life of Japanese people.

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