Influence of the Extent of Westernization of Lifestyle on the Progression of Preclinical Atherosclerosis in Japanese Subjects

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To clarify the influence of a westernized lifestyle on the risk factors for atherosclerosis and preclinical atherosclerosis in Japanese subjects, we surveyed a Japanese population and Japanese immigrants in the United States. Based on the extent of westernization of their lifestyle, the subjects were classified as Japanese (J), first generation Japanese-Americans (JA-I), and second or later generation Japanese-Americans (JA-II). The consumption of animal fat and simple carbohydrates increased in the order of J, JA-I, and JA-II, while the subjects with strenuous physical activity decreased in the same order. The waist-hip ratio, fasting insulin level, serum cholesterol and triglyceride levels, and prevalence of hypertension increased in the same order as the dietary changes. The carotid intima-media wall thickness and the plaque size, which are indexes of preclinical atherosclerosis, also increased in the order of J, JA-I, and JA-II. These data indicate that a westernized lifestyle aggravates the risk factors for atherosclerosis and influences the progression of preclinical atherosclerosis, in correspondence with the extent of westernization. 


Key words: Lifestyle, Carotid intima-media wall thickness, Japanese-American

Introduction

The lifestyle of the Japanese has become progressively more westernized since World War II. Although the total energy intake has not changed over the past 50 years, the fat intake has increased 3.8-fold and the consumption of carbohydrates has decreased by 30% (1). Along with these changes, the serum cholesterol (CH) level has also changed. The mean CH level in men aged 50-59 years was 181 mg/dl in 1970 and increased to 198 mg/dl by 1990. It also increased from 194 mg/dl to 208 mg/dl in women (2). The difference in the serum CH level of the same age populations from the United States and Japan decreased from 48mg/dl to 23mg/dl for men, and from 51mg/dl to 29mg/dl for women between 1970 and 1990.

(2). These changes might be associated with an increase in the incidence of coronary artery disease (CAD) in the Japanese population. However, no significant changes of the age-adjusted mortality rate for heart disease have been observed over several decades. Furthermore, it has been reported that the incidence of fatal CAD in the U.S. population was 4.7-fold higher for men and 3.9-fold higher for women than in the Japanese population (3).

The reason why the incidence of CAD is still lower in Japan than in the United States despite the increase of CH with westernization of the lifestyle is not clear.

To investigate the influence of the extent of westernization of the lifestyle on the risk factors for atherosclerosis and on the progression of preclinical atherosclerosis, we studied Japanese and Japanese-Americans with the same genetic background but different lifestyles.

Subjects and methods

The subjects were Japanese living in Hiroshima (J: n =
645) and Japanese migrants living in Hawaii and Los Angeles or their descendants (Japanese-Americans, n = 1,193). The Japanese-Americans were divided into first generation migrants, who were born in Japan (JA-I), and second or later generation persons, who were born in the United States (JA-II), to distinguish the extent of westernization of their lifestyles (Table 1). The study was performed in 1992, 1993 and 1995.

Measurements were taken in the early morning after an overnight fast. All patients were weighed in their underweaer, their height was determined using a stadiometer, and the body mass index (BMI) was subsequently calculated as the weight in kilograms divided by the square of the height in meters. The waist circumference was measured at the level of the umbilicus, the hip circumference was measured at the level of the greater trochanter, and the waist-hip ratio was calculated.

Blood pressure was measured using a sphygmomanometer in a standardized fashion with the subjects in the sitting position. Subjects with a systolic blood pressure ≥140 mmHg and/or a diastolic blood pressure ≥90 mmHg were diagnosed as having hypertension.

A 75-g glucose tolerance test was performed after the physical measurements had been obtained. Serum samples were rapidly separated and frozen at −80°C. The frozen samples were packed with dry ice and brought back to Japan by plane and stored at −80°C with the samples obtained in Japan. All samples were analyzed at the same time in one laboratory within one month after sample collection. Serum glucose was determined by the glucose oxidase method. Serum insulin was measured with a commercial radioimmunoassay kit.

Serum total CH (TCH), triglycerides (TG), and HDL-CH were determined using enzymatic methods with a 736-60E Auto Analyzer (Hitachi, Tokyo, Japan). HDL was separated using the phosphorus-tungsten precipitation method[4]. LDL-CH was calculated by Friedewald’s equation[5]. Assays for serum lipids were calibrated using Q-PAK Chemistry Control Serum I and II (Technichan Instrument Corp., New York, USA).

The resting ECG was recorded in each subject and classified according to the Minnesota code[6]. To evaluate the severity of preclinical atherosclerosis, the carotid intima-media wall thickness (IMT) was measured using B-mode ultrasonography (EUB-405X, Hitachi, Tokyo, Japan) with a 10-MHz probe[7]. A standard protocol was used to scan the near and far walls of the left and right common carotid arteries, as well as the bifurcation and the internal and external carotid arteries in three different longitudinal projections (anterior, lateral, and posterior). Plaque was defined as a local "hill"-like thickening of the intima >1.1 mm. In each projection, the site of maximum thickness (including plaque) was detected by checking the arterial walls from the common carotid artery to the internal carotid artery. Then the IMT was measured at the site of maximum thickness and at two other points (1 cm upstream and 1 cm downstream from this site), and the three measurements were averaged. The greatest of the six average IMT values obtained in this way was used as the representative value. All measurements were performed by a single physician using the same equipment to avoid methodological influences. The inter-observer variability (determined in five subjects on 2 occasions) was 3.6 to 4.7%.

<table>
<thead>
<tr>
<th>Table 1. Characteristics of Study Subjects</th>
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<tbody>
<tr>
<td>Men</td>
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<tr>
<td>N</td>
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<tr>
<td>Age (years)</td>
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<tr>
<td>Body mass index (kg/m²)</td>
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<tr>
<td>Total cholesterol (mg/dl)</td>
</tr>
<tr>
<td>Triglyceride (mg/dl)</td>
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<tr>
<td>LDL-cholesterol (mg/dl)</td>
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<tr>
<td>HDL-cholesterol (mg/dl)</td>
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<tr>
<td>Systolic BP (mmHg)</td>
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<tr>
<td>Diastolic BP (mmHg)</td>
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<td>Fasting-IR (μU/mL)</td>
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</table>

Values are Mean ± SE  
J: Japanese in Hiroshima  
JA-I: First generation Japanese-Americans  
JA-II: Second or more later generation Japanese-Americans  
* p < 0.05, ** p < 0.005; *** p < 0.0005 vs J  
1' p < 0.05, 1" p < 0.005; 1"' p < 0.0005 vs JA-I  
All variables were adjusted for age and sex except age.
The dietary history was obtained by three well-trained dietitians in the Japanese and Japanese-American population(8). The amount per meal, the frequency of intake per week (or month), and the cooking method of each food group were ascertained through interviews. The nutritional value of each food group was determined using the Nutritive Value of American Foods in Common Units (Agriculture Handbook No.456) for the Japanese-Americans(9) and the Standard Tables of Food Composition in Japan for the Japanese subjects(10).

Physical activity was evaluated by questionnaire. The occupation, as well as the daily duration of walking, standing, sitting, leisure time, and exercise were ascertained in detail. According to the labor category of the Japanese Ministry of Health and Welfare, the level of physical activity was classified as strenuous, moderate, or light.

In the present analyses, we found 14% of the subjects to be diabetic, 21% with impaired glucose tolerance, and 65% with normal glucose tolerance (WHO criteria)(11) in the Japanese-Americans. The representative values in the Japanese were 8%, 24% and 68%, respectively. Subjects with diabetes, liver disease, renal disease, and treatment with anti-hypertensive and/or lipid-lowering drugs were excluded. The study was approved by the ethics committee of Hiroshima University School of Medicine and by the Council of the Hiroshima Kenjin-kai Association (an association of immigrants from Hiroshima Prefecture, Japan) in Hawaii and Los Angeles. All subjects gave informed consent to participation.

### Statistical methods

Data were analyzed using SAS Version 6.10 (SAS Institute, Cary, NC) and the results are given as the mean ± SE. The mean values were compared by Student's unpaired t-test or by age-and sex-adjusted analysis of covariance (ANCOVA) as appropriate. TG and insulin data were converted to logarithmic values when they did not fit the normal distribution.

### Results

No marked differences in total energy intake were observed between J, JA-I, and JA-II. However, the consumption of animal protein, animal fat, vegetable fat, and simple carbohydrates increased in the order of J, JA-I, and JA-II among men, while the intake of complex carbohydrates decreased in the same order. Similar trends were also observed in women (Fig. 1).

The percentage of male subjects performing strenuous physical activity was highest among J, and decreased in the order of JA-I and JA-II. In women, the percentage of subjects performing strenuous physical activity was also highest among J, and there were few such women in the JA-I and JA-II populations.

BMI was lowest in J and increased in the order of JA-I and JA-II among men, but women showed similar BMI levels among the three groups. On the other hand, the waist-hip ratio was lowest in J and increased in the order.
of JA-I and JA-II in both men and women (Fig. 2). TCH, LDL-CH and TG levels increased in the order of J, JA-I, and JA-II. HDL-CH was highest in J, but the difference between JA-I and JA-II was less clear. Systolic blood pressure was higher in JA-II than in the other two groups (Table 1). The frequency of hypertension was 29% in J, 32% in JA-I, and 38% in JA-II (p < 0.05, v.s. J), when the treated subjects were included. The fasting insulin level (F-IRI) increased in the order of J, JA-I, and JA-II (Table 1), and insulin resistance (HOMA) showed a similar trend (data not shown). Even after adjusting for gender, age, and BMI, F-IRI was positively correlated with TG and with blood pressure, while it was negatively correlated with HDL-CH. These correlations increased in the order of J, JA-I, and JA-II (Table 2).

In JA-II, IMT was 1.25 ± 0.03 mm, and this value was significantly higher than in JA-I (1.01 ± 0.04 mm, p < 0.05) or J (0.98 ± 0.03 mm, p < 0.01). The plaque size was 2.82 ± 0.05 mm in JA-II, which was significantly larger than in JA-I (2.52 ± 0.07 mm, p < 0.001) or J (1.82 ± 0.04 mm, p < 0.001) (Fig. 3). The highest incidence of abnormal Q waves on the resting ECG was seen in JA-II (4.7%), followed by JA-I (3.8%), and J (0.8%, p < 0.05 v.s. JA-II).

**Discussion**

JA-I immigrants lived a Japanese lifestyle for part of their life, while JA-II were born and raised in the United States. Thus, the extent of westernization of the lifestyle increased in the order of J, JA-I, and JA-II. Our data suggested that the influence of a westernized lifestyle on Japanese eating habits caused a qualitative, but not quantitative change. Physical activity also decreased in the subjects with more advanced westernization of lifestyle. We found that lifestyle changes affected obesity and risk factors for atherosclerosis depending on the extent of westernization. However, the influence of a westernized lifestyle on obesity, as evaluated by BMI, was less apparent in women than men. A recent National Nutrition Survey in Japan also showed that BMI has changed less in women than in men over the past several decades (12). Thus, women are probably more concerned about obesity than men for cosmetic reasons. However, the waist-hip ratio increased in the order of J, JA-I and JA-II for men as well as women, showing that westernization of lifestyle promoted the accumulation of visceral fat in Japanese persons, corresponding to the degree of lifestyle westernization. Visceral fat actively secretes adipocytokines
Table 2. Age, sex, and BMI adjusted partial correlation coefficients between fasting IRI and metabolic indices

<table>
<thead>
<tr>
<th></th>
<th>Japanese</th>
<th>Japanese-Americans</th>
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<tr>
<td></td>
<td>I</td>
<td>II</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>0.144</td>
<td>0.045</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>0.176*</td>
<td>0.393**</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>-0.122*</td>
<td>-0.201*</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>0.023</td>
<td>0.010</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>0.064</td>
<td>0.120</td>
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</table>

I: First generation Japanese-Americans
II: Second or more later Japanese-Americans
*p < 0.05, **p < 0.005

(13) that potentiate insulin resistance (14) and the progression of atherosclerosis (15). Since the waist-hip ratio increased stepwise despite the absence of a difference of BMI in women, it may be more important to evaluate visceral fat accumulation as an index of obesity in women. Classical risk factors, such as TCH, LDL-CH and TG increased in association with the extent of westernization of lifestyle. Among Japanese-Americans living in Seattle, the mean CH level was found to exceed that of U.S. subjects (16), although animal fat intake by the Japanese-Americans was still lower than that by U.S. subjects (8,17).

Thus, it seems likely that Japanese-Americans might be unable to compensate for an excess of dietary CH, suggesting the existence of racial differences in CH metabolism.

Our data clearly indicate that westernization of lifestyle enhances insulin resistance, and the accumulation of visceral fat may be an important cause, as mentioned above. Furthermore, increasing insulin resistance (as evaluated by F-IRI) was associated with changes of lipids and blood pressure even after adjustment for the BMI, suggesting that visceral fat may be an important cause of metabolic syndrome.

It is difficult to compare the impact of changes in the risk factors for atherosclerosis on the progression of atherosclerotic disease in Japanese and Japanese-Americans. The incidence of CAD is influenced by many factors such as the genetic background, the standard of medical care, disease prevention strategies, and the extent and duration of exposure to risk factors for atherosclerosis. In the present study, we measured the IMT as a parameter of preclinical atherosclerosis. IMT and plaque size increased in the order of J, JA-I, and JA-II, corresponding to the extent of the change in the risk factors for atherosclerosis. A similar trend was observed for the detection of abnormal Q waves in the ECG. Accordingly, it appears likely that in Japanese, when risk factors for atherosclerosis are aggravated by a westernized lifestyle, atherosclerosis progresses along with the extent of westernization.

The duration of exposure to risk factors is important in determining the progression of atherosclerosis. Differences in the risk factors for atherosclerosis corresponding to IMT changes in our Japanese and Japanese-American subjects might have resulted from long-term exposure to different levels of risk factors. However, the CH levels of the Japanese and U.S. populations have been getting closer in recent years (2). Indeed, there were no significant differences in TCH between the Japanese and Japanese-Americans after 1996 in our survey (18). This may have resulted from the effect of CH-lowering strategies pursued in the United States and the continuing westernization.
ization of lifestyle in Japan. As a consequence, the IMT values of Japanese and Japanese-Americans might be expected to become closer in the future. Until now, the incidence of CAD has not been increasing in the Japanese population. This might be due to the relatively short duration of exposure to risk factors for atherosclerosis, and because many Japanese foods contain abundant anti-atherosclerotic factors such as antioxidants, even though the diet has been somewhat westernized.

In conclusion, the Japanese are not an "atherosclerosis-resistant" population, and atherosclerosis may progress along with an increase of risk factors due to a more westernized lifestyle. Avoiding excessive westernization of lifestyle might be important for preventing atherosclerosis in the Japanese population.

References


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