

Westernization of Lifestyle and Atherosclerosis in the Japanese: Lessons from the Hawaii – Los Angeles – Hiroshima Study

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Japanese Americans include Japanese individuals migrating from Japan to the United States (first-generation Japanese Americans [JA-1]) and their offspring (second- or later-generation Japanese Americans [JA-2]). Although Japanese Americans share their genetic predisposition with the Japanese, their lifestyles have been westernized rapidly and extensively. We conducted a medical survey for atherosclerosis among Japanese Americans living in Hawaii and Los Angeles and native Japanese living in Hiroshima for 50 years since 1970 (the Hawaii–Los Angeles–Hiroshima Study) and obtained the following results:

(1) In the 1990s, a westernized lifestyle induced hyperlipidemia among Japanese Americans, and based on the evaluation of the carotid artery intima-media wall thickness (IMT), atherosclerosis was apparently more advanced in Japanese Americans than in native Japanese. In addition, the advancement of atherosclerosis corresponded to the degree of westernization of lifestyles in JA-1 and JA-2.

(2) In the 2010s, the serum total cholesterol and low-density lipoprotein cholesterol levels in native Japanese were significantly higher than those in Japanese Americans, and the difference in the progression of carotid artery IMT was smaller between native Japanese and Japanese Americans.

(3) Maintaining a healthy Japanese lifestyle since childhood may suppress future worsening of risk factors for atherosclerosis (such as obesity and diabetes mellitus) and contribute to atherosclerosis prevention in the Japanese.

Key words: Atherosclerosis, Japanese Americans, Lifestyle, Westernization

1. Introduction

The incidence and mortality of coronary heart disease in Japan are lower than of those in Western countries such as the United States. Do the Japanese have any genetic characteristics that protect them against atherosclerosis?

In the late 19th century, many Japanese emigrated from Japan to the United States and other countries. The lifestyles of Japanese migrants who were born in Japan and immigrated to the United States (first-generation Japanese Americans [JA-1]) have changed rapidly from the Japanese lifestyle to the

American lifestyle, i.e., they became “westernized.” Their offspring who were born and brought up in the United States (second- or later-generation Japanese Americans [JA-2]) have been exposed to the American lifestyle for a longer period (**Fig. 1**).

In recent years, more Japanese have emigrated from Hiroshima to other countries than from any other prefecture. We conducted a medical survey among Japanese Americans living in Hawaii and Los Angeles and native Japanese living in Hiroshima for 50 years since 1970. We compared and analyzed the survey results obtained from these two Japanese populations sharing the same genetic predisposition

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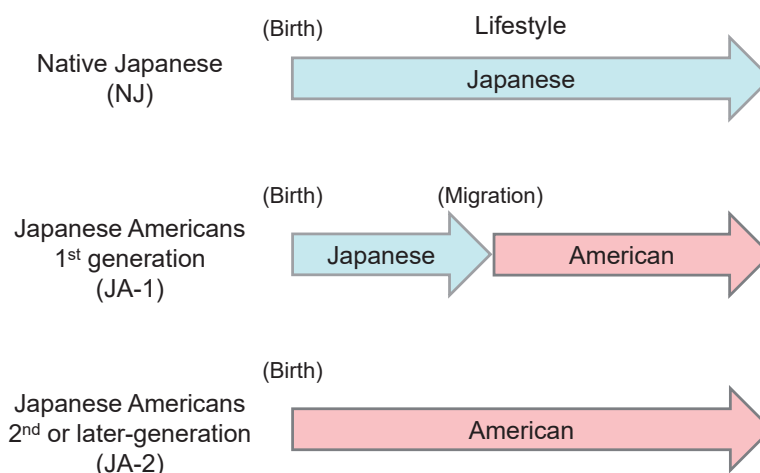


Fig. 1. Differences in lifestyles between native Japanese (NJ) and Japanese Americans (JA). First-generation (JA-1) and second- or later-generation (JA-2) Japanese Americans were exposed to the American lifestyle at different time points for different periods.

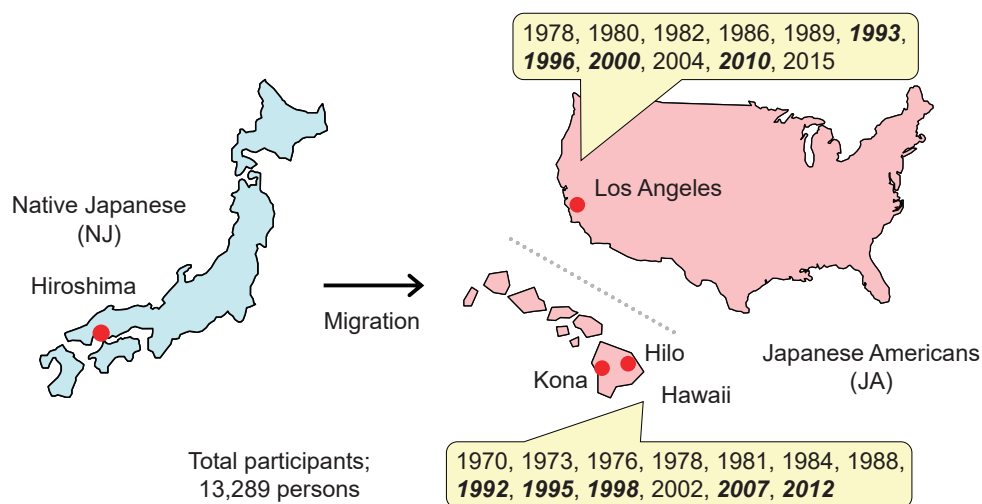


Fig. 2. Number of subjects and the year of the medical survey of Japanese Americans. Since 1970, a medical survey was conducted 13 times on the island of Hawaii and 11 times in Los Angeles. The data used in this article were collected in the years indicated in italics.

but living in different environments to clarify the influence of a westernized lifestyle on the health condition of Japanese (the Hawaii – Los Angeles – Hiroshima Study)^{1, 2)}. In this review, we summarize how the association between westernization of lifestyles and atherosclerosis in the Japanese has changed over time.

2. Overview of the Medical Survey of Japanese Americans

We initiated a medical survey of Japanese Americans in Hilo and Kona on the island of Hawaii

in 1970 and Los Angeles, California in 1978. Health checkups were performed every few years. By 2015, 24 rounds of the survey were conducted, and 13,289 participants were examined (Fig. 2)³⁾.

To conduct a medical survey of Japanese Americans, approximately 10 medical professionals from Hiroshima, including doctors, nurses, and dietitians, stayed in the United States for approximately 3 weeks, during which they performed physical examinations, blood pressure measurements, nutritional surveys, urinalyses, blood tests, 75-g oral glucose tolerance tests (OGTTs), and electrocardiographies. Since the 1990s, we measured the carotid artery

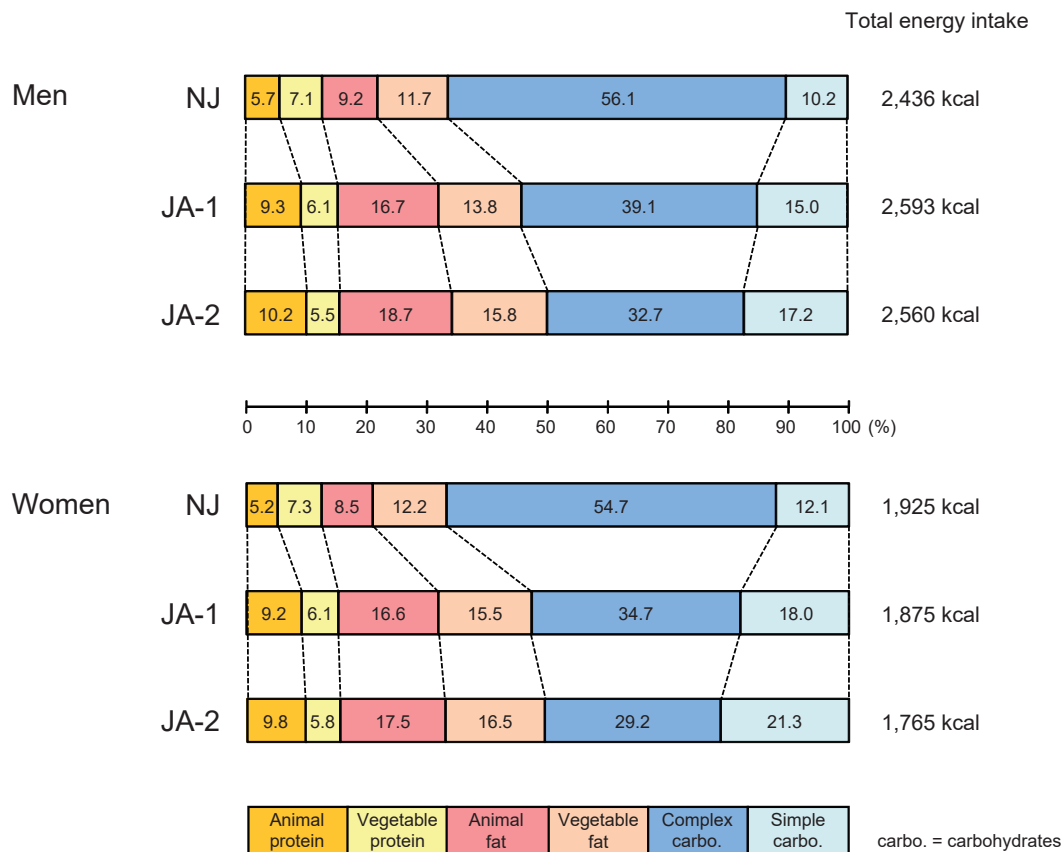


Fig. 3. Comparison of nutrient intakes between native Japanese and the two generations of Japanese Americans (cited from reference 4)

Survey from 1992 to 1995

594 native Japanese (NJ; 273 men and 321 women), 477 first-generation Japanese Americans (JA-1; 181 men and 296 women), and 549 second- or later-generation Japanese Americans (JA-2; 164 men and 385 women)

intima-media wall thickness (IMT) using ultrasonography to evaluate atherosclerosis. The control group comprised native Japanese participants who underwent lifestyle-related disease screening conducted in Hiroshima. We compared the survey results obtained during the same period from the two Japanese populations in the United States and Japan.

Both Japanese American and native Japanese participants were classified into a normal glucose tolerance group (NGT; a fasting serum glucose level <110 mg/dL and a 2-h serum glucose level <140 mg/dL after OGTT), a diabetes mellitus group (DM; a fasting serum glucose level \geq 126 mg/dL or a 2-h serum glucose level \geq 200 mg/dL after OGTT), and an impaired glucose tolerance group (IGT; fasting serum glucose and 2-h serum glucose levels between those of the NGT and DM groups). Obesity was defined as a body mass index (BMI) of \geq 25 kg/m². Hypertension was defined as systolic blood pressure \geq 140 mmHg or diastolic blood pressure \geq 90 mmHg

or both.

All participants received a description of the study procedure, and they provided written informed consent. This epidemiological study was conducted according to the Declaration of Helsinki and was approved by the Ethics Committee of Hiroshima University.

3. Comparison between Native Japanese and Japanese Americans with Respect to Generation

3.1) Comparison of Nutrient Intakes and Physical Activity

In the 1992–1995 survey, the nutritional survey results of Japanese Americans, divided into JA-1 and JA-2 with respect to generation, were compared with those of native Japanese (Fig. 3)⁴. Although the total energy intakes in men were almost comparable among the three groups, the highest total energy intake in

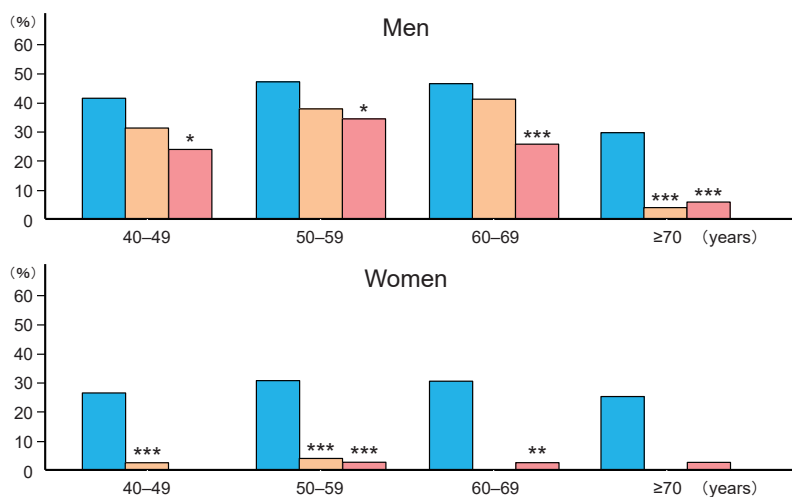


Fig. 4. Comparison of the percentage of subjects involved in strenuous physical activity between native Japanese and the two generations of Japanese Americans with respect to the age group (cited from reference 4)

Survey from 1992 to 1995

594 native Japanese (NJ; 273 men and 321 women), 477 first-generation Japanese Americans (JA-1; 181 men and 296 women), and 549 second- or later-generation Japanese Americans (JA-2; 164 men and 385 women)

Blue column: NJ, orange column: JA-1, pink column: JA-2

* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$ vs. NJ

women was observed in native Japanese, followed by JA-1 and JA-2. Furthermore, regarding the proportions of nutrient intake, proportions of consumption of animal protein, animal fat, vegetable fat, and simple carbohydrates increased in both men and women in the order of native Japanese, JA-1, and JA-2, whereas the proportions of complex carbohydrate consumption decreased in both men and women in the same order.

In the same report⁴⁾, the percentage of male subjects involved in strenuous physical activity was the highest in native Japanese and decreased in the order of JA-1 and JA-2 (Fig. 4). The percentage of female subjects in this category was also the highest in native Japanese; however, it was low in JA-1 and JA-2. The prevalence of hypertension was 29% in native Japanese, 32% in JA-1, and 38% in JA-2, and it was significantly higher in JA-2 than in the other two groups.

3.2) Comparison of Carotid Atherosclerosis

Carotid artery IMT was compared in the 1992–1995 survey (Fig. 5)⁴⁾. The IMT in JA-1 was almost comparable with that in native Japanese, whereas the IMT in JA-2 was significantly greater than that in the other two groups. This indicated that even among Japanese individuals, the progression of atherosclerosis is notable among those living an American lifestyle for a longer period after birth.

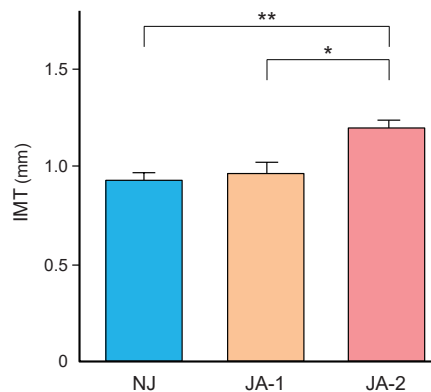


Fig. 5. Comparison of carotid artery intima-media wall thickness (IMT) between native Japanese and the two generations of Japanese Americans (cited from reference 4)

Survey from 1992 to 1995

Native Japanese (NJ; $n = 594$), first-generation Japanese Americans (JA-1; $n = 477$), and second- or later-generation Japanese Americans (JA-2; $n = 549$)

* $P < 0.05$, ** $P < 0.01$

4. Comparison of Japanese Americans with Respect to Generation and the Presence or Absence of *Kibei* Experience

Some JA-2s who were born in the United States stayed with their relatives in Japan from childhood to adolescence and returned to the United States after receiving education in Japan (Fig. 6). We refer to this

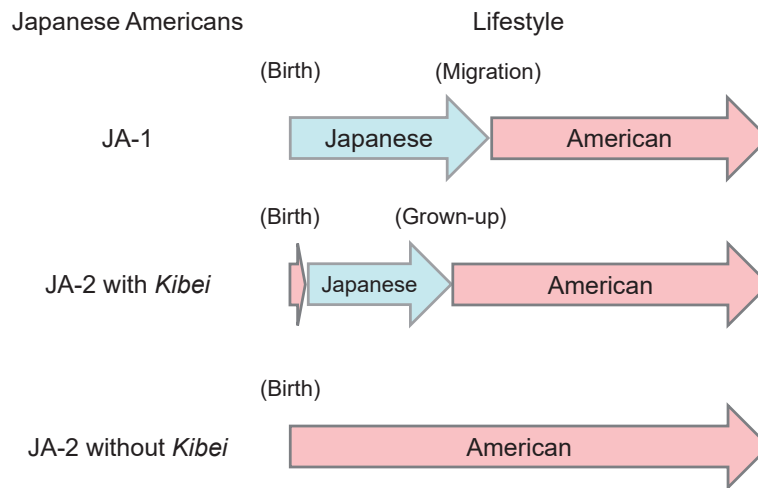


Fig. 6. What is “*Kibei*”?

Some second- or later-generation Japanese Americans (JA-2) were born in the United States, after which they stayed in Japan for some time during their childhood. They returned to the United States after receiving school education in Japan (JA-2 with *Kibei*).

experience as “*Kibei*” (meaning, “return to the United States” in Japanese). This *Kibei* subgroup spent a certain period of their childhood living a Japanese lifestyle and escaped from the American lifestyle.

4.1 Comparison of Carotid Atherosclerosis

In the 1998–2000 survey, after excluding Japanese Americans who were diagnosed with DM using OGTT, we compared the carotid artery IMTs in subjects with NGT and IGT in each generation, as well as in the JA-2 with and without *Kibei* subgroups (Fig. 7). In subjects with NGT and IGT, the IMT in the JA-2 without *Kibei* subgroup was significantly greater than that in the JA-1 and JA-2 with *Kibei* subgroups; the IMT in the JA-2 with *Kibei* subgroup was comparable with that in the JA-1 subgroup.

4.2 Comparison of the Prevalence of Obesity and DM

In the 2007–2010 survey, the Japanese American participants were divided into three subgroups (i.e., JA-1, JA-2 with *Kibei*, and JA-2 without *Kibei*). We compared the prevalence of obesity and DM in each subgroup with that in native Japanese (Fig. 8)⁵. The prevalence of obesity gradually increased in the order of native Japanese, JA-1, and JA-2 with *Kibei*; moreover, the prevalence in the JA-2 without *Kibei* subgroup was markedly higher at nearly 50%. Furthermore, the prevalence of DM was higher in Japanese Americans than in native Japanese. Although the highest prevalence was observed in the JA-2 without *Kibei* subgroup, the prevalence was almost comparable among the three Japanese American

subgroups.

The results of the cross-sectional analyses revealed that Japanese lifestyles during childhood, as in the case of the JA-1 and JA-2 with *Kibei* subgroups, could prevent better the development of obesity and DM and the progression of atherosclerosis compared with those living an American lifestyle since birth, as in the case of the JA-2 without *Kibei* subgroup. Thus, to prevent the development of lifestyle-related and atherosclerotic diseases in Japanese individuals, “dietary education,” especially the acquisition of Japanese-style dietary habits in childhood, may be important.

5. Transitions in the Progression of Atherosclerosis and Serum Lipid Levels between Native Japanese and Japanese Americans

5.1 Progression of Carotid Atherosclerosis according to Aging in 1998 and 2012

As shown in Fig. 9, we compared the age-related LOWESS regression lines of carotid artery IMT between native Japanese and Japanese Americans who were not treated for DM or dyslipidemia. In the 1998 survey, the LOWESS regression line of Japanese Americans was situated above that of native Japanese (Fig. 9A)⁶. Furthermore, Japanese Americans reached a carotid artery IMT of 1.1 mm, approximately 20 years earlier than native Japanese. These data demonstrated that atherosclerosis was more advanced in Japanese Americans than in native Japanese.

However, in the 2012 survey, despite the small

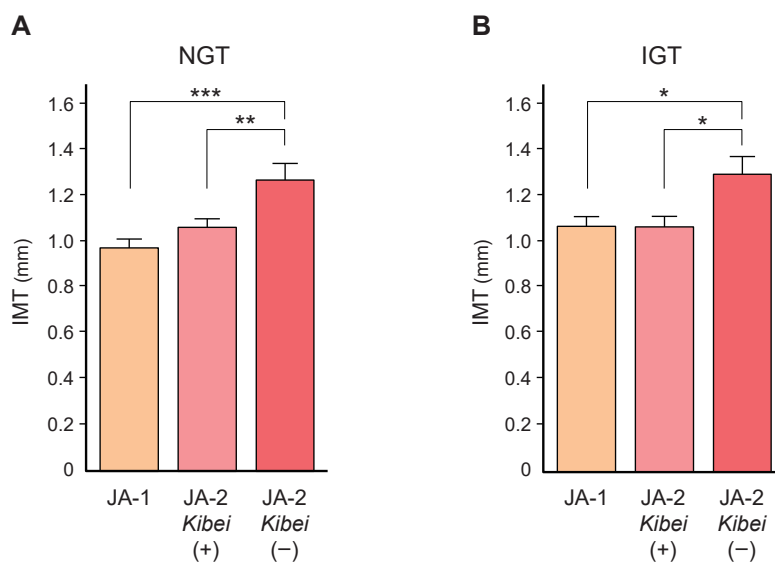


Fig. 7. Comparison of carotid artery intima-media wall thickness (IMT) in Japanese Americans with respect to generation and the presence or absence of *Kibei* experience in subjects with normal glucose tolerance (NGT) and impaired glucose tolerance (IGT)

Survey from 1998 to 2000

(A) NGT group ($n=527$): first-generation Japanese Americans (JA-1; $n=192$) and second- or later-generation Japanese Americans (JA-2) with the *Kibei* subgroup [*Kibei* (+); $n=111$] or without the *Kibei* subgroup [*Kibei* (-); $n=224$]

(B) IGT group ($n=118$): JA-1 ($n=49$) and JA-2 with the *Kibei* subgroup [*Kibei* (+); $n=39$] or without the *Kibei* subgroup [*Kibei* (-); $n=30$]

* $P<0.05$, ** $P<0.01$, *** $P<0.001$

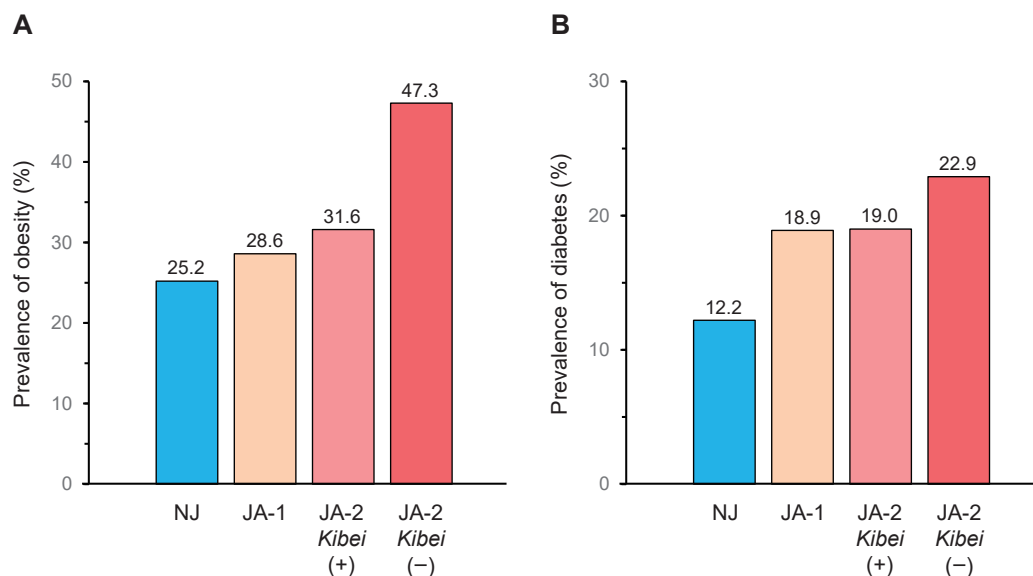


Fig. 8. Comparison of the prevalence of obesity (A) and diabetes mellitus (B) among native Japanese, first-generation Japanese Americans, and second- or later-generation Japanese Americans with or without *Kibei* (cited from reference 5)

Survey from 2007 to 2010

Native Japanese (NJ; $n=516$), first-generation Japanese Americans (JA-1; $n=444$), second- or later-generation Japanese Americans (JA-2) with the *Kibei* subgroup [*Kibei* (+); $n=79$] or without the *Kibei* subgroup [*Kibei* (-); $n=258$]

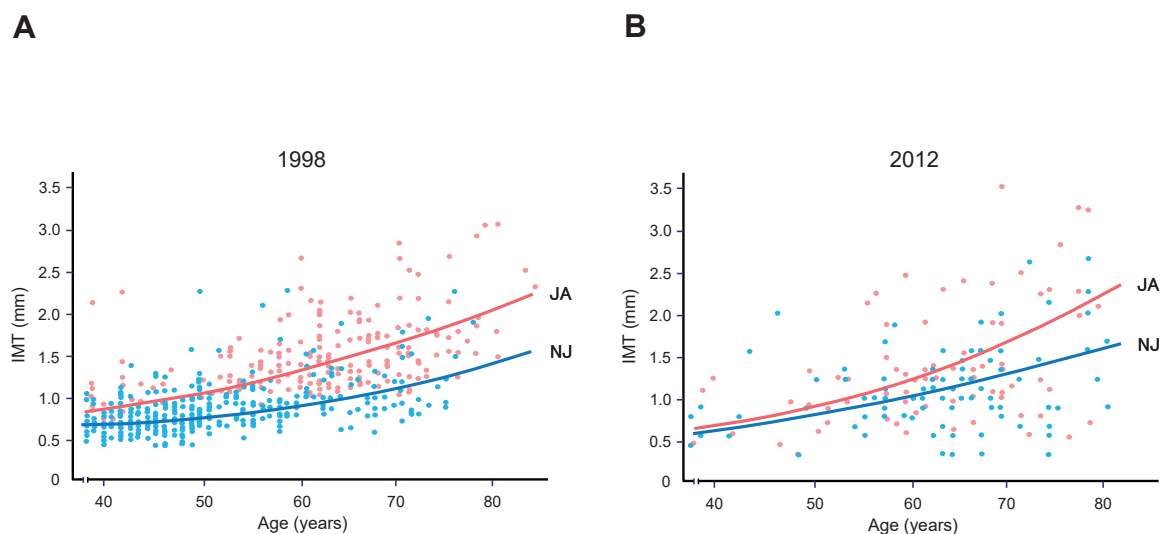


Fig. 9. Comparison of the association of age with carotid artery intima-media wall thickness (IMT) between native Japanese and Japanese Americans

(A) Survey in Hawaii in 1998 (cited from reference 6): native Japanese (NJ; $n=271$) and Japanese Americans (JA; $n=222$) excluding those on pharmacotherapy for diabetes mellitus (DM) or dyslipidemia

(B) Survey in Hawaii in 2012 (cited from reference 7): native Japanese (NJ; $n=115$) and Japanese Americans (JA; $n=112$) excluding those on pharmacotherapy for DM or dyslipidemia

LOWESS regression lines are shown.

number of subjects, the LOWESS regression lines of native Japanese and Japanese Americans were closer, mainly because of the elevation of the line of native Japanese (Fig. 9B)⁷. To investigate the cause of this change in the carotid artery IMT, we compared the nutrient intake. In the 2012 survey, the intake of Japanese Americans living in Hawaii consisted of 12.1% protein, 35.5% fat, and 52.4% carbohydrates, whereas the intake of native Japanese in the same year consisted of 14.5% protein, 26.4% fat, and 59.1% carbohydrates, which shows that Japanese Americans consumed a relatively high-fat diet.

5.2) Changes in Serum Lipid Levels

Fig. 10 shows changes in serum lipid levels over the past 30 years. Although the 1978–1988 survey showed significantly higher levels of serum total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), and triglyceride (TG) in Japanese Americans than in native Japanese², these differences were not noted in the 1998 survey^{6, 8}. However, serum TC and LDL-C levels in native Japanese were significantly higher than those in Japanese Americans in the 2012 survey⁷.

Furthermore, in the 1992–1995 survey, serum TC, LDL-C, and TG levels increased in the order of native Japanese, JA-1, and JA-2⁴. However, in the 2007–2010 survey, serum TC levels were significantly

lower in JA-2 than in JA-1 and native Japanese because the percentage of subjects undergoing treatment for dyslipidemia was significantly higher in JA-2 (37.4%) than in JA-1 (22.3%) and native Japanese (21.3%)⁵.

5.3) Intake of Trans Fatty Acids

Trans fatty acids are highly capable of inducing atherosclerosis. The use of trans fatty acids has been restricted in the State of California since July 2008. Thus, in the 2010 survey, we measured serum levels of elaidic acids, which are typical trans fatty acids, and found that serum elaidic acid levels in Japanese Americans living in Los Angeles were significantly higher than those in native Japanese⁹. However, the subsequent differences in the restrictions on the use of trans fatty acids between Japan and the United States might influence the changes in serum lipid levels and the progression of atherosclerosis in the near future.

Compared with JA-1, JA-2 who has fewer language barriers might procure useful information easily and receive appropriate treatment. These factors might have influenced the reversal of serum lipid levels in native Japanese and Japanese Americans, as observed in our recent surveys, and could contribute to the change in the age-related LOWESS regression lines of carotid artery IMT between the two Japanese populations.

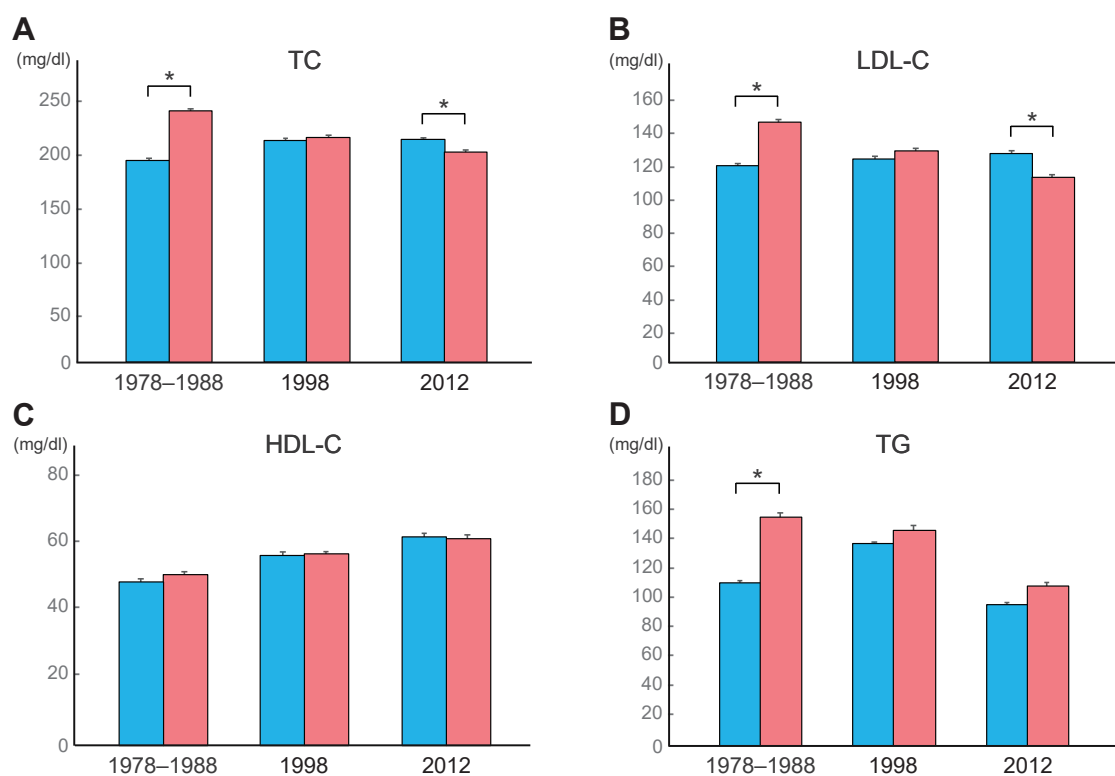


Fig. 10. Year-wise changes in serum lipid levels between native Japanese and Japanese Americans (cited from references 2, 6, and 7) (A) serum total cholesterol (TC), (B) low-density lipoprotein cholesterol (LDL-C), (C) high-density lipoprotein cholesterol (HDL-C), and (D) triglyceride (TG) levels
Blue column: native Japanese, pink column: Japanese Americans
* $P < 0.05$

6. Conclusions

Based on the results of this long-term medical survey comparing native Japanese and Japanese Americans (JA-1 and JA-2), we found that a westernized lifestyle induced the development of obesity, DM, hypertension, dyslipidemia, and the progression of atherosclerosis in association with the degree of westernization of the lifestyle among Japanese individuals.

A longer residence time in the United States could aggravate the risk factors and atherosclerosis, indicating “the negative acculturation effect”¹⁰⁾ among Japanese living in the United States. However, our recent survey results revealed that JA-2 who lived a more advanced westernized lifestyle had lower serum cholesterol levels, showing “the reverse negative acculturation.”

We also found that living in Japan during childhood impeded the progression of atherosclerosis in the JA-2 with *Kibei* subgroup. Thus, it is important to adopt and maintain the Japanese lifestyle from childhood to prevent the development of

atherosclerotic diseases.

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References

- 1) Kawate R, Yamakido M, Nishimoto Y, Bennett PH, Hamman RF, Knowler WC: Diabetes mellitus and its vascular complications in Japanese migrants on the Island of Hawaii. *Diabetes Care*, 1979; 2: 161-170
- 2) Egusa G, Murakami F, Ito C, Matsumoto Y, Kado S, Okamura M, Mori H, Yamane K, Hara H, Yamakido M: Westernized food habits and concentrations of serum lipids in the Japanese. *Atherosclerosis*, 1993; 100: 249-255

- 3) Yoneda M, Kobuke K: A 50-year history of the health impacts of Westernization on the lifestyle of Japanese Americans: A focus on the Hawaii-Los Angeles-Hiroshima Study. *J Diabetes Investig*, 2020; 11: 1382-1387
- 4) Egusa G, Watanabe H, Ohshita K, Fujikawa R, Yamane K, Okubo M, Kohno N: Influence of the extent of westernization of lifestyle on the progression of preclinical atherosclerosis in Japanese subjects. *J Atheroscler Thromb*, 2002; 9: 299-304
- 5) Shiwa M, Yoneda M, Nakanishi S, Oki K, Yamane K, Kohno N: Japanese lifestyle during childhood prevents the future development of obesity among Japanese-Americans. *PLoS One*, 2015; 10: e0120804
- 6) Watanabe H, Yamane K, Fujikawa R, Okubo M, Egusa G, Kohno N: Westernization of lifestyle markedly increases carotid intima-media wall thickness (IMT) in Japanese people. *Atherosclerosis*, 2003; 166: 67-72
- 7) Kubota M, Yoneda M, Watanabe H, Egusa G: Progression of Carotid Atherosclerosis in Two Japanese Populations with Different Lifestyles. *J Atheroscler Thromb*, 2017; 24: 1069-1074
- 8) Watanabe H, Yamane K, Egusa G, Kohno N: Influence of Westernization of Lifestyle on the Progression of IMT in Japanese. *J Atheroscler Thromb*, 2004; 11: 330-334
- 9) Itcho K, Yoshii Y, Ohno H, Oki K, Shinohara M, Irino Y, Toh R, Ishida T, Hirata KI, Yoneda M: Association between Serum Elaidic Acid Concentration and Insulin Resistance in Two Japanese Cohorts with Different Lifestyles. *J Atheroscler Thromb*, 2017; 24: 1206-1214
- 10) Ro A: The longer you stay, the worse your health? A critical review of the negative acculturation theory among Asian immigrants. *Int J Environ Res Public Health*, 2014; 11: 8038-8057