J Atheroscler Thromb, 2017; 24: 1206-1214.
http://doi.org/10.5551/jat.39164

Original Article

Association between Serum Elaidic Acid Concentration and Insulin Resistance in Two Japanese Cohorts with Different Lifestyles

Kiyotaka Itcho[1], Yoko Yoshii[1], Haruya Ohno[1], Kenji Oki[1], Masakazu Shinohara[3], Yasuhiro Irino[2], Ryuji Toh[2], Tatsuro Ishida[3], Ken-ichi Hirata[3] and Masayasu Yoneda[1]

[1]Department of Molecular and Internal Medicine, Graduate School of Biomedical and Health Sciences, Hiroshima University, Hiroshima, Japan
[2]Division of Evidence-Based Laboratory Medicine, Kobe University Graduate School of Medicine, Kobe, Japan
[3]Division of Cardiovascular Medicine, Department of Internal Medicine, Kobe University Graduate School of Medicine, Kobe, Japan

***Aim*: Many cohort studies have shown that increased trans fatty acid (TFA) intake increases the risk of developing coronary heart disease. However, whether TFA intake is directly associated with the development of diabetes mellitus (DM) remains unknown.**
***Methods*: We performed the 75-g oral glucose tolerance test in two Japanese cohorts: a cohort of 454 native Japanese living in Hiroshima, Japan, and a cohort of 426 Japanese-Americans living in Los Angeles, USA, who shared identical genetic predispositions but had different lifestyles. Serum elaidic acid concentration was measured and compared, and its association with insulin resistance was assessed.**
***Results*: Serum elaidic acid concentrations were significantly higher in the Japanese-Americans (median, 18.2 μmol/L) than in the native Japanese (median, 11.0 μmol/L). The serum elaidic acid concentrations in the native Japanese DM group (16.0 μmol/L) were significantly higher compared with those in the normal glucose tolerance (10.8 μmol/L) and impaired glucose tolerance (11.7 μmol/L) groups. Multiple linear regression analyses showed that serum elaidic acid concentrations were significantly positively associated with homeostasis model assessment for insulin resistance (HOMA-IR) values after adjusting for various factors.**
***Conclusions*: These results suggest that excessive TFA intake worsens insulin resistance and increases the risk of developing DM even in the native Japanese, whose intakes of animal fat and simple carbohydrates were presumed to be lower than those of the Japanese-Americans.**

See editorial vol. 24: 1199-1201

Key words: Trans fatty acid, Elaidic acid, Insulin resistance, Diabetes mellitus

Introduction

Trans fatty acids (TFAs) are a type of unsaturated fatty acid that contains double bonds in a trans configuration. Unsaturated fatty acids are classified into two forms, trans and cis, based on the orientation of the hydrogen atoms forming the double bonds; the majority of natural unsaturated fatty acids exist in the cis form. However, TFAs are produced from cis-unsaturated fatty acids by partial hydrogenation during the industrial process of manufacturing hydrogenated oil from vegetable oil. Hydrogenated oil manufactured by this process is widely used to produce margarine, shortening, and other products because of its commercial value and convenience.

Many cohort studies conducted in Europe and the United States have shown that increased TFA intake increases the risk of developing coronary heart disease[1-7]. However, whether TFA intake is directly

Address for correspondence: Masayasu Yoneda, Department of Molecular and Internal Medicine, Graduate School of Biomedical and Health Sciences, Hiroshima University, 1-2-3 Kasumi, Minami-ku, Hiroshima, 734-8551, Japan
E-mail: masayone17@hiroshima-u.ac.jp
Received: November 28, 2016
Accepted for publication: March 26, 2017

Table 1. Clinical characteristics of the study subjects

	Native Japanese	Japanese-Americans	*P* value
N (men/women)	454 (159/295)	426 (182/244)	
NGT/IGT/DM	341/97/16	323/70/33	
Age (years)	57.7 ± 15.1	59.4 ± 14.4	0.089
BMI	22.8 ± 3.0	22.3 ± 3.7	0.018
SBP (mmHg)	126 ± 18	131 ± 18	< 0.001
DBP (mmHg)	77 ± 11	82 ± 11	< 0.001
FSG (mg/dL)	93.0 ± 9.6	90.3 ± 11.6	< 0.001
2-h SG (mg/dL)	121.3 ± 36.2	118.1 ± 45.6	0.262
FIRI † (μU/mL)	3.89 (3.16-5.55)	4.76 (3.49-8.66)	< 0.001
2-h IRI † (μU/mL)	42.18 (27.24-64.92)	50.72 (29.43-80.25)	0.007
HOMA-IR †	0.89 (0.71-1.28)	1.07 (0.74-2.02)	< 0.001
HOMA-β †	52.0 (40.3-75.5)	77.7 (51.6-120.0)	< 0.001
TG † (mg/dL)	86.5 (62.0-120.0)	108.5 (75.8-150.3)	< 0.001
HDL-C (mg/dL)	62.5 ± 14.2	61.2 ± 16.1	0.195
LDL-C (mg/dL)	126.6 ± 31.6	129.0 ± 36.2	0.289
Elaidic acid † (μmol/L)	11.0 (9.5-13.5)	18.2 (14.1-24.5)	< 0.001

Data are expressed as the means ± SD, median (interquartile range) or number. † Parameters were transformed logarithmically before analysis. *P* values were calculated by *t*-test. DBP, Diastolic blood pressure; DM, Diabetes mellitus; FIRI, Fasting immunoreactive insulin; FSG, Fasting serum glucose; HDL-C, high-density lipoprotein-cholesterol; HOMA-IR, Homeostasis model assessment of insulin resistance; HOMA-β, Homeostasis model assessment of β-cell function; IGT, Impaired glucose tolerance; LDL-C, low-density lipoprotein-cholesterol; NGT, Normal glucose tolerance; SBP, Systolic blood pressure; TG, Triglyceride; 2-h IRI, Immunoreactive insulin at two hours after an oral glucose load; 2-h SG, Serum glucose at two hours after an oral glucose load.

associated with the development of diabetes mellitus (DM) remains unknown. Although four long-term observational studies on the association between the development of DM and TFA intake have been reported, the results vary[8-11]. Short-term interventional studies in humans have demonstrated no significant changes in glucose tolerance or insulin resistance in healthy adults consuming TFAs[12-14], whereas TFA intake adversely affected insulin resistance in obese adults with a history of DM[15]. In other words, the results of these studies suggest that TFA intake may aggravate insulin resistance in certain types of individuals.

The World Health Organization (WHO) recommends a mean TFA intake of less than 1% of the total energy intake[16]. Europe and the United States, where significant amounts of TFAs are consumed, have started restricting the use of TFAs because of their potential to cause arteriosclerotic diseases. In California, USA, the use of oil, shortening, or margarine containing artificial TFAs within a food facility has been banned since 2010. In contrast, no food containing TFAs are regulated in Japan, where TFA intake is reportedly less. However, a recent report indicated that the estimated TFA intake by some groups of Japanese, mainly young adults living in cities, exceeded the amount recommended by the WHO[17].

In 1970, we started an epidemiological study targeting Japanese-Americans, titled the Hawaii-Los Angeles-Hiroshima Study, and conducted medical surveys in Hawaii and Los Angeles every few years, totaling 24 surveys until 2015. Comparing the native Japanese in Hiroshima, Japan with a Japanese lifestyle and Japanese-Americans in the United States with an American lifestyle and who shared identical genetic predispositions, we have reported that the prevalence rates of obesity, type 2 DM, and metabolic syndrome are significantly higher in the Japanese-Americans than in the native Japanese[18-21]. However, as observed globally, the prevalence of DM in Japan has been increasing in recent years, suggesting that even the eating habits of native Japanese are increasingly becoming westernized.

Aim

After observing increased TFA intake in Japan, we compared the concentrations of serum elaidic acid, which is most commonly found in processed food among the many subtypes of TFAs, in the native Japanese living in Hiroshima and the Japanese-Americans living in Los Angeles, California, using a 2010 medical survey. Then, we investigated the association between serum elaidic acid concentrations and insulin resistance.

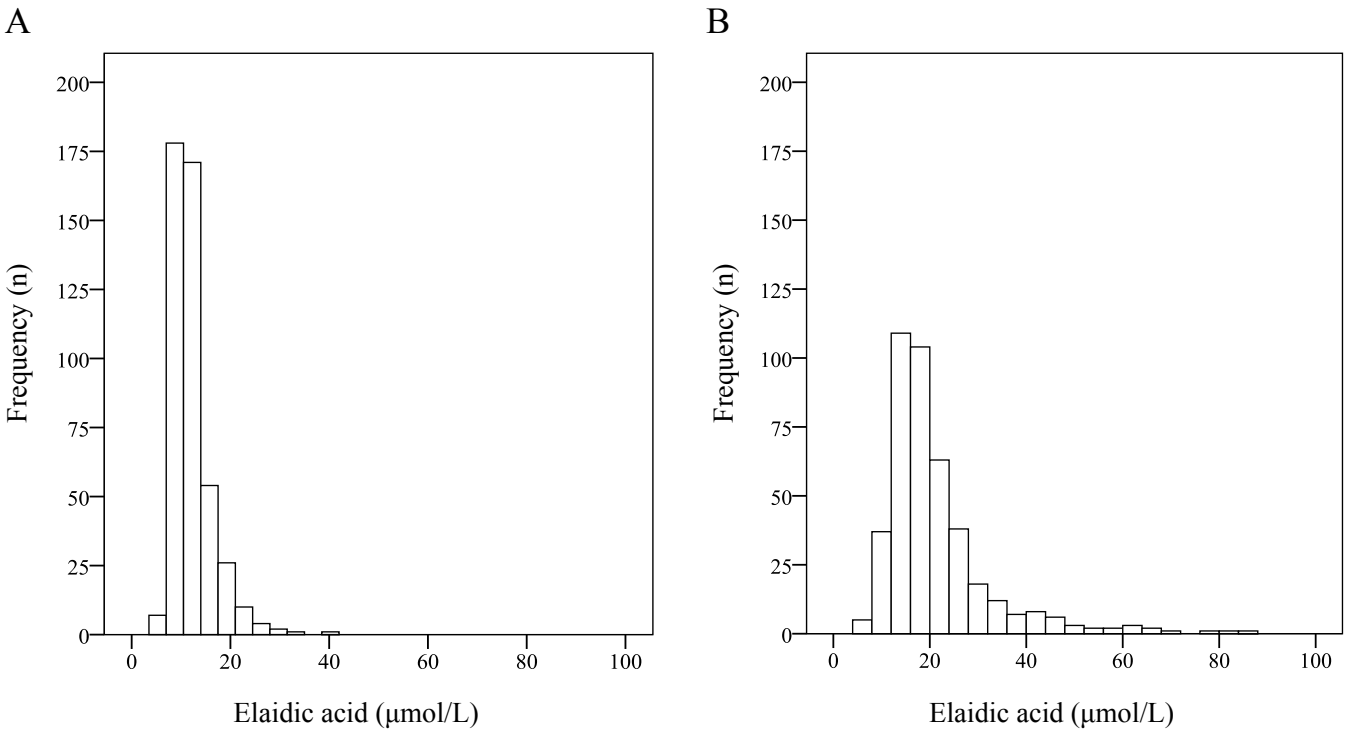


Fig. 1. Distribution of serum elaidic acid concentrations in 454 native Japanese (A) and 426 Japanese-Americans (B).

Methods

Research Design and Methods

This study was a cross-sectional analysis of data collected as part of the Hawaii-Los Angeles-Hiroshima Study. Our study included 552 native Japanese living in Hiroshima who underwent a medical checkup in 2009 and 608 Japanese-Americans living in Los Angeles who underwent a medical checkup in 2010. All participants, except for those under treatment for DM, underwent a 75-g oral glucose tolerance test (OGTT) and were divided according to OGTT results into the following three groups: normal glucose tolerance (NGT), impaired glucose tolerance (IGT), and DM. NGT was defined as a fasting serum glucose level of <110 mg/dl and a serum glucose level of <140 mg/dl at 2 h after OGTT. DM was defined as a fasting serum glucose level of ≥ 126 mg/dl and/or a serum glucose level of ≥ 200 mg/dl at 2 h after OGTT or as treatment of previously diagnosed diabetes. IGT was diagnosed in participants who did not meet the criteria of either NGT or DM[22]. After excluding the participants under treatment for dyslipidemia and those with a fasting serum glucose levels ≥ 140 mg/dl, 454 native Japanese and 426 Japanese-Americans were ultimately included in this study. All participants received an explanation of the study procedures and provided written informed consent. This study was approved by the ethics committee of Hiroshima University.

Biochemical Analysis

Blood samples were collected from all participants after overnight fasting, and serum samples were stored at -80℃ until analysis. Serum glucose was measured using the hexokinase method. Immunoreactive insulin (IRI) levels were measured using the double-antibody radioimmunoassay. Homeostasis model assessment was used to estimate β-cell function (HOMA-β) and insulin resistance (HOMA-IR)[23]. Triglyceride (TG) levels were measured using an enzymatic method. High-density lipoprotein-cholesterol (HDL-C) and low-density lipoprotein-cholesterol (LDL-C) were measured using a homogeneous assay (MetaboLead HDL-C and Determiner L LDL-C, respectively, Kyowa Medex, Tokyo, Japan).

Measurement of Serum Elaidic Acid Concentrations

Elaidic acid concentrations were measured by gas chromatography/mass spectrometry (GC−MS QP2010; Shimadzu, Kyoto, Japan) at the Integrated Center for Mass Spectrometry at Kobe University Graduate School of Medicine, according to a previously reported procedure[24].

Statistical Analysis

Data were expressed as means with standard devi-

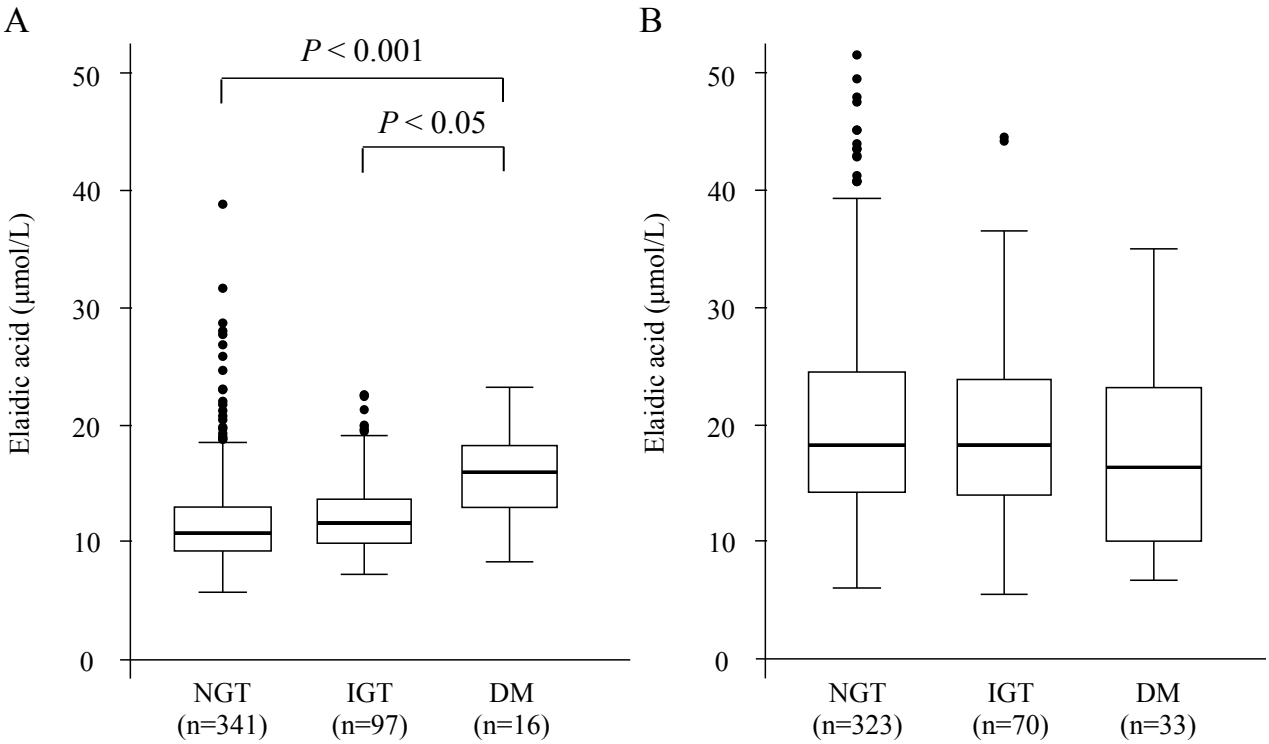


Fig. 2. Comparisons of serum elaidic acid concentrations by glucose tolerance status in native Japanese (A) and Japanese-Americans (B). Parameters were transformed logarithmically before analysis. Statistical analyses were performed by ANOVA followed by Bonferroni's test for multiple comparisons.

ation or as medians (25th−75th percentiles) depending on the data distribution. Parameters with a skewed distribution were logarithmically transformed before analysis. This transformation was performed for fasting IRI (FIRI), IRI at 2 h after an oral glucose load (2-h IRI), HOMA-IR, HOMA-β, TG, and elaidic acid measurements. The differences in parameters between two groups were analyzed by unpaired *t*-tests, while the differences in parameters between three groups were analyzed by the one-way analysis of variance (ANOVA). The correlation between elaidic acid concentration and each parameter was assessed by Pearson's coefficient. Furthermore, regression analyses were performed to assess the associations between HOMA-IR and each metabolic parameter. In regression analyses, glucose tolerance was considered a categorical variable. *P* values of <0.05 were considered to indicate statistical significance. IBM SPSS Statistics, version 24.0 (IBM Corp., Armonk, NY) was used for the analyses.

Results

The characteristics of the study participants are shown in **Table 1**. No significant difference was observed in age between the two cohorts. Systolic blood pressure (SBP) and diastolic blood pressure (DBP) were significantly higher in the Japanese-Americans. Body mass index (BMI) and fasting serum glucose levels were higher in the native Japanese, whereas FIRI, 2-h IRI, HOMA-IR, HOMA-β, and TG levels were significantly higher in the Japanese-Americans. The median serum elaidic acid concentrations were 11.0 μmol/L in the native Japanese and 18.2 μmol/L in the Japanese-Americans, significantly higher in the Japanese-Americans than in the native Japanese. The distribution of serum elaidic acid concentrations showed that the concentrations in the Japanese-Americans tended to be higher overall and more varied compared with those of the native Japanese (**Fig. 1**).

Next, serum elaidic acid concentrations were analyzed according to glucose tolerance status (**Fig. 2**). In the native Japanese, the median serum elaidic acid concentrations were 10.8, 11.7, and 16.0 μmol/L in the NGT, IGT, and DM groups, respectively, a significantly higher median in the DM group than in the other groups. However, the median serum elaidic acid concentrations in the Japanese-Americans were 18.4, 18.4, and 16.3 μmol/L in the NGT, IGT, and DM groups, respectively, with no significant differences between the three groups.

The associations between insulin resistance and

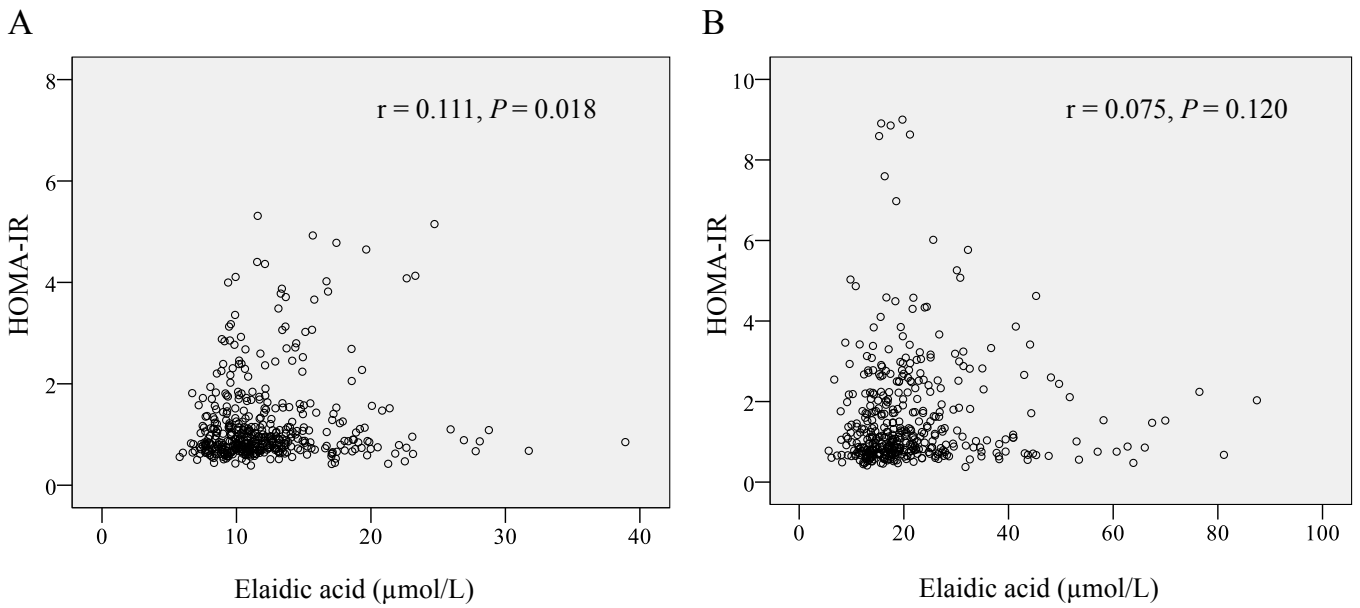


Fig. 3. Correlations of serum elaidic acid concentrations and HOMA-IR in 454 native Japanese (A) and 426 Japanese-Americans (B). Parameters were transformed logarithmically before analysis. Pearson's correlation coefficients (*r*) and *P* values are given.

serum elaidic acid concentrations were also assessed. Although a significant positive correlation was observed between HOMA-IR values and serum elaidic acid concentrations in the native Japanese, no significant correlation was observed in the Japanese-Americans (**Fig. 3**).

To closely evaluate the associations between insulin resistance and serum elaidic acid concentrations in the native Japanese, simple linear regression analyses were performed on the association between HOMA-IR values and each metabolic parameter (**Table 2**). BMI, SBP, DBP, LDL-C, TG, and serum elaidic acid concentrations were significantly positively associated with HOMA-IR values, whereas sex and HDL-C levels were significantly negatively associated with these values. Furthermore, multiple linear regression analyses showed a significant positive association between serum elaidic acid concentrations and HOMA-IR values after adjustment for sex, age, BMI, SBP, DBP, glucose tolerance, HDL-C, and LDL-C levels; however, no significant association was observed after adjustment for TG levels (**Table 3**).

Table 2. Relationships between HOMA-IR and other parameters in native Japanese

	β	*P* value
Age (years)	−0.019	0.693
Sex	−0.150	0.001
BMI	0.504	<0.001
SBP (mmHg)	0.159	0.001
DBP (mmHg)	0.285	<0.001
TG † (mg/dL)	0.355	<0.001
HDL-C (mg/dL)	−0.291	<0.001
LDL-C (mg/dL)	0.164	<0.001
Elaidic acid † (μmol/L)	0.111	0.018

β, Standardizes regression coefficients. † Parameters were transformed logarithmically before analysis. Data were analyzed by a simple linear regression analysis.

Discussion

In this study, we first revealed that in a 2010 survey, the absolute serum elaidic acid concentrations differed significantly between native Japanese living in Japan and Japanese-Americans living in the United States, who shared identical genetic predispositions but had different lifestyles. Furthermore, the DM group had higher concentrations even in the native Japanese whose serum elaidic acid concentrations were lower compared with those of the Japanese-Americans; the native Japanese showed an independent positive association between concentration and insulin resistance.

Although two of the four prospective studies showed no significant association between TFA intake and the incidence of DM[9, 10], another study that followed 84,204 female nurses for 14 years showed a significant association[8]. In these three studies, the total TFA intake was estimated based on the results of dietary surveys. The different results may have reflected errors in the estimation of TFA intake or variations in

Table 3. Relationships of serum elaidic acid concentrations in native Japanese by regression analysis with HOMA-IR as the dependent variable

	β	*P* value
Not adjusted	0.111	0.018
Adjusted for age, sex	0.131	0.006
Adjusted for age, sex, and BMI	0.089	0.033
Adjusted for age, sex, and SBP	0.135	0.004
Adjusted for age, sex, and DBP	0.108	0.019
Adjusted for age, sex, and NGT/IGT/DM	0.113	0.018
Adjusted for age, sex, and HDL-C	0.114	0.014
Adjusted for age, sex, and LDL-C	0.100	0.036
Adjusted for age, sex, and TG †	−0.031	0.538

β, Standardized regression coefficients. † Parameters were transformed logarithmically before analysis. Data were analyzed by each multiple regression model.

TFA intake during the follow-up period. Wang *et al.* assessed the association between TFA intake and the incidence of DM while simultaneously estimating the intake of each TFA subtype and measuring blood TFA concentrations to complement these limitations. They reported that blood concentrations of t-16:1n9 and t-18:1 (elaidic acid) TFAs were significantly positively correlated with the incidence of DM[11]. However, blood TFA concentrations were analyzed as a ratio to blood total fatty acid concentration. Because this ratio is affected by other intrinsic fatty acids, Wang *et al.* recommended additional studies using absolute blood TFA concentrations, which may more accurately reflect TFA intake. In the present study, we measured absolute serum concentrations of elaidic acid among TFA subtypes and observed significantly lower concentrations in native Japanese living in Hiroshima than those in Japanese-Americans living in Los Angeles. Because TFAs are not intrinsically synthesized, serum TFA concentrations seem to reflect dietary intake. Presumably, great differences in lifestyles, especially the contents of meals, still existed between Japan and the United States in 2010.

Next, we demonstrated that the DM group of the native Japanese cohort had serum elaidic acid concentrations as high as those observed in the Japanese-Americans. Furthermore, this study revealed that serum elaidic acid concentrations were significantly positively associated with HOMA-IR values in the native Japanese. These results suggested that excessive TFA intake might be one of the factors that worsen insulin resistance in this population. Although the mechanism of how TFAs aggravate insulin resistance remains unknown in many aspects, studies with animal models reported the following. A study in rats indicated that the consumption of a high-TFA diet weakens insulin sensitivity in adipocytes, changes the adipocyte plasma membrane fatty acid composition and fluidity[25], increases the expression of resistin messenger RNA, and decreases the expression of peroxisome proliferator-activated receptor γ and lipoprotein lipase messenger RNA[26]. Moreover, excessive TFA intake in mice also reportedly increases the expression of genes associated with lipogenesis in the liver, including those for sterol regulatory element-binding proteins, consequently inducing insulin resistance and fatty liver[27].

However, there were no significant differences in serum elaidic acid concentrations between the NGT, IGT, and DM groups in the Japanese-Americans. Moreover, no significant correlations between serum elaidic acid concentrations and HOMA-IR values were observed in the Japanese-Americans. The HOMA-IR values of the IGT and DM groups were significantly higher than those of the NGT group in the Japanese-Americans (**Supplemental Fig. 1**). This result indicates that the worsening of insulin resistance is an important factor for the development of DM in Japanese-Americans. We previously reported that Japanese-Americans have higher insulin resistance than native Japanese[19] and that the intakes of animal fat and simple carbohydrates were markedly higher in Japanese-Americans than in native Japanese[28, 29]. Accordingly, the effect of TFA intake on the development of DM is presumed to be relatively greater in native Japanese whose intake of animal fat and simple carbohydrates are lower compared with that of Japanese-Americans.

This study has several limitations. First, in the native Japanese, an independent significant positive association was observed between serum elaidic acid concentrations and HOMA-IR values, but this association was not observed after adjusting for TG levels. A possible reason for this may be that, because fatty acid is a major component of TG, an increase in TG leads to an increase in total fatty acids, including elaidic

acid. In fact, a regression model showed a linear association between TG and elaidic acid (data not shown). Second, this study is a cross-sectional study that was conducted in 2010, and data were collected from Japanese-Americans living in Los Angeles when the partial regulation on TFAs was implemented in California. Further studies are needed to collect data on serum elaidic acid concentrations in Japanese-Americans under the current regulations.

Conclusion

The results of the present study demonstrated that serum elaidic acid concentrations in the native Japanese were significantly lower compared with those in the Japanese-Americans living in the United States and observed an independent significant positive association between serum elaidic acid concentrations and HOMA-IR values in the native Japanese. In the native Japanese, TFA intake may have aggravated insulin resistance and increased the risk of developing DM. Similar to the United States, regulation of TFAs may also become an important policy for the future prevention of DM in Japan.

Acknowledgments

This work was supported by the members of the Hiroshima Kenjin-kai Association of Southern California.

Funding Disclosure

The authors received no specific funding for this article.

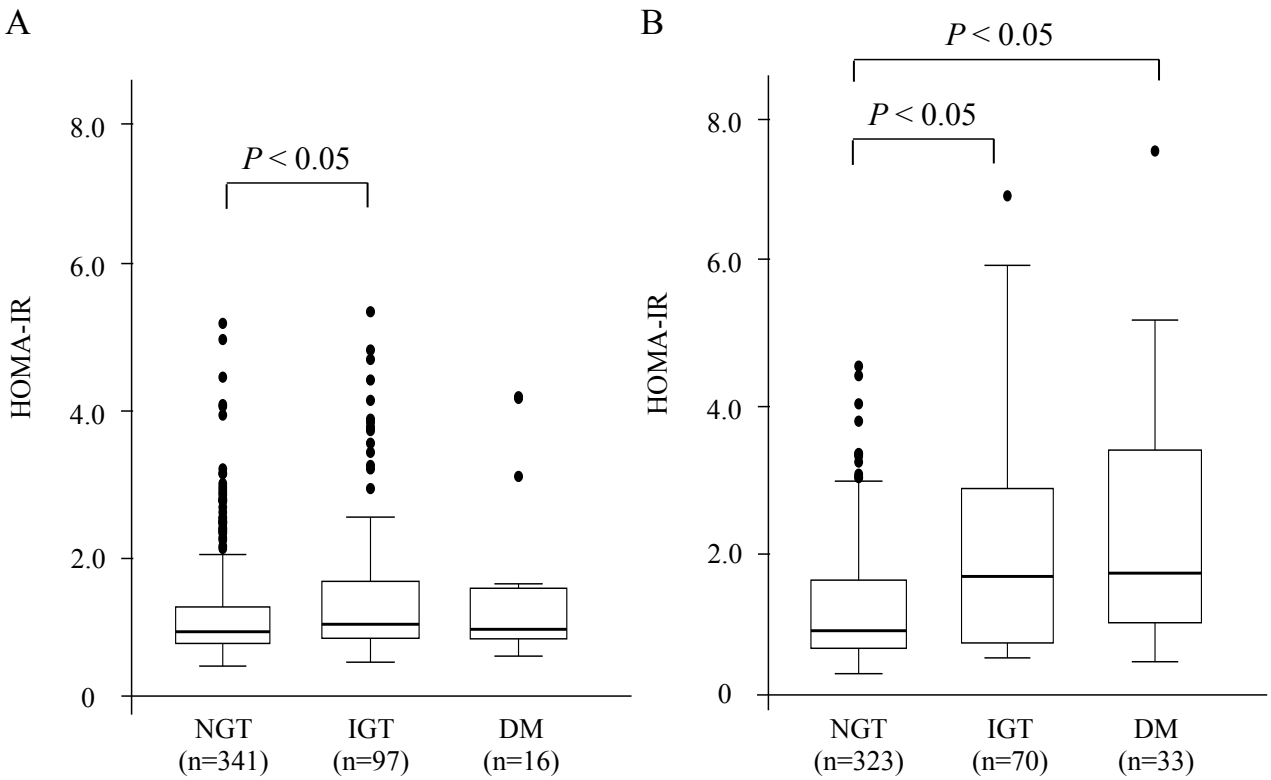
Conflicts of Interest

None.

References

1) Oh K, Hu FB, Manson JE, Stampfer MJ, Willett WC: Dietary fat intake and risk of coronary heart disease in women: 20 years of follow-up of the nurses' health study. Am J Epidemiol, 2005; 161: 672-679
2) Ascherio A, Rimm EB, Giovannucci EL, Spiegelman D, Stampfer M, Willett WC: Dietary fat and risk of coronary heart disease in men: cohort follow up study in the United States. BMJ, 1996; 313: 84-90
3) Pietinen P, Ascherio A, Korhonen P, Hartman AM, Willett WC, Albanes D, Virtamo J: Intake of fatty acids and risk of coronary heart disease in a cohort of Finnish men. The Alpha-Tocopherol, Beta-Carotene Cancer Prevention Study. Am J Epidemiol, 1997; 145: 876-887
4) Oomen CM, Ocké MC, Feskens EJ, van Erp-Baart MA, Kok FJ, Kromhout D: Association between trans fatty acid intake and 10-year risk of coronary heart disease in the Zutphen Elderly Study: a prospective population-based study. Lancet Lond Engl, 2001; 357: 746-751
5) Aro A, Kardinaal AF, Salminen I, Kark JD, Riemersma RA, Delgado-Rodriguez M, Gomez-Aracena J, Huttunen JK, Kohlmeier L, Martin BC: Adipose tissue isomeric trans fatty acids and risk of myocardial infarction in nine countries: the EURAMIC study. Lancet Lond Engl, 1995; 345: 273-278
6) Baylin A, Kabagambe EK, Ascherio A, Spiegelman D, Campos H: High 18: 2 trans-fatty acids in adipose tissue are associated with increased risk of nonfatal acute myocardial infarction in costa rican adults. J Nutr, 2003; 133: 1186-1191
7) Clifton PM, Keogh JB, Noakes M: Trans fatty acids in adipose tissue and the food supply are associated with myocardial infarction. J Nutr, 2004; 134: 874-879
8) Salmerón J, Hu FB, Manson JE, Stampfer MJ, Colditz GA, Rimm EB, Willett WC: Dietary fat intake and risk of type 2 diabetes in women. Am J Clin Nutr, 2001; 73: 1019-1026
9) van Dam RM, Willett WC, Rimm EB, Stampfer MJ, Hu FB: Dietary fat and meat intake in relation to risk of type 2 diabetes in men. Diabetes Care, 2002; 25: 417-424
10) Meyer KA, Kushi LH, Jacobs DR, Folsom AR: Dietary fat and incidence of type 2 diabetes in older Iowa women. Diabetes Care, 2001; 24: 1528-1535
11) Wang Q, Imamura F, Ma W, Wang M, Lemaitre RN, King IB, Song X, Biggs ML, Delaney JA, Mukamal KJ, Djousse L, Siscovick DS, Mozaffarian D: Circulating and dietary trans fatty acids and incident type 2 diabetes in older adults: the Cardiovascular Health Study. Diabetes Care, 2015; 38: 1099-1107
12) Tardy A-L, Lambert-Porcheron S, Malpuech-Brugère C, Giraudet C, Rigaudière J-P, Laillet B, Leruyet P, Peyraud JL, Boirie Y, Laville M, Michalski MC, Chardigny JM, Morio B: Dairy and industrial sources of trans fat do not impair peripheral insulin sensitivity in overweight women. Am J Clin Nutr, 2009; 90: 88-94
13) Lovejoy JC, Smith SR, Champagne CM, Most MM, Lefevre M, DeLany JP, Denkins YM, Rood JC, Veldhuis J, Bray GA: Effects of diets enriched in saturated (palmitic), monounsaturated (oleic), or trans (elaidic) fatty acids on insulin sensitivity and substrate oxidation in healthy adults. Diabetes Care, 2002; 25: 1283-1288
14) Louheranta AM, Turpeinen AK, Vidgren HM, Schwab US, Uusitupa MI: A high-trans fatty acid diet and insulin sensitivity in young healthy women. Metabolism, 1999; 48: 870-875
15) Christiansen E, Schnider S, Palmvig B, Tauber-Lassen E, Pedersen O: Intake of a diet high in trans monounsaturated fatty acids or saturated fatty acids. Effects on postprandial insulinemia and glycemia in obese patients with NIDDM. Diabetes Care, 1997; 20: 881-887
16) Uauy R, Aro A, Clarke R, Ghafoorunissa, L'Abbé MR, Mozaffarian D, Skeaff CM, Stender S, Tavella M: WHO Scientific Update on trans fatty acids: summary and conclusions. Eur J Clin Nutr, 2009; 63: 68-75
17) Yamada M, Sasaki S, Murakami K, Takahashi Y, Okubo

H, Hirota N, Notsu A, Todoriki H, Miura A, Fukui M, Date C: Estimation of trans fatty acid intake in Japanese adults using 16-day diet records based on a food composition database developed for the Japanese population. J Epidemiol, 2010; 20: 119-127
18) Hara H, Egusa G, Yamakido M, Kawate R: The high prevalence of diabetes mellitus and hyperinsulinemia among the Japanese-Americans living in Hawaii and Los Angeles. Diabetes Res Clin Pract, 1994; 24: S37-S42
19) Nakanishi S, Okubo M, Yoneda M, Jitsuiki K, Yamane K, Kohno N: A comparison between Japanese-Americans living in Hawaii and Los Angeles and native Japanese: the impact of lifestyle westernization on diabetes mellitus. Biomed Pharmacother, 2004; 58: 571-577
20) Yoneda M, Yamane K, Jitsuiki K, Nakanishi S, Kamei N, Watanabe H, Kohno N: Prevalence of metabolic syndrome compared between native Japanese and Japanese-Americans. Diabetes Res Clin Pract, 2008; 79: 518-522
21) 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
22) Committee of the Japan Diabetes Society on the Diagnostic Criteria of Diabetes Mellitus, Seino Y, Nanjo K, Tajima N, Kadowaki T, Kashiwagi A, Araki E, Ito C, Inagaki N, Iwamoto Y, Kasuga M, Hanafusa T, Haneda M, Ueki K: Report of the committee on the classification and diagnostic criteria of diabetes mellitus. J Diabetes Investig, 2010; 1: 212-228
23) Matthews DR, Hosker JP, Rudenski AS, Naylor BA, Treacher DF, Turner RC: Homeostasis model assessment: insulin resistance and beta-cell function from fasting plasma glucose and insulin concentrations in man. Diabetologia, 1985; 28: 412-419
24) Mori K, Ishida T, Yasuda T, Hasokawa M, Monguchi T, Sasaki M, Kondo K, Nakajima H, Shinohara M, Shinke T, Irino Y, Toh R, Nishimura K, Hirata K: Serum trans-fatty acid concentration is elevated in young patients with coronary artery disease in Japan. Circ J, 2015; 79: 2017-2025
25) Ibrahim A, Natrajan S, Ghafoorunissa R: Dietary trans-fatty acids alter adipocyte plasma membrane fatty acid composition and insulin sensitivity in rats. Metabolism, 2005; 54: 240-246
26) Saravanan N, Haseeb A, Ehtesham NZ, Ghafoorunissa: Differential effects of dietary saturated and trans-fatty acids on expression of genes associated with insulin sensitivity in rat adipose tissue. Eur J Endocrinol, 2005; 153: 159-165
27) Obara N, Fukushima K, Ueno Y, Wakui Y, Kimura O, Tamai K, Kakazu E, Inoue J, Kondo Y, Ogawa N, Sato K, Tsuduki T, Ishida K, Shimosegawa T: Possible involvement and the mechanisms of excess trans-fatty acid consumption in severe NAFLD in mice. J Hepatol, 2010; 53: 326-334
28) 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
29) Egusa G, Yamane K: Lifestyle, serum lipids and coronary artery disease: comparison of Japan with the United States. J Atheroscler Thromb, 2004; 11: 304-312



Supplemental Fig. 1. Comparison of HOMA-IR by glucose tolerance in native Japanese (A) and Japanese-Americans (B). Parameters were transformed logarithmically before analysis. Statistical analyses were performed by ANOVA followed by Bonferroni's test for multiple comparisons.