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Roles of Trans and ω Fatty Acids in Health; Special References to Their Differences between Japanese and American Old Men

Akikazu Takada, Fumiko Shimizu and Shinji Koba

Abstract

Omega and trans-fatty acids play important roles in atherogenesis of vascular system. In this review, we discuss such roles in health; there are much differences in coronary heart disease (CHD) rates between the US and Japan. Fatty acids profiles in the plasma are related to risks of CHD. There have been few studies that compared plasma levels of fatty acids, including trans-fatty acids, in people in Japan and the US. Plasma levels of long-chain omega-3 fatty acids (docosahexaenoic acid [DHA] and eicosapentaenoic acid [EPA]) were higher in Japanese men, and omega-6 fatty acids (e.g., arachidonic acid [AA]) were lower compared with American men. American people had higher plasma levels of the major industrially produced trans-fatty acids (IP-TFAs; elaidic and inoelaidic acids), and levels of the potentially cardioprotective, primarily ruminant-derived trans-fatty acid, palmitoelaidic acid (POA) were higher in Japanese men. Plasma levels of saturated or monounsaturated fatty acids were also higher in American men. Only intakes of preference drinks have significant correlation with plasma levels of palmitoelaidic acid and linoelaidic acid. The higher levels of DHA and EPA, along with the lower levels of the IP-TFAs, are consistent with the markedly lower risk for coronary heart disease in Japan vs. the US.

Keywords: trans-fatty acids, omega fatty acids, lipid, DHA, EPA, arachidonic acid, palmitoelaidic acid, elaidic acid, linoelaidic acid, food, protein, carbohydrate, preference drink, coffee, tea, cholesterol, GRP120, insulin, GLP-1

1. Introduction

Coronary heart disease (CHD) is the leading cause of death worldwide, and certain dietary fatty acids (FAs) are known to play an important role in CHD risk [1]. It has been reported that higher intakes of industrially produced trans-fatty acids (IP-TFA) [2] and of saturated fatty acids (SFAs) are associated with increased risk for CHD [3, 4] and that higher intakes of both the omega-6 (n-6) polyunsaturated fatty acids (PUFAs) and the omega-3 PUFAs are associated with lower risk of CHD [5, 6]. Intakes of the PUFAs (especially the omega-3 class) and IP-TFAs are considered to be biomarkers strongly

linked to risks. Because risk for CHD is much lower in Japan than in the US [7], we tried to compare the FA profiles in Japanese and American men over the age of 50.

1.1 Configurations of trans-fatty acids and their origins

Trans-fatty acids have at least one double bond in the trans configuration and formed during partial hydrogenation of vegetable oils. This process is used for the conversion of vegetable oils to semisolid fats used for margarines.

Most of trans-fatty acids isomers are monosaturated with carbon number 18 (trans type octadecenoic acid (t-C18:1)). Trans type octadecenoic acids contained in foods are classified 13 isomers depending upon the location of the double bond (**Figure 1**). These trans isomers are produced industrially or naturally. The largest amounts of industrially produced trans-fatty acids are elaidic acids (t9-C18:1) and those of naturally produced forms are vaccenic acid (t11-C18:1) [8].

In the cis forms of fatty acids, hydrogen atoms are present on the same side of the bond, which causes a bend in the fatty acid chain, whereas the trans form has hydrogen atoms in the opposite sides of the chain, which straightens the fatty acid chain (upper figure). There are many isomers in carbon 18 fatty acids. Elaidic acid has the double bond at the ninth carbon atom (t9-18:1). Oleic acid has the double bond at the same location (c9-18:1). Partially hydrogenated oils contain mixture of isomers in which the trans form may be detected anywhere between the 4th and 14th carbon. Smaller amounts of isomers with a second trans double bond (trans,trans-18:2) are also present.

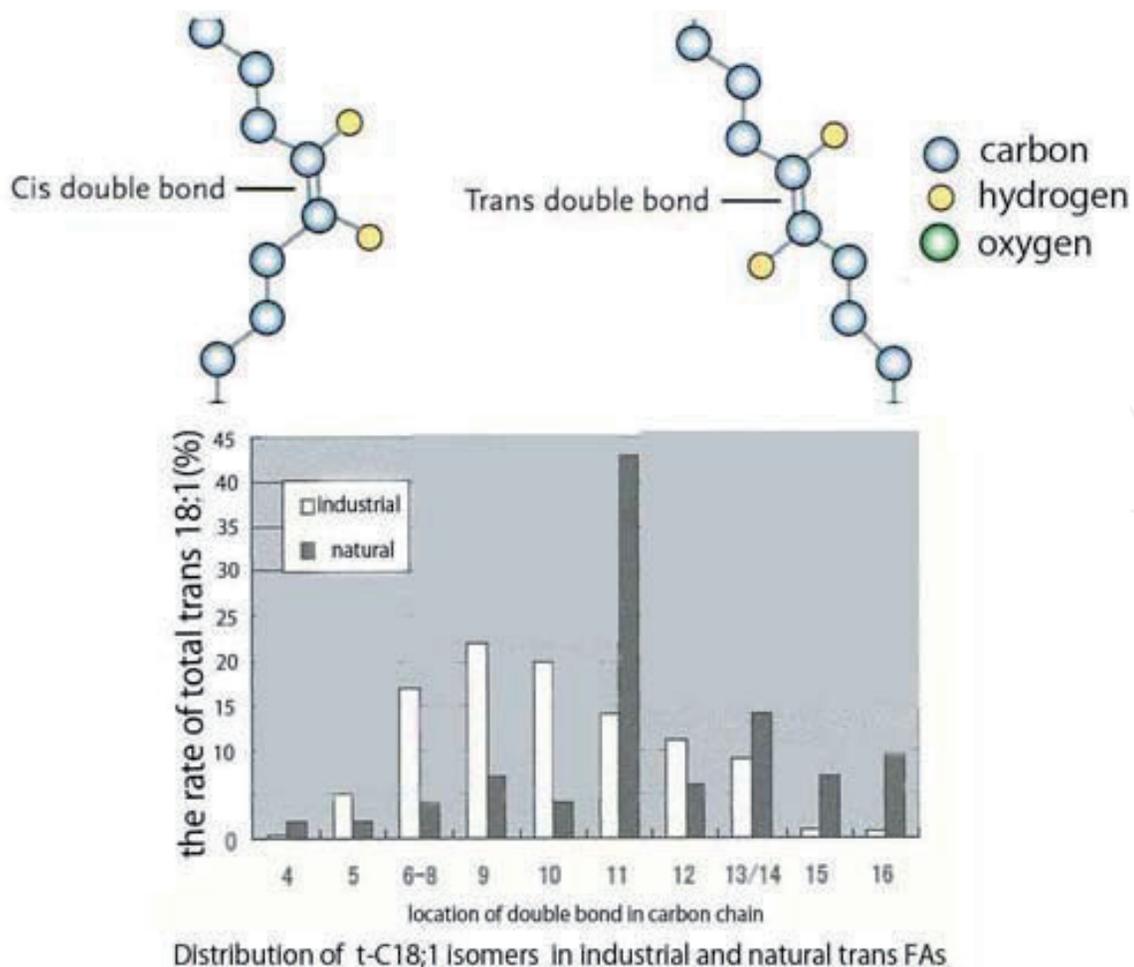


Figure 1.
The configuration of cis and trans forms of the double bond.

1.2 Molecular mechanisms of trans-fatty acids

Fatty acids modulate cell functions. They change membrane fluidity and responses of membrane receptors. Fatty acids not only bind to membrane receptors but also bind to and modulate nuclear receptors that regulate gene transcription, peroxisome-proliferator-activated receptors, liver X receptor, and sterol regulatory element-binding protein 1 [9] (**Figure 2**). Fatty acids modulate metabolic and inflammatory responses of the endoplasmic reticulum [10].

Trans-fatty acids change the secretion, lipid composition, and the size of apoB100 produced by hepatic cells [11, 12]. In hepatocytes, trans-fatty acids increase the accumulation and secretion of free cholesterol and cholesterol esters [11]. Trans-fatty acids increase plasma activity of cholesteryl ester transfer protein [13], which may result in decreases in plasma levels of high density lipoprotein (HDL) and increase in the levels of low density lipoprotein (LDL) and very low density lipoprotein (VLDL).

Trans-fatty acids modulate monocyte and macrophage functions resulting in increase in the production of tissue necrosis factor (TNF)- α and interleukin-6 [14]. Endothelial dysfunctions are caused by trans-fatty acids, and arterial dilatation is impaired due to nitric oxide [15].

Fatty acid metabolism of adipocytes was affected by trans-fatty acids, causing reduced triglyceride uptake, reduced esterification of cholesterol, and increased production of free fatty acids [16]. In animal studies, the gene expression was changed by the consumption of trans-fatty acids in adipocytes. These gene products are peroxisome-proliferator-activated receptor- γ , resistin, and lipoprotein lipase [17].

Trans-fatty acids may affect plasma lipid levels due to changes in hepatocytes of the production, secretion, and catabolism of lipoproteins and plasma levels of

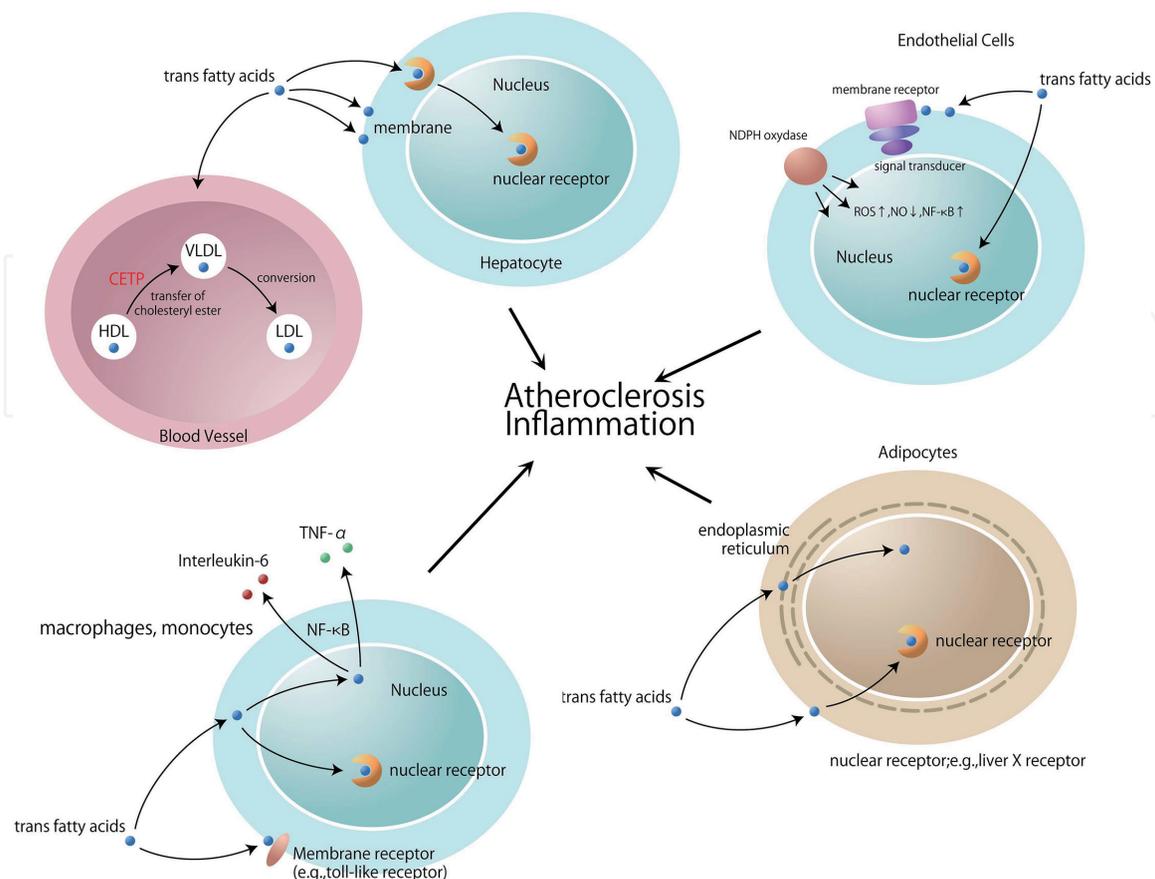


Figure 2.
Effects of trans-fatty acids.

cholesteryl ester transfer protein (CETP) (upper left panel). In adipocytes, trans-fatty acids change fatty acid metabolism and, possibly, inflammatory responses. When trans fats are taken, nitric acid-dependent endothelial dysfunction is observed and circulating adhesion molecules increase. Trans fat modulates monocyte and macrophage function (lower left panel). Membrane receptors may affect subcellular mechanisms. These receptors localize with and are influenced by specific membrane phospholipids (upper right panel) such as endothelial nitric oxide synthetase or toll-like receptors. Trans-fatty acids may bind to nuclear receptors-regulating gene transcription such as liver X receptor (lower left panel).

1.3 Effects on cardiovascular diseases

Trans-fatty acids may increase the risks of coronary heart disease (CHD). In a meta-analysis of four prospective cohort studies, a 2% increase in energy intake from trans-fatty acids was shown to be associated with a 23% increase in the incidence of CHD [18–21].

There are many papers showing increased risks of CHD in patients with high fatty acids levels [22–25]. These data are obtained using cohorts of Western populations.

Koba et al. [26] recently reported using Japanese adult males that total trans-fatty acids levels were similar between acute coronary syndrome (ACS) and control subjects. Palmitelaidic acid levels were lower in ACS patients and were significantly directly associated with HDL cholesterol (HDL-C) and n-3 polyunsaturated FA (n-3 PUFA). Linoleic trans isomers (total C18:2 TFA) and primary industrially produced TFA (IP-TFAs) were significantly higher in ACS patients. Total trans-C18:1 isomers were comparable between ACS and control.

1.4 Intakes of trans-fatty acids in people of US and Japan

Allison et al. [27] used food intake data from 1989 to 1991 Continuing Survey of Food Intakes by Individuals (CSFII) and the trans-fatty acid contents of specific foods, which were calculated from a data base of the US Department of Agriculture. These data show the mean levels of trans-fatty acids intakes of US population.

The average percentage of energy ingested as trans-fatty acids was 2.6%, and the average percentage of total fat ingested as trans-fatty acids was 7.4%. Across all age and gender groups examined, estimates ranged from 2.6 to 2.8% and 7.1 to 7.9%, respectively [27].

In Japan, mean total fat and trans-fatty acid intake was 56.9 g/day (27.7% total energy) and 1.7 g/day (0.8% total energy), respectively, for women and 66.8 g/day (25.5% total energy) and 1.7 g/day (0.7% total energy) for men [28].

Recent studies indicate that the average trans-fatty acids intake was estimated to be 0.92–0.96 g/day, which was 0.44–0.47% of total daily energy intakes [29].

These data indicate that Japanese take far less amounts of trans-fatty acids compared with American.

1.5 Omega fatty acids

Intakes of long-chain ω -3 fatty acids (eicosapentaenoic acid (EPA), docosapentaenoic acid (DPA), and docosahexanoic acid (DHA)) found in fish, and fish oils has been shown to be related to the low incidence of coronary heart disease in the Inuit people of Greenland [30].

We do not review roles of such fatty acids in health and disease in details.

Figure 3 summarizes roles of EPA in causing various dysfunctions of the body.

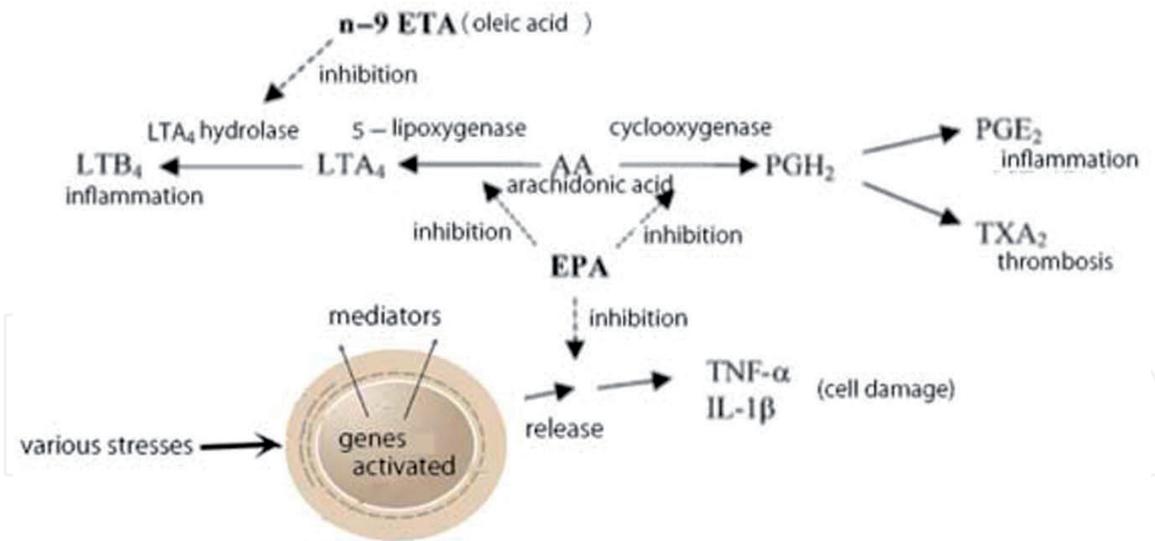


Figure 3.
 Roles of EPA in the prevention of cell damage, inflammation, or thrombosis.

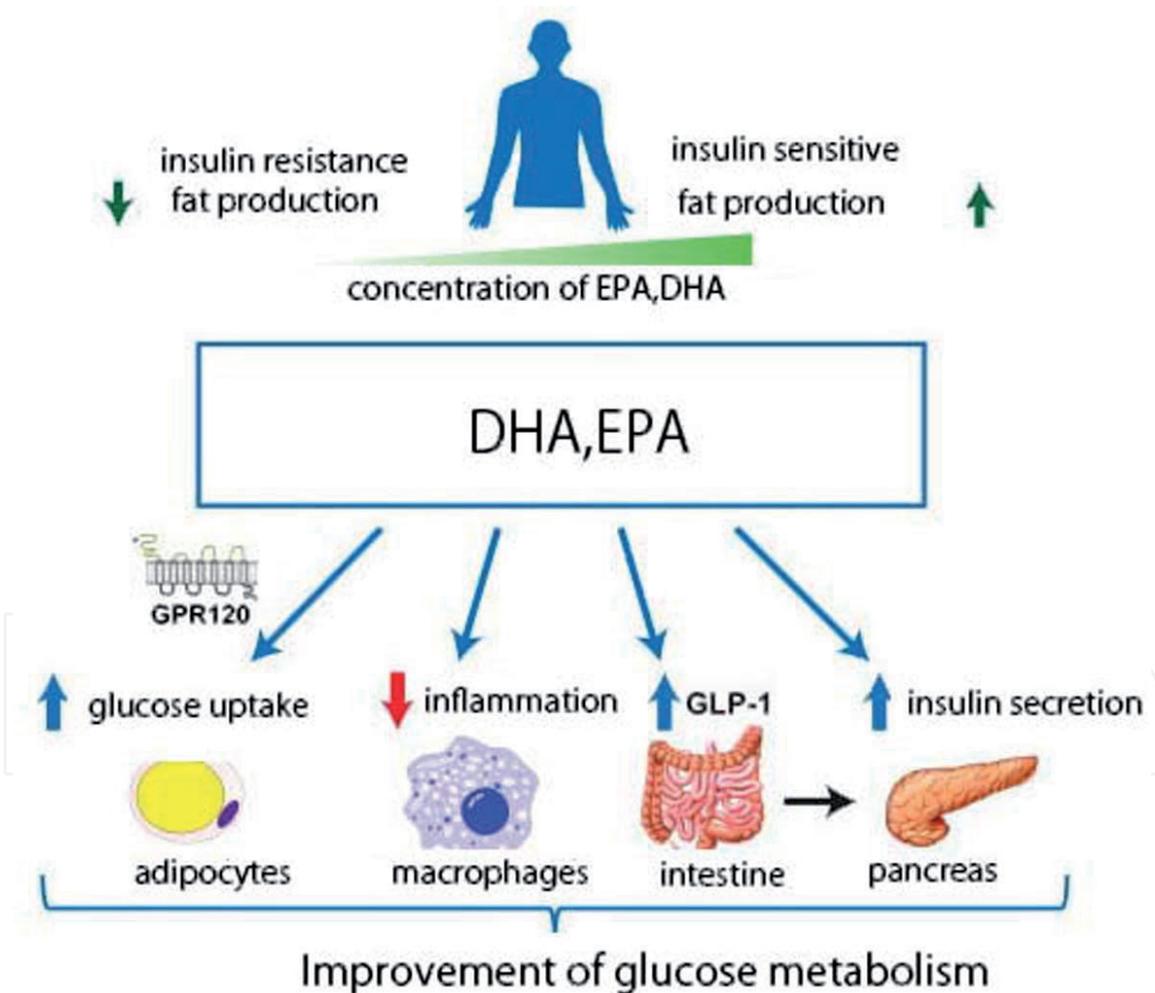


Figure 4.
 Function of G-protein-coupled receptor 120 as a receptor of DHA and EPA.

Arachidonic acid (n-6 polyunsaturated fatty acid “PUFA”) is converted to PGH₂ (prostaglandin H₂, which is converted to prostaglandin E₂, inflammatory mediator) or to TXA₂ (thromboxane A₂), causing thrombosis. AA is also converted to LTA₄ (leukotriene A₂), then to leukotriene B₄, inflammatory mediator [31].

Cells produce TNF- α or interleukin (IL)-1 β , which cause cell damages.

EPA inhibits such processes, preventing cell damages, inflammation, and thrombosis. DHA may work in the similar ways as EPA.

1.6 ω fatty acid receptor

GPR120 is proposed to function as an ω -3 FA receptor/sensor in pro-inflammatory macrophages and mature adipocytes. By signaling through GPR120, DHA and EPA mediate potent anti-inflammatory effects to inhibit both TLR (toll-like receptor) and TNF- α inflammatory signaling pathways [32].

DHA and EPA stimulate GRP 120 and cause a decrease of glucose uptake by adipocytes, inhibit inflammation by macrophages, secrete glucagon-like peptide 1 (GLP-1), and increase insulin secretion by pancreas (**Figure 4**).

These data suggest that DHA and EPA may be effective for prevention and treatment of cardiovascular disease and diabetes mellitus.

2. Differences of plasma levels of fatty acids between Japanese and American old men

2.1 Materials and methods

2.1.1 Participants

In Japan, we recruited 44 male volunteers older than 50. They were friends and family members of the research team for this study [33, 34]. Exclusion criteria included the use of medications to treat diabetes, hyperlipidemia, hypertension, and/or cardiovascular disease (CVD). Smokers were also excluded. The 76 US men were participants in the Chicago Area Sleep Study, a prospective cohort study to examine risk factors for the development of sleep disorders [35]. This cohort excluded men with known sleep disturbances but did not exclude for the chronic conditions excluded in the Japanese cohort. We collected blood samples after an overnight fast, and plasma was isolated for fatty acid analysis. We obtained an informed consent prior to conducting the protocol which had been approved by the Ethical Committee of Showa Women's University and Saiseikai Shibuya Satellite Clinic. The Chicago Area Sleep Study was approved by the Northwestern University Institutional Review Board.

2.2 Analyses of plasma samples

Fatty acids levels were measured in plasma obtained from ethylenediamine tetraacetic acid anticoagulated blood samples. Samples were frozen at -80°C until analyzed at Omegaquant, LLC (Sioux Falls, SD, USA). After thawing, an aliquot of plasma was combined (1.40 parts) with the methylating mixture (boron trifluoride in methanol [14%], toluene, and methanol [35/30/35, vv]), shaken at 100°C for 45 min. After cooling, 40 parts of both hexane and distilled water were added. After briefly vortexing, the samples were spun to separate layers, and an aliquot of the hexane layer that contained the fatty acid methyl esters was analyzed by gas chromatography as previously described.

2.3 Statistical analysis

Student's t test was used for the comparison of two groups, and $p < 0.05$ was considered as significant difference. Results are expressed as mean \pm SD. Spearman's correlation tests were used to examine statistical significance.

3. Results

The ages of the two cohorts was reasonably similar (Japan, 61 ± 10 and US, 57 ± 5 years), as were the body mass indexes (24.9 ± 3.7 vs. 25.1 ± 3.4 kg/m²) (**Figure 5**).

Of the fatty acids that constituted at least 1% of the total in either cohorts, those that are significantly higher in Japanese men than US men were as follows: palmitic, palmitoleic, arachidic, EPA, and DHA. Those that were lower in the Japanese men were as follows: linoleic acid (LA), dihomo-gamma linolenic acid (DGLA), and AA (**Table 1**).

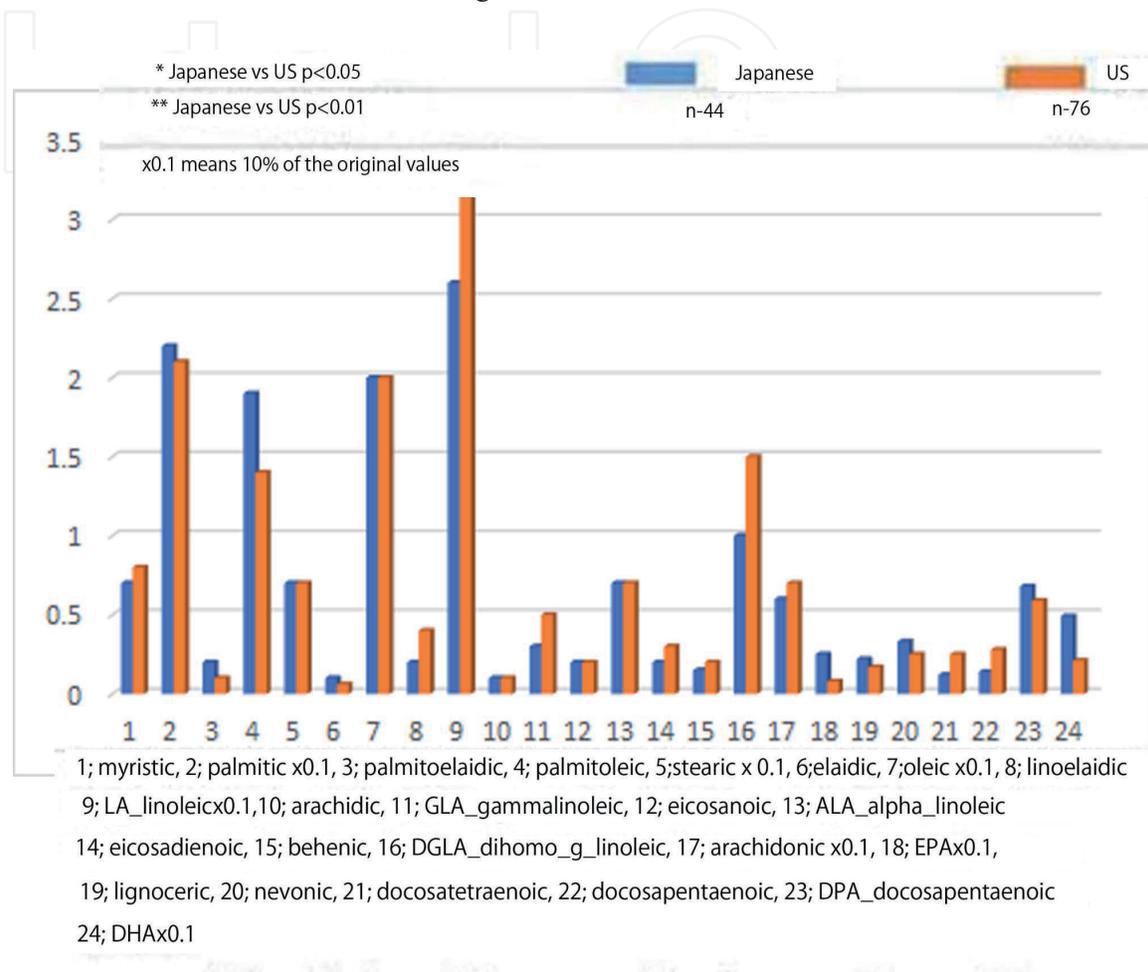


Figure 5.
 Profiles of plasma levels of fatty acids of Japanese and American old men.

	Japanese (n = 44)	American (n = 76)
Age	62.4 ± 9.6	57.5 ± 4.3
Height (m)	1.68 ± 0.07	1.70 ± 0.1
Weight (kg)	68.8 ± 10.9	74.4 ± 12.1
Body mass index (BMI)	24.3 ± 3.2	25.3 ± 3.4
Total cholesterol (mg/dL)	209.9 ± 32.3	185 ± 33.5
Triglyceride (mg/dL)	126.4 ± 81.3	118.0 ± 62.8
HDL-C (mg/dL)	60.9 ± 16.6	54.0 ± 15.7
LDL-C (mg/dL)	123.8 ± 30.2	107.0 ± 29.6
Fasting blood glucose (mg/dL)	91.7 ± 16.3	97 ± 22.3

Table 1.
 Backgrounds of various parameters of healthy old men in Japan and US.

Figure 6 compares plasma levels of palmitoelaidic, elaidic, and linoelaidic acids. IP-TFAs (elaidic and mainly industrially produced linoelaidic), although of low abundance in both cohorts, were considerably higher in the US than in Japan. Palmitoleic was slightly but significantly higher in Japan (Figure 7).

Plasma levels of DHA and EPA are higher in Japanese than American old men; on the other hand, plasma levels of arachidonic acid and dihomoγlinoleic acid are higher in American than Japanese old men.

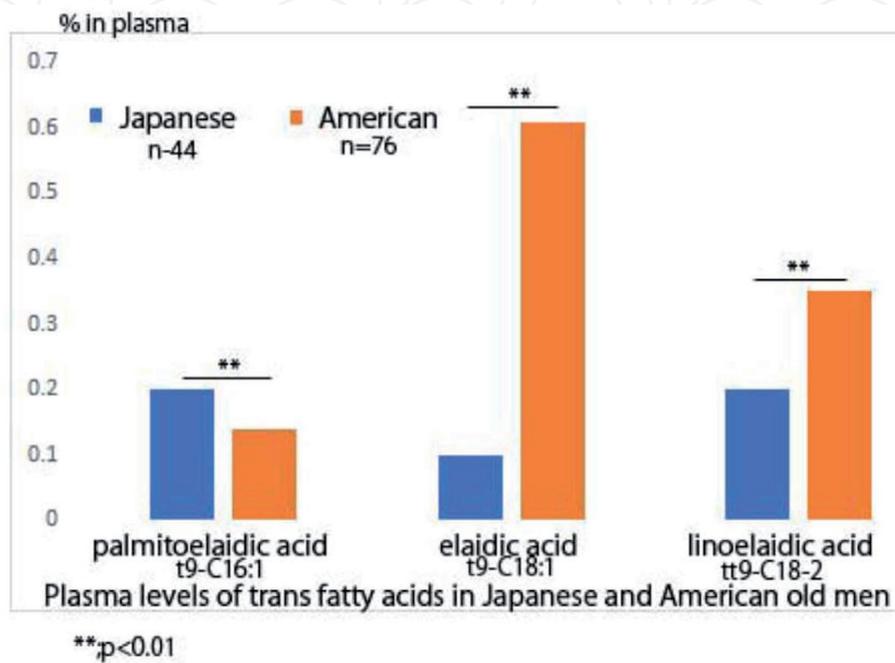


Figure 6.
Plasma levels of trans-fatty acids in Japanese and American old men.

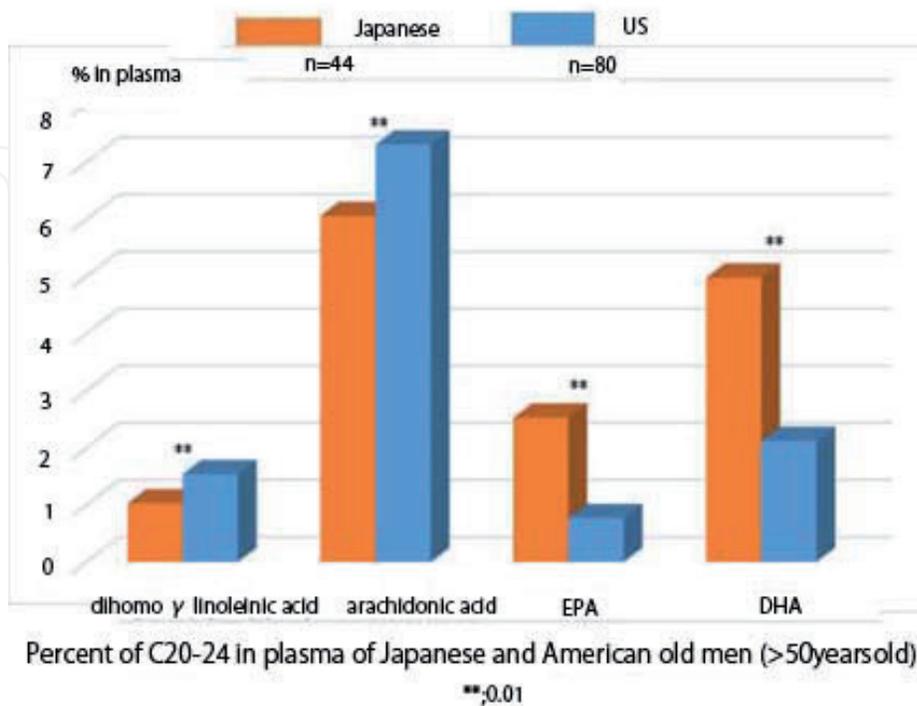


Figure 7.
Comparison of plasma levels of C20–22 fatty acids between Japanese and American old men.

Plasma fatty acids (% of total)	Japanese (n = 44)	US (n = 76)	ss
Myristic	0.7 ± 0.2	0.85 ± 0.34	**
Palmitic	22.3 ± 1.3	21.23 ± 2.13	*
Palmitoelaidic (trans)	0.2 ± 0.1	0.14 ± 0.07	**
Palmitoleic	1.9 ± 0.6	1.45 ± 0.80	**
Stearic	7.0 ± 0.7	7.24 ± 0.83	
Elaidic (trans)	0.1 ± 0.01	0.61 ± 0.34	**
Oleic	20.0 ± 2.6	19.96 ± 3.34	
Linoelaidic (trans)	0.2 ± 0.1	0.35 ± 0.12	**
Linoleic (LA)	26.3 ± 4.0	32.83 ± 5.24	**
Arachidic	0.13 ± 0.04	0.13 ± 0.04	
Gamma linolenic	0.3 ± 0.1	0.53 ± 0.27	**
Eicosenoic	0.2 ± 0.04	0.15 ± 0.05	
Alpha-linolenic	0.7 ± 0.2	0.72 ± 0.32	
Eicosadienoic	0.2 ± 0.03	0.29 ± 0.07	**
Behenic	0.15 ± 0.02	0.20 ± 0.10	**
Dihomo-gamma linolenic (DGLA)	1.0 ± 0.2	1.56 ± 0.37	**
Arachidonic (AA)	6.0 ± 1.1	7.38 ± 2.18	**
Eicosapentaenoic (EPA)	2.5 ± 1.3	0.77 ± 0.60	**
Lignoceric	0.22 ± 0.10	0.18 ± 0.07	*
Nervonic	0.33 ± 0.18	0.26 ± 0.10	*
Docosatetraenoic	0.12 ± 0.04	0.26 ± 0.11	**
Docosapentaenoic (n6)	0.14 ± 0.04	0.18 ± 0.08	**
Docosapentaenoic (n3)	0.68 ± 0.26	0.59 ± 0.14	*
Docosahexaenoic (DHA)	5.0 ± 1.5	2.14 ± 0.85	**

ss, statistical significance.
 * $p < 0.05$.
 ** $p < 0.01$.

Table 2.
 Comparison of fatty acids profiles between Japanese and American men.

Table 2 summarizes plasma levels of important fatty acids between Japanese and American men.

4. Food intakes and plasma levels of fatty acids

Participants were given self-administered diet history questionnaires and described answers on each item by recollection of diets they took (7 days dietary recall). We used a brief-type self-administered diet history questionnaire (BDHQ) by using which the Japanese Ministry of Health, Labour and Welfare reports National Nutrition Surveys. From these questionnaires, we calculated the intakes of energy and varieties of foods such as proteins, carbohydrates, lipids vitamins, etc.

4.1 Results

Table 3 shows that only preference drinks such as tea and coffee had significant correlations with plasma levels of palmitoelaidic acid and linoelaidic acid.

	Palmitelaidic	Elaidic	Linoelaidic
Energy	0.319	-0.135	0.181
Protein	0.239	0.031	0.034
Animal protein	0.233	0.135	0.034
Vegetable protein	0.193	-0.081	0.152
Lipid	0.187	0.120	0.034
Animal lipid	0.188	0.154	0.094
Vegetable lipid	0.167	0.027	-0.066
Carbohydrate	0.188	-0.197	0.138
Na	0.128	0.033	-0.073
K	0.223	-0.015	0.137
Ca	0.099	0.263	-0.021
Mg	0.283	-0.003	0.143
Phosphorus	0.230	0.088	0.020
Iron	0.193	-0.120	0.112
Zinc	0.109	0.081	0.072
Copper	0.211	-0.066	0.163
Mn	0.422	-0.059	0.113
Retinol	0.307	-0.195	0.054
β-Carotene	-0.001	-0.049	-0.005
Vit D	0.295	-0.001	-0.066
Tocopherol	0.167	-0.049	-0.004
Vit K	0.098	0.014	0.083
Vit B1	0.095	0.119	0.098
Vit B2	0.246	0.169	0.135
Niacine	0.320	-0.012	0.081
Vit B6	0.239	-0.036	0.129
Vit B12	0.353	-0.090	0.049
Folic acid	0.333	-0.120	0.080
Pantothenic acid	0.299	0.120	0.083
Vit C	0.214	-0.040	0.034
Saturated fatty acids	0.209	0.144	0.112
Monovalent fatty acids	0.156	0.126	-0.004
Multivalent fatty acids	0.179	0.024	-0.062
Cholesterol	0.221	-0.025	0.125
Soluble dietary fiber	0.133	-0.080	0.155
Insoluble dietary fiber	0.125	-0.047	0.076
Total dietary fiber	0.082	0.027	0.089
Salt	0.128	0.033	-0.073
Preference drinks	0.586**	-0.263	0.511*

Mean ± SD.

**p* < 0.05.

***p* < 0.01.

Table 3.
Correlations between foods intake and plasma levels of fatty acids.

5. Discussion

Fatty acids are major components of blood vessels. So their changes exert tremendous impact to pathophysiology of cardiovascular system.

Epidemiological studies repeatedly showed that Japanese people had lower incidence of CVD, compared with American people [7]. As discussed below, kinds of intaken foods, life-styles, and genetics may contribute to such differences.

We thought the measurements of fatty acids composition in plasma may help to elucidate such differences between Japanese and American people.

We compared plasma levels of fatty acids between Japanese and American men over 50 years of age. We found, not surprisingly, that levels of EPA and DHA are higher in Japanese than American and that levels of arachidonic acid are lower in Japanese. Although both Japanese and American take meat, egg, and fish, fish has far more omega-3 fatty acids compared to eggs. When we eat larger amounts of omega-3 fatty acids such as DHA and EPA, omega-3 fatty acids are known to replace omega-6 fatty acids in cell membrane [36]. The omega-3 fatty acids are found predominantly in oily fish, whereas arachidonic acid (the major long chain omega-6 fatty acid) is contained in meats and eggs and can be synthesized (albeit very slowly) [37]. The differences between Japanese and US men in regard to the consumption of these types of foods can help explain these differences in blood levels [38]. The other major finding of this study was the lower levels of IP-TFA such as linoelaidic acid in Japanese vs. the US men.

Currently, CHD death rates in Japan are 3× lower for women and 4× lower for men (ages 35–74) compared with the US. Among 30 countries for which the American Heart Association provided CHD death rates in its 2017 Statistical Update [7], Japan had the second and third lowest rates (men and women, respectively) compared with the US. Sekikawa et al. [39] showed in 2014 that the calcification of the coronary artery was twice in American compared with Japanese men, but the calcification of Hawaiian Japanese was similar to that of people on the US mainland.

These results do not necessarily prove differences of CVD incidences between Japanese and American are due to foods and lifestyle. Since Japanese immigrants to the US have increased CHD mortality [40], although still lower US Whites, it appears that some genetic variabilities between American and Japanese must be responsible for this difference. However, the possibility that differences in dietary fatty acid patterns may contribute to this phenomenon is the subject of this report.

We found that the levels of the long-chain omega-3 fatty acids such as EPA and DHA were 2–3× higher in Japan vs. the US. The relationship of fish and dietary omega-3 fatty acids and cardiovascular disease (CVD) has been investigated in numerous studies and comprehensive reviews and recommendations exist. Still controversies exist. A recent meta-analysis of randomized trials with omega-3 fatty acids [41] did not find a statistically significant reduction in CVD mortality, but in these researches, some important factors were said to be ignored [42–44]. Other systematic reviews have reported mortality benefits for omega-3 fatty acids [45, 46], and omega-3 biomarker levels have been strongly associated with risk for fatal CHD in still other meta-analyses [47, 48]. Hence, higher omega-3 levels could at least partly explain the lower CHD risk in Japan.

We also found that IP-trans-fatty acid such as linoelaidic acid was lower in Japan than US. The reported intake of IP-TFA is 75% lower in Japan than in the US, again supporting the observed differences in biomarker levels. Circulating 18:2 trans-fatty acids was shown to be most adversely associated with total mortality, mainly due to the increased risk of CVD [23]. It was also positively associated with total mortality and CHD.

It may be surprising that TFA is not necessarily adverse for health. Some are beneficial for health. In a recent study from Germany, total trans-fatty acids in erythrocyte membranes were shown to be inversely associated with mortality, but this was mainly driven by the naturally occurring 16:1 trans (trans-palmitoleic acid) [49]. As to relationship between IP-TFA or SFA intakes and CHD mortality, excessive intakes of both had a greater impact on risk for CHD in the US compared with Japan, whereas insufficient intakes of omega-6 PUFAs had about the same impact on risk in both countries [50].

Our results also indicate that plasma levels of SFAs are higher in American than in Japanese. Saturated fatty acids are considered to be one of the dietary risk factors of CVD, primarily because these fats raise LDL-cholesterol levels. Many health and government organizations have recommended the reduction of intakes of SFAs to lower the incidence of CVD. Although this difference in SFA plasma levels may also be one of the reasons that Americans have a higher mortality rate for CVD than Japanese, plasma saturated (and monounsaturated) fatty acids are claimed to be relatively poor markers of dietary SFA (saturated fatty acid) intake [51].

Plasma fatty acid profiles in older men from Japan and US differed in many ways that are consistent with the lower rate of CHD in the former country. Efforts to lower TFA levels and increase EPA + DHA levels may help lower risk for CHD in the US, and current trends in Japan toward a more western diet [52] should be discouraged.

As to relationship between TFA or SFA intakes and CHD mortality, excessive intakes of both had a greater impact on risk for CHD in the US compared with Japan, whereas insufficient intakes of omega-6 PUFAs had about the same impact on risk in both countries [50]. As stated above, naturally occurring trans fats are consumed in smaller amounts (about 0.5% of total energy intake) in meats and dairy products from cows, sheep, and other ruminants; these trans fats are produced by the action of bacteria in the ruminant stomach [22]. Since trans-fatty acids are not used in foods in Japan, all the trans-fatty acids must come from meat or dairy products. We found that there was no relationship between various foods intake and plasma levels of trans-fatty acids in Japanese old men. Only intakes of preference drinks such as tea and coffee had significant relationship with plasma levels of palmitoelaidic acid and linoelaidic acid. These results seem to indicate that plasma levels of trans-fatty acids are not derived from foods but derived by intestinal microbes.

Human gut microbes are important in neural, endocrine, and immune communication with the host [53]. Communication is considered to be bidirectional. Mediators of microbiota-gut-brain communication affected by microbial metabolism include short-chain fatty acids, neurotransmitters such as serotonin, γ -aminobutyric acid (GABA), hormones such as cortisol, and immune system mediators such as quinolinic acid [51].

In conclusion, some of trans-fatty acids may be produced by hydrogenation of fatty acids by gut microbes.

6. Conclusion

We here report our results of comparison of plasma levels of fatty acids between healthy old men in Japan and the US.

The higher levels of DHA and EPA, along with the lower levels of the IP-TFAs, are consistent with the markedly lower risk for coronary heart disease in Japan vs. the US.

Various foods intake may not affect plasma levels of trans-fatty acids in Japanese old men except for preference drinks such as tea or coffee.

The higher levels of DHA and EPA, along with the lower levels of the IP-TFAs, are consistent with the markedly lower risk for coronary heart disease in Japan vs. the US.

Our results also indicate that plasma levels of SFAs are higher in American than in Japanese. Saturated fatty acids are considered to be one of the dietary risk factors of CVD, primarily because these fats raise LDL-cholesterol levels.

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Experiments were designed and performed by all of the authors. AT and WSH wrote the manuscript. Statistical analyses were done by FS. All authors read the manuscript and approved the final version. All the authors take responsibility for the final content.

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